Screening for Oral Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

Description: Update of the 2004 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for oral cancer.

Methods: The USPSTF reviewed the evidence on whether screening for oral cancer reduces morbidity or mortality and on the accuracy of the oral screening examination for identifying oral cancer or potentially malignant disorders that have a high likelihood of progression to oral cancer.

Population: This recommendation applies to asymptomatic adults aged 18 years or older who are seen by primary care providers. This recommendation focuses on screening of the oral cavity performed by primary care providers and not dental providers or otolaryngologists.

Recommendation: The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for oral cancer in asymptomatic adults.

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For author affiliation, see end of text.
* For a list of USPSTF members, see the Appendix (available at www.annals.org).
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The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

SUMMARY OF RECOMMENDATION AND EVIDENCE

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for oral cancer in asymptomatic adults. (I statement)

See the Clinical Considerations section for additional information and suggestions for practice regarding the I statement.

See the Figure for a summary of the recommendation and suggestions for clinical practice.

Appendix Table 1 describes the USPSTF grades, and Appendix Table 2 describes the USPSTF classification of levels of certainty about net benefit (both tables are available at www.annals.org).

RATIONALE

Importance

Oral cavity cancer (or oral cancer) and pharyngeal cancer include cancer of the lip, oral cavity, and pharynx (nasopharynx, oropharynx, and laryngopharynx). Ninety percent of all cases of oral cavity and pharyngeal cancer are classified as squamous-cell carcinoma (1). An estimated 41,380 new cases of and 7,890 deaths from cancer of the oral cavity and pharynx will occur in 2013 (2). At the time of diagnosis, more than 50% of persons with oral and pharyngeal cancer have regional or distant metastases (3). Screening for oral cancer may be helpful if potentially malignant disorders can be identified earlier and treated successfully.

Oral and oropharyngeal cancer have different causes. Oral cavity cancer is predominantly caused by tobacco and alcohol use. Oropharyngeal cancer, another subset of neck and head cancer, includes human papillomavirus (HPV) as an important risk factor. The incidence and mortality rate of oral cancer has been decreasing in the United States presumably because of reduced tobacco and alcohol use. However, HPV-related oropharyngeal cancer is increasing...
in incidence. Oropharyngeal cancer includes lesions of the tonsil, oropharynx, and base of the tongue. The epidemiology of HPV-related oropharyngeal cancer is evolving and could have important implications for identifying high-risk populations that might benefit from screening.

**Detection**

The USPSTF found inadequate evidence that the oral screening examination accurately detects oral cancer.

**Benefits of Detection and Early Treatment**

The USPSTF found inadequate evidence that screening for oral cancer and treatment of screen-detected oral cancer improves morbidity or mortality.

**Harms of Detection and Early Treatment**

The USPSTF found inadequate evidence on the harms of screening. No study reported on harms from the screening test or from false-positive or false-negative results. Potential diagnostic harms are primarily related to the harms of biopsy for suspected oral cancer or its potential precursors. Harms of treatment for screen-detected oral cancer and its potentially malignant precursors (leukoplakia and erythroplakia) may result from complications of surgery (first-line treatment), radiation, and chemotherapy. The natural history of screen-detected oral cancer or potentially malignant disorders is unclear; thus, the magnitude of overdiagnosis due to screening is unknown.

**USPSTF Assessment**

The USPSTF concludes that the evidence is insufficient to determine the balance of benefits and harms of screening for oral cancer in asymptomatic adults by primary care providers.

**CLINICAL CONSIDERATIONS**

**Patient Population Under Consideration**

This recommendation applies to asymptomatic adults aged 18 years or older who are seen by primary care providers. This recommendation focuses on screening (visual inspection and palpation) of the oral cavity performed by primary care providers and not dental providers or otolaryngologists.

**Assessment of Risk**

Tobacco and alcohol use are major risk factors for oral cancer. A total of 20% to 30% of cases of oral cancer worldwide are attributable to cigarette smoking (1). In the United States, up to 75% of cases of oral cancer may be attributable to tobacco and alcohol use (4). Additional risk factors include male sex, older age, use of betel quid, ultraviolet light exposure, infection with *Candida* or bacterial flora, and a compromised immune system (1).

