Cancer Screening in the United States, 2018: A Review of Current American Cancer Society Guidelines and Current Issues in Cancer Screening

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Abstract: Each year, the American Cancer Society publishes a summary of its guidelines for early cancer detection, data and trends in cancer screening rates from the National Health Interview Survey, and select issues related to cancer screening. In this 2018 update, we also summarize the new American Cancer Society colorectal cancer screening guideline and clarify a clarification in the language of the 2013 lung cancer screening guideline. CA Cancer J Clin 2018;68:297-316. © 2018 American Cancer Society.

Keywords: breast neoplasms, cervical neoplasms, colorectal neoplasms, lung neoplasms, mass screening, ovarian neoplasms, prevention and control, prostate neoplasms

Introduction

The American Cancer Society (ACS) provides an annual report for health care professionals and the public that summarizes the current ACS cancer screening guidelines, including current recommendations, updates, and guidance related to early cancer detection when a direct recommendation for screening cannot be made. This annual report also includes the most recent 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 guidelines reviews, as well as the more detailed individual cancer screening guideline updates, are published as standalone articles and are available online. Table 1 shows the recent history of ACS guideline updates as well as those in progress.3-19

In this update of ACS cancer screening guidelines, we describe the current guidelines (Table 2) and issues that influence screening for breast cancer, cervical cancer, colorectal cancer (CRC), and prostate cancer; clarify our current recommendations for lung cancer screening with low-dose computed tomography (LDCT); and provide a comparison of ACS recommendations with those of other groups, 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 as measured by average and total years of life lost.20 In 2018, the ACS estimated that there would be 266,120 cases of invasive breast diagnosed in US women and 40,920 deaths.21 After a period of declining delay-adjusted, age-standardized breast cancer incidence rates (1999-2004), incidence increased by an average of 0.4%
While declines in death rates are seen in all racial/ethnic groups, a large disparity in age-adjusted death rates emerged between black and white women during the 1980s and has continued to increase for several decades, although these differences have stabilized in recent years. During 2011 through 2015, death rates were 42% higher in black women than in white women.\textsuperscript{22}

The ACS guideline for breast cancer screening in average-risk women was updated in 2015.\textsuperscript{5} An update of the ACS breast cancer screening guideline for women at higher than average risk, which previously was updated in 2007,\textsuperscript{4} is currently underway.

In 2015, the ACS issued a strong recommendation that average-risk women aged 45 years and older should undergo regular mammography screening and a qualified recommendation that women aged 40 to 44 years should have an opportunity to begin screening before age 45 years (Table 2). The designations of the recommendations as “strong” and “qualified” were made in accordance with the criteria of Grading of Recommendations Assessment, Development and Evaluation (GRADE). The ACS recommends that women aged 45 to 54 years and those aged 40 to 44 years who choose to begin screening before age 45, should be screened annually, and women aged 55 years and older should transition to biennial screening or can continue annual screening if that is their preference. 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).\textsuperscript{5} A strong recommendation conveys the consensus that the benefits of adherence to the intervention outweigh the undesirable effects and that most patients would choose the intervention. A qualified recommendation indicates there is clear evidence of benefit (or harm), but less certainty about either the balance of benefits and harms, or about patients’ values and preferences, which could lead to different individual decisions.\textsuperscript{23}

The ACS breast cancer screening guideline emphasizes annual screening from aged 40 to 54 years, because it has been demonstrated that annual mammography screening in premenopausal women significantly reduces the risk of being diagnosed with an advanced breast cancer compared with biennial screening.\textsuperscript{24} In this analysis, annual screening did not confer the same advantage in postmenopausal women, except for women who were currently receiving menopausal hormone therapy. On the basis of these findings, the ACS recommended that women aged 55 years and older can transition to biennial screening or, if it is their preference, continue annual screening. The ACS does not set a stopping age for breast cancer screening but acknowledges the potential for women aged 75 years and older who

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\textbf{CANCER SITE} & \textbf{YEAR (REFERENCE)} \\
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Breast cancer & 2003: Complete update (Smith 2003) \\
& 2007: Guidelines for MRI use in high-risk women (Saslow 2007) \\
& 2015: Complete update (Oeffinger 2015) \\
& 2018: Update for women at increased and high risk underway \\
Cervical cancer & 2002: Complete update (Saslow 2002) \\
& 2007: Guidelines for HPV vaccine use (Saslow 2007) \\
& 2012: Complete update (Saslow 2012) \\
& 2015: Update related to follow-up of HPV-negative ASCUS (Smith 2015) \\
& 2016: Complete update for HPV vaccine use guideline (Saslow 2016) \\
& 2017: Update related to HPV vaccine use (Smith 2017) \\
& 2018: Update initiated \\
Colorectal cancer & 2001: Complete update (Smith 2001) \\
& 2003: Technology update (Levin 2003) \\
& 2006: Update for postpolypectomy and postcolorectal cancer resection surveillance (Rex 2006, Winawer 2006) \\
& 2008: Complete update (Levin 2008) \\
& 2018: Complete update (Wolf 2018) \\
Endometrial cancer & 2001: Guidance for counseling, shared decision making, and high-risk women (Smith 2001) \\
Prostate cancer & 2001: Guidance for shared decision making related to testing for early detection, and screening recommendations for higher risk men (Smith 2001) \\
& 2010: Complete update (Wolf 2010) \\
& 2019: Update planned \\
Lung cancer & 2001: Guidance for shared decision making (Smith 2001) \\
& 2011: Interim guidance on lung cancer screening (Smith 2012) \\
& 2013: Complete update (Wender 2013) \\
& 2018: Clarification in the guideline wording (this report) \\
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Abbreviations: ASCUS, atypical squamous cells of undermined significance; HPV, human papillomavirus; MRI, magnetic resonance imaging.

per year from 2004 to 2014.\textsuperscript{20} Age-adjusted breast cancer mortality rates have declined 39% from 1989 through 2015,\textsuperscript{22} with an estimated 322,600 deaths averted in US women over this period. Unfortunately, these overall favorable statistics are not shared equally among all populations.
| CANCER SITE | POPULATION | TEST OR PROCEDURE | RECOMMENDATION |
|-------------|------------|-------------------|----------------|
| Breast      | Women aged 40-54 y | Mammography | Women should undergo regular screening mammography starting at age 45 y; women aged 45-54 y should be screened annually; women should have the opportunity to begin annual screening between the ages of 40 and 44 y. |
|             | Women aged ≥ 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 of 10 y or longer. |
| Cervix      | Women, aged 21-29 y | Pap 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. |
|             | Women, aged 30-65 y | Pap test and HPV DNA test | 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 | Pap test and 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, aged 45-75 y, for all tests listed | Fecal immunochemical test (FIT) [annual], or High-sensitivity guaiac-based fecal occult blood test (HSgFOBT) [annual], or Multitarget stool DNA test (mt-sDNA), [every 3 y per manufacturer’s recommendation], or Colonoscopy [every 10 y], or CT colonography (CTC) [every 5 y], or Flexible sigmoidoscopy (FS) [every 5 y] | Adults aged 45 y and older should undergo regular screening with either a high-sensitivity stool-based test or a structural (visual) exam, depending on patient preference and test availability. As part of the screening process, all positive results on non-colonoscopy screening tests should be followed up with timely colonoscopy. Adults in good health with a life expectancy of greater than 10 y should continue screening through the age of 75 y. Screening decisions should be individualized, based on patient preferences, life expectancy, health status, and prior screening history. If a decision is made to continue screening patient should be offered options as listed above. |
|             | Men and women aged 76-85 y | | Individuals should be discouraged from continuing screening. |
| 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 aged 55-74 y in good health with at least a 30-pack-y history of smoking | Low-dose helical CT | Annual screening in adults who: • currently smoke or have quit within the past 15 years; and • have at least a 30 pack-year smoking history; and • receive evidence-based smoking cessation counseling, if they are current smokers; and • have undergone a process of informed/shared decision making that included information about the potential benefits, limitations, and harms of screening with low-dose CT; and • have access to a high-volume, high quality lung cancer screening and treatment center. |
| Prostate    | Men, aged ≥50 y | Prostate-specific antigen test (PSA) with or without digital rectal examination (DRE) | 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. |

