

Screening for Asymptomatic Carotid Artery Stenosis: U.S. Preventive Services Task Force Recommendation Statement

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Description: Update of the 2007 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for carotid artery stenosis.

Methods: The USPSTF commissioned a systematic review to synthesize the evidence on the accuracy of screening tests, externally validated risk-stratification tools, the benefits of treatment of asymptomatic carotid artery stenosis with carotid endarterectomy (CEA) or carotid angioplasty and stenting (CAAS), the benefits from medications added to current standard medical therapy, and the harms of screening and treatment with CEA or CAAS.

Population: This recommendation applies to adults without a history of transient ischemic attack, stroke, or other neurologic signs or symptoms.

Recommendation: The USPSTF recommends against screening for asymptomatic carotid artery stenosis in the general adult population. (D recommendation)

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* 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 recommends against screening for asymptomatic carotid artery stenosis (CAS) in the general adult population. (D recommendation)

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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

Stroke is a leading cause of death and disability in the United States. Although asymptomatic CAS is a risk factor for stroke, it causes a relatively small proportion of strokes.

Detection

The most feasible screening test for CAS (defined as 60% to 99% stenosis) is ultrasonography. Although adequate evidence indicates that this test has high sensitivity and specificity, in practice, ultrasonography yields many false-positive results in the general population, which has a low prevalence of CAS (approximately 0.5% to 1%). There are no externally validated, reliable tools that can determine who is at increased risk for CAS or for stroke when CAS is present. Adequate evidence indicates that the accuracy of screening by auscultation of the neck is poor.

Benefits of Detection and Early Intervention

There is no direct evidence on the benefits of screening for CAS. Adequate evidence indicates that in selected trial participants with asymptomatic CAS, carotid endarterectomy (CEA) performed by selected surgeons reduces the absolute incidence of all strokes or perioperative death by

Figure. Screening for asymptomatic carotid artery stenosis: clinical summary of U.S. Preventive Services Task Force recommendation.

Annals of Internal Medicine



SCREENING FOR ASYMPTOMATIC CAROTID ARTERY STENOSIS CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Adults without a history of transient ischemic attack, stroke, or other neurologic signs or symptoms
Recommendation	Do not screen for asymptomatic carotid artery stenosis in the general adult population. Grade: D
Risk Assessment	The major risk factors for carotid artery stenosis include older age, male sex, hypertension, smoking, hypercholesterolemia, diabetes mellitus, and heart disease.
Screening Tests	All screening strategies, including ultrasonography with or without confirmatory tests (digital subtraction or magnetic resonance angiography), have imperfect sensitivity and could lead to unnecessary surgery and result in serious harms, including death, stroke, and myocardial infarction. There is no evidence that screening by auscultation of the neck to detect carotid bruits is accurate or provides benefit.
Balance of Benefits and Harms	The harms of screening for asymptomatic carotid artery stenosis outweigh the benefits.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on many factors related to stroke prevention, including screening for hypertension, screening for dyslipidemia, the use of nontraditional coronary heart disease risk factors, counseling on smoking, and counseling on healthful diet and physical activity. In addition, the USPSTF recommends the use of aspirin for persons at increased risk for cardiovascular disease. These recommendations are available on the USPSTF Web site (www.uspreventiveservicestaskforce.org).

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to www.uspreventiveservicestaskforce.org.

approximately 3.5% compared with (outdated) medical management. However, this difference is probably smaller with current optimal medical management (1). The magnitude of these benefits would be smaller in asymptomatic persons in the general population. For the general primary care population, the magnitude of benefit is small to none. There is no evidence that identification of asymptomatic CAS leads to any benefit from adding or increasing medication doses (beyond current standard medical therapy for cardiovascular disease prevention).