Sexually transmitted oral HPV infection (HPV-16) has recently been recognized as an increasingly important...
risk factor for oropharyngeal cancer. In the United States, the prevalence of oropharyngeal cancer due to oral HPV infection is probably as high as 80% to 95% (5). The prevalence of oral HPV infection is associated with age, sex, number of sexual partners, and number of cigarettes smoked per day. The effect of multifactorial risk assessment and screening for risk factors on oral cancer morbidity and mortality is unknown (1).

Screening Tests

The primary screening test for oral cancer is a systematic clinical examination of the oral cavity. According to the World Health Organization and the National Institute of Dental and Craniofacial Research, an oral cancer screening examination should include a visual inspection of the face, neck, lips, labial mucosa, buccal mucosa, gingiva, floor of the mouth, tongue, and palate. Mouth mirrors can help visualize all surfaces. The examination also includes palpating the regional lymph nodes, tongue, and floor of the mouth. Any abnormality that lasts for more than 2 weeks should be reevaluated and considered for biopsy (1, 6).

Oropharyngeal cancer is difficult to visualize and is usually located at the base of the tongue (the back third of the tongue), the soft palate (the back part of the roof of the mouth), the tonsils, and the side and back walls of the throat. A comprehensive examination of the oropharynx may require referral to a dental provider or specialist, which is outside the scope of this recommendation.

Additional tests proposed as adjuncts to the oral cancer screening examination include toluidine blue dye staining, chemiluminescent and autofluorescent lighting devices, and brush cytology. These screening and adjunct tests have not been adequately tested in primary care nondental settings. Although there is interest in screening for oral HPV infection, medical and dental organizations do not recommend it. Currently, no screening test for oral HPV infection has been approved by the U.S. Food and Drug Administration (FDA). Evaluating the accuracy of tests that detect oral HPV infection is a potentially promising area of research.

Suggestions for Practice Regarding the I Statement

This recommendation is intended for primary care providers and does not pertain to dental providers or otolaryngologists. Dental care providers and otolaryngologists may conduct a comprehensive examination of the oral cavity and pharynx during the clinical encounter. In deciding whether to screen for oral cancer, primary care providers should consider the following factors.

Potential Preventable Burden

Up to 75% of cases of oral cancer may be attributed to tobacco and alcohol use (4). Since 1979, the incidence rate of oral cavity cancer in the United States has been decreasing because of the reduced consumption of alcohol and smoking prevalence (1).

During this period, the incidence of HPV-positive oropharyngeal squamous-cell carcinoma has increased. Cancer registry data have shown that from 1988 to 2004, HPV-negative oropharyngeal cancer has decreased from 2.0 cases to 1.0 case per 100,000 persons and HPV-positive oropharyngeal cancer has increased more than 3-fold from 0.8 case to 2.6 cases per 100,000 persons (7). The overall prevalence of oral HPV infection is estimated to be 6.9% in adults aged 14 to 69 years in the United States. However, HPV prevalence can be as high as 20% for persons who have more than 20 lifetime sexual partners or currently use tobacco (more than 1 pack of cigarettes per day) (8).

The prevalence of type-specific HPV-16 oral infection is estimated at 1% in adults aged 14 to 69 years (an estimated 2.13 million infected persons) (8). Human papillomavirus-16 is associated with approximately 85% to 95% of cases of HPV-positive oropharyngeal cancer (5). Therefore, the increasing role of oral HPV infection as a risk factor for oropharyngeal cancer may warrant future assessment of the independent effect of HPV-16 on incidence and outcomes of oropharyngeal cancer and the health effect of screening persons who are HPV-16–positive.