Abbreviations: CT, computed tomography; HPV, human papillomavirus; MRI, magnetic resonance imaging; Pap, Papanicolaou. *All individuals should become familiar with the potential benefits, limitations, and harms associated with cancer screening.*
are in good health with an expected longevity of 10 or more years to benefit from continuing mammography screening. In applying clinical judgment about longevity, clinicians should use mortality indices that incorporate age, comorbidities, and functional status.25,26 In addition, women should be provided opportunities for individualized decision making to consider the potential benefits and harms and incorporate health priorities and patient preferences.27

In the update of the breast cancer screening guideline, the ACS Guideline Development Group (GDG) addressed the question of age-specific breast cancer screening recommendations by evaluating the burden of disease and evidence related to the benefit, limitations, and harms associated with screening examinations. To address the enduring debate about whether screening should begin at age 40 or 50, the GDG first chose to examine the age-related burden of disease in smaller age ranges instead of comparing women aged 40 to 49 with those aged 50 years and older (or aged 40-49 vs 50-59 years), noting that women aged 40 to 49 years represent a cohort of over 22 million women. In their examination of risk in 5-year age groups, it was apparent that the absolute 5-year risk among women aged 45 to 49 years (0.9%) and those aged 50 to 54 years (1.1%) was similar (vs. 0.6% for women aged 40-44), as was the proportion of all annual incident breast cancer cases (10% and 12%, respectively, vs. 6% for women aged 40-44 years) and incidence-based mortality (10% and 11%, respectively, vs. 7% for women aged 40-44 years), which represents the proportion of annual breast cancer deaths attributable to an age at diagnosis rather than an age at death. In addition, the age-specific, incidence-based person-years of life lost, an indicator of premature mortality, also was similar for women aged 45 to 49 years and aged 50 to 54 years (approximately 15% of the total annual person-years of life lost for all women was attributable to a diagnosis of breast cancer in each age group).5 This examination of the burden of disease within 5-year age groups revealed that traditional comparisons of women in their 40s with women aged 50 years and older obscured similarities among women aged 45 to 49 years and aged 50 to 54 years—adjacent age cohorts representing over 11 million women each. Also noteworthy was the observation that more than one-third of all breast cancer deaths each year are attributable to diagnoses after age 70 years.5 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.

The systematic review of the evidence related to the benefit of mammography screening included evidence from randomized clinical trials (RCTs) and observational studies of modern service screening.28 The review revealed consistent evidence across all study designs that invitation or exposure to mammography screening, compared with usual care, is associated with reduced breast cancer mortality overall, as well as in age-specific subgroups.28 The magnitude of the observed mortality reductions varied across the different study designs; from 15% to 54% fewer deaths were associated with mammography screening, depending on the study design and whether the mortality reduction was associated with invitation versus exposure to screening.

In addition to consideration of the burden of disease and the benefit of breast cancer screening, the systematic review also examined the harms associated with screening, including false-positive findings associated with being recalled for further evaluation, false-positive biopsy results, the anxiety that may be associated with each, overdiagnosis, and radiation exposure. With respect to overdiagnosis, the GDG found little persuasive evidence regarding the fraction of breast cancers that are overdiagnosed, particularly for in situ versus invasive cases. Most published estimates were judged to be either unreliable or provably excessive. Instead, the GDG focused on harms that are better quantified and understood. Further, observed and estimated harms differ quantitatively in terms of their occurrence and qualitatively in terms of the effect, importance, and degree of adverse effects experienced by different women. Overall, the GDG judged that the benefits of screening significantly outweighed the harms both overall and within age-specific subgroups for which breast cancer screening was recommended directly or as an acceptable choice.

Screening Women at High Risk

In 2007, the ACS issued a guideline for women who were known or likely carriers of a breast cancer gene (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 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-degree and second-degree relatives on both the maternal and paternal sides. Annual MRI and mammography also are recommended for women who were treated for Hodgkin disease with radiation to the chest between ages 10 and 30 years and women with Li-Fraumeni, Cowden, and Bannayan-Riley-Ruvalcaba syndromes.4 At the time these recommendations were issued, there was insufficient evidence to recommend MRI and mammography for women at elevated risk because of other risk factors. At this time, the ACS is updating its guideline for women at increased and high risk.
Studies of New Breast Imaging Technologies

Two trials of new screening technologies are underway at this time. The Tomosynthesis Mammographic Imaging Screening Trial (TMIST) is designed to compare the performance of conventional full-field digital mammography (FFDM), which produces flat-plane, 2-dimensional (2D) images of the breast, with a newer technology: digital breast tomosynthesis (DBT), which produces both 2D and 3D images of the breast. The unique feature of DBT is the ability to take images of the breast from different angles to produce a 3D image, which allows radiologists to look through the breast, eliminating the influence of overlapping layers of breast tissue that can obscure the ability to see cancer or give the appearance of an abnormality when none is present. Although studies already have demonstrated that DBT tends to have superior performance compared with 2D mammography in terms of both sensitivity and specificity, there is interest in determining whether DBT is superior to FFDM in reducing the rate of advanced breast cancer. TMIST opened in July 2017 and enrollment is open to women aged 45 to 74 years who were planning to have a routine screening mammogram. The study plans to enroll 165,000 women by the end of 2020. Women participating in the trial will be randomized to undergo 4 rounds of routine screening with either FFDM or DBT. As noted above, the primary objective is to measure the proportion of women diagnosed with advanced breast cancer during the study period. Secondary objectives include agreement on breast lesion pathology between local and study pathologists for all benign and malignant breast lesions, correlation between imaging features and histologic and genetic features, comparison of diagnostic and performance characteristics (predictive value, sensitivity, specificity, recall rates, biopsy rates, etc) of FFDM and DBT, costs associated with each technology, interval cancer rates, and mortality outcomes.

