Cancer Screening

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Faculty

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Faculty Disclosure

Contributing faculty, Lori L. Alexander, MTPW, ELS, MWC, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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Division Planners Disclosure

The division planners have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for physicians, physician assistants, and nurses who may intervene to improve cancer screening rates.

Accreditations & Approvals

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Disclosure Statement

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Course Objective

The purpose of this course is to concisely provide the evidence-based guidelines and recommendations for cancer screening in order to improve healthcare professionals' adherence and ultimately increase overall screening rates, leading to improvements in public health.

Learning Objectives

Upon completion of this course, you should be able to:

1. Identify trends in cancer screening for the most common cancers.
2. Discuss disparities in adherence to cancer screening guidelines, including the impact of race/ethnicity, gender, age, socioeconomic status, and other factors.
3. Evaluate controversies in cancer screening recommendations and the creation of guidelines.
4. Describe breast cancer screening recommendations and possible factors affecting nonadherence.
5. Outline guideline recommendations for cervical cancer screening.
6. Identify colorectal cancer screening guidelines.
7. Assess recommendations for lung cancer screening and possible adherence issues.
8. Summarize available prostate cancer screening recommendations.
9. Describe oral cancer screening recommendations.
10. Evaluate guideline recommendations for ovarian cancer screening and factors affecting adherence.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Lung, colorectal, breast, and prostate cancer are the leading causes of cancer-related deaths in the United States [1]. Together, these cancers accounted for an estimated 46% of all cancer-related deaths, or more than 273,000 deaths, in 2016 [1]. Appropriate screening has the potential to reduce this substantial mortality by detecting cancer at earlier stages, when cure is most possible. Screening guidelines have been developed for these cancers (as well as for cervical cancer), but the appropriateness of cancer screening has been heavily debated, with questions related to several aspects, including the age at which to begin screening, the age at which screening can safely be discontinued, the method used for screening, the screening interval, the definition of risk, and specific recommendations according to risk. Another significant issue is overdetection and overtreatment of certain cancers.

Improving cancer screening rates is a priority and is included in the objectives for the Healthy People initiative. These objectives set target goals for 2020 based on a 10% improvement from recent data on breast and cervical cancer screening and prostate cancer screening counseling; the target rate is higher for increasing the proportion of people who have colorectal screening [2].

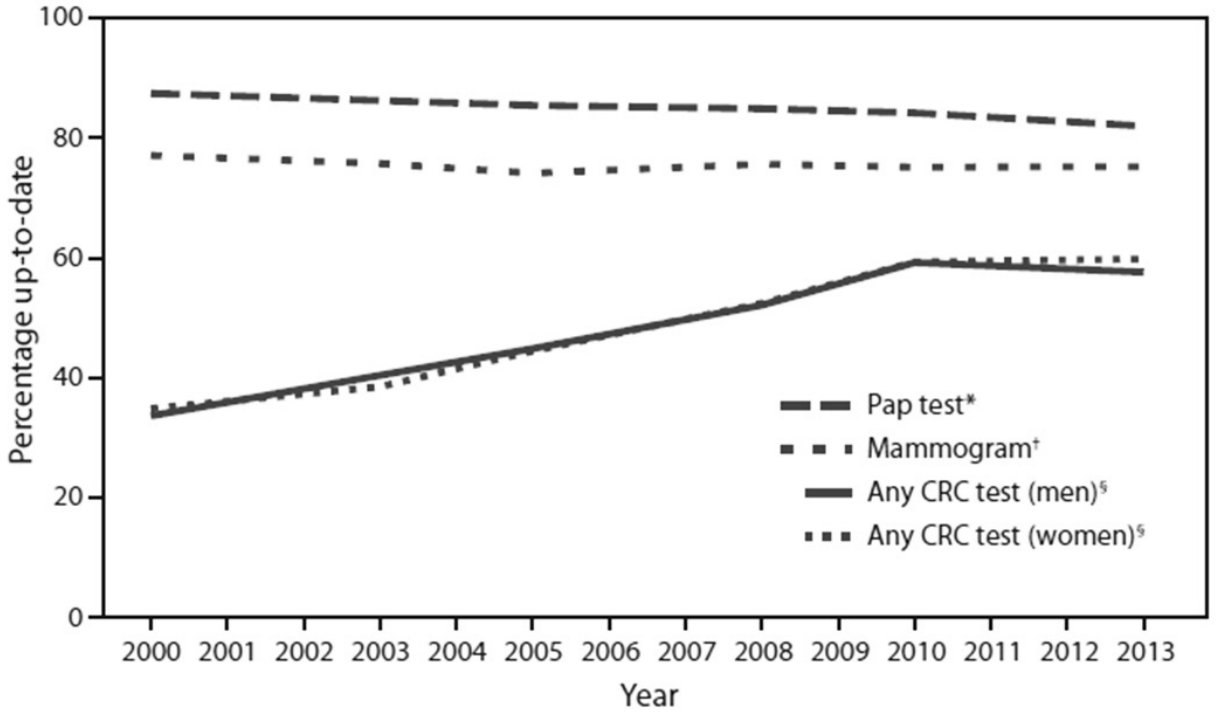
According to data from the 2010 National Health Interview Survey (NHIS), the rates of screening for breast and colorectal cancer screening met the goals set in Healthy People 2010, but the rate of cervical cancer screening fell short of the target (***Table 1***) [3; 4]. (A later analysis of data from the 2012 Behavioral Risk Factor Surveillance System [BRFSS] survey showed a higher rate [65.1%] of colorectal cancer screening [5].) All three rates are considerably below the targets set for 2020, so improvement is needed [2]. Progress toward meeting Healthy People 2020 cancer screening targets was not observed in 2013 compared with 2010. Mammography use remained essentially stable, Pap test use declined, and colorectal cancer test use was essentially unchanged (***Figure 1***) [221].

2010 CANCER SCREENING RATES COMPARED WITH HEALTHY PEOPLE TARGETS FOR 2010 AND 2020

Objective for Screening and Counseling	Target for 2010	Reported Rate 2010	Target for 2020
Breast cancer			
Increase the proportion of women ≥40 years of age who had breast cancer screening with mammography within past 2 years	70%	72.4%	81.1%
Cervical cancer			
Increase the proportion of women 21 to 65 years of age who had cervical cancer screening with Pap test within past 3 years	90%	83.0%	93.0%
Colorectal cancer			
Increase the proportion of adults who have ever had colorectal cancer screening	50%	58.6%	70.5%
Prostate cancer			
Increase the proportion of men who have discussed with their healthcare provider the advantages and disadvantages of screening with prostate-specific antigen	—	14.4%	15.9%

Source: [2; 3; 4] *Table 1*

PERCENTAGE OF ADULTS UP TO DATE WITH SCREENING FOR BREAST, CERVICAL, AND COLORECTAL CANCER, BY TEST, SEX, AND YEAR—UNITED STATES, 2000–2013



CRC = colorectal cancer; Pap = Papanicolaou.
*Among women 21 to 65 years of age with no hysterectomy
†Among women 50 to 74 years of age
§Among persons 50 to 75 years of age

Source: Reprinted from Sabatino SA, White MC, Thompson TD, et al. Cancer screening test use—United States, 2013. MMWR. 2015;64(17):464-468. *Figure 1*

2013 CANCER SCREENING RATES ACCORDING TO RACE/ETHNICITY

Cancer Screening[a]	Screening Rate					
	Overall	White	Black	AI/AN	Asian	Hispanic
Breast	72.5%	72.6%	72.6%	73.4%	72%	66.5%
Cervical	80.5%	81.2%	82.2%	83.1%	70.1%	76.9%
Colorectal	57.8%	58.4%	57.9%	48.3%	49.5%	41.5%

[a]Breast cancer screening defined as mammography within the past two years, and cervical cancer screening defined as Pap testing within the past three years.
AI/AN = American Indian/Alaska Native.

Source: [4] *Table 2*

The screening rates reflect disparities according to race/ethnicity as well as socioeconomic demographics. In general, screening rates are lowest among Asian and Hispanic populations and highest among white and black populations (***Table 2***) [221]. Rates were substantially lower for people who had been residents of the United States for fewer than 10 years, approximately 40.8%, 66%, and 19.3% for breast, cervical, and colorectal cancer screening, respectively [221]. Low rates were also associated with an educational level of less than high school and lack of health insurance. In another review of data on cancer screening, researchers found that screening rates were higher for cancer survivors than for the general population [6].

This course provides an overview of the major issues in cancer screening, appropriate adherence to guidelines and barriers to adherence, controversies regarding guideline criteria, and the effect of screening on mortality. Also included are detailed recommendations for the five major cancer types for which guidelines on screening and counseling have been developed: breast, cervical, colorectal, lung, and prostate cancers. Recommendations for other cancers of concern are included as well. Lastly, strategies to enhance cancer screening are also discussed.

ISSUES IN CANCER SCREENING

The overall goal of health screening is to discover a condition in a person who has no signs or symptoms of the condition [7]. In 1968, the World Health Organization (WHO) defined 10 principles for an appropriate screening test that remain relevant today [7; 8]:

- The condition to be screened for should be an important health problem, either because of a high prevalence or a major cause of death.
- The condition should have a recognizable latent or early symptomatic stage.
- The natural history of the condition, from latency to overt disease, should be adequately understood.
- There should be an accepted treatment for the disease.
- The screening test should be acceptable to the population.
- Facilities for diagnosis and treatment should be available.
- There should be an agreed policy on whom to treat as patients.
- The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
- Case-finding should be a continuing process and not a "once and for all" project.

With regard to cancer screening specifically, the National Cancer Institute (NCI) notes that at least two requirements must be met for screening to be efficacious [8]:

- A test or procedure must be available to detect cancers earlier than if the cancer were detected as a result of the development of symptoms.
- Evidence must be available that treatment initiated earlier as a consequence of screening results in an improved outcome.

Early detection and treatment offer potential benefits of reduced morbidity and longer survival; however, these benefits alone do not define a cancer screening test as effective. Rather, the standard criterion for effective screening is evidence of a decrease in cause-specific mortality in randomized controlled trials [8]. This definition of efficacy is often misunderstood by the general public as well as by clinicians, who may consider screening to be effective if it increases early detection and improves survival. This misinterpretation was demonstrated in a study of clinicians' understanding of screening in which more than 300 primary care physicians were presented with scenarios about the effect of

two hypothetical screening tests. In that study, significantly more physicians said they would recommend a screening test associated with an increase in 5-year survival from 68% to 99% compared with a screening test associated with a decrease in cancer mortality from 2 to 1.6 per 1,000 persons (69% vs. 23%) [9]. Nearly half (47%) of the physicians said that detecting more cases of cancer in a screened population than an unscreened one was proof that screening saves lives.

The validity of a screening test is usually measured in terms of four factors [8]:

- Sensitivity: The ability of the test to correctly identify people who have the disease
- Specificity: The ability of the test to correctly identify people who do not have the disease
- Positive predictive value: The proportion of people with a positive test result who actually have the disease
- Negative predictive value: The proportion of people with a negative test result who actually do not have the disease

Sensitivity is a measure of the false-negative rate (i.e., the number of negative results among people who have the disease), whereas specificity is a measure of the false-positive rate (i.e., the number of positive results among people who do not have the disease) [7]. The positive predictive value of a screening test depends primarily on the prevalence of disease in the population being screened; the higher the prevalence, the higher the positive predictive value [8]. Thus, for a cancer with a low prevalence, most positive screening test results will be false-positive results.

Guidelines for cancer screening are developed by expert panels from a variety of organizations, including the American Cancer Society (ACS), specialty organizations, and the U.S. Preventive Services Task Force (USPSTF). Guidelines from the ACS are developed by an expert panel and based primarily on other evidence-based screening guidelines, although some criteria may differ. Expert panels from specialty organizations craft guidelines based on evidence from the literature on the effectiveness and safety of the screening test and may supplement the guideline with recommendations based on consensus or expert opinion when evidence is lacking. The USPSTF is an independent panel of experts in prevention and evidence-based medicine that issues evidence-based recommendations about clinical preventive services with a goal of improving public health across the United States. The Task Force focuses on the benefits and harms of a screening test and recommends a screening test only when there is sufficient evidence that the benefits outweigh the harms. The USPSTF guidelines center on recommendations for asymptomatic, average-risk individuals seen in the primary care setting; most specialty organizations also include recommendations for higher risk individuals in their guidelines. The general public is most likely to be familiar with guidelines from the ACS rather than those from other organizations.

ADHERENCE TO CANCER SCREENING GUIDELINES

In general, adherence to cancer screening guidelines is suboptimal. This suboptimal adherence relates not only to clinicians' underuse of appropriate screening but also to overuse and misuse [10; 11]. Underuse is evident in low cancer screening rates and is typically a result of low uptake by people and lack of healthcare professional recommendation. Overuse and misuse are primarily related to the use of screening for patients in non-recommended age-groups and misinterpretation or lack of awareness of patient risk [12; 13; 14; 15]. For example, screening for breast and colorectal cancer is often offered to women younger than the guideline-recommended age, cervical cancer screening is commonly offered at more frequent intervals than recommended, and prostate and lung cancer screenings are often offered to people at average risk when recommended only for people at high risk. Overuse has also been related to cancers for which screening is not recommended, such as ovarian cancer [16; 17].

BARRIERS TO APPROPRIATE CANCER SCREENING	
Related Factors	**Documented Barriers**
Patient	Race/ethnicity Attitude toward screening Education level Income level Level of trust in health care Obesity Access to health care Availability of health insurance Lack of clinician recommendation Knowledge of appropriate screening (related to risk)
Healthcare professional	Age and gender Practice type Attitude about screening guidelines or the recommending organization Patient concerns or preferences for screening Perception of patient risk Concern about medical-legal risk Reimbursement and payment issues Changing and conflicting guidelines Unfamiliarity with definition of efficacy of screening
Practice/system	Lack of practice policies regarding guidelines Lack of office-based systems for ordering and following through on screening tests Lack of insurance coverage
Source: [6; 10; 11; 13; 14; 15; 18; 19; 20; 21; 22; 23; 24; 25; 26; 27; 28; 29; 30; 31; 32; 221]	*Table 3*

Inappropriate screening is associated with patient-related, healthcare professional-related, and healthcare system-related barriers (***Table 3***). These barriers must be identified and understood in order to improve rates of appropriate screening. The rapid rate at which many screening guidelines change, the presence of conflicting guidelines from different organizations, and the increasing complexity of cancer screening make it difficult for both healthcare professionals and their patients to understand the best screening options [18]. Some barriers vary according to cancer type, but others are common overall.

Patient-Related Barriers

Patient-related factors have included race/ethnicity, attitude toward screening, obesity, education level, income level, level of trust, access to health care, and availability of health insurance [6; 11; 13; 19; 20; 21; 22; 221]. Lack of healthcare professional recommendation has also been a barrier noted by patients, with one meta-analysis showing that it was the most often cited barrier [23; 24]. This finding highlights the importance of clinicians enhancing their adherence to guidelines and recommending appropriate screening to their patients.

Healthcare Professional-Related Barriers

Among healthcare professional-related factors, age and gender, practice type, specialty area, attitude about screening guidelines or the recommending organization, patient concerns or preferences for screening, perception of patient risk, concern about medical-legal risk, and reimbursement and payment issues have been associated with adherence to appropriate screening [10; 14; 15; 18; 19; 25; 26; 27; 28; 29; 30; 31; 32]. As noted, many clinicians do not understand the accurate definition of effective cancer screening, which can also influence recommendations.

Adherence to guideline recommendations is also lacking in terms of patient-clinician discussion about options for screening modalities and the benefits and harms of screening. For example, many primary care providers do not discuss all colorectal screening options with their patients [33]. Also, although guidelines for prostate cancer screening emphasize informed decision making, most men have reported that they had no shared decision making [26; 34].

Determining Patient Risk

An issue further complicating decision making about cancer screening is the difference in recommendations for the general (average-risk) population and for people at high risk because of a variety of factors (e.g., age, comorbidities, genetic testing, previous cancer). Many healthcare professionals are not only unfamiliar with the recommendations for high-risk patients but also have difficulty identifying patients who are at high risk. Some surveys have found that physicians recommended cancer screening because they estimated their patient's risk as being high [14; 26]. In contrast, other studies have shown that healthcare providers did not offer appropriate screening to their patients who are at high risk because of a comorbidity or family history [29; 31]. Both healthcare professionals and patients have been reported to be unfamiliar with screening guidelines for survivors of childhood cancer, who may be at high risk for certain cancers in adulthood [27; 28].