Potential Harms

Suspected oral cancer or its precursors (such as erythroplakia, due to its high risk for transformation to cancer) detected through examination require confirmation by tissue biopsy, which may lead to harms. Harms of treatment of screen-detected oral cancer and its potential precursors (leukoplakia and erythroplakia) may result from complications of surgery, radiotherapy, and chemotherapy. The natural history of screen-detected oral cancer is not well-understood, and as a result, the harms from overdiagnosis and overtreatment are unknown.

Current Practice

In a 2008 survey of U.S. adults, 29.4% of those aged 18 years or older reported ever having an oral cancer examination in which a physician, dentist, or other health professional pulled on their tongue or palpated their neck. It is unknown what percentage of these examinations were conducted by dentists rather than physicians or other health professionals. Adults aged 40 years or older are more likely to have ever had an examination than those aged 18 to 39 years, despite smoking status. Adults who are most at risk for oral cancer (current smokers aged >40 years) are less likely to have ever had an oral cancer examination than former smokers or adults who have never smoked (1).

Other Approaches to Prevention

The USPSTF recommends that clinicians screen all adults for tobacco use, recommend against tobacco use,
and provide tobacco cessation interventions for those who use tobacco products (9). The USPSTF also recommends screening and behavioral counseling interventions in primary care settings to reduce alcohol misuse by adults (10).

**OTHER CONSIDERATIONS**

**Research Needs and Gaps**

One of the most important research needs is a randomized, controlled trial assessing the benefits and harms of oral cancer screening in U.S. persons who are at increased risk, such as those with a history of tobacco and heavy alcohol use. Continued research is needed to determine the accuracy of primary care providers, dental hygienists, dentists, or other trained persons screening U.S. patients who are at increased risk. Also needed is longitudinal follow-up of screening studies applicable to the United States that will show the health effect of screening for oral cancer and a clear understanding of who is at high risk in the United States. In addition, given the higher risks for death from oral cancer among African Americans and men, more research is warranted about the risks and benefits of screening in these populations.

If HPV continues to become a more clinically significant risk factor for oropharyngeal cancer, the benefits of screening for HPV and selection of populations for oral cancer screening based on HPV status will need to be assessed. As the epidemiology evolves, the most effective screening examination will need to be determined. No screening test for oral HPV infection has been approved by the FDA. More research is needed to determine the benefits and harms of screening for oropharyngeal cancer. Other areas of research include learning about the natural history of oral HPV infection.

Vaccines that reduce the risk for HPV infection are available. Whether current vaccines can prevent infection at noncervical sites and help reduce the risk for oropharyngeal cancer is unknown. Research is needed to assess the efficacy of HPV vaccines in preventing infection at noncervical sites and in decreasing the risk for oropharyngeal cancer.

**DISCUSSION**

**Burden of Disease**

According to a report from the Centers for Disease Control and Prevention and National Cancer Institute, there were 35,807 cases of oral and pharyngeal cancer in the United States in 2009, the most recent year of data available (2). Nearly three fourths of all cases occur in men, making it the eighth most common cancer in men (it is the 14th most common cancer in women) in the United States.

More than one half of all persons with oral and pharyngeal cancer have regional or distant metastases at diagnosis. Relative 5-year survival is 82.4% for localized disease, 55.5% for regional lymph node spread, and 33.2% for distant metastases (1, 3). Patients with HPV-positive oropharyngeal cancer are diagnosed an average 5 years younger and have better survival than patients with HPV-negative oral cancer (4).

African Americans previously had higher incidence rates of oral and pharyngeal cancer than white persons. However, current data indicate a change in racial or ethnic incidence rates, such that white men and women now have higher incidence rates (3). This change in incidence is ascribed to increases in HPV-related oral and pharyngeal (including oropharyngeal) cancer in white persons, along with a reduction in HPV-related and non–HPV-related oral and pharyngeal cancer in African Americans (11). American Indian and Alaska Native, Asian and Pacific Islander, and Latino men and women have lower incidence rates than white and African American men and women. Mortality rates are substantially higher in African Americans and in men; mortality rates in American Indian and Alaska Native men are about the same as in white men, but Asian, Pacific Islander, and Latino men have lower mortality rates than white men (3).