The second trial is the Abbreviated Breast MRI and Digital Tomosynthesis Mammography in Screening Women with Dense Breasts study (hereafter, the AB-MRI trial), which is focused on women with significant mammographic breast density. Abbreviated MRI is a new approach to using MRI technology with an abbreviated protocol consisting of just one precontrast and one postcontrast acquisition and the derived images. The potential advantage is that the examination takes less time to perform compared with a full-protocol MRI (3 minutes vs 17 minutes), takes less time to interpret (2.8 seconds vs 28 seconds), and can be done at a lower cost. Kuhl et al reported the first feasibility study of abbreviated MRI in a prospective study of 443 asymptomatic women at moderately increased risk who had normal digital mammograms and also had heterogeneously or extremely dense breasts. Eleven early-stage breast cancers were detected, for a cancer detection rate of 18.2 per 1000. This new approach of using MRI to screen women with significant mammographic breast density led to interest in comparing abbreviated breast MRI with DBT. Approximately 1450 women aged 40 to 75 years with mammographically dense breasts have been randomized to either a study arm that first undergoes DBT followed by AB-MRI, or to a comparison group that first undergoes AB-MRI followed by DBT. Each woman will follow the same protocol again after 1 year; then, all women will be followed for 3 years. Data collection is scheduled to be complete in 2018. The primary objective of the AB-MRI investigators will be to compare the initial rates of detection of invasive cancers using abbreviated MRI and DBT in women with significant mammographic breast density. Secondary objectives include comparison of screening outcomes, including predictive value, recall rates, short-term follow-up, sensitivity, and specificity; short-term quality of life related to diagnostic testing and willingness to return for testing; and factors associated with willingness to return for screening for each technology. Additional endpoints include comparison of tumor biology of invasive cancers and ductal carcinoma in situ detected on AB-MRI and DBT; and to estimate the incident cancer rate during 3 years after the year-1 AB-MRI/DBT, when patients return to standard screening.

Screening for Cervical Cancer

The ACS estimates that 13,240 women will be diagnosed with invasive cervical cancer, and 4170 women will die from the disease in 2018. 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. For the period from 2006 through 2014, delay-adjusted cervical cancer incidence rates have nonsignificantly decreased at an average annual percentage rate of 0.3% per year; and, between 2003 and 2014, cervical cancer mortality rates have declined at an average annual rate of 0.8%. The 2012 joint guideline of the ACS, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology recommends screening strategies and options based on a woman’s age, screening history, and choice of screening tests:

Women Aged 21 to 65 Years

- Screening for cervical cancer should begin at age 21 years. Women under age 21 years should not be screened regardless of the age of sexual initiation or other risk factors.
- For women aged 21 to 29 years, screening with cytology alone every 3 years is recommended. Human papillomavirus (HPV) testing should not be used to screen women in this age group, either as a standalone test or as a cotest with cytology.
• For women aged 30 to 65 years, the preferred approach is cotesting every 5 years. It is also acceptable for women to continue to be screened every 3 years with cytology alone.

• Women with an HPV-negative atypical squamous cells of undetermined significance result should return for screening in 3 years.

• Recommended screening practices should not change on the basis of a woman’s HPV vaccination status.

Women Aged Greater Than 65 Years

• 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. Women with an HPV-negative atypical squamous cells of undetermined significance result should be regarded as negative for the purpose of discontinuing screening. Once screening is discontinued, it should not resume for any reason, including if a woman has a new sexual partner.

• After spontaneous regression or appropriate management of cervical intraepithelial neoplasia grade 2 (CIN2), CIN3, or adenocarcinoma in situ, routine screening should continue for at least 20 years (even if this extends screening past age 65 years).

Additional details for managing cervical cancer screening in women who have abnormal findings or are at different risk are detailed in the guideline.8,33

Special Considerations

These recommendations are intended 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 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.

Authors of the 2012 guideline anticipated the emergence of hrHPV testing as a standalone screening test for cervical cancer and noted unresolved issues, which included the lack of management strategies for positive results, the lack of standards for HPV assays, and the potential implications of false-negative results, stating: “Although hrHPV testing alone-based screening approaches appear promising, the lack of a well-defined and evaluated management strategy for positive tests precludes their practical implementation in the majority of clinical settings in the United States at this time. There are no data to estimate how the clinical performance of cytology (as a follow-up test) would be affected by a priori knowledge of positive HPV status. The lack of an internal standard for specimen adequacy for some HPV assays may provide false reassurance among a small number of women whose negative screening results may be a function of specimen inadequacy rather than the true absence of disease. Such an event is less common with cytology, because specimen adequacy assessment is a routine component of the evaluation, and inadequacy prompts intervention and follow-up on the part of the clinician and patient. Thus, the inclusion of cytology with hrHPV testing (ie, cotesting) provides some additional reassurance against testing errors because of specimen inadequacy, although the benefits in terms of sensitivity and negative predictive values are only incremental. Implications, such as cost effectiveness of and adherence to implementing such a major change in the current US opportunistic screening setting, require further evaluation and planning.”

In 2014, the US Food and Drug Administration (FDA) approved an HPV DNA test for primary cervical cancer screening (ie, a standalone test without concomitant cytology testing). As of this writing, only 2 hrHPV DNA tests are approved for primary screening. In 2015, interim clinical guidance was developed for providers interested in primary HPV testing as a screening approach.34 Although there is merit to a high-risk HPV (hrHPV) testing-only screening strategy for cervical cancer screening, there remain substantial concerns about the specificity of primary hrHPV screening, excess rates of colposcopy, and treatment for nonneoplastic HPV lesions detected by primary hrHPV screening. Other concerns include lack of a well-defined and evaluated strategy to manage hrHPV-positive women, inadequate information to define appropriate screening intervals for women who are hrHPV-negative, lack of data on testing errors because of specimen inadequacy, questions about cost effectiveness, and concerns about access to hrHPV testing and adherence to screening recommendations within the current US opportunistic screening setting. These issues have been brought to the forefront by the US Preventive Services Task Force (USPSTF) draft update of their recommendations for cervical cancer screening, which eliminate cotesting after age 30 years in favor of hrHPV testing alone every 5 years.35 Although there is little question that hrHPV-alone testing eventually will dominate cervical cancer screening, there is uncertainty about the best strategy for screening, whether an hrHPV-alone strategy is feasible for all women in all settings, and whether health care professionals and women accustomed to annual Pap
testing and Pap testing combined with hrHPV cotesting every 5 years are ready to accept a strategy with lower sensitivity.

A follow-up report of 4 European RCTs, of which 3 of the 4 screening trials tested at 3-year intervals, reported that HPV-based screening provides 60% to 70% greater protection against invasive cervical carcinomas compared with cytology only. In this evaluation by Ronco et al., detection of invasive cervical cancer was similar for both screening strategies (HPV-based screening and cytology) during the first 2.5 years of follow-up but was significantly lower in the HPV-based screening arm in long-term follow-up (up to 8 years).

Kaiser Permanente of Northern California (KPNC) has data on cotesting at 3-year intervals, with over 1 million women representing nearly 2.5 million person-years of follow-up. Using the KPNC data, Gage et al reported that screening with primary HPV testing every 3 years showed similar or better reassurance against precancer and cancer versus 3-year-interval screening with Pap testing (CIN3+: 0.069% vs 0.19% [P < .0001]; cancer: 0.011% vs 0.020% [P < .0001]) and 5-year-interval cotesting (CIN3+: 0.069% vs 0.11% [P < .0001]; cancer: 0.011% vs 0.014% [P = .21]). Their findings indicated the clear superiority of 3-year and 5-year cotesting compared with Pap testing alone every 3 years and a small but clear incremental advantage of cotesting over hrHPV testing alone in terms of lower rates of CIN3+ and invasive cancer rates in women with negative tests. However, it is the negative hrHPV test in cotesting that is contributing to the negative predictive value. Gage et al designed the analysis in anticipation of primary HPV testing every 3 years and so described 3-year, 4-year, and 5-year outcomes. A negative hrHPV test every 3 years provided greater protection than a negative Pap test every 3 years or a negative cotest every 5 years. Gage et al concluded that the optimal interval for primary hrHPV testing has not been established, and it may be every 4 or 5 years. However, at this time, no prospective studies have evaluated outcomes of primary hrHPV testing every 5 years.