Harms of Detection and Early Intervention

Adequate evidence indicates that both the testing strategy for CAS and treatment with CEA can cause harms. Although screening with ultrasonography has few direct harms, all screening strategies, including those with or without confirmatory tests (that is, digital subtraction or magnetic resonance angiography), have imperfect sensitivity and specificity and could lead to unnecessary interventions and result in serious harms. In selected centers similar to those in the trials, CEA is associated with a 30-day stroke or mortality rate of approximately 2.4%; reported rates are as high as approximately 5% in low-volume centers and 6% in certain states (1). Myocardial infarctions

(MIs) are reported in 0.8% to 2.2% of patients after CEA. The 30-day stroke or mortality rate after carotid angioplasty and stenting (CAAS) is approximately 3.1% to 3.8%. The overall magnitude of harms of screening and subsequent treatment of asymptomatic CAS is small to moderate depending on patient population, surgeon, center volume, and geographic location.

USPSTF Assessment

The USPSTF concludes with moderate certainty that the harms of screening for asymptomatic CAS outweigh the benefits.

CLINICAL CONSIDERATIONS

Patient Population Under Consideration

This recommendation applies to adults without a history of transient ischemic attack, stroke, or other neurologic signs or symptoms. It was based on evidence of the benefits and harms of screening using ultrasonography to detect narrowing of the carotid arteries. A previous USPSTF review on the assessment of carotid intima-media thickness in 2009 found insufficient evidence to support its use as a screen for coronary heart disease risk. For this

recommendation, the USPSTF did not review new evidence on ultrasonography to characterize carotid plaque structure or intima-media thickness and their association with cardiovascular disease events. However, clinicians considering using ultrasonography to characterize carotid plaque to stratify patient risk for cardiovascular disease should consider the same harms that the USPSTF evaluated for this recommendation (stroke, MI, and death from CEA) because surgery may result from this screen.

Assessment of Risk

The major risk factors for CAS include older age, male sex, hypertension, smoking, hypercholesterolemia, diabetes mellitus, and heart disease. Despite evidence on important risk factors, there are no externally validated, reliable methods to determine who is at increased risk for CAS or for stroke when CAS is present.

Screening Tests

Although screening with ultrasonography has few direct harms, all screening strategies, including those with or without confirmatory tests (that is, digital subtraction or magnetic resonance angiography), have imperfect sensitivity and specificity and could lead to unnecessary surgery and result in serious harms, including death, stroke, and MI. There is no evidence that screening by auscultation of the neck to detect carotid bruits is accurate or provides benefit.

Useful Resources

The USPSTF has made recommendations on many factors related to stroke prevention, including screening for hypertension, screening for dyslipidemia, the use of non-traditional coronary heart disease risk factors, counseling on smoking, and counseling on healthful diet and physical activity. In addition, the USPSTF recommends the use of aspirin for persons at increased risk for cardiovascular disease. These recommendations are available on the USPSTF Web site (www.uspreventiveservicestaskforce.org).

OTHER CONSIDERATIONS

Research Needs and Gaps

Valid and reliable tools are needed to determine which persons are at high risk for CAS or for stroke due to CAS and who might experience harm from treatment with CEA or CAAS. Studies comparing CEA or CAAS with current standard medical therapy are needed. The planned CREST-2 (Carotid Revascularization Endarterectomy versus Stenting Trial 2) may provide important data for future recommendations. CREST-2 will study 2400 patients with greater than 70% stenosis who are randomly assigned to CAAS with intensive medical management versus intensive medical management alone or to CEA with intensive medical management versus intensive medical management alone.

DISCUSSION

Burden of Disease

Stroke is a leading cause of death and disability in the United States. Mortality from all strokes has decreased substantially over the past 5 decades; improved blood pressure control is believed to be the most important factor accounting for this decrease (2). Other factors, including treatment and control of diabetes and hyperlipidemia, are also reported to be important contributors. Most strokes are ischemic (80% to 90%), and approximately 10% to 20% are from hemorrhagic causes.