Changing or Conflicting Guidelines

Cancer screening guidelines are updated frequently as compelling evidence emerges. Although updated guidelines are heavily promoted to clinicians, especially primary care providers, remaining up-to-date on specific screening criteria is difficult. In addition, most types of cancer have multiple guidelines, and although these guidelines are in general agreement, areas of disagreement may exist. Areas of discrepancy add to the challenge of decision making for clinicians as well as patients [18]. Together, changing and conflicting guidelines, as well as lack of knowledge about definitions of high risk, contribute substantially to suboptimal rates of adherence to screening guidelines [12; 13; 14; 16; 25; 35; 36; 37; 38].

System-Related Barriers

As noted, financial issues that affect access to care are a primary system-related barrier to cancer screening [4; 21; 39; 40]. A source of usual care is an important factor in cancer screening rates, with lower screening rates for people who lack a usual source of care. In the case of colorectal cancer screening, the screening rate is approximately 21% for people who do not have a usual source of care compared with 62% for people who do. The corresponding rates are approximately 36% and 75% for breast cancer screening and 65% and 86% for cervical cancer screening [221]. Cancer screening rates are also much lower for people with no health insurance than for people with insurance. In fact, screening rates for individuals who have insurance or a usual source of care are higher than the overall screening rates, highlighting the role of these two factors in improving cancer screening rates (***Table 4***).

CONTROVERSIES

Effect of Screening on Mortality

The impact of screening on mortality rates is the issue that generates the most controversy about appropriate cancer screening. Since the 1990s, the number of cancers diagnosed at later stages has decreased substantially [1]. Although regular cancer screening is likely to have contributed to this decline, the effect is not always clear. One exception is colorectal cancer screening, which has been shown to be associated with reduced colorectal cancer-specific mortality [41; 42]. Data are conflicting for other cancers. Guidelines for prostate cancer screening with prostate-specific antigen (PSA) were updated in 2012 when evidence showed little benefit in reduction of mortality among the general male population [43].

CANCER SCREENING RATES ACCORDING TO HEALTH INSURANCE STATUS				
Type of Screening	**Screening Rate**			
	Total	**No Insurance**	**Private Insurance[a]**	**Public Insurance**
Breast cancer	72.5%	38.5%	79.9%	66.4%
Cervical cancer	80.5%	62.0%	86.3%	78.8%
Colorectal cancer	57.8%	23.5%	63.0%	58.7%
[a]Includes military insurance				
Source: [221]				*Table 4*

Most recently, low-dose spiral computed tomography (LDCT) was recommended for lung cancer screening based on the findings of the National Lung Screening Trial (NLST), in which LDCT decreased the relative risk of lung cancer-specific death compared with chest x-ray alone [44]. However, a systematic analysis found that two smaller trials showed no benefit in terms of mortality [45]. Conflicting results of mortality reduction have led researchers to scrutinize the benefits and harms of cancer screening and to consider the populations who would benefit the most from screening.

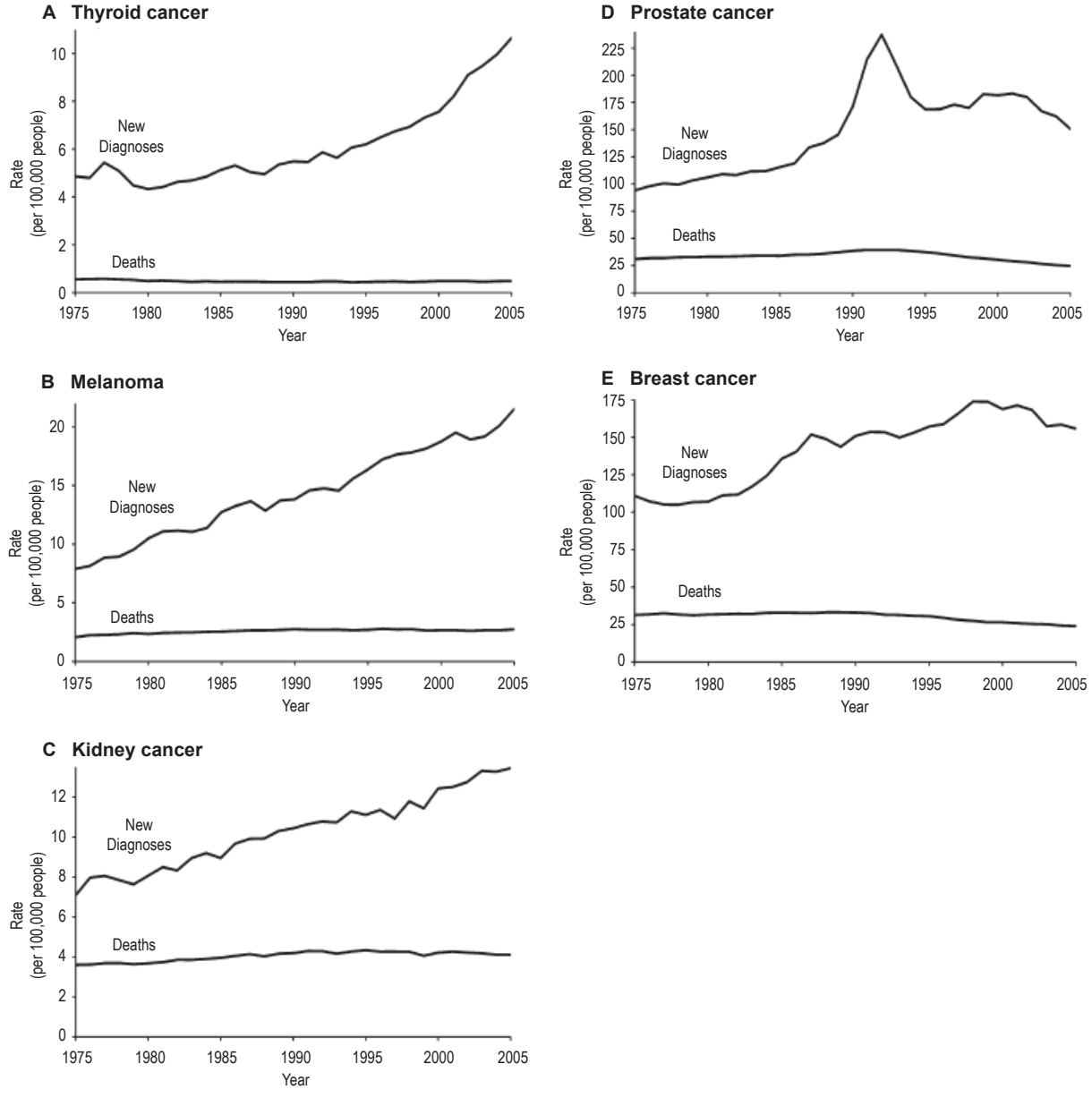
Overdiagnosis

Overdiagnosis is perhaps the most important harm associated with cancer screening, as it can have long-term effects on physical and emotional health [46]. Cancer overdiagnosis is defined as the diagnosis of a cancer that would otherwise not subsequently cause symptoms or death because of either lack of progression, slow growth, or even regression [46]. Overdiagnosis is distinct from a high rate of false-positive results, as overdiagnosis refers to a tumor that meets the pathologic criteria for cancer, whereas false-positive results do not [46].

Overdiagnosis is determined by analyzing long-term data from screening trials and population-based rates of cancer incidence and cancer-related mortality. In screening trials, the number of cancers in a screened group is initially higher than in an unscreened group because of the early detection that screening offers. However, over time, the number of cancers in an unscreened group is expected to increase and become similar to that in a screened group, as more cancers become clinically evident as they progress [46]. Thus, overdiagnosis is represented by an excess of cancers in a screened group years after a screening trial has been completed [46]. With population-based data, overdiagnosis is determined by comparing the rate of new diagnoses with the rate of mortality; if the mortality rate does not increase over time as the incidence increases, overdiagnosis is the most likely reason. For example, a review of 30-year data on incidence and mortality from the Surveillance, Epidemiology, and End Results (SEER) database showed that the rates of diagnosis for five cancers increased, but the mortality rates did not (***Figure 2***) [46]. The increase in the rates of new diagnoses was associated with an increased uptake of screening or greater use of imaging to detect cancers. Decreasing mortality rates for breast and prostate cancer may be the result of improvements in treatment, as well as increased screening, but evidence from randomized controlled trials support an effect of overdiagnosis. Few improved treatments have been put into practice for thyroid or kidney cancer or melanoma (during the time of the data), which means the gap in new diagnoses and mortality is most likely related to overdiagnosis [46].

Overdiagnosis has been associated most often with breast, prostate, and lung cancer. There is little evidence of overdiagnosis with screening for either cervical or colorectal cancer (with conventional methods), because the rate of diagnosis of both cancers is decreasing [46].

RATE OF NEW DIAGNOSES AND DEATH IN FIVE CANCERS IN THE SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS DATA FROM 1975 TO 2005



Source: Reprinted, with permission, from Welch H, Black WC. Overdiagnosis in cancer. J Natl Cancer Inst. 2010;102(9):605-613.

Figure 2

Age at Which to Stop Screening

The age at which cancer screening may be stopped has been debated for many cancers, and a lack of clear guidance on an ending age in some guidelines has an impact on clinicians' decision making [47]. In addition, multiple screening guidelines for the same type of cancer may recommend different age cutoffs [47; 48]. For example, at one time, three organizations recommended three different ending ages for mammography, and a fourth organization specified no age limit [48]. An important reason for the lack of clarity about ending ages is that people older than 75 years of age have been excluded from most trials of cancer screening tests, and extrapolating data on a younger population to an older one is difficult [48].

Some expert panels have noted that the presence of comorbidities and life expectancy are better determinants of an ending age than a chronologic age. Consideration of comorbidities addresses the diversity in health status within the older population [47]. Determining life expectancy is important because the weight of benefit versus harm is distinct in the older population. Older adults are unlikely to benefit from cancer screening if they have a life expectancy of less than 5 years. In a meta-analysis of survival data from nine randomized controlled trials around the world, survival curves for people screened for breast and colorectal screening did not separate significantly until more than 5 to 10 years after the start of screening [49]. The authors concluded that screening for these two types of cancer is most appropriate for people with a life expectancy of more than 10 years.

In contrast, the potential harms associated with screening are immediate, and the risk for harm is greater among older people. Among the greatest harms is the detection and treatment of a cancer that would not have become clinically significant within an older person's remaining lifetime [48]. Other potential harms include complications related to diagnostic tests and psychologic distress related to false-positive results or anxiety related to the screening test itself or to a cancer diagnosis [48]. These harms may be greater in the older population, as tests and follow-up procedures may be more difficult, painful, or frightening in people with cognitive or sensory problems [48].

BREAST CANCER

Widespread breast cancer screening has been available for more than three decades, and as researchers gain a better understanding of the natural history of the disease and of the efficacy of screening modalities, the guidelines have changed over that time. At least six major organizations have developed evidence-based guidelines for breast cancer screening, and some inconsistency among them remains (***Table 5***) [39; 50; 51; 52; 53; 54].

RECOMMENDATIONS FOR WOMEN AT AVERAGE RISK

Starting Age

The National Comprehensive Cancer Network (NCCN), the American College of Obstetrics and Gynecology (ACOG), and the Society of Breast Imaging/American College of Radiology (SBI/ACR) recommend screening mammography beginning at 40 years of age for women with average risk for the disease and no symptoms [50; 51; 52]. The American College of Physicians (ACP) determined that clinicians should discuss the potential benefits and harms of screening mammography with women 40 to 49 years of age and base decisions about screening on these benefits and harms, as well as on a woman's preferences and breast cancer risk profile [54]. Physicians should order biennial mammography screening if an informed woman requests it.

The USPSTF had also recommended a starting age of 40 years, but in 2009 (and reaffirmed in 2016), the Task Force changed the recommended starting age to 50 years, stating that the absolute reduction in breast cancer-related mortality is greater for women 50 to 74 years of age than for women 30 to 49 years of age [53]. The USPSTF noted that, according to pooled breast cancer mortality data, 1,904 women 39 to 49 years of age must be screened in order to prevent one breast cancer death; that number decreased to 1,339 for women 50 to 59 years of age, and 377 to women 60 to 69 years of age [53]. The Task Force also reported age-specific screening results from the Breast Cancer Surveillance Consortium (BCSC). These data show that the following number of women in each age-group would need to have mammography to diagnose one case of breast cancer [53]:

- 40 to 49 years of age: 556 women
- 50 to 59 years of age: 294 women
- 60 to 69 years of age: 200 women
- 70 to 79 years of age: 154 women
- 80 to 89 years of age: 143 women

RECOMMENDATIONS FOR BREAST CANCER SCREENING FOR AVERAGE-RISK WOMEN			
Organization (Year)	**Screening Recommendations**		
	Imaging	**Clinical Breast Exam**	**Self-Exam**
U.S. Preventive Services Task Force (2016)	Age 50 to 74 years: Biennial mammography Age ≥75 years: Evidence is insufficient to assess benefits and harms	Not addressed	Awareness of breast changes; discuss changes with physician
American College of Physicians (2019)	Age 40 to 49 years: Individualized assessment of risk for discussion of benefits and harms of screening mammography, as well as woman's preferences Age 50 to 74 years: Offer biennial mammography Age 75 and older or life expectancy less than 10 years: Do not screen.	Not addressed	Not addressed
American Cancer Society (2015)	Age 45 to 54 years: Annual mammography (40 to 44 years, optional); Age 55 years and older: Biennial screening (annual optional); Less than 10 year life expectancy: No screening	Not recommended	Not recommended
National Comprehensive Cancer Network (2015)	Age ≥40 years: Annual mammography	Age ≥25 years but <40 years: Every 1 to 3 years Age ≥40 years: Annually	Breast awareness
American College of Obstetrics and Gynecology (2011)	Age ≥40 years: Annual mammography	Age 20 to 39 years: Every 1 to 3 years Age ≥40 years: Annually	Age ≥20 years: Breast awareness
Society of Breast Imaging/ American College of Radiology (2010)	Age ≥40 years: Annual mammography; end screening when life expectancy is <5 to 7 years	Not addressed	Not addressed
Source: [50; 51; 52; 53; 54; 220]			*Table 5*

For women younger than 50 years of age, the USPSTF guideline echoes the ACP statement, noting that the decision is an individual one and should be based on a woman's values regarding the benefits and risks [53].

Despite the USPSTF recommendation of 50 years as a starting age, some experts continue to advocate the younger starting age of 40 years. In fact, the three other guidelines on breast cancer screening that recommend a starting age of 40 years were published after the USPSTF guidance. In its guideline, the ACOG notes that, although the incidence of breast cancer is lower among women in their 40s, the sojourn time (i.e., time between mammographic detection of a small breast cancer and the time the cancer is large enough to be symptomatic) is short in this age-group (about 2 years) [51]. As such, the window of opportunity to detect early-stage cancer is smaller, and more frequent screening for this age-group should be considered.

To evaluate the impact of the higher starting age recommended by the USPSTF, researchers reviewed screening mammographies at a single institution between 2007 and 2010 and found that women 40 to 49 years of age accounted for approximately 33% of all screened women and for about 20% of the screen-detected cancers, half of which were invasive [55]. The authors suggested that these findings were useful for patient-clinician discussions about when to start screening.

In a review of invasive breast cancers diagnosed between 1990 and 1999 and followed up through 2007, investigators found that 29% of 609 confirmed breast cancer-related deaths were among women who had been screened, and 71% were among women who had never been screened or who had been screened more than 2 years previously [56]. The median age at the time of diagnosis of the fatal cancers was 49 years. The authors encouraged initiation of regular screening before 50 years of age.

A modeling study found that biennial screening for women 50 to 69 years of age would reduce mortality by 15%, averting approximately five breast cancer-related deaths per 1,000 women [57]. Lowering the starting age to 40 years would change the mortality decrease to 16% and avert one more breast cancer-related death per 1,000 women. With regard to annual screening, mortality would be reduced 20% for women 50 to 69 years of age (averting approximately eight deaths per 1,000 women) and 22% for women 40 to 69 years of age (averting approximately seven deaths per 1,000 women) [57].

Ending Age

The USPSTF recommends screening mammography until 74 years of age and concluded that there was insufficient evidence to assess the benefits and harms of screening mammography for women 75 years of age and older [53]. The SBI/ACR expert panel notes that screening should be stopped when the life expectancy is less than 5 to 7 years (on the basis of age or comorbidities) or when abnormal results would not prompt action because of age or comorbidities [52]. Similarly, the ACS recommends that screening continue for patients "as long as their overall health is good and they have a life expectancy of 10 years or longer" [39]. The ACOG guideline states that there is no consensus on the age limit for screening mammography but notes that the benefits of screening decrease with increasing age compared with the harms associated with overtreatment [51]. The guideline recommends that physicians discuss the continuation of screening with their female patients older than 75 years of age. The NCCN guideline does not specify an ending age, noting that the high incidence of breast cancer in older women merits continued screening. The guideline also notes that screening recommendations be tailored according to an individual woman's health status, with screening not recommended for women who have severe comorbidities and limited life expectancy [50].