There are concerns related to the feasibility of hrHPV-only testing at this time. First, there are only 2 FDA approved hrHPV-only tests, which likely means access issues will result in some women having to rely on Pap-only testing. Second, what is evident in the observational study from KPNC is that longer screening intervals are associated with some (albeit small) increased cancer risk. While the rate of false-positive findings with a 3-year primary hrHPV testing interval would be higher, the transition to primary hrHPV-alone testing may be more readily accepted by women and health care providers with a shorter testing interval that offers similar protection to the 5-year cotesting strategy. This especially may be the case if implementation of primary hrHPV-alone testing in the United States faces the hurdle of limited choice and availability of the test for screening.

Vaccination Against HPV

Persistent HPV infection accounts for virtually all of cervical cancers; 90% of anal cancers; 70% of oropharyngeal cancers; and 60% to 70% of vaginal, vulvar, and penile cancers. Although 3 HPV vaccines have been approved by the FDA, the 9-valent HPV vaccine is the only vaccine currently offered in the United States. An estimated 29,100 HPV-associated cancer cases could be averted annually with broad application of the HPV-9 vaccine.

HPV vaccination results in lower prevalence of HPV-related cervical abnormalities and, subsequently, a lower positive predictive value of cytology. In Alberta, Canada, where school-based HPV vaccination was implemented in 2008, Kim et al assessed the influence of vaccination on Pap test cytology results using databases that linked vaccination and cervical cancer screening results. Kim et al reported reduced prevalence of HPV-related cervical abnormalities, particularly high-grade cervical abnormalities. Similar findings from Australia, one of the earliest countries to implement HPV vaccination, showed that detection rates of histologically confirmed high-grade cervical abnormalities and high-grade cytology were significantly lower for vaccinated women (any dose) compared with unvaccinated women. Those reports concluded that these and similar favorable results of vaccine effect on pathology outcomes will reduce the positive predictive value of the cytology screening test. Also, the reduced prevalence of cervical abnormalities could result in fewer women referred to colposcopy, potentially disrupting the benefit-harm balance of current screening strategies.

The ACS recommends vaccination of all children at ages 11 and 12 years to protect against HPV infections that lead to several cancers and precancers. The vaccination series can be started beginning at age 9 years. In October 2016, after FDA approval of a new dosing schedule for HPV vaccination, the Advisory Committee on Immunization Practices recommended a new 2-dose schedule for girls and boys who initiate the vaccination series at ages 9 through 14 years. Late vaccination for those not vaccinated at the recommended ages should be completed as soon as possible. Three doses remain recommended for those who initiate the vaccination series at ages 15 through 26 years and for immunocompromised persons. Providers should inform unvaccinated men and women aged 22 to 26 years that vaccination may not be effective in lowering their cancer risk. It is important that all women, regardless of whether they have been vaccinated, get screened for cervical cancer and precancers according to current recommendations. The ACS endorses the Advisory Committee on Immunization Practices updated recommendation as follows: For persons initiating vaccination before their 15th birthday, the
recommended immunization schedule is 2 doses of HPV vaccine. The second dose should be administered 6 to 12 months after the first dose (0, 6-month to 12-month schedule).10

The ACS partners with the Centers for Disease Control and Prevention on 2 initiatives aimed at increasing HPV vaccination rates and ultimately reducing the incidence of and mortality from HPV-associated cancers and cervical 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. Additional information is available on the National HPV Vaccination Roundtable web site.45

The HPV VACs (Vaccinate Adolescents against Cancers) Program 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 CRC

The ACS estimates that 140,250 new cases of CRC will be diagnosed in women and men, and 50,630 women and men will die from this disease during 2018.21 CRC incidence and mortality rates have been declining for the past 2 decades among adults aged 50 years and older, which is largely attributable to the contribution of screening to prevention and early detection.46 Among people aged 50 years and older, CRC incidence declined by 32% between 2000 and 2013, and CRC mortality has declined by 34% between 2000 and 2014, although, as described below, mortality has increased among those younger than 50 years, which is attributable to the rising incidence of CRC in successive age cohorts born between 1950 and 1990.47 CRC incidence and mortality also remain higher in blacks than any other racial/ethnic group, with incidence rates 20% higher and mortality rates 40% greater in blacks than in non-Hispanic whites.48

The ACS updated its guideline for CRC screening in individuals at average risk in 2018. The ACS recommends that adults aged 45 years and older with an average risk of CRC undergo regular screening with either a high-sensitivity stool-based test or a structural (visual) exam, depending on patient preference and test availability. As a part of the screening process, all positive results on non-colonoscopy screening tests should be followed up with timely colonoscopy.17 The ACS Guideline Development Group applied the Grades of Recommendations, Assessment, Development and Evaluation (GRADE) criteria in developing and rating the recommendations. The recommendation to begin screening at age 45 years is a qualified recommendation. The recommendation for regular screening in adults aged 50 years and older is a strong recommendation.23 As noted earlier, a strong recommendation conveys the consensus that the benefits of adherence to the intervention outweigh the undesirable effects and that most patients would choose the intervention. A qualified recommendation indicates there is clear evidence of benefit (or harm), but less certainty about either the balance of benefits and harms, or about patients’ values and preferences, which could lead to different individual decisions.23 The options for CRC screening are: fecal immunochemical test (FIT) annually, high sensitivity guaiac-based fecal occult blood test (HsgFOBT) annually, multi-target stool DNA test (mTS–sDNA) every 3 years, colonoscopy every 10 years, CT colonography (CTC) every 5 years, flexible sigmoidoscopy (FS) every 5 years. The ACS further recommends (qualified recommendations) that: 1) average-risk adults in good health with a life expectancy of greater than 10 years continue CRC screening through the age of 75 years; 2) clinicians individualize CRC screening decisions for individuals aged 76 through 85 years, based on patient preferences, life expectancy, health status, and prior screening history; 3) clinicians discourage individuals over age 85 years from continuing CRC screening.

The age of 45 years to initiate CRC screening in average-risk adults is the most significant change from previous ACS CRC screening guidelines.16 The recommendation for an earlier starting age was based on the prolonged trends in disease burden showing increases in CRC incidence and mortality in persons under age 50 years47,49 and modeling analyses showing efficient strategies for CRC screening starting at age 45 years.50,51

In contrast to the 2008 ACS guideline, which prioritized screening options that had a higher potential to prevent CRC through the detection of adenomatous polyps, the 2018 CRC screening guideline does not prioritize among screening tests, emphasizing instead that screening utilization and adherence could be improved by offering a choice of tests at the time of referral to CRC screening. Health professionals should provide guidance to adults about the benefits, limitations, and potential burdens associated with screening test options and assist them in making a choice and completing screening.52 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 manufacturer’s instructions, or the limited sensitivity observed with one-time testing would make stool testing a poor choice. In contrast, evidence from randomized clinical trials and modeling has shown that a
commitment to annual testing with high-sensitivity stool tests can result in reduced risks of developing CRC and of dying from CRC that rival the reductions achieved with colonoscopy. Single-panel gFOBT in the medical office using a stool sample collected during a digital rectal exam is not recommended for screening, due to its very low sensitivity for advanced adenomas and cancer. The ACS acknowledges the potential for men and women aged 75 years and older who are in good health to benefit from continuing screening and recommends that the screening decision be individualized in older persons based on overall health status and prior screening history. Individuals over age 85 years should be discouraged from continuing CRC screening.