In a population-based U.S. study from 1999, the age-adjusted incidence rates for ischemic stroke subtypes were 40 per 100 000 persons for stroke due to cardioembolic causes, 27 per 100 000 persons for stroke due to atherosclerosis causes, 25 per 100 000 persons for lacunar stroke (small vessel disease), and 52 per 100 000 persons for stroke due to unknown causes (3). Strokes resulting from large artery atherothrombotic disease (such as CAS) in previously asymptomatic patients (the focus of this recommendation) account for a relatively small proportion of all strokes.

The best available data from U.S.-based studies report that the overall estimated prevalence of CAS (defined as 70% or 75% to 99% stenosis) is 0.5% to 1% (1). Studies have found that the condition is more prevalent in older adults, smokers, persons with hypertension, and persons with heart disease. Evidence shows that the incidence of stroke caused by CAS has been decreasing (1). Research has not shown any single risk factor or clinically useful risk-stratification tool that can reliably and accurately distinguish between persons who have clinically important CAS and those who do not.

Scope of Review

In 2007, the USPSTF recommended against screening for asymptomatic CAS in the general adult population. To update its recommendation, the USPSTF commissioned a systematic review to synthesize the evidence on the accuracy of screening tests, externally validated risk-stratification tools, the benefits of treatment of asymptomatic CAS with CEA or CAAS, the benefits from medications added to current standard medical therapy, and the harms of screening and treatment with CEA or CAAS.

Accuracy of Screening Tests

Three meta-analyses and 3 primary studies assessed the accuracy or reliability of duplex ultrasonography (DUS) to detect CAS (1). A good-quality meta-analysis included studies published from 1966 to 2003 and used digital subtraction angiography as the reference standard (4). Authors reported a sensitivity of 98% (95% CI, 97% to 100%) and a specificity of 88% (CI, 76% to 100%) for detecting CAS of 50% or greater. Sensitivity and specificity for detecting CAS of 70% or greater were 90% (CI, 84% to 94%) and 94% (CI, 88% to 97%), respectively. This evidence is lim-

ited by the lack of reporting on whether (or what proportion of) asymptomatic patients were included.

The reliability of DUS to detect potentially clinically important CAS is limited. A good-quality meta-analysis reported wide variation in measurement properties between laboratories, with clinically important variation in the magnitude of the variation (4). Potential sources of heterogeneity of measurements include differences in patients, study designs, equipment, techniques, and methods of classification or training. One study of 1006 carotid arteries reported poor agreement between readers for the differentiation of stenoses of less than 70% (45% agreement; $\kappa = 0.26$ [CI, 0.23 to 0.29]) but excellent agreement for stenoses of 70% or greater (96% agreement; $\kappa = 0.85$ [CI, 0.83 to 0.87]) (5). Results of DUS screening can also vary on the basis of the type of scanner, the velocity cut points or ratios used, the Doppler angle employed, and inherent variability between facilities and observers (1, 6).

Four studies assessed the use of auscultation for carotid bruits to detect CAS (7–10). Reported sensitivity ranged from 46% to 77%, and specificity ranged from 71% to 98%. However, none of the studies used angiography as a gold standard, and only 2 studies involved patients from the general population.

No externally validated risk-stratification tools can reliably distinguish between persons who have clinically important CAS and those who do not or those who will experience harm after treatment with CEA or CAAS.

Effectiveness of Early Detection and Treatment

There are no studies on the direct benefit of screening for asymptomatic CAS. Three randomized, controlled trials (RCTs) evaluated the benefit of treating asymptomatic CAS with CEA: ACAS (Asymptomatic Carotid Atherosclerosis Study) (11), VACS (Veterans Affairs Cooperative Study) (12), and ACST (Asymptomatic Carotid Surgery Trial) (13). These RCTs studied 5226 patients randomly assigned to treatment of asymptomatic CAS with CEA or medical therapy alone and followed the patients for 2.7 to 9 years. Two of the studies (ACAS and VACS) were conducted in North America, and ACST was conducted in 30 countries, primarily in Europe. The mean age of patients was 65 to 68 years, and they were required to have at least 50% (VACS) or 60% (ACAS and ACST) stenosis of the carotid artery. In the 2 North American trials, most patients (87% to 95%) were white. Two thirds of the patients in ACAS and ACST and all of the patients in VACS were men.