The U.S. Preventive Services Task Force concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women 75 years of age or older.

(https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/breast-cancer-screening1?ds=1&s=breast%20cancer. Last accessed January 19, 2017.)

Strength of Recommendation: I (Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.)

Screening Interval

The NCCN, the ACOG, and the SBI/ACR recommend that screening be done every year for women 40 years of age and older; the USPSTF recommends screening every 2 years for women 50 years of age and older; and ACS recommends screening every year for women 45 to 54 years of age, and every other year beginning at 55 years of age [50; 51; 52; 53; 220]. The ACP recommends biennial screening [54].

Using modeling, Mandelblatt et al. evaluated the effects of different schedules of mammography screening and found that screening every 2 years achieves most of the benefit of annual screening but with less harm [57]. Specifically, screening every 2 years retained an average of 81% of the benefit of annual screening with about half the number of false-positive results.

Although the ACOG recommends a range (1 to 2 years) for the screening interval, the guideline notes that annual mammography offers the best chance for early detection and treatment. The ACOG bases its recommendation for the screening interval primarily on the sojourn time. The greatest predictor of sojourn time is age, with the shortest average sojourn time (2 to 2.4 years) associated with an age of 40 to 49 years; the longest average sojourn time (4 to 4.1 years) is associated with an age of 70 to 74 years [51].

Preliminary findings from a retrospective review of data on 300 women with screen-detected breast cancers provide further support for more frequent screening. The investigators divided the women according to screening interval (less than 1.5 years, 1.5 to 3 years, and more than 3 years) [58]. After controlling for age, breast density, high-risk status, and family history of breast cancer, the authors found that the rate of positive lymph nodes was significantly higher in the groups with the longer intervals (8.7%, 20.5%, and 15.4%, respectively).

Screening Methods

Film mammography is the screening method recommended in all guidelines [50; 51; 52; 53; 54; 220]. The USPSTF concluded that the current evidence is insufficient to assess the additional benefits and harms of either digital mammography or magnetic resonance imaging (MRI) instead of film mammography as the recommended screening method [53]. Similarly, the ACP recommends additional research on the benefits and harms of other screening modalities [54].

Some studies have supported the use of ultrasound as an adjunct to mammography for women with dense breast tissue. However, no organization recommends ultrasound in this context. The SBI/ACR guideline states that ultrasound may be considered as an adjunct to mammography for women with dense breast tissue, whereas the ACR Appropriateness Criteria notes that, although ultrasound may enhance cancer detection in women with dense breast tissue, such screening is associated with a high rate of false-positive results and is time-consuming [52; 59]. The NCCN notes that there is insufficient evidence to support the routine use of ultrasound as adjunct screening for women with dense breast tissue and no other risk factors [50]. A systematic review found no sound evidence to support the routine use of breast ultrasound as an adjunct to mammography for screening women at average risk [62].

Since the publication of screening guidelines, meta-analyses of large randomized trials have shown that the detection rate is slightly higher for digital mammography compared with film mammography. However, the data on the benefit of digital mammography have been conflicting; in one meta-analysis, the higher detection rate was found primarily among women 60 years of age and older, whereas in the other, the detection rate was higher among women younger than 50 years of age [60; 61]. The NCCN notes that digital mammography appears to benefit young women and women with dense breasts [50].

Clinical Breast Examination

Clinical breast examination has been shown to add incremental value to screening mammography, which can miss 10% to 15% of palpable masses [63]. However, the effectiveness of clinical breast examination is limited; in a large study of women 40 years of age or older, the sensitivity of clinical breast examination for detection of cancer was 58.8% and the specificity was 93.4% [64]. In addition, the rate of false-positive screening results is higher with the combination of mammography and clinical breast examination than with mammography alone.

The NCCN and the ACOG agree that women 40 years of age and older should have an annual clinical breast examination [50; 51]. The USPSTF notes that there is insufficient evidence to assess the additional benefits and harms of clinical breast examination beyond screening mammography for women in this age-group [53].

With regard to younger women, the ACOG recommends clinical breast examination every 1 to 3 years for women 20 to 39 years of age, and the NCCN recommends this examination every 1 to 3 years for women 25 to 39 years of age [50; 51]. The USPSTF concluded that the evidence is insufficient to assess the additional benefits and harms of clinical breast examination (in addition to screening mammography) for women 40 years of age or older [53].

Breast Self-Examination

The term "breast self-examination" has been replaced by the concept of "breast self-awareness," which describes a woman's understanding of the normal appearance and feel of her breasts. No time interval is associated with breast self-awareness, as it had been with self-examination, but the goal is for women to pay attention to any change and report it to her clinician. The USPSTF, the ACOG, and the NCCN have embraced the use of this newer concept [50; 51; 53]. The ACOG endorses educating women about breast self-awareness beginning at 20 years of age. These organizations all note that women may continue with traditional monthly self-examinations if they wish, but the USPSTF has recommended against clinicians teaching breast self-examination [53]. The ACS specifically recommends against breast self-examination [220].

RECOMMENDATIONS FOR HIGH-RISK WOMEN

According to the ACS, the average lifetime risk of breast cancer for women is estimated to be 12.3% [65]. Several models are available to estimate a woman's risk for breast cancer. The first of these models, the Gail model, includes the following risk factors: current age, race, age at menarche, age at first live birth (or nulliparity), number of first-degree relatives with breast cancer, number of previous benign breast biopsies, and atypical hyperplasia in a previous breast biopsy [66]. An interactive risk-assessment tool based on the Gail model is available on the NCI website at https://www.cancer.gov/bcrisktool. Other models rely primarily on family history; these models, which include the Claus, BRCAPRO, Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA), and Tyrer-Cuzick models, are used most commonly to estimate risk on the basis of *BRCA* mutations [50; 67; 68; 69; 70]. The Gail model is the only model that has been validated for black women as well as white women [52].

In a systematic review and meta-analysis (66 studies), researchers found that the following factors increased the risk of breast cancer for women 40 to 49 years of age [71]:

- Extremely dense breasts
- First-degree relative with breast cancer
- Previous breast biopsy
- Second-degree relatives with cancer
- Heterogeneously dense breasts
- Current oral contraceptive use
- Nulliparity
- Age 30 years or older at the time of first birth

Clinicians should discuss screening beginning at 40 years of age for their patients who have any one of these factors [71]. The NCCN notes that women who are 35 years of age or older and have a 5-year risk of invasive breast cancer of 1.7% or more according to the modified Gail model should have more aggressive breast cancer screening [50]. Other studies have identified additional factors that increase the risk of breast cancer, including radiation therapy to the chest at a younger age (10 to 30 years), diagnosis of lobular carcinoma in situ, and a history of personal breast cancer [28; 50].

As well, several syndromes, most of which are rare, carry an increased risk of breast cancer, with the likelihood of cancer developing at an early age. The most notable of these syndromes is hereditary breast and ovarian syndrome, which is associated with mutations in *BRCA1* and *BRCA2* genes. This syndrome is associated with a lifetime risk for breast cancer of 41% to 90% [72]. In a meta-analysis, the mean cumulative risk of breast cancer by 70 years of age was 57% for the *BRCA1* mutation and 49% for the *BRCA2* mutation [73].

Some syndromes primarily known for their association with an increased risk of gastrointestinal cancers also increase the risk for breast cancer. Peutz-Jeghers syndrome, an autosomal dominant inherited disorder characterized by intestinal hamartomatous polyps (primarily, germline mutation of the *STK11/LKB1* gene), is associated with a 45% risk of breast cancer by 70 years of age [72; 74]. Hereditary diffuse gastric cancer syndrome is an autosomal dominant susceptibility for diffuse gastric cancer (associated with mutation of the *CDH1* gene) and carries a 52% risk of lobular cancer of the breast by 75 years of age [72]. Lynch syndrome, an autosomal dominant cancer susceptibility caused by germline mutations in the DNA mismatch repair (MMR) genes (*MLH1*, *MSH2*, *MSH6*, and *PMS2*), carries a substantially increased risk of many types of cancer, but data on an increased risk of breast cancer have conflicted (finding a possible 18% risk by 70 years of age) [72]. In a meta-analysis of molecular studies, 13 of 21 risk studies showed no significant association of breast cancer risk with Lynch syndrome, whereas eight studies did show a significant association, with a risk ranging from twofold to 18-fold compared with the general (average-risk) population [75].

Cowden syndrome is also associated with an increased risk of breast cancer. This syndrome, linked to germline mutations in the *PTEN* gene, is characterized by multiple hamartomas; the estimated cumulative lifetime risk of breast cancer is 85% [76]. Cancer usually develops in individuals who are in their 30s or 40s [72]. Li-Fraumeni syndrome, typically associated with germline mutations in the *TP53* gene, is rare (approximately 400 families in the United States) [72]. However, the risk of cancer is substantial; the odds of having cancer are 1,075-fold higher for women with Li-Fraumeni syndrome with mutation of *TP53* than for women without this mutation [77]. Breast cancer is the primary cancer that develops in association with the syndrome and can occur in the 20s or earlier [72].

Starting Age

The age at which screening should start varies according to the high-risk feature (***Table 6***) [50; 52; 72; 220]. In general, the NCCN and the ACS recommend a starting age of 30 years, with the SBI/ACR guideline stating that screening for high-risk women should begin by 30 years of age but not before 25 years of age [52; 72; 220].

Screening Methods

As with screening for average-risk women, mammography is the primary method for breast cancer screening. Other imaging modalities, such as ultrasound and contrast-enhanced MRI, have been evaluated as adjuncts to mammography for women at intermediate or high risk. Ultrasound plus mammography in this setting has improved the detection rate compared with mammography alone; however, it is also associated with a low positive predictive value, an increased biopsy rate, and substantial physician time [78; 79]. Similarly, the combination of mammography with either ultrasound or MRI has resulted in a higher cancer detection yield among high-risk women but also an increase in false-positive findings [80]. The findings of a systematic review (11 nonrandomized studies) suggested that screening with both MRI and mammography may rule out breast cancer lesions better than mammography alone among women who are known or likely to have an inherited predisposition for breast cancer [81]. The NCCN recommends the combination of mammography and MRI for this population, and the SBI/ACR guideline adds that ultrasound of the breast can be used for women who cannot have MRI [50; 52; 72].

BREAST CANCER SCREENING OR SURVEILLANCE ACCORDING TO HIGH-RISK FACTORS		
Risk Factor	**Recommendation for Screening**	
	NCCN	**SBI/ACR**
Age 35 years or older and 5-year risk of invasive breast cancer of 1.7% or more according to the modified Gail model	Annual mammography plus clinical breast examination every 6 to 12 months Breast awareness	—
Lifetime risk of more than 20% according to risk models that rely primarily on family history	Annual mammography plus clinical breast examination every 6 to 12 months beginning 10 years before youngest affected family member (but not younger than 30 years of age) Consider annual breast MRI beginning at same time. Referral to genetic counseling Breast awareness	Annual mammography and MRI by 30 years of age but not before 25 years of age) or 10 years before age of youngest affected family member
Radiation therapy (RT) to the chest at a younger age (10 to 30 years)	Women <25 years of age: Annual clinical breast examination beginning 8 to 10 years after RT Women ≥25 years of age: Annual mammography plus clinical breast examination every 6 to 12 months beginning 8 to 10 years after RT or at 40 years of age (whichever comes first) and recommended annual breast MRI Breast awareness	Annual mammography and MRI beginning 8 years after RT; mammography before 25 years of age is not recommended
Lifetime risk of more than 20% based on history of lobular carcinoma in situ or ADH/ALH	Annual mammography plus clinical breast examination every 6 to 12 months beginning at the time of diagnosis but not less than 30 years of age Consider annual MRI Breast awareness	Annual mammography from time of diagnosis; annual MRI may also be considered
Personal history of breast cancer	Annual mammography and history and physical examination every 4 to 6 months for 5 years, then every 12 months	Annual mammography
Suggested or known hereditary breast and ovarian cancer syndrome (*BRCA1* or *BRCA2* mutations)	Women: Annual MRI with contrast (preferred) or mammography (if MRI unavailable) at 25 to 29 years of age—may individualize the starting age based on family history if breast cancer diagnosis under 30 years of age is present Annual mammography and MRI with contrast at 30 to 75 years of age Consider screening on an individual basis after 75 years of age Clinical breast examination every 6 to 12 months starting at 25 years of age Breast awareness starting at 18 years of age	Annual mammography and MRI beginning at 30 years of age but not before 25 years of age
	Men: Clinical breast examination every 12 months starting at 35 years of age Breast self-exam starting at 35 years of age	—

Table 6 continues on next page.

BREAST CANCER SCREENING OR SURVEILLANCE ACCORDING TO HIGH-RISK FACTORS *(Continued)*		
Risk Factor	**Recommendation for Screening**	
	NCCN	**SBI/ACR**
Peutz-Jeghers syndrome	Annual mammography and MRI plus clinical breast examination every 6 months beginning around 25 years of age	—
Lynch syndrome	Optimal screening strategy uncertain	—
Cowden syndrome	Annual mammography and breast MRI starting at 30 to 35 years of age or 5 to 10 years before the earliest known breast cancer in the family (whichever comes first) Clinical breast examination every 6 to 12 months starting at 25 years of age or 5 to 10 years before the earliest known breast cancer in the family (whichever comes first) Breast awareness starting at 18 years of age	—
Li-Fraumeni syndrome	Annual breast MRI with contrast (preferred) or mammography and starting at 20 to 29 years of age (or individualized based on earliest age of onset in family) Annual mammography and breast MRI at 30 to 75 years of age Clinical breast examination every 6 to 12 months starting at 20 to 25 years of age or 5 to 10 years before the earliest known breast cancer in the family if before 20 years (whichever comes first) Breast awareness starting at 18 years of age	—
ADH = atypical ductal hyperplasia, ALH = atypical lobular hyperplasia, NCCN = National Comprehensive Cancer Network, SBI/ACR = Society of Breast Imaging/American College of Radiology.		
Source: [50; 52; 72; 75; 114; 220]		*Table 6*

Screening Interval

The intervals for imaging and clinical breast examination also vary according to the high-risk feature [50; 52; 72]. In general, imaging is recommended annually and clinical breast examination is recommended every 6 to 12 months.

EFFECTS OF SCREENING

Several studies have documented the benefits and harms associated with breast cancer screening mammography, and an understanding of both is crucial for determining the net benefit for patients. Evidence shows that the balance of benefits to harms in breast cancer screening strongly supports the use of routine screening [39; 53].

Benefits

Among the benefits of breast cancer screening is a greater likelihood of detecting cancer at an early stage. An analysis of 30-year data on screening mammography in the United States demonstrated that screening was associated with an absolute increase of 122 cases of early-stage breast cancer per 100,000 women [82]. Some experts have proposed that early detection is not as important as it once was because of advances in breast cancer treatment, especially adjuvant therapy; however, analysis of this issue has shown that overall survival is considerably better for node-negative disease compared with later stages, supporting the value of

early detection [83]. Early detection also means a greater range of treatment options, many of which are less aggressive than those needed for later stage cancers [39].

Earlier detection has led to a reduction in mortality in breast cancer screening, although the magnitude of that reduction is unclear. Breast cancer screening has been widely encouraged as essential for the early detection of cancer and promoted as "saving lives." But the issue of decreased mortality as a result of early detection with screening has been debated.

Some studies of population-based mammography screening in England have shown no significant effect of screening on mortality [84; 85]. A review of the effectiveness of the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) on mortality rates from 1990 to 2004 found that the screening rate was significantly associated with a decrease in mortality within the same year; however, changes in the screening rate were not related to breast cancer-related mortality in subsequent years [86].

A meta-analysis done as part of the USPSTF literature review showed that reductions in mortality differ among age-groups. Screening with mammography reduced breast cancer-related mortality by 15% for women 39 to 49 years of age, by 14% for women 50 to 59 years of age, and by 32% for women 60 to 69 years of age [87]. Investigators conducting a Cochrane review also found that screening was associated with a significant reduction in mortality but that screening had no effect on mortality when only trials with adequate randomization were considered [88]. These authors estimated that screening reduced mortality by approximately 15%, but with an absolute reduction of about 0.05% per year for a woman of average risk [88]. The Cochrane review excluded observational studies, which have shown a positive effect of mammography [63].

In a review on the issue of the effect of screening on mortality, investigators noted that in the four most recent high-profile reviews (USPSTF analysis, Cochrane review, UK Independent Review, and EUROSCREEN), the reduction in mortality ranged from 14% to 48% [83]. These reductions translated to a range in the number needed to screen (or invite to screen) of 111 to 2,000 to prevent one breast cancer-related death. In an effort to explain the wide range, the authors analyzed the data from the perspective of only one scenario (as defined in the UK Independent Review) and found a narrower range, from 64 to 257, in the number needed to screen (or invite to screen) to prevent one breast cancer-related death [83].