In 2017, the U.S. Multi-Society Task Force (USMSTF), a group comprising representatives from the American Gastroenterology Association, the American College of Gastroenterology, and the American Society for Gastrointestinal Endoscopy, updated their recommendations for CRC screening. In the update, the USMSTF recommended adults at average risk for CRC begin annual screening for CRC at age 50 years but that African Americans should initiate routine screening at age 45 years. The USMSTF also recommended discontinuation of screening upon reaching age 75 years for persons who have prior negative screening or those with less than 10 years of life expectancy. The USMSTF listed recommended screening methods using a new ranked approach that divides screening methods into 3 tiers based on performance features, costs, and other considerations. First-tier tests (colonoscopy every 10 years and annual FIT) are considered the cornerstone of screening. Second-tier tests include CT colonography every 5 years, an mt-sDNA test every 3 years, and flexible sigmoidoscopy every 5 to 10 years; and capsule colonoscopy every 5 years is the sole third-tier test.

CRC Trends in Younger Individuals

Although CRC incidence and mortality rates in the United States have fallen steadily for more than 20 years among people aged 55 years and older, incidence rates among younger individuals have increased during this period. By using Surveillance, Epidemiology, and End Results data from 1974 through 2013, researchers calculated incidence rate ratios and used age-period-cohort modeling to examine trends in CRC incidence by tumor location, age at diagnosis, and year of birth. These analyses demonstrated that the risk of CRC decreased sequentially for birth cohorts from 1890 to 1950 but has increased for every generation born since 1950. This rise is fueled disproportionately by increases in rectal cancer; the age-specific risk of colon cancer for someone born in 1990 is double that of someone born in 1950 and, for rectal cancer, the risk has quadrupled. Currently, 20% of CRC cases are diagnosed in individuals younger than 55 years, and nearly one-third (29%) of rectal cancers are diagnosed in patients younger than 55 years.

Previous reports on this phenomenon have focused on the increase in CRC among those younger than 50 years; however, the analysis by Siegel et al demonstrates that risk is also rising in individuals aged 50 to 54 years—increasing 0.5% per year since the mid-1990s. While guidelines from all major organizations recommend CRC screening starting at age 50 years for individuals at average risk, screening rates remain much lower among those aged 50 to 54 years, and the rising CRC rate in this group is believed to reflect missed opportunities for prevention attainable through screening that have benefited adults aged 55 years and older.

Delay in diagnosis is another common and concerning feature of young-onset CRC. One study found that the median time for initial clinical presentation after the onset of symptoms was twice as long for patients with young-onset CRC compared with older patients (60 days vs 30 days) and that patients with young-onset CRC experienced a longer time to diagnosis after symptom recognition (128 days vs 79 days). A study of patients with rectal cancer found that the time from symptom onset to treatment was more than 4 times longer for patients younger than 50 years (217 days) compared with adults aged 50 years and older (58 days). This delay may be because of failure on the part of both patients and primary care clinicians to consider CRC as a potential cause of symptoms, resulting in a less aggressive diagnostic approach than that taken in older individuals who present with similar symptoms. Young individuals are also more likely than older patients to be diagnosed with distant versus localized stage CRC. Whether this stage shift is associated with delays in diagnosis is unclear.

It has been reported that young-onset CRC occurs disproportionately in blacks and other minority groups in the United States, and lower survival has been documented for non-Hispanic black patients with young-onset CRC compared with young Hispanic and non-Hispanic white patients. An analysis of recent data suggests a developing shift in the racial pattern of CRC mortality in younger individuals. By using Surveillance, Epidemiology, and End Results data from 1974 through 2014, investigators examined CRC deaths in those younger than 55 years by racial background and observed a disproportionate fraction of deaths among blacks compared with white adults younger than 55 years. There was a trend of decreasing mortality in all groups until 2004, at which time there was a 1% increase annually, from 3.9 of 100,000 to 4.3 of 100,000 in 2014. This increase has been observed almost entirely in white individuals, among whom rates are increasing 1.4% annually.
Mortality continued to decrease during this period for black individuals and those of other races.

The underlying causes of the increased incidence of early-onset CRC are not fully understood. Approximately 4 in 10 individuals with early-onset disease have a family history of CRC or a risk-inducing genetic mutation and thus, their elevated risk is potentially identifiable, whereas the remaining 60% are labeled “sporadic.” Various traditional CRC risk factors likely are contributing to the upward trend in early-onset disease, including the obesity epidemic, the increasing prevalence of type II diabetes mellitus, a rise in sedentary lifestyle, and higher consumption of processed and red meats in the under 50 population. In addition to these risk factors, recent studies suggest that many sporadic cases of early-onset CRC have features that differentiate them clinically, pathologically, and molecularly from traditional cases of CRC diagnosed in older individuals. Efforts are underway to better characterize these distinguishing features, understand the interplay between molecular-genetic factors and environmental/behavioral risks, and use this information to enhance risk assessment and intervention.

Investigators are exploring the causes of early-onset CRC and ways to reverse this trend, but there are measures that can be taken immediately to address the worsening morbidity and mortality of CRC in younger adults. Recognition of at-risk individuals will require better collection and utilization of family history information and will be enhanced by routine genetic testing with a comprehensive cancer gene panel for all patients with early-onset CRC. Efforts must also be taken to raise awareness among clinicians and the public of the increased prevalence of CRC in young and middle-aged adults and to encourage the prompt and thorough evaluation of symptomatic patients (ie, those with rectal bleeding, unexplained weight loss, abdominal pain, etc) regardless of age. Implementation of and adherence to the new ACS recommendation to begin screening at age 45 are expected to mitigate the increasing CRC burden in younger adults. The ACS also will continue actively monitoring ongoing research regarding early-onset CRC and studies investigating screening outcomes in individuals younger than 50 years of age.

**Recommendations for High-Risk Adults**

The ACS and other organizations recommend more intensive surveillance for individuals at higher risk for CRC. 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 post-polypectomy and post-colorectal cancer resection surveillance. Those guidelines have since been updated by the USMSTF. Individuals at higher risk for CRC 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 with a history of inflammatory bowel disease of significant duration; 5) individuals with a known or suspected presence of 1 of 2 hereditary syndromes, specifically, Lynch syndrome (hereditary nonpolyposis colon cancer) or familial adenomatous polyposis; or 6) individuals with a history of abdominal or pelvic radiation for a previous cancer. 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. The USMSTF also has issued new recommendations for genetic evaluation and management of Lynch syndrome.

Knowledge and implementation of these high-risk screening recommendations by clinicians is suboptimal. Larger proportions of patients with young-onset CRC have a family history of CRC (25% vs 17% in older patients) and confirmed or probable hereditary cancer syndromes (7% vs 1% in older patients). In many cases, these risk factors are not recognized until patients are diagnosed with CRC, resulting in more missed opportunities for prevention and early detection. Even in oncology practices, the collection and appropriate management of cancer family history information is disturbingly low. A study of oncology practices participating in an oncologist-led, practice-based quality assessment and improvement program found that capture of complete CRC family history in CRC patients was poor (22%), and only one-quarter of patients at risk for hereditary cancers were referred for genetic counseling and/or testing. And, although the risk of CRC and young-onset CRC in this group is significantly higher than that in the general population, less than one-half of these individuals are adherent with risk-based guidelines for screening.