**Scope of Review**

The previous USPSTF recommendation found no evidence that screening for oral cancer led to improved health outcomes and no evidence on the harms of screening or the benefits of early treatment (12). To update its previous recommendation, the USPSTF reviewed evidence to answer the following questions: 1) Does screening for oral cancer reduce morbidity or mortality? and 2) How accurate is the screening oral examination for identifying oral cancer or potentially malignant disorders that have a high likelihood of progression to oral cancer? The focus of this recommendation is screening (visual inspection and palpation) of the oral cavity performed by primary care providers and not dental providers or otolaryngologists.

**Accuracy of Screening Tests**

No evidence was found on screening for oral cancer in the general or high-risk U.S. population. Seven studies (\(n = 49,120\)) examined the performance characteristics of the oral screening examination. These studies were generally conducted in settings with an increased incidence of and mortality rate from oral cancer (India and Taiwan) compared with U.S. rates. The studies also had considerable heterogeneity in who performed the screening and greatly varied in test performance characteristics (1). Across the 7 studies, sensitivity for oral cancer or potentially malignant disorders ranged from 18.0% to 94.3% and specificity ranged from 54.0% to 99.9%. The positive predictive value ranged from 17.0% to 86.6%, and the negative predictive value ranged from 73.0% to 99.3% (1). Two studies in the United Kingdom assessed oral examinations performed by general dentists in older adults (aged \(> = 40\) years) who were at increased risk because of alcohol and tobacco use and in a mixed sample with unknown risk factors. The dental examination in the high-
risk sample \((n = 2027)\) showed a sensitivity of 74%, specificity of 99%, and positive predictive value of 67%, whereas the study of patients with unknown risk factors found a sensitivity of 71%, specificity of 99%, and positive predictive value of 86%. Although the patients in the U.K. study may be similar to those in the U.S. population, the results of these studies are limited by an imperfect reference standard (comparison with a “more expert” examiner), by combining the detection of potentially malignant disorders with that of oral cancer, and by an unclear delineation of high-risk status. These results would need to be confirmed by studies with longitudinal follow-up (1).

When compared with expert or trained screening examinations, self-examinations in 2 studies performed in India and the United Kingdom were insensitive (18% and 33%, respectively) (1). Toluidine blue was not found to significantly improve screening for premalignant or malignant lesions, did not affect the incidence of oral cancer, and did not improve outcomes (1 study). No acceptable evidence for other adjunctive devices was found in the literature (1).

**Effectiveness of Early Detection and Treatment**

No direct evidence was available on whether screening reduces morbidity or mortality in general or high-risk U.S. populations. One fair-quality, randomized, controlled trial of home-based screening for oral cancer by advanced health workers \((n = 191,873)\) conducted in Kerala, India, found no statistical difference in oral cancer mortality rates between screening and control groups after 9 years of follow-up (rate ratio, 0.79 [95% CI, 0.51 to 1.22]) (1, 10). After an additional screening round and 15 years of follow-up, oral cancer mortality ratios were of similar magnitude and not statistically significant (13). Screened participants were diagnosed with oral cancer at earlier stages with a greater 5-year survival than control participants, possibly as a result of lead-time bias (1, 14).

A post hoc subgroup analysis of participants in the Kerala study who reported tobacco and alcohol use \((n = 84,600)\) found a significant reduction in oral cancer mortality rates in those assigned to the screening group (rate ratio, 0.66 [CI, 0.45 to 0.95]). A similar post hoc analysis at 15 years suggested a decreased but still significant oral cancer mortality reduction in the screening group (rate ratio, 0.76 [CI, 0.60 to 0.97]) (13). However, the subgroup analyses do not meet high-quality criteria. The results of the overall study and the post hoc subgroup analysis do not provide sufficient evidence on screening because of limited applicability to the U.S. population and methodological limitations, such as inadequate accounting for clustering in the results, low adherence to follow-up, imbalance in baseline risk factors, possible lead- and length-time bias, and not reporting harms of screening or how lesions were treated. In addition, these participants commonly chewed paan (a carcinogenic compound containing areca nut and betel leaf), which is not used in the United States and affects the generalizability of this study. India also has higher oral cancer incidence, prevalence, and mortality, as well as a different health care system, than the United States, which also affects the applicability of the study results in the U.S. population (1, 14).