The review of 30-year data on mammography screening in the United States demonstrated that since screening began, breast-cancer related mortality among women 40 years of age and older has decreased 28% (from 71 to 51 deaths per 100,000 women) [82]. The degree of this decrease that can be attributed to screening is unclear. As noted, screening reduces mortality by increasing the number of breast cancers detected at an early stage, with a concomitant decrease in the number of breast cancers detected at a late stage. The 30-year data, however, demonstrated that the absolute increase in early-stage breast cancer (122 cases per 100,000 women) was accompanied by an absolute decrease of eight late-stage cancers per 100,000 women [82].

These findings reflect an important issue in determining the effect of screening on mortality: the role of improved treatments in decreasing mortality. Modeling studies have found a wide range for the effect that can be attributed to screening—ranging from 28% to 65% [89]. However, the 30-year data suggest that the effect of screening is at the low end of that range [82]. These data also showed a greater decrease in mortality among women younger than 40 years of age (who were not routinely screened) than among women 40 years of age and older (42% compared with 28%). This difference further supports a greater effect of improved treatment rather than screening. In a Norwegian study, the effect of

screening was calculated to be approximately 33% [90]. The WHO notes that breast cancer screening reduces mortality 20% to 30%, but only in women 50 years of age or older who live in high-income countries where screening coverage is more than 70% [91].

Harms

The harms associated with screening mammography include false-positive and false-negative results, the potential need for additional procedures, and overdiagnosis. The safety of mammography in terms of exposure to radiation has been evaluated, and the risk is considered to be moderate and not enough to deter women older than 40 years of age from being screened [92]. The risk associated with radiation exposure is also offset by the benefits of screening [63].

False-Positive and False-Negative Results

Studies have shown that the cumulative risk for a false-positive result after 10 mammograms is 21% to 50% [87; 93]. Analysis of data from the BCSC demonstrates that the rate of false-positive results varies according to age, with the highest rate (within one screening round) found among women 40 to 49 years of age (97.8 per 1,000 screened) and the lowest rate found among women 80 to 89 years of age (59.4 per 1,000 screened) [87]. False-positive results are associated with medical, psychologic, and financial effects related to follow-up tests. Among women screened annually between 40 and 69 years of age, two or more abnormal test results will occur and an unnecessary biopsy will be done in approximately 16% of women [87; 93]. Complications may occur as a result of these procedures, especially in older women or women in poor health [93]. The anxiety associated with false-positive results is also an important consideration. In a meta-analysis of European studies, a false-positive result caused breast cancer-specific psychologic distress that lasted for as long as 3 years and was associated with a likelihood of not returning for the next appropriate screening mammography [94].

The BCSC data demonstrate that the rate of false-negative results is low and also varies according to age, with the lowest rate found among women 40 to 49 years of age (1.0 per 1,000 screened) and the highest rate found among women 70 to 79 years of age (1.5 per 1,000 screened) [87]. False-negative results may provide false reassurance to women (and their healthcare providers) about the lack of breast cancer as well as delay necessary treatment.

Potential Need for Additional Procedures

Mammographic findings also commonly lead to additional procedures. Additional imaging is done in 56.3 to 84.3 women per 1,000 screened, with the highest rate among women 40 to 49 years of age [87]. The rate of biopsy is lower, ranging from 12.2 per 1,000 screened for women 70 to 79 years of age to 9.3 per 1,000 screened for women 40 to 49 years of age. An estimated 47 women per 1,000 screened 40 to 49 years of age will have additional imaging to diagnose one case of invasive breast cancer, and an estimated five women per 1,000 screened of the same age will have a biopsy to diagnose one case of invasive breast cancer [87]. These numbers are lower for other age-groups, ranging from eight to 22 per 1,000 screened for additional imaging and 1.5 to three per 1,000 screened for biopsy [87].

Overdiagnosis

According to data from randomized trials, the magnitude of overdiagnosis in breast cancer (detected by mammography) is estimated to be 10% to 25%, although the USPSTF notes that no data are specific for U.S. trial samples and reports a much lower rate of overdiagnosis of less than 1% to 10% [87; 93]. Many of these overdiagnosed cancers are ductal carcinoma in situ [39; 93]. The 30-year data on breast cancer screening in the United States indicate that breast cancer was overdiagnosed in 1.3 million women; in 2008 alone, breast cancer was overdiagnosed in more than 70,000 women, which represents about 31% of all breast cancers diagnosed [82]. Similarly, the rate of overdiagnosis and overtreatment was estimated to be 30% in the Cochrane meta-analysis [88]. Those authors found higher rates of lumpectomy, mastectomy, and radia-

tion therapy among screened women than among unscreened women and estimated that for every 2,000 women invited for screening throughout 10 years, 10 healthy women will receive unnecessary treatment for an overdiagnosed breast cancer.

CLINICIAN ADHERENCE TO GUIDELINE RECOMMENDATIONS

The results of surveys of primary care clinicians have shown that appropriate use of breast cancer screening is suboptimal, and rates vary across specialties. Some surveys have asked respondents to indicate their screening recommendation in the context of vignettes. In one such survey, 75% of respondents said they would offer screening mammography to an asymptomatic woman 35 years of age [14]. In another survey, 36% of respondents recommended screening that was inconsistent with recommended guidelines for an asymptomatic woman who was 51 years of age and not at high risk for breast cancer; the inconsistency was primarily related to the use of nonrecommended tests, such as MRI and ultrasound [95]. In a third survey, 44% of respondents recommended clinical breast examination and mammography for a woman older than 50 years of age who had a limited life expectancy [96].

Knowledge gaps about breast cancer screening exist among gynecologic care providers as well. Although 93% of respondents said they were aware of the revised guidelines for breast cancer screening [37]:

- 51% did not provide the correct starting age
- 72% said that the USPSTF recommends teaching breast self-examination
- 54% did not agree with the statement "Women between 50 and 74 years of age are recommended to have screening mammography."

These gaps in knowledge correlated with clinicians' beliefs about screening. For example, 95% of physicians believed that mammography for women 40 to 49 years of age was "very" or "somewhat" effective, and 76% believed that self-examination was "very" or "somewhat" effective [37].

CERVICAL CANCER

Screening for cervical cancer has been available since the middle of the 20th century. Its effectiveness is reflected by the move of cervical cancer from the leading cause of cancer-related deaths among women to the rank of 14th [97]. The goal of cervical cancer screening is to reduce the morbidity and mortality associated with cervical cancer through the detection of invasive cancer at an early stage as well as to detect preinvasive lesions that can be treated before malignant transformation [97].

At least two major guidelines on cervical cancer screening are available; one was developed by the USPSTF, and the other was created jointly by the ACS, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology (ACS/ASCCP/ASCP) (***Table 7***) [97; 98]. Both guidelines were updated in 2012. The ACOG participated in the development of both guidelines, and the NCCN Guidelines Panel for Cervical Cancer screening endorses the ACS/ASCCP/ASCP guideline. The recommendations in the two guidelines are consistent.

RECOMMENDATIONS FOR WOMEN AT AVERAGE RISK

Starting Age

The USPSTF and the ACS/ASCCP/ASCP recommend that cervical screening should begin at 21 years of age [97; 98]. This age was established because studies showed that screening of women in their teens was associated with few detected cases of cancer and a high number of false-positive test results [99]. Screening is not recommended for women younger than 21 years of age regardless of the age at which sexual activity began or of other risk factors [97].

Both guidelines also note that women who have received the human papillomavirus (HPV) vaccine should continue to have screening [97; 98]. Screening is not recommended for women who have had a hysterectomy with removal of the cervix who do not have a history of a high-grade precancerous lesion or of cervical cancer [97; 98].

RECOMMENDATIONS FOR CERVICAL CANCER SCREENING FOR AVERAGE-RISK WOMEN		
Screening Factor	**USPSTF**	**ACS/ASCCP/ASCP**
Starting age	21 years	21 years
Ending age	65 years if prior screenings are negative within past 10 years[a]	65 years if prior screenings are negative within past 10 years[a] and if there has been no history of CIN2+ within the past 20 years
Screening method	Age 21 to 29 years: Cytology (Pap test) alone Age 30 to 65 years: Cytology alone or cytology plus HPV testing	Age 21 to 29 years: Cytology (Pap test) alone Age 30 to 65 years: Cytology plus HPV testing (preferred) or cytology alone
Screening interval	Age 21 to 29 years: Every 3 years Age 30 to 65 years: Every 3 years for cytology alone; every 5 years for cytology plus HPV testing	Age 21 to 29 years: Every 3 years Age 30 to 65 years: Every 3 years for cytology alone; every 5 years for cytology plus HPV testing
[a]Adequate prior screenings is defined as three consecutive negative cytology results (or two consecutive negative co-testing results) within the past 10 years, with the most recent test occurring within the past 5 years. ACS/ASCCP/ASCP = American Cancer Society/American Society for Colposcopy and Cervical Pathology/American Society for Clinical Pathology, CIN2+ = cervical intraepithelial neoplasia of grade 2 or higher, HPV = human papillomavirus, Pap = Papanicolaou, USPSTF = U.S. Preventive Services Task Force.		
Source: [97; 98]		*Table 7*

Ending Age

The USPSTF recommends the discontinuation of screening at 65 years of age for women who have had adequate prior screenings and are not otherwise at high risk for cervical cancer, as screening offers little to no benefit for women in this age-group [98]. Adequate prior screening is defined as three consecutive negative cytology results (or two consecutive negative co-testing results) within the past 10 years, with the most recent test occurring within the past 5 years. The recommendation in the ACS/ASCCP/ASCP guideline is similar, with the added note that screening can be discontinued after 65 years of age for women who have no history of cervical intraepithelial neoplasia grade 2 or higher within the past 20 years [97]. In addition, screening should not begin again in older women for any reason, including a new sexual partner.

Screening Method

Cytology (Papanicolaou [Pap] testing) remains the primary method for cervical cancer screening. Pap test alone is recommended for women 21 to 29 years of age and is acceptable for women 30 to 65 years of age [97]. No clinically important differences have been found between liquid-based cytology and conventional cytology [98]. Since the discovery that persistent HPV infection is integral to the development of cervical cancer, combination testing (co-testing) with cytology and HPV testing has been proposed, and the ACS/ASCCP/ASCP guidelines states a preference of co-testing for women 30 to 65 years of age [97]. The USPSTF notes a comparable ratio of benefits to harms in both methods and does not indicate a preference [98]. The USPSTF recommends HPV testing alone every five years as an alternative to cytology testing [98].

According to the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology, women 30 to 65 years of age should be screened with cytology and HPV testing every five years (preferred) or cytology alone every three years (acceptable).

(https://www.asccp.org/asccp-guidelines. Last accessed October 11, 2018.)

Level of Evidence: Expert Opinion/Consensus Statement

AMERICAN SOCIETY FOR COLPOSCOPY AND CERVICAL PATHOLOGY CONSENSUS GUIDELINES FOR SCREENING AFTER ABNORMAL RESULTS OF SCREENING	
Results	**Recommendation**
Cytology: unsatisfactory; HPV: unknown or negative (all women)	Repeat cytology testing in 2 to 4 months; if result is negative, resume routine screening, and if result remains unsatisfactory, refer for colposcopy
Cytology: unsatisfactory; HPV: positive (women 30 years of age and older)	Repeat cytology testing in 2 to 4 months; if result is negative, resume routine screening, and if result remains unsatisfactory, refer for colposcopy
Cytology: atypical squamous cells of undetermined significance; HPV: negative	Co-testing in 3 years; if result is negative, resume routine screening
Cytology: atypical squamous cells of undetermined significance; HPV: not done	Repeat cytology testing in 1 year is acceptable; if result is negative, resume routine screening with cytology
Cytology: reported as negative with an absent or insufficient EC/TZ component (women 21 to 29 years of age)	Routine screening (HPV testing is unacceptable)
Cytology: reported as negative with an absent or insufficient EC/TZ component (women 30 years of age or older); HPV: not done or result not known	HPV testing is preferred; if result is negative, resume routine screening, and if result is positive, repeating co-testing in 1 year is acceptable (If HPV testing is not done, repeating cytology in 3 years is acceptable)
EC/TZ = endocervical/transformation zone.	
Source: [101]	*Table 8*

Screening Interval

Screening for cervical cancer was long recommended at an interval of every year. However, studies showed that annual testing (by any method) led to few cancers prevented, with an excess of unnecessary procedures and treatments [97]. A modeling study showed that among women 30 to 64 years of age who had negative results on three or more consecutive Pap tests, screening every 3 years was associated with an average excess risk of cervical cancer of approximately three per 100,000 women compared with annual screening for 3 years [100].

Both updated guidelines now recommend screening with cytology alone every 3 years for women 21 to 29 years of age [97; 98]. For women 30 to 65 years of age, the screening interval can be lengthened to 5 years if screening includes includes HPV testing or the combination of cytology and HPV testing; cytology alone every 3 years is an acceptable alternative. The ACS emphasizes the new screening interval with the statement, "Women at any age should NOT be screened annually by any screening method" [39].

Follow-Up Screening

A positive HPV result with a negative cytology result occurs in approximately 11% of women 30 to 34 years of age and in 2.6% of women 60 to 65 years of age [98]. Direct referral for colposcopy should not be done for women who have a negative cytology result with a positive HPV result [97]. Instead, the ACS/ASCCP/ASCP guideline recommends that repeat co-testing be done in 12 months for women with these results. If either repeat test is positive, colposcopy is recommended; if both tests are negative, routine screening may be resumed [97]. Alternatively, women who have a negative cytology result and a positive HPV result may have HPV genotype-specific testing for HPV16 alone or for HPV16/18. Colposcopy is recommended if either test is positive; if testing results are negative, co-testing should be repeated in 12 months.

The ASCCP also developed consensus guidelines for the management of abnormal results of cervical cancer screening [101]. The recommendations address screening intervals for cytology results of unsatisfactory findings, atypical squamous cells of undetermined significance, and negative findings with an absent or insufficient endocervial/transformation zone (***Table 8***).

RECOMMENDATIONS FOR HIGH-RISK WOMEN

High risk for cervical cancer is defined as exposure in utero to diethylstilbestrol (DES) or a compromised immune system because of chemotherapy, organ transplantation, chronic treatment with corticosteroids, or infection with human immunodeficiency virus [39; 97]. The USPSTF and the multisociety guideline do not include recommendations for high-risk women.

Women who know or believe they were exposed to DES in utero should have a pelvic examination annually, and a regular Pap test as well as a four-quadrant Pap test should be done [102]. There is no specific age at which to stop screening for this population [39].

The ACS recommends following guidelines of the U.S. Public Health Service and the Infectious Disease Society of America for screening of women with a compromised immune system [39]. These guidelines indicate that cervical screening be carried out twice within the first year after diagnosis or treatment and annually thereafter. As with women exposed to DES, there is no specific age at which to stop screening [39].

The lifetime risk of cervical cancer is 10% for women with Peutz-Jeghers syndrome, and the NCCN recommends annual pelvic examination and cytology testing beginning at 18 to 20 years of age [114]. Transvaginal ultrasound may also be considered.

EFFECTS OF SCREENING

Since screening for cervical cancer began, the incidence and mortality rates associated with the disease have decreased substantially. For example, the introduction of cervical cancer screening to a previously unscreened population reduces the incidence of cervical cancer by 60% to 90% within 3 years [98]. A meta-analysis demonstrated that screening with cytology was associated with a 62% reduction in the risk of invasive cervical cancer, compared with no screening [104]. In the United States, since 2004, the incidence of cervical cancer has decreased by 2.1% per year among women younger than 50 years of age and by 3.1% per year in women older than 50 years of age [39]. During that same time, mortality rates have remained stable overall but have decreased by 2.6% per year among black women [39].

The primary harms associated with cervical cancer screening are anxiety related to false-positive results and the potential for further testing [97; 98]. Screening every 3 years is associated with approximately 760 colposcopies per 1,000 women, and the predicted number of colposcopies increases with shorter screening intervals [97]. Evidence of overdiagnosis with cervical cancer screening is lacking, as the rate of diagnosis of cervical cancer has decreased over time, in part because of the detection and treatment of precancerous lesions [46].

Although beneficial for screening, co-testing is associated with potential harms when the results of HPV testing are positive. Some women prefer to know their HPV status, but negative psychologic effects associated with knowing a positive result have been documented [98]. Approximately 5% to 17% of women 30 years of age or older with positive HPV results will have no evidence of high-grade precancerous lesions; additional testing and possible treatment in these cases is associated with anxiety, potential complications, and a risk of infertility [98].