**Quality Issues in Follow-Up Colonoscopy**

Most CRC screening in the United States is completed with colonoscopy, and all adults who are screened with other testing options and have a positive test result should undergo further evaluation with colonoscopy. In 2016, we described the challenges to assuring that all adults who undergo colonoscopy receive a high-quality test and, in 2017, we explored in greater detail the impact of key quality factors (adenoma detection rate, performance characteristics of stool tests) on CRC outcomes.
Appropriate follow-up of abnormal stool test findings is another key component of high-quality screening, and is included in the recommendation wording of the updated 2018 ACS guideline. Stool tests serve as the first in a 2-step screening process, wherein step 2 is the follow-up evaluation of all positive gFOBTs, mt-sDNA tests, or FITs with colonoscopy. The screening process is not complete until the patient undergoes a colonoscopy to determine whether the abnormal stool test result signals the presence of a cancer, an advanced adenomatous polyp, or other pathology. For this reason, CRC screening guidelines from all organizations recommend colonoscopy after a positive stool test. Yet colonoscopy follow-up of positive stool blood test results is highly variable, and delays and outright failures to perform follow up colonoscopy have been widely documented. One study comparing completion rates among 4 health systems in the United States found that rates of colonoscopy follow-up at 12 months varied from as low as 58% to 83%, revealing both a wide range of follow-up rates and a need for improvement among both the lowest and highest performing systems. The importance of colonoscopy follow-up of a positive FOBT is illustrated by recent studies in which investigators quantified the negative impact both of failure to receive colonoscopy (n = 10,778). The investigators found a 1.64-fold increased risk of CRC death in the noncolonoscopy group overall. When the quality of the follow-up colonoscopy was also considered (with colonoscopy completion to the cecum used as a proxy measure for high quality), the risk of CRC death was nearly twice as high (hazard ratio, 1.92) in the noncolonoscopy group compared with the colonoscopy group. A US study compared CRC outcomes among individuals based on the time to follow-up colonoscopy after a positive FIT result. Seven intervals were investigated, ranging from less than 31 days to greater than 12 months. The researchers found a significantly higher risk of any CRC, advanced-stage disease, and stage II and IV CRC when follow-up colonoscopy was performed more than 10 months after a positive FIT result compared with colonoscopy occurring within 8 to 30 days. Factors at the patient, provider, and systems levels are implicated in the failure to receive timely follow-up colonoscopy. A recent review of interventions to improve follow-up colonoscopy after a positive stool test found that patient navigator and provider feedback may improve timely follow-up, but evidence for other system-level interventions is unclear.

**Testing for Early Prostate Cancer Detection**

Prostate cancer is the most common cancer, apart from skin cancer, diagnosed among men in the United States, with an
estimated 164,690 new cases and 29,430 deaths expected in 2018. Overall, prostate cancer incidence and mortality rates have been declining in both black and white men since the early 1990s, but age-adjusted incidence rates among black men remain 75% higher than those among non-Hispanic white men, and mortality rates among black men are more than double. The current ACS guideline for the early detection of prostate cancer was published in 2010 and states that men who have at least a 10-year life expectancy should have an opportunity to make an informed/shared decision with their health care provider about whether to be tested for prostate cancer with serum prostate-specific antigen (PSA), with or without DRE, 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 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 a PSA test, with or without DRE (DRE is recommended along with PSA for men with hypogonadism, because of reduced sensitivity of PSA); 2) for men with PSA levels less than 2.5 ng/mL, screening intervals can be extended to every 2 years, and screening should be conducted yearly for men with PSA levels of 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 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. Factors that increase the risk of prostate cancer include African American race, a family history of prostate cancer, increasing age, an abnormal DRE, and age-specific PSA level. 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. For example, a widely used risk calculator, the Prostate Cancer Prevention Trial (PCPT) Prostate Cancer Risk Calculator, first available in 2006, was updated in 2012 to include the ability to predict risk of low-grade (Gleason grade < 7) versus high-grade prostate cancer, to aid decisions about biopsy and other decisions. The calculator is based on findings from nearly 6,000 men in the placebo arm who were followed annually with PSA and DRE, and most of whom underwent biopsy at the end of the trial regardless of prior PSA and DRE findings. The calculator is applicable to men ages 55 and older without a prior diagnosis of prostate cancer and who have DRE and PSA results less than a year old. An alternative approach to risk stratification that integrates age, age-specific PSA levels, and risk factors into prostate cancer screening recommendations and consideration of referral for biopsy has been proposed by investigators at the Memorial Sloan Kettering Cancer Center (MSKCC). The MSKCC recommendations start screening men at age 45 years, with the interval for further screening based on initial and subsequent PSA levels. Vickers and colleagues argue that the risk stratification approach that distinguishes the MSKCC recommendations from other guidelines identifies men at higher risk for lethal prostate cancer and reduces the risk of overdiagnosis and overtreatment. Prostate cancer screening recommendations have been influenced by the conflicting results from 2 large, prospective RCTs of prostate cancer screening that were published in 2009. A large European RCT, the European Randomized Study of Screening for Prostate Cancer (ERSPC), observed a statistically significant prostate cancer mortality reduction (21%) associated with invitation to prostate cancer screening, while a large US RCT, the Prostate, Lung, Colorectal, and Ovarian Screening Trial (PLCO), observed no reduction in prostate cancer mortality associated with an invitation to screening. Reconciling the different outcomes of these RCTs has focused on differences in protocols and speculative accounts but, by and large, people with differing views on prostate cancer screening identify with the outcome of one or the other trial (ie, prostate cancer screening either is or is not associated with a reduction in prostate cancer mortality). The USPSTF judged that the benefit of prostate cancer screening was small, citing the PLCO findings, and focusing on the absolute mortality reduction in the ERSPC, namely, the likelihood that a man undergoing PSA testing would avoid a death from prostate cancer, which is different than the relative mortality reduction (20% in the ERSPC), ie, the reduction in the risk of
dying from prostate cancer relative to deaths that would have occurred without screening. 87 One difference that stood out in comparing the 2 studies was the very high rate of screening (estimated to be greater than 80%)88 in the control group from the PLCO trial versus the ERSPC trial; one group of investigators judged that this high rate significantly limited the ability of the PLCO trial to observe a difference in mortality between the group invited to screening and the control group. 89

Tsodikov et al sought to reconcile the differences in the observed mortality reductions between the 2 studies in terms of their implementation and practice settings and the intensity of screening. 90 The study included investigators from both trials and from the Prostate Cancer Working Group of the Cancer Intervention and Surveillance Modeling Network. The study methodology included performing a traditional statistical analysis, including a combined analysis of the 2 studies, assuming a common effect of screening, which showed that invitation to screening was estimated to result in a statistically significant 16% reduction in prostate cancer mortality. However, the novel methodology of the study was to estimate the intensity of screening in each study group by estimating the mean lead time (MLT) gained in each arm of the 2 trials. The MLT is the average time that diagnosis is advanced by screening. The conventional approach to the analysis of RCT data is to compare outcomes in the experimental group compared with the control group, what the authors describe as “all or nothing.” If non-adherence to the randomization assignment in a trial is modest (some invited to screening do not attend/some not invited to screening seek testing outside of the trial), then the advantage of the intention-to-treat analysis is preserved. However, it is obvious that treating men in the PLCO control group as if they did not undergo screening introduces considerable measurement error in the analysis of outcomes. To overcome this bias, the investigators treated the MLT as a covariate to capture the level of screening in both arms of both studies. In a study with no contamination, the MLT will be zero in the control group, because their cancers will be detected after symptoms appear (ie, no lead time), whereas a control group that has high rates of contamination will have MLTs that approach those of the intervention group, because screening is taking place in both study arms. After adjustment for the MLT in modeling the risk of prostate cancer death on each arm of the study, the investigators observed similar reductions per year of MLT in the risk of prostate cancer death. Given the MLTs on each study’s screening arm, this amounted to estimated reductions in prostate cancer death from 25% to 31% in the ERSPC trial and from 27% to 32% in the PLCO trial. By using data from both trials and a novel analysis, the authors concluded that screening in the 2 studies had a similar and significant effect on reducing the risk of prostate cancer death, but they also acknowledged that this benefit must be weighed against the potential harms associated with screening. 90 Thus, even though these new findings provide support for the conclusion that screening is associated with a reduced risk of prostate cancer death, the importance of informed/shared decision making about screening is not diminished.