The evidence has important limitations, including the lack of studies focusing on a population identified by screening in primary care. In addition, many of the enrolled patients were not completely asymptomatic. Although study patients were required to be recently asymptomatic for the carotid artery under study, 20% to 24% had a history of contralateral CEA and 25% to 32% had a history of contralateral transient ischemic attack or stroke

in trials reporting baseline data for these characteristics. ACST allowed the enrollment of patients who had a transient ischemic attack or stroke attributable to the carotid artery under study if it occurred more than 6 months before enrollment, and ACAS included patients if their symptoms referable to the contralateral artery occurred more than 45 days before enrollment. Medical therapy varied across trials and was not clearly defined or standardized, although all patients received aspirin in ACAS and VACS. Surgeons were highly selected and were required to submit records of their 50 most recent cases (ACAS and ACST) or previous 24 months performing CEA (VACS); they were selected on the basis of demonstrated low morbidity and mortality rates. In addition, the ACAS and ACST trial protocols did not allow further enrollment of patients by surgeons or institutions that showed unacceptably high morbidity or mortality during the trial.

In general, the RCTs reported results combining stroke and death outcomes during the perioperative period 30 days after surgery and during the time subsequent to this period. Pooled estimates from the 3 RCTs found that, compared with patients receiving medical treatment alone, 2.0% fewer patients randomly assigned to CEA had perioperative stroke or death and subsequent ipsilateral stroke. Pooled estimates on the outcome of death, perioperative stroke, or any subsequent stroke reported that 3.5% fewer patients treated with CEA had this outcome than those in medical treatment groups (1).

No studies compared CAAS with medical therapy or studied the incremental benefit of additional medications beyond current standard medical therapy.

Potential Harms of Screening and Treatment

No studies examined the direct harms of screening. Although angiography is less commonly used now as a confirmatory test, harms from it occurred in 2 of the previously discussed RCTs. In ACAS, 1.2% of patients (5 of 414) who had angiography developed strokes, and 1 of these patients died. In VACS, 0.4% of patients (3 of 714) had nonfatal strokes after angiography (1).

The 3 previously discussed RCTs, 8 studies based on additional trials, and 8 cohort studies provided data on harms of treatment. Four of the additional trials include the CASANOVA (Carotid Artery Stenosis with Asymptomatic Narrowing: Operation Versus Aspirin) trial (14), the MACE (Mayo Asymptomatic Carotid Endarterectomy) trial (15), CREST (16, 17), and the SAPPHERE (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) trial (18). The MACE and CASANOVA trials were conducted in the early 1990s and included 252 patients with 50% to 99% CAS, confirmed by angiography, who were randomly assigned to treatment with CEA. Patients in both trials were predominantly male (56% to 63%); most (60% to 64%) had hypertension, and 42% to 44% had coronary artery disease. Data on harms were provided by 2 other multicenter RCTs (CREST and

the SAPPHIRE trial), which compared CEA with CAAS. The SAPPHIRE trial required that participants have at least 1 condition suggesting high surgical risk (for example, age >80 years, severe pulmonary disease, or contralateral carotid occlusion). Prevalence of hypertension in CREST and the SAPPHIRE trial was 85% to 88%, prevalence of diabetes in the trials was 25% to 33%, and prevalence of coronary artery disease was 81% in the SAPPHIRE trial and 44% in CREST. In both trials, interventionalists had to demonstrate low complication rates before participating. Eight multicenter cohort studies using Medicare claims and enrollment databases reported perioperative harms of CEA.

Pooled analysis of data from 6 trials ($n = 3435$) showed that 2.4% (CI, 1.7% to 3.1%) of patients died or had a stroke in the 30-day period after CEA, which was 1.9% more (CI, 1.2% to 2.6%) than in the medical therapy groups in the 3 trials ($n = 5223$) directly comparing CEA with medical therapy (1). Pooled data from cohort studies showed a 3.3% rate of death or stroke after CEA at 30 days. One cohort study on harms from CAAS, the CREST lead-in study, found a stroke or death rate of 3.8% (CI, 2.9% to 5.1%) (19). A meta-analysis of 2 trials ($n = 6152$) found a stroke or death rate of 3.1% (CI, 2.7% to 3.6%) after CAAS (1).