CLINICIAN ADHERENCE TO GUIDELINE RECOMMENDATIONS

Clinician adherence to guideline recommendations has been suboptimal, with most nonadherent practice related to overuse. Despite the updated guidelines for longer screening intervals, especially with co-testing, many healthcare professionals continue to recommend annual screening.

In a survey that included vignettes, 2,087 primary care providers were asked when they would recommend that a woman (30 to 60 years of age) return for her next Pap test. For the scenario of a woman who had normal results on three consecutive Pap tests, with either a negative HPV test or no HPV test results available, nearly three-quarters of participants responded with a recommendation that was earlier than that recommended in guidelines [105]. For the scenario of a woman who had negative results on co-testing and had not had a previous Pap test, approximately 90% responded with a recommendation that was sooner than that recommended in guidelines [105].

Similar results were found in a survey of ACOG members. Of the 366 respondents to the survey, 74% said they continued to recommend annual screening to women 21 to 29 years of age, and 53% said they continued to recommend annual screening to women 30 years of age and older [15]. Respondents noted that they recommended shorter intervals because they thought their patients were uncomfortable with longer intervals and that patients would not maintain annual examinations if they did not need screening [15].

In a survey of 1,111 primary care clinicians, approximately 48% of respondents recommended a Pap test for a woman who was 18 years of age and not sexually active [96]. According to the 2010 NHIS data, 58% of women 65 years of age and older (without hysterectomy) reported having a Pap test within the past 3 years. Considering just the NHIS data on hysterectomy status and age, cervical cancer screening was overused in approximately 14 million women [106].

Overuse is also related to hysterectomy status and age. In the same survey of primary care clinicians, approximately 77% of respondents said they would recommend a Pap test at least annually for a woman 35 years of age who had a hysterectomy for benign reasons [96]. Analyzing data from the 2010 NHIS, researchers found that among women who reported having a hysterectomy, 34% said they had had a Pap test done in the previous year [106].

COLORECTAL CANCER

Colorectal cancer screening has been recommended since 1980, and guidelines have been updated over the years to accommodate advances in screening modalities. At least four guidelines for colorectal cancer screening are currently available, and the ACP has developed a guidance statement based on these guidelines [103; 107; 108; 109; 110]. Two other guidelines address surveillance after the detection of polyps or after treatment for colorectal cancer [111; 112]. In addition, the ACR developed Appropriateness Criteria for screening options in the category of gastrointestinal imaging [113]. Recommendations are primarily consistent across guidelines.

RECOMMENDATIONS FOR INDIVIDUALS AT AVERAGE RISK

The ACP recommends that clinicians carry out individualized assessment of risk for colorectal cancer in all adults [110]. Average risk is defined as no personal or family history of inflammatory bowel disease, adenoma, or colorectal cancer or high-risk genetic syndromes [103; 107].

Starting Age

All guidelines recommend beginning colorectal cancer screening at 50 years of age for people at average risk for the disease [103; 107; 108; 109; 110]. The 2009 update of the American College of Gastroenterology (ACG) guideline recommends that screening begin at 45 years of age for black individuals because of the higher incidence of colorectal cancer and related mortality in that population, as well as an earlier average age at the time of diagnosis [109].

RECOMMENDATIONS FOR COLORECTAL CANCER SCREENING FOR AVERAGE-RISK MEN AND WOMEN BEGINNING AT 50 YEARS OF AGE		
Screening Recommendation		**Notes**
Method	**Interval**	
Flexible sigmoidoscopy	5 years	May be performed alone or in conjunction with annual stool-based test
Colonoscopy	10 years	Repeat in 5 years if polyps found
CT colonography	5 years	—
Stool-based test (FOBT or FIT)	1 year	Must have high sensitivity for detecting cancer
Stool DNA test ($_s$DNA)	Uncertain	—
Double-contrast barium enema	5 years	Recommended only in the ACS/USMSTF/ACR guideline
CT = computed tomography, FIT = fecal immunohistochemical test, FOBT = fecal occult blood test.		
Source: [103; 107; 108; 109; 110]		*Table 9*

Ending Age

Most guidelines do not specify an ending age. The USPSTF recommends against routine colorectal cancer screening for people older than 75 years of age, although the Task Force acknowledges that there may be considerations to support screening in an individual patient 76 to 85 years of age [108]. The ACP recommends against screening for people who are older than 75 years of age or who have a life expectancy of fewer than 10 years [110]. The risks associated with colonoscopy increase with age, and decision making on screening for older men and women should be individualized according to the specific benefits and harms for a person [110]. Lee et al. estimated that it took 10.3 years before one colorectal cancer-related death was prevented among 1,000 people screened [49]. The authors suggest that the findings indicate that colorectal cancer screening should be done only for people who have a life expectancy of at least 10 years.

Screening Methods

Seven methods for colorectal screening—used alone or in combination—are currently available and recommended (***Table 9***):

- Colonoscopy
- Fecal occult blood test (FOBT)
- Fecal immunochemical test (FIT)
- Fecal DNA testing
- Flexible sigmoidoscopy
- CT colonography (virtual colonoscopy)
- Double-contrast barium enema

The guideline developed jointly by the ACS, the U.S. Multi-Society Task Force on Colorectal Cancer, and the ACR (ACS/USMSTF/ACR) categorizes these screening options either as methods that detect adenomatous polyps and cancer or that primarily detect cancer [107]. The goals of colorectal cancer screening should be prevention and early detection; thus, screening methods designed to detect adenomatous polyps and cancer should be encouraged [103; 107]. The ACS/USMSTF/ACR guideline states that it is the "strong opinion" of each of the three organizations that prevention of colorectal cancer should be the primary goal of screening.

The wide range of screening methods is unique to colorectal cancer, and in general, patients can choose the option that is best for them in terms of access, comfort, and convenience. The risks and benefits of the methods vary, and patient preference should be a factor [107]. The ACG recommends that clinicians establish a "preferred strategy" for colorectal cancer screening, as this approach provides advantages (clinician-patient discussions are easier, and the likelihood that a

patient is offered screening is greater) compared with offering several options [109].

Colonoscopy

Colonoscopy is often considered to be the preferred screening method in evidence-based guidelines as well as in clinical practice [5; 103; 109; 115; 116]. According to patient-reported screening, approximately 62% of colorectal cancer screenings in 2012 were done with colonoscopy, and physician surveys have shown that the number of colonoscopies ordered had increased somewhat or substantially for 73% of respondents [5; 116]. Colonoscopy requires an extensive bowel cleansing preparation and dietary restrictions before the procedure and sedation during the procedure.

Compared with stool-based testing, colonoscopy offers the advantage of visualization and examination of the entire colon as well as removal of polyps in the same procedure. As the standard for colorectal cancer screening, colonoscopy is the screening method that is used to evaluate the efficacy of other screening options. Although colonoscopy offers many benefits compared with the other screening options, it is not fail-safe. Studies have indicated that colonoscopy is associated with a miss rate for cancer of 5% and a miss rate for large adenomas of 6% to 12% [107].

Flexible Sigmoidoscopy

Flexible sigmoidoscopy also allows for visualization of the colon and removal of polyps in one procedure, but only the lower half of the colon can be visualized [103]. In the NCI's Prostate, Lung, Colorectal, and Ovarian Cancer Screening (PLCO) trial, approximately 44% of undetected cancers were related to a limitation of sigmoidoscopy—37% were beyond the area that could be examined with the sigmoidoscope and 7% were attributed to inadequate depth of insertion of the sigmoidoscope [117]. The authors suggested that if colonoscopy had been used instead, an additional 15% to 19% of colorectal cancers may have been detected [117]. Sigmoidoscopy requires less bowel preparation than that for colonoscopy, and the procedure is usually done without sedation. Colonoscopy is required as follow-up if polyps larger than 1 cm are found [103].

Sigmoidoscopy may be done alone or in combination with stool-based testing [103; 107; 108; 109; 110]. The use of sigmoidoscopy for screening has been declining. More than half of primary care physicians reported that their sigmoidoscopy volume had decreased somewhat or substantially [116].

Stool-Based Testing

The ACS/USMSTF/ACR guideline notes that the FOBT or FIT used for screening should have at least 50% sensitivity [107]. This guideline also states that patients should perform stool testing at home, adhering to the manufacturer's recommendations on collecting the sample and the number of samples to collect. FOBT on a single specimen collected during a digital rectal examination (DRE) in a healthcare setting is not recommended. Immunochemical tests have been shown to have better sensitivity than guaiac-based tests and are more patient-friendly [107; 118; 119]. The ACG recommends FIT as a preference over FOBT [109]. FOBTs of lower sensitivity have been associated with reduced mortality related to colorectal cancer, but modeling studies suggest that tests with higher sensitivity are associated with a greater number of life-years gained [108]. FOBT is the second most commonly used screening method (10.4%) [5].

Another stool-based screening method, fecal DNA testing, has been shown to be accurate, but evidence on a screening interval is lacking. The USPSTF concluded that the evidence is insufficient to assess the benefits and harms of fecal DNA testing as a screening method for colorectal cancer [108]. The NCCN acknowledges that emerging evidence supports the accuracy of FDA-approved fecal DNA testing for screening but does not recommend an optimal interval; every three years is suggested [103]. The ACS/USMSTF/ACR guideline lists fecal DNA testing as an acceptable screening option, and the ACG lists the test as an "alternative" option [107; 109].

Stool-based testing may be used alone or in combination with flexible sigmoidoscopy, but the combination was used in less than 1% of colorectal cancer screenings in 2012 [5; 103; 107; 110]. Annual stool-based testing should not be done in combination with colonoscopy [103]. Positive results on any stool-based test require follow-up testing with colonoscopy.

CT Colonography

CT colonography is minimally invasive and does not require sedation, but if polyps are noted, a colonoscopy must be done as follow-up [103; 107]. The USPSTF concluded that there is insufficient evidence to assess the benefits and harms of CT colonography as a screening method [108]. Other guidelines, however, note that CT colonography is an acceptable screening option [103; 107; 109]. As of 2016, the NCCN has added CT colonography as a primary screening modality for average-risk individuals [103].

Double-Contrast Barium Enema

Only the ACS/USMSTF/ACR guideline includes double-contrast barium enema as an option [107]. The ACG guideline notes that CT colonography replaces double-contrast barium enema as an option [109].

Screening Interval

The colorectal cancer screening interval depends on the screening method used and the results of screening. Stool-based tests are recommended annually, with or without flexible sigmoidoscopy every 5 years (regardless of the findings) [103; 107; 110]. Colonoscopy should be done every 10 years; if polyps are found, the procedure should be done every 5 years [103; 107]. The recommended interval for CT colonography is 5 years, and the interval for double-contrast barium enema is also 5 years [103; 107; 109; 110].

The results of modeling have shown that colorectal cancer screening among the average-risk population would result in approximately equally effective life-years gained (assuming 100% adherence) with three screening options: colonoscopy every 10 years; high-sensitivity FOBT every year; and flexible sigmoidoscopy every 5 years, with high-sensitivity FOBT every 3 years [108].

RECOMMENDATIONS FOR HIGH-RISK POPULATIONS

Several distinct populations of men and women are at high risk for colorectal cancer and should be offered more aggressive cancer screening. These high-risk populations include people with a family history of colorectal cancer or a personal history of known or suspected hereditary syndromes, adenomatous polyps, or colorectal cancer [103; 111; 112; 114]. A family history of polyps is no longer a risk that prompts more aggressive screening, unless the polyps are advanced adenomas [103; 109; 114].

Lynch syndrome is the most common familial colorectal cancer syndrome, and it confers an increased risk of several types of cancer, with colon cancer being the greatest risk for carriers of the *MLH1* and *MSH2* gene mutations [114]. The risk of colon cancer up to 70 years of age is 40% to 80% (compared with 5.5% for the general population), with a mean age at onset of 44 to 61 years [114]. The lifetime risk of colon cancer is 40% to 50% for individuals with juvenile polyposis syndrome, and screening should begin around 15 years of age [114]. For individuals with the rare Peutz-Jeghers syndrome, the lifetime risk of colon cancer is 39%, and colonoscopy should begin in the late teenage years and be done every 2 to 3 years [114].

The American College of Physicians recommends using optical colonoscopy as a screening test in patients who are at high risk for colorectal cancer.

(http://annals.org/aim/fullarticle/1090701. Last accessed October 11, 2018.)

Level of Evidence: Expert Opinion/Consensus Statement

RECOMMENDATIONS FOR COLORECTAL CANCER SCREENING FOR HIGH-RISK MEN AND WOMEN			
Risk Factor	**Screening Recommendations**		
	ACS/USMTF/ACR	**NCCN**	**ACG**
Family history			
One first-degree relative with colorectal cancer or advanced adenoma diagnosed before 60 years of age OR two first-degree relatives with colorectal cancer or advanced adenoma	Colonoscopy every 5 years beginning at 40 years of age, or 10 years younger than age at diagnosis of the youngest affected relative	Colonoscopy every 5 years beginning at 40 years of age, or 10 years younger than age at diagnosis of the youngest affected relative	Colonoscopy every 5 years beginning at 40 years of age, or 10 years younger than age at diagnosis of the youngest affected relative
Second-degree relative with colorectal cancer diagnosed before 50 years of age	—	Colonoscopy every 5 to 10 years beginning at 50 years of age	—
Colorectal cancer or adenomatous polyps in first-degree relative diagnosed at 60 years of age or older OR in two second-degree relatives with colorectal cancer	Screening options as for average-risk individuals, but beginning at 40 years of age	—	—
Personal history			
Adenomatous polyp	1 or 2 small tubular adenomas with low-grade dysplasia: Colonoscopy at 5 to 10 years 3 to 10 adenomas or 1 adenoma >1 cm or any adenoma with villous features or high-grade dysplasia: Colonoscopy at 3 years	Low-risk adenomatous polyps: Repeat colonoscopy within 5 years; if no polyps, repeat every 10 years Advanced or multiple adenomatous polyps: Repeat colonoscopy within 3 years; if no polyps, repeat within 5 years	—
Inflammatory bowel disease, chronic ulcerative colitis, or Crohn disease	Colonoscopy every 1 to 2 years with biopsies for dysplasia, beginning 8 years after the onset of pancolitis	Colonoscopy every 1 to 2 years beginning 8 to 10 years after onset of symptoms of pancolitis	—
Hereditary syndromes			
Lynch syndrome (*MLH1* and *MSH2* mutations)	Colonoscopy every 1 to 2 years beginning at 20 to 25 years of age or 10 years younger than age at diagnosis of the youngest affected relative	Colonoscopy every 1 to 2 years beginning at 20 to 25 years of age or 2 to 5 years younger than age at diagnosis of the youngest affected relative if diagnosed before 25 years of age	Colonoscopy every 2 years beginning at 20 to 25 years of age and then annually after 40 years of age
Juvenile polyposis syndrome	—	Colonoscopy every year if polyps found or every 2 to 3 years if no polyps found beginning around 15 years of age	—
Peutz-Jeghers syndrome	—	Colonoscopy every 2 to 3 years beginning in the late teenage years	—

ACG = American College of Gastroenterology, ACS/USMSTF/ACR = American Cancer Society/U.S. Multisociety Task Force on Colorectal Cancer/American College of Radiology, NCCN = National Comprehensive Cancer Network.

Source: [103; 107; 109; 114] *Table 10*

Starting Age and Screening Interval

In general, screening for high-risk men and women should begin at 40 years of age, or 10 years younger than the age of the youngest affected relative at the time of colorectal cancer diagnosis [103; 109]. Screening should begin earlier for individuals with hereditary syndromes, as noted (***Table 10***) [103; 107; 109; 114]. Colonoscopy is the recommended method for colorectal cancer screening for high-risk adults [103; 109].

EFFECTS OF SCREENING

Benefits

There is convincing evidence that colorectal screening, with any method, detects cancer at an early stage, detects precursor lesions, and is associated with better outcomes [108; 121]. The incidence of colorectal cancer has been decreasing over the past several years, primarily because of increases in screening uptake, which allows for detection and removal of precancerous and early-stage cancerous polyps [1]. Follow-up data from the National Polyp Study showed that removal of polyps led to a 53% reduction in mortality; after a median of 15.8 years of follow-up, there were 12 colorectal cancer-related deaths in the screened group compared with an expected 25.4 deaths in the general population (based on incidence-based colorectal cancer-related mortality in the SEER database) [122].

A retrospective review of data on 354 patients with colorectal cancer in a Veterans Administration hospital showed that colorectal cancer was diagnosed by screening in 34% [123]. Compared with colorectal cancer diagnosed by symptom evaluation, screen-detected cancers were more often found at an earlier stage, were more likely to be treated with a curative-intent procedure, and were associated with better 5-year survival rates [123].