Screening for Endometrial Cancer

The ACS estimates that 63,230 women will be diagnosed with endometrial cancer, and 11,350 women will die from this disease in 2018. 21 Uterine corpus cancer incidence has increased by 1.2% per year between 2005 and 2014, and mortality rates similarly increased during this period. 20 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. 12 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 they should be strongly encouraged to immediately report these symptoms to a clinician (Table 2). Women at very high risk for endometrial cancer because of: 1) known Lynch syndrome 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) families with suspected autosomal-dominant predisposition to colon cancer in the absence of genetic testing results, should consider beginning annual testing for early endometrial cancer detection at age 35 years. The evaluation of endometrial histology with the endometrial biopsy is still the standard for determining the status of the endometrium. 91 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, accounting for an estimated 234,030 new cases in 2018. 21 Lung cancer also is the leading cause of death from cancer in men and women, accounting for an estimated 154,050 deaths in 2018, which is approximately 26% of all cancer deaths in the United States. 21 Trends in lung cancer incidence and mortality vary by sex. Incidence rates in men have been declining since the 1980s, and, between 2010 and 2014, the average delay-
TABLE 4. 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 lung 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 non-lung-related incidental finding. <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.
- 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.

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 undergoing 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 y
- 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.

Abbreviations: LDCT, low-dose computed tomography.

adjusted incidence rates declined by 2.9% per year.20,21 For women, declines in incidence lagged behind those of men. Incidence rates in women did not begin declining until the mid-2000s as a result of historical differences in smoking patterns and cessation but, between 2010 and 2014, the average delay-adjusted incidence rates declined by 1.4% per year. Among men, mortality rates have declined by 43% since 1990; and, among women, mortality rates have declined by 17% since 2002.20,21

Clarification in the Wording of the ACS Lung Cancer Screening Guideline

In 2013, the ACS recommended that: “Clinicians should ascertain the smoking status and smoking history of their patients aged 55 to 74 years. Clinicians with access to high-volume, high-quality lung cancer screening and treatment centers should initiate a discussion about lung cancer screening with patients aged 55 to 74 years 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 following benefits, uncertainties, and harms of screening.”19

Most organizations that recommend lung cancer screening do so directly and may or may not stress the importance of informed or shared decision making.92-95 The ACS guideline for lung cancer screening has been interpreted by some to be a recommendation for shared decision making about lung cancer screening rather than a direct recommendation for lung cancer screening accompanied by adequate provision of information about the benefits, limitations, and harms of screening (or informed/shared decision making). Although the 2013 guideline publication stated that there was sufficient evidence of an overall benefit to support a recommendation for screening, the recommendation wording about initiation of a discussion suggests that the balance of benefits and harms was judged to be uncertain or at least highly subject to individual patient preferences. Typically, a recommendation for shared decision making is reserved for cancer screening tests in which there is uncertainty over whether benefits exceed harms and where patients are expected to differ in the value they place on those potential outcomes (as is the case with the current prostate cancer screening guideline issued by the ACS and most other organizations).

In 2017, the ACS GDG adopted this clarification and revised wording of the ACS recommendation for lung cancer screening with LDCT:

The ACS recommends annual screening for lung cancer with LDCT in adults aged 55 to 74 years in relatively good health who:
- Currently smoke or have quit within the past 15 years; and
- Have at least a 30-pack-year smoking history; and
- Receive evidence-based smoking-cessation counseling, if they are current smokers; and
- Have undergone a process of informed/shared decision making that included information about the potential benefits, limitations, and harms of screening with LDCT (Table 4); and
- Have access to a high-volume, high-quality lung cancer screening and treatment center.

The 2013 guideline statement included an emphasis on a high priority given to smoking-cessation counseling for current smokers who are considering screening as one of the core elements of the discussion about lung cancer screening. 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. In this clarification and update, the importance of smoking-cessation counseling is more clearly stated as an important element of the process of identifying high-risk adults who are eligible for lung cancer screening.

This clarification properly places the emphasis as intended on a positive recommendation for screening based on randomized trial evidence of screening efficacy in reducing lung cancer mortality and a judgment that the balance between potential benefits and harms is favorable. The recommendation continues to affirm the necessary conditions of appropriate selection of individuals to be screened, an opportunity for each patient to be provided information and to gain an understanding of the screening process and possible outcomes, and access to high-quality screening and follow-up (Table 5).

In late 2016, the ACS established the National Lung Cancer Roundtable (NLCRT), a national coalition of public, private, and voluntary organizations, and invited individuals, dedicated to reducing the incidence of and mortality from lung cancer in the US through coordinated leadership, strategic planning, and advocacy. The NLCRT’s focus is on promoting increased lung cancer awareness, prevention, early detection, and assurance of optimal therapy through public education, provider education, targeted research, and health policy initiatives. This roundtable is similar to other ACS supported roundtables, such as the National Colorectal Cancer Roundtable (NCCRT) in that it is intended to serve as a catalyst to stimulate greater levels of collaborative engagement among member organizations’ efforts to address key lung cancer issues, or to take on challenges that are not likely to be addressed by any one organization. The work of the Roundtable is guided by its strategic plan with direction and input from its Steering Committee. Through the efforts of its Task Groups, the NLCRT will advance initiatives that focus on primary care, tobacco cessation, shared decision-making, implementation of screening programs, access to high quality screening, triage for appropriate diagnostic evaluation and therapy, and an end to the stigma and nihilism associated with a diagnosis of lung cancer. The first NLCRT Annual Meeting was held in December 2017.

**Testing for Early Ovarian Cancer Detection**

Although the annual incidence of ovarian cancer is low compared with that of breast cancer and precursor lesions of the cervix, it is the most lethal of the gynecologic cancers. Approximately 22,240 women will be diagnosed with ovarian cancer in 2018, and 14,070 will die from the disease. Fewer than one-half of women diagnosed with ovarian cancer survive longer than 5 years and, although the 5-year survival of patients with localized ovarian cancer is greater than 90%, only 15% of all patients are diagnosed with localized disease.