**Potential Harms of Screening and Treatment**

A potentially important harm of screening for oral cancer is adverse effects from biopsy or surgery performed on oral lesions that would have regressed spontaneously or not have progressed to cancer during a patient’s lifetime (overdiagnosis and overtreatment). There was insufficient evidence on harms from the screening test or from false-positive or false-negative results.

**Estimate of Magnitude of Net Benefit**

The USPSTF found inadequate evidence on the diagnostic accuracy, benefits, and harms of screening for oral cancer. Therefore, the USPSTF was unable to determine the balance of benefits and harms.

**How Does Evidence Fit With Biological Understanding?**

The oral cancer examination is designed to detect oral cancer or potentially malignant disorders at earlier stages. However, visual examination or biopsy cannot reliably distinguish potentially malignant disorders from lesions that may spontaneously regress or not progress (overdiagnosis), and evidence that earlier treatment improves health outcomes is lacking. Test performance characteristics for the oral screening examinations also varied widely.

The natural history of oropharyngeal cancer is not well-understood. Knowledge of this particular cancer is evolving as more is learned about the association between oropharyngeal cancer and HPV. More evidence is needed to address effective screening strategies, treatment, and primary prevention. Clinical outcomes may differ among countries on the basis of predominant cause because patients with HPV-positive oropharyngeal cancer are generally diagnosed younger and survive longer than patients with HPV-negative oral cancer.

**Response to Public Comments**

A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 9 April to 6 May 2013. In response to these comments, the USPSTF added additional language to the Rationale, Clinical Considerations, and Discussion sections to emphasize that the recommendation statement applies to primary care providers and not dental providers. Additional language was added throughout the recommendation statement to further define oral cancer and oropharyngeal cancer. Language addressing HPV vaccination and screening tools was added to the Research Needs and Gaps section. Clarifying language about adjunct screening tools was added to the Accuracy of Screening Tests section. Additional language was also added to describe the oral cavity examination in the Clinical Considerations section.
Screening for Oral Cancer

UPDATE OF THE PREVIOUS USPSTF RECOMMENDATION

In 2004, the USPSTF issued an I statement for screening for oral cancer because it found no evidence that screening for oral cancer led to improved health outcomes and no evidence on the harms of screening or the benefits of early treatment (12).

In the current recommendation, the USPSTF found inadequate evidence that the oral screening examination accurately detects oral cancer. It also found inadequate evidence that screening for oral cancer and treatment of screen-detected oral cancer improves morbidity or mortality. The evidence for screening for oral cancer remains insufficient; therefore, the USPSTF is unable to make a recommendation in favor of or against screening (I statement).

RECOMMENDATIONS OF OTHERS

The American Academy of Family Physicians concluded that the current evidence is insufficient to assess the balance of benefits and harms of screening for oral cancer in asymptomatic adults (15). The American Cancer Society recommends that adults aged 20 years or older who have periodic health examinations should have the oral cavity examined as part of a cancer-related checkup (16).

The American Dental Association recommends that patients who use tobacco or have periodic health examinations should have the oral cavity examined as part of a cancer-related checkup (16).

The evidence for screening for oral cancer remains insufficient. The American Cancer Society concluded that the current evidence is insufficient to assess the balance of benefits and harms of screening for oral cancer (16).

The American Dental Association recommends that patients who use tobacco or have periodic health examinations should have the oral cavity examined as part of a cancer-related checkup (16).

From the U.S. Preventive Services Task Force, Rockville, Maryland.

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Potential Conflicts of Interest: Dr. Moyer: Support for travel to meetings for the study or other purposes: Agency for Healthcare Research and Quality. Disclosure forms from USPSTF members can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M13-2568.