In a meta-analysis (nine studies), flexible sigmoidoscopy was associated with a 28% reduction in mortality compared with no screening [121]. Similar reviews have shown that FOBT (either annually or biennially) led to a 14% to 15% reduction in colorectal cancer-related mortality [121; 124]. The positive impact of FOBT was supported by the results of long-term follow-up of more than 46,000 people (50 to 80 years of age) in the Minnesota Colon Cancer Control Study [41]. The participants in this study were randomly assigned to usual care (control) or to annual or biennial FOBT. Through 30 years of follow-up, screening reduced colorectal cancer-related mortality by 32% (annual screening) and 22% (biennial screening) compared with no screening. There was no reduction in all-cause mortality. The findings in this population suggest that the effect of screening persists after screening has stopped [125].

Another large, long-term study provides evidence of the effect of endoscopic screening on mortality. In this study, nearly 89,000 participants in the Nurses' Health Study and the Health Professionals Follow-up Study were followed up for more than 22 years. Compared with no endoscopic screening, sigmoidoscopy and colonoscopy were associated with a lower incidence of distal colorectal cancer, and colonoscopy was associated with a modestly lower incidence of proximal colon cancer as well [42]. The total number of colorectal cancers diagnosed was 1,164 in the group that had no screening, 82 in the group that had endoscopic polypectomy, 348 in the group that had sigmoidoscopy, and 221 in the group that had colonoscopy. Multivariate analysis demonstrated that these data represent incidence reductions of 43%, 40%, and 56%, respectively. Both types of endoscopic screening were also associated with lower mortality. The number of deaths in the no-screening group was 349, compared with 73 and 52 in the sigmoidoscopy and colonoscopy groups, respectively. According to multivariate analysis, these data represent mortality reductions of 41% and 68%. An analysis of trends in the incidence of colorectal cancer and related mortality from 1975 to 2006 demonstrated an overall decrease in the incidence of colorectal cancer, with modeling estimating that half of the decline in mortality could be attributed to screening [126].

Harms

Harms are more likely with endoscopic screening than with stool-based testing, but the rates are low. The potential harms of stool-based testing are related primarily to follow-up colonoscopy for positive results [107; 108]. Evidence of overdiagnosis with colorectal cancer screening is lacking, as the rate of diagnosis of colorectal cancer has decreased over time, in part because of the detection and treatment of precancerous polyps [46].

One analysis of data on flexible sigmoidoscopy indicates a rate of serious complications of 0.34 per 1,000 procedures, whereas other studies have shown that fewer than one colonic perforation occurs in 20,000 examinations [107; 127]. A meta-analysis found that a major complication was reported for 0.08 cases among more than 60,000 flexible sigmoidoscopy screenings and nearly 6,000 follow-up colonoscopies [121]. Colonoscopy is associated with a higher rate of serious complications (e.g., perforations, hemorrhage, diverticulitis, cardiovascular events, severe abdominal pain, and death), with an estimated 2.8 serious complications per 1,000 procedures [127]. Complications related to the sedation required for the procedure may also occur.

CLINICIAN ADHERENCE TO GUIDELINE RECOMMENDATIONS

Surveys have demonstrated that guideline-consistent recommendations most often relate to screening intervals and starting age, whereas lack of adherence is primarily related to overuse and use of nonpreferred screening methods [10; 14; 25; 38]. However, the rates of adherence vary, and only 19% of physicians make guideline-consistent recommendations across all screening methods [10]. Evidence of underuse is found in surveys of patients that have shown a lack of clinician recommendation as a primary reason for not participating in screening [10; 24; 128].

Overuse has been related to both the starting and ending age, with greater overuse among younger people and variation in rates among the screening methods recommended [10]. In a 2007 survey of a national representative sample of more than 1,200 primary care clinicians, FOBT was the method most commonly recommended to patients younger than the guideline-recommended starting age (41%); flexible sigmoidoscopy and double-contrast barium enema were recommended in approximately 11% and 10%, respectively, with colonoscopy recommended in 3% [10]. Of 721 primary care physicians who responded to a survey with a vignette describing an asymptomatic woman, 35 years of age, seen for a routine office visit, approximately 39% said they would offer colorectal screening, most often FOBT alone (43%) [14]. Some, but not all, of this overuse was due to the physician's perception of the patient's risk.

One-third of healthcare professionals have reported that they stop recommended colorectal cancer screening for healthy patients at the recommended age of 75 years, with most continuing screening until 80 years of age [25; 129]. Rates of overuse are lower for older individuals and again vary according to screening method; screening was recommended past the ending age for 4.4% of patients using double-contrast barium enema, 3% with flexible sigmoidoscopy or colonoscopy, and 0.8% with FOBT [10].

Overuse has also been related to screening intervals, primarily with endoscopy, for which the intervals are longest. Approximately 44% of physicians recommended colonoscopy at shorter-than-recommended intervals, and 23% recommended more frequent sigmoidoscopy [10]. In contrast, only 0.2% of physicians recommended more frequent FOBT.

In discussions with patients about screening options, most healthcare professionals recommend colonoscopy (95%), followed by FOBT (80%), flexible sigmoidoscopy alone (25%), and FOBT and sigmoidoscopy (23%) [10]. Approximately 21% of healthcare professionals recommend any

of three screening methods (colonoscopy, sigmoidoscopy, FOBT) and 23% recommend either type of endoscopy [10]. Patients have reported lack of knowledge about FOBT, which may, in part, reflect a lack of clinicians' discussion of this screening option [128].

Inappropriate use of a screening method was found in a survey of more than 1,000 primary care providers, in which 25% of respondents used FOBT for a single specimen collected in the office and 53% used FOBT in the office and as home testing [130].

LUNG CANCER

Screening for lung cancer is the most recent screening test to be adopted, with evidence to support screening emerging in 2011 [44]. Until then, trials of screening tools such as chest radiography and sputum cytology had shown no decrease in lung cancer-related mortality [131; 132; 133]. Screening trials began to show benefit with LDCT, including reductions in lung cancer-specific and all-cause mortality. Recommendations from specialty organizations followed, and the USPSTF published its systematic review in July 2013 and its recommendation in December 2013 [45; 120; 134; 135; 136; 137].

RECOMMENDATIONS FOR INDIVIDUALS AT AVERAGE RISK

Lung cancer screening is not recommended for asymptomatic persons with low or moderate risk for lung cancer. The definition of low or moderate risk differs slightly among guidelines. The NCCN guideline defines low risk as an age younger than 50 years and/or a history of smoking of less than 20 pack-years [135]. Moderate risk is defined as an age 50 years or older and a history of smoking or secondhand smoke exposure of 20 pack-years or more with no additional risk factors. The American College of Chest Physicians (ACCP) defines low or moderate risk as an age younger than 55 years, a history of smoking of fewer than 30 pack-years, or smoking cessation more than 15 years previously [136]. Guidelines also recommend against screening for people with severe comorbidities that would preclude potentially curative treatment and/or limit life expectancy [44; 45; 120; 136].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The American Cancer Society recommends clinicians with access to high-volume, high-quality lung cancer screening and treatment centers initiate a discussion about lung cancer screening with patients 55 to 74 years of age 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.

(https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21172. Last accessed October 11, 2018.)

Level of Evidence: Expert Opinion/Consensus Statement

RECOMMENDATIONS FOR HIGH-RISK POPULATIONS

High risk for lung cancer was defined in the largest randomized controlled trial of lung cancer screening trial in the United States to date (50,000 individuals), the NLST [44]. In that trial, high risk was based on patient age and smoking history (i.e., number of pack-years, smoking status, and time since smoking cessation), with the following criteria:

- Age of 55 to 74 years
- History of current or former smoking
- Smoking history of at least 30 pack-years
- Smoking cessation of fewer than 15 years for former smokers

This definition of high risk is based on research showing that the incidence of lung cancer is relatively low before 50 years of age but increases with age, especially after the age of 60 years, and that age-specific incidence rates increase with cumulative exposure to tobacco smoke [135; 137]. Guidelines have modeled the definition of high risk on these criteria. Analysis of data from 2010 has indicated that approximately 8.6 million people in

the United States (5.2 million men and 3.4 million women) were eligible for lung cancer screening based on the NLST eligibility criteria [138]. However, this number represents only approximately 27% of all individuals in whom lung cancer is diagnosed in the United States [139]. Other risk models are being explored to determine if the inclusion of additional risk factors will help better select candidates for screening.

Starting and Ending Age

The American Society of Clinical Oncology (ASCO), the NCCN, the ACS, and the ACCP, with input from the American Thoracic Society (ATS), collaborated on a literature review on lung cancer screening from which evidence-based guidelines were developed [45]. According to these guidelines, screening is recommended for individuals 55 to 74 years of age who are current or former smokers who have (or had) smoked for at least 30 pack-years and, if a former smoker, who has quit within the past 15 years [45]. Guidelines established individually by these organizations, as well as by the American Lung Association, define high risk similarly [135; 136; 141; 142; 143]. In its own guideline, the ATS notes that screening may begin at 50 years of age for individuals who have a 20 pack-year history of smoking and one additional comorbidity that results in a 5% cumulative risk of lung cancer developing over the next 5 years [144].

Guidelines note that it is crucial for the harms associated with lung cancer screening to be balanced with the benefits [45; 135; 136; 137]. In its review of screening strategies to determine the best balance of benefits and harms, the USPSTF found that an age of 55 to 80 years (with the same defined smoking-related risk factors) was associated with a reasonable balance of benefits and harms [120; 137]. In addition, the Task Force found that screening focused on persons with a smoking history of 40 pack-years or more resulted in the lowest number of screening examinations per death averted and thus the least harm in terms of radiation exposure, risk for overdiagnosis, and consequences of false-positive results [137].

Guidelines recommend that screening be offered only in settings that can provide the comprehensive care that was provided to participants in the NLST; such settings must offer multidisciplinary coordinated care along with a comprehensive process for screening, interpretation of screening images, management of the findings, and expert evaluation and treatment of potential cancers [45; 134; 136; 142]. The ACCP also recommends that screening be accompanied by counseling, with a complete discussion of the potential benefits and harms [136]. In addition, it is recommended that healthcare professionals emphasize to their patients the importance of smoking cessation, noting that screening is not a substitute for quitting [45; 135; 136].

Screening Methods

LDCT is the recommended method for lung cancer screening, as it has shown to be associated with higher sensitivity than chest radiography or sputum cytology, either alone or in combination, with LDCT leading to a high percentage (60% to 80%) of lung cancers being detected at stage 1 [137; 145; 146]. In the NLST, the sensitivity and specificity of LDCT, based on the initial screen, was 93.8% and 73.4%, respectively, compared with 73.5% and 91.3% for chest radiography [44]. In addition, neither chest radiography nor sputum cytology—once or at regular intervals—has been shown to decrease mortality, and thus, neither is recommended for screening [45; 136; 137; 142; 147; 148]. In a meta-analysis of trials in which different frequencies of chest radiography were compared, frequent screening was associated with an 11% relative increase in lung cancer-related mortality compared with less frequent screening [148]. There was a trend toward lower lung cancer-related mortality with the combination of chest radiography and sputum cytology (compared with chest radiography alone), but the difference was not significant [148].

Screening Interval

Although the ACCP noted that the effective frequency or duration of screening has not been determined, guidelines recommend annual screening [45; 120; 135; 136; 142]. According to estimates from modeling studies performed by the Cancer Intervention and Surveillance Modeling Network (CISNET), annual screening for the defined high-risk group provided greater benefit in decreasing lung cancer-related mortality than screening every 2 or 3 years [137].

EFFECTS OF SCREENING

Because of the limited time that lung cancer screening has been available, few data are available to rigorously assess its benefits and harms. The most compelling benefit of screening with LDCT is the resultant reductions in lung cancer-specific and all-cause mortality, driven mostly by an earlier stage at the time of diagnosis [137]. The harms are primarily associated with high rates of false-positive results and the potential for overdiagnosis [137].

The NLST demonstrated a 20% reduction in lung cancer-related mortality and a nearly 7% reduction in all-cause mortality in the high-risk population screened [44]. The number needed to screen to prevent one death from lung cancer was 320. It has been estimated that if lung cancer screening with LDCT was implemented in all eligible individuals in the United States, 12,000 lung cancer-related deaths could potentially be averted [138].

Lung cancers in the NLST were diagnosed at an earlier stage. According to 2009 data (before screening was recommended), lung cancer was localized at the time of diagnosis in approximately 15% of individuals [1]. In the first 3 years of screening in the NLST, 63% of participants who had positive results on LDCT had early-stage lung cancer (stage IA or IB), and 21% had late-stage disease (stage IIIB or IV); these results compared with 48% and 31%, respectively, for positive results on chest radiography [44].

Rates of false-positive results with LDCT screening are high. Overall, studies have shown that screening with LDCT has identified small nodules in 10% to 50% of individuals screened, and the vast majority of these nodules will be found to be benign [136]. In the NLST, 96.4% of the positive screening results in the LDCT group were false-positive (compared with 94.5% in the radiography group) [44]. The rate of biopsy for nodules later found to be benign has varied, with an average of approximately 30% [136]. False-positive results are associated with psychologic distress for patients and the potential for unnecessary follow-up procedures or treatment. Over the three rounds of screening in the NLST, approximately 72% of individuals with a positive result had diagnostic follow-up of some type, 59% had a clinical procedure, and 4% had a surgical procedure [44]. Major complications in individuals with nodules that proved to be benign were rare (0.1%) [44].

The rate of false-negative results for LDCT has ranged from 0% to 20% [137]. Establishing a larger nodule size as the threshold for a positive result will increase the specificity but decrease the sensitivity of the test.

Overdiagnosis is also associated with lung cancer screening, and the rates have varied. Analysis of data from the NSLT indicated that 18.5% of all lung cancers detected with LDCT were indolent and thus represent overdiagnosis [149]. The likelihood of overdiagnosis varied according to histologic type, with a rate of 22.5% for non-small cell lung cancer and 78.9% for bronchioalveolar lung cancer. Modeling studies by CISNET estimate that 9.5% to 11.9% of screen-detected cancers are overdiagnosed [137; 150]. Further research is needed to more fully assess the benefits and harms of lung cancer screening with LDCT.

CLINICIAN ADHERENCE TO GUIDELINE RECOMMENDATIONS

Many healthcare professionals screened for lung cancer before it was recommended, with most using screening tools that have not been associated with decreased mortality. For example, in a survey of 962 physicians (family physicians, general practitioners, and general internists), 55% said they had ordered chest radiography and fewer than 5% had ordered sputum cytology; 22% had ordered LDCT [13]. Several physician-related factors associated with lung cancer screening (before it was recommended) were identified [13; 36]:

- Perception of a screening test's effectiveness
- Attitude toward recommended screening guidelines
- Practice experience
- Perception of a patient's risk for lung cancer
- Reimbursement and payment for screening
- Concern about litigation
- Patient request for screening

Since the publication of guidelines for lung cancer screening, a small study of 15 leading academic medical centers that offer screening showed that 11 (73%) of the centers limit screening to individuals at high risk as defined in the NLST; one center followed expanded selection criteria, and three centers offered lung cancer screening to any individuals who had participated in shared decision making with a physician [151].

PROSTATE CANCER

Prostate cancer screening with PSA and/or DRE was once recommended routinely for the early detection of prostate cancer in average risk men. However in the late 2000s, as evidence increasingly showed no benefit in mortality and a high likelihood for harm, many expert panels updated their screening recommendations in 2012 and 2013 (***Table 11***) [39; 43; 152; 153; 154; 155]. Informed decision-making is integral in selecting approaches to prostate cancer screening, with every guideline emphasizing the need to discuss the potential benefits, harms, and limitations associated with screening with their male patients.

RECOMMENDATIONS FOR MEN AT AVERAGE RISK

Overall, experts recommend against routine screening for most men and emphasize the need to consider life expectancy and the patient's age and risk factors for prostate cancer.

Age for Discussion about Screening

The age to start a discussion about screening varies slightly among the guidelines. The earliest age is 45 years, recommended in the NCCN guideline, which suggests measurement of the PSA level beginning at this age and that clinicians talk to patients about the risks and benefits of a baseline DRE [155]. The ACP recommends a discussion for men 50 to 69 years of age, and the American Urological Association strongly recommends shared decision making for men 55 to 69 years of age, as the benefit of screening appears to be greatest for men in this age-group [152; 153]. The ACS recommends that the potential benefits and substantial harms of screening be discussed with men who are 50 years of age or older and have a life expectancy of at least 10 years. The USPSTF guideline does not address an age at which to begin a discussion but does emphasize that shared decision making should take place [43].