Currently, no organization recommends screening average-risk women for ovarian cancer. Screening and diagnostic methods for ovarian cancer include pelvic examination, cancer antigen 125 (CA 125) as a tumor marker, transvaginal ultrasound (TVU), and potentially multimarker panels and bioinformatic analysis of proteomic patterns. In 2011, the PLCO RCT report on ovarian cancer screening with CA 125 and TVU concluded that simultaneous screening with a fixed threshold of CA 125 and TVU, compared with usual care, did not reduce ovarian cancer mortality. Based largely on the PLCO results, 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, likewise, that there was adequate evidence that screening for ovarian cancer can lead to important harms, mainly surgical interventions, in women without ovarian cancer.

A promising approach to ovarian cancer screening has been demonstrated by the UK Collaborative Trial of Ovarian Cancer Screening, which currently is assessing the efficacy of a multimodal screening strategy (MMS) including annual CA 125 screening using a risk of ovarian cancer algorithm and TVU as a second-line test, ultrasound alone, and usual care in an RCT involving asymptomatic 202,638 women ages 50-74 years recruited from 13 centers in the UK. The risk of ovarian cancer algorithm measures changes in CA 125 over time over a baseline measure rather than with a single cutoff point, as has traditionally been used and was used in the PLCO study, and has shown improved sensitivity for smaller tumors without measurably increasing the false-positive rate. The initial analysis of trial data has shown nonsignificant mortality reductions over years zero through 14 of 15% (95% confidence interval, −3% to 30%; P = .10) associated with MMS and 11% (95% confidence interval, −7% to 27%; P = .21) associated with TVU. However, in the analysis in which prevalent cases

| TABLE 5. Eligibility Criteria for the National Lung Screening Trial |
|----------------------|------------------|------------------|
| **Age** | 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; 1 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 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 |
were censored, MMS was associated with a statistically significant 20% mortality reduction \( (P = 0.021) \) and a 28% mortality reduction for cases diagnosed in years 7 through 14. The authors described these findings as “encouraging” but cautioned that further follow-up\(^{104}\) was needed before policy decisions about the value of MMS ovarian cancer screening could be made.

**Surveillance of Cancer Screening: Colorectal, Breast, Cervical, Prostate, and Lung 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.\(^{105}\) The most recent data available are from the 2015 NHIS and were provided in 2017.\(^{11}\) In this 2018 report, we provide some of these data in graphic form. Figure 1 displays cancer screening prevalence for colorectal, breast, and cervical cancer between 2005 and 2015, when CRC screening increased from 46.8% to 62.6% because of increasing use of colonoscopy. In 2015, CT colonography use was uncommon, and the inclusion of this test did not alter overall CRC screening prevalence estimates. Cervical cancer screening prevalence declined slightly between 2005 and 2015, from 85.4% to 81.6%, and there has been little change in breast cancer screening since 2005. Prostate cancer screening rates were stable between 2005 and 2010 but declined by 18% between 2010 and 2013, when the proportion of men reporting a PSA test in the past year for routine reasons declined from 37.8% to 30.8% according to NHIS data, and the rates remained stable between 2013 and 2015.\(^{106}\) Additional nationwide studies indicate that only 36% of men report shared decision making for prostate cancer screening and that discussions are often inadequate and fail to fully address the benefits, risks, and uncertainties of PSA testing.\(^{107,108}\) There are limited data on LDCT for lung cancer screening in community practice, although a recent ACS study using 2010 and 2015 NHIS data estimated the proportion of high-risk current and former smokers (who quit in the past 15 years) who had undergone LDCT for lung cancer screening in the past year did not change and remained below 4%.\(^{109}\)

In 2015, CRC screening prevalence ranged from 49.4% in Asians and 49.9% in Hispanics to 65.4% in non-Hispanic whites and was over twice as high among insured (59.6%) adults ages 50 to 64 years compared with the uninsured (25.1%). The proportion of women receiving mammographic screening in the past year ranged from 45.7% in Hispanic women to 55.4% in non-Hispanic black women and was over 2.5 times greater among insured women (52.5%) ages 50 to 64 years compared with uninsured women (20.9%) of the same age. Cervical cancer screening rates ranged from 73.3% in Asian women to 84.8% in non-Hispanic white women and were about one-third higher in insured women (84.4%) compared with uninsured women (60.8%).

It is important to note that, while the NHIS is nationally representative and is a 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 accounted for in part (but not in full) by the survey weighting procedures.\textsuperscript{110} Thus, in most instances, these data likely overestimate the rate of recent cancer screening. Additional information on cancer screening surveillance, including rates of screening by state and other sociodemographic factors, can be found in the periodically updated ACS Cancer Prevention and Early Detection Facts and Figures and Interactive Cancer Statistics Center.\textsuperscript{111}

Discussion

The most recent data on cancer screening rates are an ongoing cause for concern. As noted above, although CRC screening rates have steadily risen, screening rates for cervical cancer have declined since 2005; breast cancer screening rates have remained stable at an unacceptable level; and, 5 years after publication of the National Lung Screening Trial findings indicating a benefit of lung cancer screening, little lung cancer screening is taking place. The potential to significantly raise the number of adults with access to preventive care was enhanced by the increase in individuals with health care insurance resulting from the Affordable Care Act. However, the 2012 Supreme Court decision that the federal government could not force states to expand their Medicaid programs blunted the beneficial impact of the ACA. In the current political climate, there is little evidence of a commitment to expand access to health care and there continue to be attempts to repeal or weaken the ACA. Thus, increasing screening rates in those with newly acquired health insurance takes on a particular urgency. Gradually increasing colorectal cancer screening rates reflect, at least in part, the ACS, CDC, and NCCRT’s well-coordinated 80\% by 2018 screening campaign. But overall, cancer screening rates are unacceptably low and, for the most part, not increasing.

What factors chiefly account for the stagnation in screening rates? One persistent barrier to increasing screening rates is the lack of uniform appreciation of the value of cancer screening. In fact, very few preventive interventions reliably and cost-effectively reduce mortality as substantially as evidence-based cancer screening. Other barriers to screening have been known for years. While social determinants of health, such as income, insurance status, and educational achievement, are paramount factors, numerous individuals confronting relatively few barriers to screening are not up to date. Requiring individuals to bear out of pocket expenses in the form of copays or deductibles is a barrier to screening. Without a national program, the uptake of cancer screening relies on the combination of highly variable modes of health care delivery, varying from highly organized approaches as seen in some integrated delivery systems to completely nonsystematic and opportunistic delivery models. Adults who report recent cancer screening tend to have a usual source of care and receive a recommendation to undergo screening from a health care professional, and there is a higher probability that this will happen if the patient has undergone an office visit dedicated to preventive care, such as a wellness visit or checkup. Given the limited time available to patients and providers during acute and chronic care visits, it is not surprising that referrals to cancer screening and other preventive care do not consistently take place. Further, while many individuals who have a reasonable likelihood of benefiting from a cancer screen are not up to date, screening too frequently is being recommended for individuals unlikely to benefit due to short life expectancy resulting from old age and/or comorbid illness, such as advanced cancer, congestive heart failure, or dementia.

The nation has an unequivocal opportunity to reduce mortality from cancer by increasing the cancer screening rates in those most likely to benefit. Although campaigns like Cancer Screen Week, which was cosponsored by Genentech, the ACS, Stand Up to Cancer, and Rally Health, can raise awareness about the importance of cancer screening, a system that provides full access to screening, reminds adults when they are due for screening, and can track outcomes and the need for follow-up tests, would reduce demands on primary care. It also would provide a more dependable foundation for interventions focused on raising rates of regular screening. With greater uptake of regular screening, there would be a significant reduction in avoidable cancer deaths in the United States.

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