Requests for Single Reprints: Reprints are available from the USPSTF Web site (www.uspreventiveservicestaskforce.org).

References


**APPENDIX: U.S. PREVENTIVE SERVICES TASK FORCE**

Members of the U.S. Preventive Services Task Force at the time this recommendation was finalized† are Virginia A. Moyer, MD, MPH, *Chair* (American Board of Pediatrics, Chapel Hill, North Carolina); Michael L. LeFevre, MD, MSPH, *Co-Vice Chair* (University of Missouri School of Medicine, Columbia, Missouri); Albert L. Siu, MD, MSPH, *Co-Vice Chair* (Mount Sinai School of Medicine, New York, and James J. Peters Veterans Affairs Medical Center, Bronx, New York); Linda Ciofu Baumann, PhD, RN (University of Wisconsin, Madison, Wisconsin); Kirsten Bibbins-Domingo, PhD, MD (University of California, San Francisco, California); Susan J. Curry, PhD (University of Iowa College of Public Health, Iowa City, Iowa); Mark Ebell, MD, MS (University of Georgia, Athens, Georgia); Glenn Flores, MD (University of Texas Southwestern, Dallas, Texas); Francisco A.R. García, MD, MPH (Pima County Department of Health, Tucson, Arizona); Adelita Gonzales Cantu, RN, PhD (University of Texas Health Science Center, San Antonio, Texas); David C. Grossman, MD, MPH (Group Health Cooperative, Seattle, Washington); Jessica Herstein, MD, MPH (Air Products, Allentown, Pennsylvania); Wanda K. Nicholson, MD, MPH, MBA (University of North Carolina School of Medicine, Chapel Hill, North Carolina); Douglas K. Owens, MD, MS (Veterans Affairs Palo Alto Health Care System, Palo Alto, and Stanford University, Stanford, California); William R. Phillips, MD, MPH (University of Washington, Seattle, Washington); and Michael P. Pignone, MD, MPH (University of North Carolina, Chapel Hill, North Carolina).

† For a list of current Task Force members, go to www.uspreventiveservicestaskforce.org/members.htm.

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**Appendix Table 1. What the USPSTF Grades Mean and Suggestions for Practice**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
<th>Suggestions for Practice</th>
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<tbody>
<tr>
<td>A</td>
<td>The USPSTF recommends the service. There is high certainty that the net benefit is substantial.</td>
<td>Offer/provide this service.</td>
</tr>
<tr>
<td>B</td>
<td>The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.</td>
<td>Offer/provide this service.</td>
</tr>
<tr>
<td>C</td>
<td>The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.</td>
<td>Offer/provide this service for selected patients depending on individual circumstances.</td>
</tr>
<tr>
<td>D</td>
<td>The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.</td>
<td>Discourage the use of this service.</td>
</tr>
<tr>
<td>I statement</td>
<td>The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.</td>
<td>Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.</td>
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Appendix Table 2. USPSTF Levels of Certainty Regarding Net Benefit

<table>
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<tr>
<th>Level of Certainty</th>
<th>Description</th>
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<tr>
<td>High</td>
<td>The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.</td>
</tr>
<tr>
<td>Moderate</td>
<td>The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: the number, size, or quality of individual studies; inconsistency of findings across individual studies; limited generalizability of findings to routine primary care practice; and lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.</td>
</tr>
<tr>
<td>Low</td>
<td>The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: the limited number or size of studies; important flaws in study design or methods; inconsistency of findings across individual studies; gaps in the chain of evidence; findings that are not generalizable to routine primary care practice; and a lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.</td>
</tr>
</tbody>
</table>

* The USPSTF defines certainty as “likelihood that the USPSTF assessment of the net benefit of a preventive service is correct.” The net benefit is defined as benefit minus harm of the preventive service as implemented in a general primary care population. The USPSTF assigns a certainty level on the basis of the nature of the overall evidence available to assess the net benefit of a preventive service.