Screening Method

For men who elect prostate cancer screening, measurement of the PSA level is the preferred method, with repeat PSA testing based on elevated initial PSA level; DRE should be measured if warranted by elevated an PSA level in a second test [155]. PSA in combination with DRE provides better predictive value than either method alone, but standalone DRE should not be performed. The positive predictive value of DRE in men with normal PSA levels is only 4% to 11% [155]. The sensitivity of PSA testing is higher than that of DRE, especially for tumors that are more aggressive [156]. However,

RECOMMENDATIONS FOR PROSTATE CANCER SCREENING		
Organization (Year)	**Screening Recommendation**	**Notes**
National Comprehensive Cancer Network (2016)	No routine screening	Begin risk-benefit discussion about baseline DRE and PSA screening at 40 years of age.
American Urological Association (2013)	No routine screening	Decisions should be individualized for men younger than 55 years of age who are at high risk. Shared decision making should take place for men 55 to 69 years of age, for whom screening is of greatest benefit.
American College of Physicians (2013)	No routine screening with PSA for average-risk men younger than 50 years of age, men older than 69 years of age, or men with a life expectancy of less than 10 to 15 years	Clinicians should inform their patients 50 to 69 years of age about the limited potential benefits and substantial harms of screening.
American Cancer Society (2013)	No routine screening	Discuss the potential benefits, risks, and uncertainties associated with prostate cancer screening with men who have a life expectancy of at least 10 years; prostate cancer screening should not occur without an informed decision-making process.
U.S. Preventive Services Task Force (2012)	No routine screening	—
American Society of Clinical Oncology (2012)	Discourage general screening for men with a life expectancy of ≤10 years, as the harms outweigh the benefits.	Discuss the individual appropriateness of screening with men who have a life expectancy >10 years.
DRE = digital rectal examination, PSA = prostate-specific antigen.		
Source: [39; 43; 152; 153; 154; 155]		*Table 11*

the PSA level can vary as a result of several factors (e.g., recent ejaculation, instrumentation, infection, trauma) [155]. For this reason, an elevated PSA level should prompt a repeat test.

RECOMMENDATIONS FOR MEN AT HIGH RISK

The ACS recommends two different starting ages for screening men at high risk for prostate cancer, depending on risk factors [39]:

- 45 years of age for black men and men who have a father or brother in whom prostate cancer was diagnosed before 65 years of age
- 40 years of age for men who have multiple family members in whom prostate cancer was diagnosed before 65 years of age

The NCCN recommends baseline PSA testing and consideration of DRE for men who are identified as being at high risk, defined as black race or family history of prostate cancer [155]. If the initial discussion of screening (at 45 years of age) results in measurement of PSA and the level is less than 1.0 ng/mL, a repeat PSA should be done every 2 to 4 years [155]. If the PSA level is 1–3 ng/mL and DRE is normal (if performed), repeat testing is recommended at one- to two-year intervals. A PSA level higher than 3.0 ng/mL with a very suspicious DRE finding should prompt a discussion of further testing, including percent-free PSA testing, 4Kscore, or prostate health index blood testing; a repeat PSA/DRE in 6 to 12 months; or a biopsy [155].

The AUA guideline notes that decisions about screening should be individualized for men younger than 55 years who are at high risk for the disease, which it defines as a positive family history or black race [152]. The USPSTF did not distinguish between men at average or increased risk for prostate cancer [43].

EFFECTS OF SCREENING

Routine screening for prostate cancer is no longer recommended because the evidence indicates that the harms far outweigh the benefits.

Benefits

The primary benefit of prostate cancer screening is a lower stage and grade of cancer at the time of diagnosis [39; 43; 156]. However, despite this benefit, an effect of screening on mortality has not been clearly demonstrated. After 13 years of follow-up in the PLCO trial, there was no benefit of annual screening on mortality [157]. A subsequent meta-analysis (five randomized controlled trials) similarly demonstrated no effect of screening on prostate cancer-specific or overall mortality [158]. However, data from the European Randomized Study of Screening for Prostate Cancer demonstrated that screening reduced the risk for prostate cancer death by 7% to 9% per year [222].

Harms

Many potential harms have been associated with prostate cancer screening, including a high rate of false-positive results and unnecessary biopsies; overdiagnosis and subsequent overtreatment; and complications [43; 152; 155; 159]. Among men who had four PSA tests, the cumulative risk for at least one false-positive result was 12.9% [43]. The false-positive rate has been reported to be 80% for a PSA cutoff of 2.5 to 4.0 ng/mL [153]. False-positive results may lead to psychologic effects as well as unnecessary biopsies or treatments. In addition, prostate biopsies have been associated with a high rate of complications, especially infection [155].

In an effort to enhance the specificity of PSA testing, variations of the PSA test have been developed, including free PSA, PSA density, PSA velocity, and complexed PSA [155]. Each has its benefits and limitations, and the AUA notes that none increases the benefit-harm ratio of screening [152]. Levels of free PSA have been shown to be significantly lower in men with prostate cancer than in men without the disease [155]. The U.S. Food and Drug Administration has approved percent-free PSA for the early detection of prostate cancer in men with PSA levels between 4 and 10 ng/mL [155]. A 25% fPSA cutoff is expected to detect 95% of prostate cancers while preventing 20% of unnecessary biopsies.

PSA density is the result of dividing the PSA level by the volume of the prostate, as measured by transrectal ultrasonography, and a higher result suggests a greater likelihood of prostate cancer [155]. Greater PSA density has correlated with the presence of prostate cancer, as well as with the pathologic stage of the tumor and its aggressiveness and progression after treatment [160]. The use of PSA density has been limited by the lack of precision of total PSA, of measurement of prostate volume, and of the need to carry out transrectal ultrasonography [155]. In addition, PSA density does not offer much benefit compared with other PSA derivatives (notably, percent-free PSA)[155].

PSA velocity is the rate at which a PSA level increases over a period of time, and it has been most helpful for longitudinal monitoring of men younger than 50 years of age who have normal PSA levels and no prostate enlargement [155]. The test is not useful for men with PSA values greater than 10 ng/mL [155]. A high PSA velocity alone should not prompt biopsy but instead aid in decision making [155]. The ratio of complexed PSA to total PSA provides information comparable to the ratio of free to total PSA, and the use of complexed PSA has been approved as a detection aid (in conjunction with DRE) for men 50 years of age or older; however, the test is not widely used in practice [155].

Rates of overdiagnosis with prostate cancer screening have been estimated at 17% to 60%, and 23% to 42% of all screen-detected prostate cancers are overtreated [43; 46; 159]. In addition, treatment of screening-detected prostate cancers has been associated with such adverse effects as incontinence and erectile dysfunction in 200 to 300 of 1,000 men treated with surgery or radiation therapy and death within one month after prostate cancer surgery in five of 1,000 men [39]. Treatment also has been associated with high rates of complication, ranging from 20% to 50% [43; 152].

Researchers continue to investigate ways to make screening more effective. Using a higher PSA threshold for biopsy for older men and less frequent screening for men with low PSA levels are strategies that may reduce the risk of overdiagnosis as well as prostate cancer-related mortality [161].

CLINICIAN ADHERENCE TO GUIDELINE RECOMMENDATIONS

According to NHIS data, the rate of prostate cancer screening among men older than 50 years of age has decreased nearly 20% since 1999 (65% compared with 46%) [6]. This decrease is thought to reflect the increasing evidence of a lack of efficacy for screening [6]. Most studies of adherence to guideline recommendations have focused on the screening rates among older men (for whom screening is not recommended) and adherence to appropriate discussion of the benefits and harms of screening. The Healthy People objective related to prostate cancer is to increase the proportion of men who have a discussion of the advantages and disadvantages of prostate cancer screening; the target in 2010 was 14.4%, and the target for 2020 is 15.9% [2].

In one study of data on 1,149 men 50 years of age or older, the rates of annual PSA testing were similar for men 50 to 74 years of age (77%) and men 75 years of age and older (75%) [162]. BRFSS data showed higher rates with older ages, with a rate of 56% for men 50 to 64 years of age, 68% for men 65 to 79 years of age, and 64% for men 80 years of age and older [12].

Other studies have shown that PSA screening rates increase with age and decline beginning at 75 years of age. NHIS data showed that the screening rate increased steadily from 24% among men 50 to 54 years of age to approximately 46% among men 70 to 74 years of age [163]. Although the rate declined after that, approximately 25% of men 85 years of age or older reported being screened. Medicare data have demonstrated a screening rate of 17% among men 80 years of age and older, with wide variation across geographic regions [164]. A study in Texas showed that the rate of any PSA screening for men 75 to 79 years of age was 49%, 45% of which had been ordered by the patient's primary care provider [165]. The rate decreased with increasing age (40% for men 80 to 84 years of age and 28% for men older than 85 years of age). Still, the overall rate was 41% for a population for whom screening is not recommended. Rates of screening have also been higher for older men with limited life expectancy, ranging from 31% to 47% [163; 166].

Despite the continued emphasis on informed decision making in prostate cancer screening, the percentage of men who report having had a discussion with their healthcare providers about screening has been suboptimal, with 64% to 73% of men reporting that they have not had a discussion of the benefits and harms of PSA screening [26; 34]. Clinician-reported rates for no discussion have been much lower, at approximately 25% [12; 32]. Even when discussions are carried out, they are often inadequate. Surveys of men have indicated that 8% had full shared decision making, whereas surveys of healthcare professionals have shown that 65% to 73% do not fully discuss the advantages and disadvantages of screening and prostate cancer treatment [12; 26].

OTHER CANCERS

The benefits and harms of screening for other types of cancers have been evaluated, and research continues to explore new methods of screening for cancers with no validated screening methods to date. Some of these cancers—pancreatic and ovarian cancer, for example—are responsible for a high number of deaths each year, but population-based screening is hampered by the lack of reliable screening tools and a low positive predictive value because of the low incidence rate.

ORAL CANCER

In 2010, an expert panel from the American Dental Association Council on Scientific Affairs developed recommendations for oral cancer screening on the basis of five systematic reviews and four clinical studies [167]. The panel concluded that community-based screening by visual and tactile examination may not alter disease-specific mortality among the general population but may decrease disease-specific mortality among people who use tobacco, alcohol, or both [167]. In addition, screening may result in detection of oral cancers at early stages of development (stages I and II). The panel found insufficient evidence to determine whether screening alters disease-specific mortality among asymptomatic people seeking dental care. There was also insufficient evidence that devices based on autofluorescence or tissue reflectance enhanced the detection of potentially malignant lesions beyond that detected by a conventional visual and tactile examination. The panel suggested that "clinicians remain alert for signs of potentially malignant lesions or early-stage cancers in all patients while performing routine visual and tactile examinations," especially for patients who use tobacco or who are considered to be heavy users of alcohol (defined as an average of more than two drinks per day for men and more than one drink per day for women) [167].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The U.S. Preventive Services Task Force concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for oral cancer in asymptomatic adults.

(http://annals.org/aim/fullarticle/1783292. Last accessed October 11, 2018.)

Strength of Recommendation: I (Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.)

Similarly, the authors of a 2013 meta-analysis on the effectiveness of screening programs for oral cancer found that population-based screening reduced the mortality rate of oral cancer only among high-risk individuals but not among individuals at average risk [168]. Visual examination as part of a screening program significantly reduced mortality by 24% among individuals with a history of alcohol or tobacco use, or both, compared with unscreened individuals [168]. However, the authors of the meta-analysis noted that the evidence was limited to one study with a high risk of bias. As with the American Dental Association review, no evidence supported a reduction in mortality with the use of other screening tools, such as toluidine blue, brush biopsy, or fluorescence imaging.

The ACS recommends that men and women 20 years of age and older should have examination of the oral cavity as part of a cancer-related check-up during periodic health examinations [39]. The USPSTF updated its recommendations on oral cancer screening in 2013. The Task Force concluded that the current evidence is insufficient to evaluate the benefits and harms of oral cancer screening in asymptomatic adults [169]. The Task Force also noted that the recommendations apply only to primary care providers and not to dental care providers or otolaryngologists [169]. The authors of a 2013 meta-analysis concluded that dental care providers should perform routine oral examinations to detect signs of premalignant disorders or oral cancer [170].

The results of surveys of primary care providers and dentists are in line with these conclusions, with oral cancer screening being carried out significantly more often by dentists than by other healthcare professionals. For example, in a study of dentists and physicians in Massachusetts, 92% of dentists said they performed an oral cancer examination in adults 40 to 55 years of age, compared with 49% of physicians [171]. In a similar survey in South Carolina, 81% of dentists and 13% of physicians reported performing oral cancer examinations at least half of the time over the past year [172]. Knowledge related to oral cancer and the examination was lacking, with 39% of dentists and 9% of physicians able to identify the two most common sites where oral cancer develops and 57% of dentists and 24% of physicians correctly identifying the most common symptom of early oral cancer [171].

OVARIAN CANCER

Ovarian cancer is the fifth leading cause of cancer-related death among women, yet the currently available tools for detecting ovarian cancer are not reliable for the early detection of the disease. These tools include pelvic examination, transvaginal ultrasound, and the tumor marker CA-125 [39]. The sensitivity and specificity are poor for pelvic examination and limited for serum CA-125 levels; studies have shown that half of early ovarian cancers produce a sufficient amount of CA-125 to cause a positive test, and the level of the antigen can be increased by noncancerous diseases and other cancers [39]. Transvaginal ultrasound can detect small ovarian masses but poorly distinguishes between cancer and benign disease [39].

The combination of CA-125 and transvaginal ultrasound for ovarian cancer screening among women at average risk was evaluated in the PLCO cancer screening trial. The study enrolled more than 78,000 women, 55 to 74 years of age, who were randomly assigned to annual screening for 6 years or usual care and were followed for a maximum of 13 years. The mortality rate was similar for both groups (3.1 ovarian cancer-related deaths per 10,000 patient-years in the group who had screening vs. 2.6 deaths per 10,000 patient-years in the group who had usual care) [173]. As a result of these and similar findings, major medical organizations agree that ovarian cancer screening is not recommended for asymptomatic women at average risk for the disease [39; 174; 175]. The USPSTF also notes that substantial harms may be involved with ovarian cancer screening, primarily due to surgical interventions for masses that are not cancerous [175].

Some hereditary syndromes increase the risk for ovarian cancer; for example, the risk of ovarian cancer is estimated to be 40% for women with breast-ovarian cancer syndrome, 18% to 21% for women with Peutz-Jeghers syndrome, and 9% for women with Lynch syndrome [72; 114]. For high-risk women who do not have prophylactic oophorectomy to prevent ovarian cancer, the combination of transvaginal ultrasound and measurement of CA-125 levels every 6 months is recommended for screening [174; 176]. Some data have shown that annual screening with these modalities is not effective, and data are limited on the effectiveness of such screening every 6 months, but guidelines note that this screening strategy is a reasonable consideration until data become available [39; 72; 174].

Surveys of healthcare professionals have shown lack of knowledge about the effectiveness of ovarian cancer screening for asymptomatic, average-risk women as well as nonadherence to the guidelines. In one survey of 1,088 physicians (family physicians, general internists, and obstetrician-gynecologists), one-third of respondents said they believed that ovarian cancer screening was effective [16]. In another survey (1,250 family physicians, general internists, and obstetrician-gynecologists), 40% said both transvaginal ultrasound and CA-125 level were effective screening tools [17]. In the latter survey, the responses of obstetrician-gynecologists were more often consistent with current guidelines; approximately 57% of obstetrician-gynecologists said neither transvaginal

ultrasound nor CA-125 level was effective for screening, compared with 34% of family practitioners and 30% of internists [16].

With regard to guideline adherence, 28% of physicians reported nonadherence to screening recommendations for women at low risk for ovarian cancer; 6% routinely ordered (or offered) ovarian cancer screening for women at low risk, and 24% routinely ordered (or offered) screening for women at medium risk [17]. The strongest predictors of nonadherence were physician belief that transvaginal ultrasound or CA-125 level was an effective screening tool, actual and physician-perceived patient risk, and patient request for ovarian cancer screening.

PANCREATIC CANCER

The risk of pancreatic cancer among the general population is low (less than 1%), and it accounts for only 3% of all cancers in men and women [1; 114]. However, the disease is the fourth leading cause of cancer-related deaths, primarily because the cancer is usually at a late stage by the time of diagnosis [1]. Unfortunately, no validated methods for pancreatic screening have been established. In 2015, the USPSTF continued to recommend against routine screening for pancreatic cancer in asymptomatic adults by any method (e.g., abdominal palpation, ultrasonography, or serologic markers) [177]. The decision was based on a lack of evidence showing a reduction in mortality, as well as the potential for significant harm related to the invasiveness of diagnostic testing, the low prevalence of the disease, and poor outcomes of treatment [177].