Other important harms after surgical intervention for CAS include MI and surgical complications. In ACST, MIs occurred in 0.6% more patients in the CEA group than in the medical group. VACS reported 4 events in the CEA group and none in the medical therapy group. One cohort study of 6 New York hospitals, which included 1378 Medicare beneficiaries who received CEA for asymptomatic CAS during 1997 to 1998, reported a 0.85% rate of nonfatal MI (20). A similar 1993 study of Medicare beneficiaries in Georgia ($n = 1002$) reported a 0.8% rate of MI and a 0.6% rate of MI-related death (21). Cranial nerve injury is another important potential harm; it occurred in 3.8% of patients (8 of 211) who received CEA in VACS, but none had permanent disability. The CASA-NOVA trial reported such CEA complications as lung embolism (1.4%), permanent cranial nerve damage (4.2%), pneumonia (1.4%), and local hematoma requiring surgery (2.8%). The total frequency of major complications (such as death, stroke, minor stroke, MI, and permanent cranial nerve damage) in the group randomly assigned to immediate surgery was 7.9%. The MACE trial reported a 1.1% rate of minor cranial nerve injury in the 36 patients randomly assigned to CEA.

The volume of patients treated by individual surgeons and centers is often suggested as an important factor that may affect outcomes. The USPSTF reviewed studies using Medicare data that reported the relationship between patient volume and adverse events after CEA. One study of Medicare beneficiaries who had CEA (350 procedures) during 1993 to 1994 in Oklahoma found combined 30-day stroke and death rates of 3.5% at high-volume hospi-

tals (>100 Medicare-covered CEAs performed over the study period) and 5.2% at low-volume centers (22). A similar study of Medicare beneficiaries who received CEA at 115 hospitals in Ohio (167 procedures) reported stroke or death rates of 0% at high-volume centers and 4.9% at low-volume centers during 1993 to 1994 (23). A major limitation of the evidence on harms associated with CEA is the dearth of recent data: All of the observational studies reporting on 30-day perioperative harms after CEA were based on data from the 1990s.

Estimate of Magnitude of Net Benefit

The USPSTF found no evidence that screening for CAS leads to additional treatment and benefit beyond standard preventive treatments based on traditional cardiovascular risk factors. In patients and surgeons similar to those in the RCTs, treatment with CEA for asymptomatic CAS can result in a net absolute reduction in stroke rates, but this benefit has been shown only in selected patients with selected surgeons and must be weighed against a small increase in nonfatal MIs. The net benefit of CEA largely depends on patients surviving the perioperative period without complications and living for at least 5 years. The magnitude of these benefits would be smaller in asymptomatic persons in the general population than among patients in RCTs.

For the general primary care population, the magnitude of benefit is small to none. Adequate evidence indicates that both the testing strategy for CAS and treatment with CEA or CAAS can cause serious harms. In selected centers similar to those in the trials, CEA is associated with a 30-day stroke or mortality rate of approximately 2.4%; reported rates are as high as approximately 5% in low-volume centers and 6% in certain states. Myocardial infarctions are reported in 0.8% to 2.2% of patients after CEA. The 30-day stroke or mortality rate after CAAS is approximately 3.1% to 3.8%. The overall magnitude of harms is small to moderate depending on patient population, surgeon, center volume, and geographic location.

The USPSTF concludes with moderate certainty that the harms of screening for asymptomatic CAS outweigh the benefits.

How Does Evidence Fit With Biological Understanding?

The medical treatment groups in the RCTs were poorly defined and probably did not include the intensive blood pressure and lipid control that is currently standard practice for the prevention of cardiovascular disease. It is difficult to determine what effect current standard medical therapy would have on comparative outcomes of medical and surgical treatments, including the potential incremental benefit of CEA.