Since the publication of the original USPSTF guideline in 2004, researchers have been exploring ways to detect early pancreatic cancer. The optimal approach would be to identify precursor lesions, which include pancreatic intraepithelial neoplasias, intraductal papillary mucinous neoplasms, or mucinous cystic neoplasms. However, current imaging studies cannot reliably visualize these lesions [178; 179]. The only known serum marker for pancreatic cancer is carbohydrate antigen CA 19-9, but it is not sensitive for early lesions [180]. A combination of methods seems to be the best approach [180]. Endoscopic ultrasound, endoscopic retrograde cholangiopancreatography, and magnetic resonance cholangiopancreatography are the imaging techniques most commonly used [178; 179; 180]. In one study, a screening protocol of CA 19-9 followed by targeted endoscopic ultrasound was found to be feasible for identifying potentially curative pancreatic adenocarcinoma [181].

High-Risk Populations

As with other cancers, most cases of pancreatic cancer are sporadic, with about 10% being related to genetic factors. Several hereditary syndromes are associated with an increased lifetime risk for pancreatic cancer; the highest estimated risk—nearly 40%—is associated with hereditary pancreatitis [178; 180]. The lifetime risk of pancreatic cancer is 11% to 36% for individuals with Peutz-Jeghers and 1% to 6% for individuals with Lynch syndrome [114]. Familial breast-ovarian cancer syndrome also confers an increased risk for pancreatic cancer, with *BRCA1* mutations associated with 2.3-fold to 3.6-fold increased risk and *BRCA2* mutations associated with a 3-fold to 10-fold increased risk [178]. Familial atypical multiple mole melanoma, another hereditary syndrome, has been associated with an increased risk for nonmelanoma cancers, including pancreatic cancer. The risk is 13-fold to 22-fold higher in individuals with this syndrome compared with the general population [178].

Familial pancreatic cancer is the occurrence of pancreatic cancer in two or more first-degree relatives in a family that is not associated with a known cancer syndrome. The causative genetic mutation has not been identified [180]. The risk for pancreatic cancer increases with the number of family members affected [180].

Recommendations for Screening

Some recommendations for pancreatic cancer screening have been established on the basis of consensus. Participants of the Fourth International Symposium of Inherited Diseases of the Pancreas recommended screening for the following populations [179]:

- Families with familial atypical multiple mole melanoma (with *p16* germline mutation) and at least one case of pancreatic cancer in a first-degree or second-degree relative
- Individuals with Peutz-Jeghers syndrome
- Individuals with hereditary pancreatitis
- Family members who have more than three pancreatic cancer cases among first-degree, second-degree, and third-degree relatives (at least one of whom is a first-degree relative)
- Known carriers of *BRCA2* mutations who have at least one case of pancreatic cancer within second-degree relatives

The Symposium participants did not reach consensus on a specific screening modality but suggested that endoscopic ultrasound is the preferred modality at many institutions, as it has been found to be the most sensitive and specific screening technique for evaluating the pancreas [179; 182]. Endoscopic retrograde cholangiopancreatography and magnetic resonance cholangiopancreatography are other options [179]. It is recommended that screening of high-risk individuals be done within research protocols with multidisciplinary teams with expertise in genetics, gastroenterology, radiology, surgery, and pathology [180].

The NCCN recommends magnetic resonance cholangiopancreatography or endoscopic ultrasound every 1 to 2 years beginning at 30 to 35 years of age for individuals with Peutz-Jeghers syndrome [114]. The NCCN makes no recommendations for pancreatic cancer screening for individuals with other hereditary syndromes.

SKIN CANCER

The rate of skin cancer has been rapidly increasing, and melanoma is the type of skin cancer with the lowest incidence but the greatest potential for morbidity and mortality [1]. Recommendations on screening for skin cancer vary, and only some specialty organizations recommend whole-body skin examination as part of routine health care or for individuals at high risk for melanoma (***Table 12***). However, the USPSTF and the AAFP state that there is insufficient evidence to assess the benefits and harms of whole-body skin examination by a clinician or of self-examination in the early detection of skin cancer [183; 193].

One reason the USPSTF does not recommend screening for skin cancer is a lack of accuracy in diagnosing melanoma. A large systematic review showed that diagnosis of melanoma by primary care providers had a sensitivity of 42% to 100% and a specificity of 98% [184]. In most of these studies, primary care providers were asked to identify melanoma from lesions with a known diagnosis, and it is not clear whether the findings can be applied to whole-body skin examination [183]. The authors of the review stated that there is insufficient evidence to determine whether there is a difference between primary care physicians and dermatologists with regard to the accuracy of diagnosis [184]. Studies have demonstrated that education improves the skills of medical students and clinicians in performing skin cancer examinations and detecting skin cancer [185; 186; 187]. In a systematic review of educational interventions about skin cancer for clinicians, 90% of studies showed a significant improvement in at least one of five outcome categories: knowledge, competence, confidence, diagnostic performance, or systems outcomes [186]. However, there was insufficient evidence to compare the effectiveness of interventions.

The USPSTF also notes that most lesions detected during skin cancer screening programs are not melanoma, which may lead to biopsy and unnecessary treatment [183]. In addition, screening also identifies thin melanomas that have little poten-

RECOMMENDATIONS FOR SKIN CANCER SCREENING		
Organization (Year)	**Screening Recommendation**	**Notes**
U.S. Preventive Services Task Force (2016)	Insufficient evidence to recommend for or against routine screening	—
American Academy of Family Physicians (2016)	Insufficient evidence to recommend for or against routine screening	—
American Academy of Dermatology (2016)	Individuals should regularly self-examine skin for signs of skin cancer and see a board-certified dermatologist if any unusual spots are found	High-risk individuals or those with a history of skin cancer should consult a dermatologist regarding screening
American Cancer Society (2013)	Skin examination should be part of cancer-related check-up during periodic health examination for all men and women 20 years of age and older.	Clinicians should counsel their patients 20 years of age or older about sun exposure. Monthly self-examination of the skin is also recommended.

Source: [39; 183; 193; 194] *Table 12*

tial for spread and that are not likely to be life-threatening; again, overtreatment may be a result [183]. The evidence is limited, however, and the USPSTF could not evaluate the magnitude of these harms. Data on benefits are also limited, with no studies in which the outcomes of a screened and an unscreened population were compared [183].

Studies have shown that both whole-body skin examination (by a healthcare professional) and self-examination of the skin are associated with thinner melanomas at the time of diagnosis [188]. Among the strongest evidence for thinner melanomas with screening is a population-based case control study in Queensland, Australia, in which a whole-body skin examination by a physician within 3 years of diagnosis was associated with a 14% lower risk of being diagnosed with a thick melanoma [189]. As a result, an estimated 26% fewer melanoma-related deaths occurred among patients who were screened compared with patients who were not. In a German study, more than 360,000 people in one state were screened with whole-body skin examination; melanoma-related mortality decreased by 47% in men and by 49% in women compared with other regions in Germany where screening was not carried out [190].

In the United States, the American Academy of Dermatology (AAD) has offered more than 2.1 million free skin cancer screenings around the country since the 1980s through its Melanoma/Skin Cancer Screening Program, and nearly 24,000 suspected melanomas have been detected [191]. Data from the first 15 years of the program showed that nearly 30% of people screened had a presumptive diagnosis of skin cancer or a precursor lesion, and about half of all people screened would not have sought screening if not for the free screening [192]. The biopsy-confirmed melanomas were more likely to be less than 1.5 mm thick compared with melanomas documented in population-based registries [192].

The ACS recommends a cancer-related checkup by a physician, including a skin examination, during a periodic health examination for people 20 years of age or older; counseling regarding sun exposure is also recommended [39]. Monthly skin self-examination is also recommended. The American Academy of Dermatology recommends that individuals act as their own health advocate by checking their body for spots, particularly individuals at high risk for malignant melanoma [194].

The USPSTF concluded that the benefit of screening is uncertain, even for individuals at high risk (defined as fair skin, age older than 65 years, presence of atypical moles, considerable history of sun exposure and sunburns, and a family history of melanoma) [183]. A survey of dermatologists showed that although 80% to 85% of respondents talk to their patients with melanoma about the risk of the disease in their first-degree relatives, fewer than 50% routinely offered to screen nearby first-degree relatives [31]. In addition, approximately 20% used medical record reminders about communicating risk to family members.

The risk of melanoma is increased for individuals with hereditary breast-ovarian cancer syndrome [72]. Although no specific guidelines for screening are available, NCCN guidelines note that whole-body skin and eye examination should be considered for men and women with this syndrome [72]. In addition, clinicians should educate their patients about monthly self-examination and need for protection against the sun.

In a survey of AAD members, one-third of respondents were aware of skin cancer screening recommendations, but 30% said they performed whole-body skin examination on all of their adult patients and 49% said they performed this examination only on patients perceived to be at increased risk [195]. The dermatologists who were aware of recommendations for skin cancer screening were not more likely to screen all adults or adults at increased risk. The most common barrier to screening was lack of time (42%); lack of financial reimbursement was not a substantial barrier (9%) [195].

TESTICULAR CANCER

In 2011, the USPSTF reaffirmed its earlier recommendation against screening for testicular cancer for asymptomatic male adolescents or adults because of the unlikelihood of benefits from such screening [196]. Self-examination is also not recommended. The Task Force notes that its recommendation is based on the low incidence of testicular cancer and the high survival rate, even when testicular cancer is detected at an advanced stage. More than 90% of newly diagnosed testicular cancers are cured; in 2016, there were 380 deaths caused by testicular cancer, with 8,720 newly diagnosed cases [1; 196].

The American Academy of Family Physicians also recommends against testicular cancer screening, and the American Academy of Pediatrics does not include screening for testicular cancer in its recommendations for preventive health care [196]. The ACS recommends that men 20 years of age and older should have testicular examination as part of a cancer-related check-up during periodic health examinations [39].

The authors of a systematic review found no published randomized controlled trials in which the effectiveness of screening for testicular cancer was evaluated [197]. The authors concluded that clinicians should discuss the risk of testicular cancer and the potential harms and benefits of screening with men who have an increased risk for testicular cancer (i.e., family history of testicular cancer, undescended testes, testicular atrophy) [197]. The NCCN recommends annual testicular exam for men with Peutz-Jeghers syndrome [114].

STRATEGIES TO IMPROVE APPROPRIATE SCREENING

Based on population-based screening rates and surveys of healthcare professionals, strategies are needed to enhance appropriate screening recommendations and to improve patients' understanding of the benefits and harms of screening. To be effective, these strategies must address identified barriers to appropriate cancer screening, and further research is needed to better understand patient-, clinician-, and system-related barriers.

CLINICIAN-DIRECTED STRATEGIES

Lack of physician recommendation is the reason given most often for people not participating in cancer screening [21; 23; 24; 128]. There is a need for improved knowledge of guidelines, but there is a greater need for a better understanding of the evidence base for guidelines to help enhance healthcare professionals' attitudes toward guidelines. Perceptions of a screening test's effectiveness and beliefs and attitudes about guidelines have been shown to be closely related to screening practices [36]. Education and resources on guideline recommendations and definitions of risk are useful. Providing assessment and feedback to clinicians has been shown to be effective as an intervention to improve rates of breast, cervical, and colorectal cancer screening [198].

PATIENT-DIRECTED STRATEGIES

Patient education is also crucial. Knowledge of the importance of screening and understanding of the benefits and harms associated with screening tests is inadequate among patients. For example, 30% of women who lived in urban areas and had public insurance said that they had never heard of either colonoscopy or sigmoidoscopy, and 55% said they had never heard of home FOBT [128]. Levels of knowledge regarding screening also vary widely and are especially low among minority populations [21; 22; 161; 200; 201]. Education helps not only to build knowledge about the importance of screening and accurate risks of cancer but also to reduce fears associated with screening methods and diagnosis. One-on-one education has been shown to be an effective intervention for improving cancer screening [198]. Healthcare professionals should target individuals in minority populations, especially individuals who have been living in the United States for fewer than 10 years.

Healthcare professionals should supplement such discussions with educational resources on cancer screening. These resources on cancer screening should be tailored to distinct minority populations and address culture-specific barriers [21; 39; 199; 200; 201]. Educational materials that address lack of evidence for a screening test as well as the potential harms may help reduce rates of inappropriate screening in response to patient requests [16]. Healthcare professionals should describe the patient's risk simply and accurately rather than telling the patient only that he or she does meet the eligibility criteria for a particular screening test [202].

As noted, rates of inappropriate screening among the older population are high, and healthcare professionals should take efforts to reduce these rates. Care is needed when discussing the end of cancer screening for older patients. It is important to explain that screening is not stopping because of a lack of attention to problems [47]. Patients and caregivers have responded well to discussions of the balance of risks and benefits, the burden of tests, the potential for complications, and quality of life [47; 203; 204].

Shared decision making about screening must also be improved to address both the benefits and potential harms of a particular screening test. An individual's values and preferences should be considered, as some people are more concerned about potential harms, whereas others value peace of mind [46; 48]. Creating a so-called balance sheet may help patients better understand the risks and harms of screening [46].

Decision aids have become an important tool with the call for enhanced patient engagement in their care. Decision aids have been shown to increase patients' involvement in their care and to improve their knowledge and perceptions, although the size of the effect has varied across studies [205]. In the setting of prostate cancer screening, the use of decision aids was associated with a decrease in the number of men who chose to have PSA screening [205]. Strong evidence indicates that incorporating personalized risk estimates into messages about breast and colorectal cancer screening enhances informed choices [126]. More research is needed on how decision aids affect rates of appropriate screening and shared decision making. In a review of 73 decision aids for breast, cervical, colon, and

prostate cancer screening, researchers found that only 36 had been evaluated for subsequent screening behavior and only 18 had been evaluated for their effect on shared decision making [206].

PRACTICE-LEVEL STRATEGIES

Several practice-related factors also have an effect on screening rates. Ensuring appropriate cancer screening involves a number of steps in clinical practice, including [207; 208]:

1. Implementing a reminder system to identify patients in need of screening
2. Ordering the screening test
3. Scheduling the screening test (or distributing stool-based testing cards)
4. Contacting people who do not carry out screening
5. Rescheduling the screening test for people who do not carry out screening
6. Tracking the results of the screening test
7. Contacting the patient with the test results
8. Scheduling referral or follow-up as necessary

Studies have shown that most primary care practices lack a system that incorporates all of these steps. For example, fewer than half of practices have a reminder system for breast and cervical cancer screening and half to two-thirds of practices do not follow all the steps necessary to ensure appropriate colorectal cancer screening [209; 210; 211]. Patient follow-through on screening has been identified as a factor in low screening rates, yet few practices have a system in place to contact patients who do not keep their screening appointment [107; 212]. Electronic reminder systems are effective for increasing screening of patients as well as of at-risk relatives [31].

Outreach efforts have been successful. Telephone outreach by Medicaid managed care organizations increased colorectal cancer screening, but automated telephone outreach with speech recognition did not [213; 214]. Direct mail outreach, either with invitations for breast or cervical cancer screening or with kits for stool-based colorectal cancer screening, has led to higher screening rates [215; 216; 217]. In one study, participation in colorectal screening was significantly higher among people who received an invitation and an enclosed FIT card and people who received an invitation for no-cost colonoscopy than among people who were offered visit-based screening (40.7% vs. 24.6% vs. 12.1%, respectively) [218]. Identifying patients eligible for screening with an electronic medical record system and mailing an FOBT card has also led to greater participation in screening [219].

SYSTEM-LEVEL STRATEGIES

Lastly, strategies must target the removal of system-level barriers, most notably, access to screening for underserved populations. Some free programs are available for uninsured women, such as the NBCCEDP. However, this program has not been fully accessed. In 2004–2006, only 9% of the 8.9 million eligible women had screening, with the rate varying according to race/ethnicity and age [140]. Clearly, other barriers in the underserved population must be addressed.

The Affordable Care Act (ACA) is expected to help improve cancer screening rates in two ways: by making insurance coverage available to more people in the United States and by requiring complete coverage for preventive services, such as cancer screening, without any cost-sharing by the patient (copayment or requirement to meet a deductible) [39]. As a provision of the ACA, Medicare now covers free screening for breast, cervical, and colorectal cancers [4].

CONCLUSION

Lung, colorectal, breast, and prostate cancers are the leading causes of cancer-related deaths in the United States, accounting for nearly half of all cancer-related deaths. Appropriate screening has the potential to reduce this substantial mortality by detecting cancer at earlier stages when cure is most possible. Appropriate screening is a complex issue, however, and adherence to established guidelines has been a challenge. Many healthcare professionals are unaware of updated guidelines, and overuse, underuse, and misuse of screening tests are common. Patient-related factors also contribute to suboptimal screening rates; rates are lowest among individuals in minority populations, persons with no usual source of care, and persons who lack health insurance.

Improving appropriate use of cancer screening is a national priority, and healthcare professionals should ensure that they are familiar with the most up-to-date guidelines for screening and that they understand their patients' level of risk. In addition, healthcare professionals should take steps to increase rates of appropriate screening in their practice by implementing strategies that have been shown to be effective, such as office policies related to screening, electronic reminders for screening, and systems that enable staff to monitor patients' participation in screening.

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