UPDATE OF PREVIOUS USPSTF RECOMMENDATION

This recommendation is an update of the 2007 recommendation on screening for CAS, which also concluded

that the general asymptomatic adult population should not be screened for the condition.

RESPONSE TO PUBLIC COMMENT

A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 18 February through 17 March 2014. All comments were reviewed and considered by the USPSTF. Many commenters agreed with the draft recommendation. Several requested clarification on the focus of this recommendation; the recommendation statement was revised to clarify that, for this recommendation, the USPSTF did not review new evidence on the use of carotid artery ultrasonography to evaluate risk for cardiovascular disease. A few commenters provided citations for related medical articles, and the USPSTF reviewed these for relevance to the current recommendation.

RECOMMENDATIONS OF OTHERS

In 2010, the American Heart Association and the American Stroke Association recommended against screening the general population for asymptomatic CAS (24). In 2011, the American College of Cardiology Foundation and the American Heart Association, in collaboration with several other organizations, including the American Stroke Association, American Association of Neurological Surgeons, American College of Radiology, American Society of Neuroradiology, Society for Vascular Surgery, and Society for Vascular Medicine, recommended against the use of carotid DUS for routine screening of asymptomatic patients with no clinical manifestations of or risk factors for atherosclerosis (25). The Society for Vascular Surgery also released a guideline in 2011 stating that routine screening to detect clinically asymptomatic CAS in the general population is not recommended (26). The American Academy of Family Physicians recommends against screening for asymptomatic CAS in the general adult population (27).

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

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Annals staff will be at these upcoming meetings:

Infectious Disease Week, Philadelphia, 9–11 October 2014 (Booth 191)

Chest, Austin, Texas, 25–30 October 2014 (Booth 1737)

Kidney Week, Philadelphia, 13–15 November 2014 (Booth 1711)

American College of Rheumatology, Boston, 16–18 November 2014 (Booth 11)

Stop by the ACP/*Annals* booth and register to be a peer reviewer or discuss your thoughts for submissions or topic coverage with *Annals* staff.

APPENDIX: U.S. PREVENTIVE SERVICES TASK FORCE

Members of the U.S. Preventive Services Task Force at the time this recommendation was finalized† are Michael L. LeFevre, MD, MSPH, *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); Kirsten Bibbins-Domingo, PhD, MD, *Co-Vice Chair* (University of California, San Francisco, and San Francisco General Hospital, San Francisco, California); Linda Ciofu Baumann, PhD, RN (University of Wisconsin, Madison, Wisconsin); Susan J. Curry, PhD (University of Iowa College of Public Health, Iowa City, Iowa); Karina W. Davidson, PhD, MAsc (Columbia University Medical Center, New York, New York); Mark Ebell, MD, MS (University of Georgia, Athens, Georgia); Francisco A.R. García, MD, MPH (Pima County Department of Health, Tucson, Arizona);

Matthew W. Gillman, MD, SM (Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, Massachusetts); Jessica Herzstein, MD, MPH (Air Products, Allentown, Pennsylvania); Alex R. Kemper, MD, MPH, MS (Duke University, Durham, North Carolina); Ann E. Kurth, PhD, RN, MSN, MPH (Global Institute of Public Health, New York, New York); Douglas K. Owens, MD, MS (Freeman Spogli Institute for International Studies, Stanford University, Stanford, California); William R. Phillips, MD, MPH (University of Washington, Seattle, Washington); Maureen G. Phipps, MD, MPH (Warren Alpert Medical School, Brown University, Providence, Rhode Island); 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.

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

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	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.	Offer/provide this service.
C	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.	Offer/provide this service for selected patients depending on individual circumstances.
D	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.	Discourage the use of this service.
I statement	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.	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.

Appendix Table 2. USPSTF Levels of Certainty Regarding Net Benefit

Level of Certainty*	Description
High	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.
Moderate	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.
Low	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.

* 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.