

# Screening for Asymptomatic Carotid Artery Stenosis

## US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

**IMPORTANCE** Carotid artery stenosis is atherosclerotic disease that affects extracranial carotid arteries. Asymptomatic carotid artery stenosis refers to stenosis in persons without a history of ischemic stroke, transient ischemic attack, or other neurologic symptoms referable to the carotid arteries. The prevalence of asymptomatic carotid artery stenosis is low in the general population but increases with age.

**OBJECTIVE** To determine if its 2014 recommendation should be reaffirmed, the US Preventive Services Task Force (USPSTF) commissioned a reaffirmation evidence review. The reaffirmation update focused on the targeted key questions on the potential benefits and harms of screening and interventions, including revascularization procedures designed to improve carotid artery blood flow, in persons with asymptomatic carotid artery stenosis.

**POPULATION** This recommendation statement applies to adults without a history of transient ischemic attack, stroke, or other neurologic signs or symptoms referable to the carotid arteries.

**EVIDENCE ASSESSMENT** The USPSTF found no new substantial evidence that could change its recommendation and therefore concludes with moderate certainty that the harms of screening for asymptomatic carotid artery stenosis outweigh the benefits.

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

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**Group Information:** The US Preventive Services Task Force (USPSTF) members are listed at the end of this article.

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### Summary of Recommendation

The USPSTF recommends against screening for asymptomatic carotid artery stenosis in the general adult population.

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See the Figure for a more detailed summary of the recommendations for clinicians. See the Practice Considerations section for a description of adults at increased risk. USPSTF indicates US Preventive Services Task Force.

**C**arotid artery stenosis is atherosclerotic disease that affects extracranial carotid arteries. Asymptomatic carotid artery stenosis refers to stenosis in persons without a history of ischemic stroke, transient ischemic attack, or other neurologic symptoms referable to the carotid arteries. The prevalence of asymptomatic carotid artery stenosis is low in the general population but increases with age.<sup>1</sup> Although asymptomatic carotid artery stenosis is a risk factor for stroke and a marker for increased risk for myocardial infarction, it causes a relatively small proportion of strokes.<sup>2</sup> Stroke is a leading cause of death and disability in the US.<sup>3</sup>

a D recommendation.<sup>4</sup> The USPSTF has decided to use a reaffirmation deliberation process<sup>5</sup> to update this recommendation. The USPSTF uses the reaffirmation process for well-established, evidence-based standards of practice in current primary care practice for which only a very high level of evidence would justify a change in the grade of the recommendation.<sup>5</sup> In its deliberation of the evidence, the USPSTF considers whether the new evidence is of sufficient strength and quality to change its previous conclusions about the evidence.

Using a reaffirmation process, the USPSTF concludes with moderate certainty that the harms of screening for asymptomatic carotid artery stenosis outweigh the benefits.

See the Figure, Table, and eFigure in the Supplement for more information on the USPSTF recommendation rationale and assessment. For more details on the methods the USPSTF uses to determine the net benefit, see the USPSTF Procedure Manual.<sup>5</sup>

### USPSTF Assessment of Magnitude of Net Benefit

#### Reaffirmation

In 2014, the US Preventive Services Task Force (USPSTF) reviewed the evidence for screening for carotid artery stenosis and issued

Figure. Clinician Summary: Screening for Asymptomatic Carotid Artery Stenosis

What does the USPSTF recommend?	For the general adult population: Do not screen for asymptomatic carotid artery stenosis. <u>Grade D</u>
To whom does this recommendation apply?	This recommendation applies to adults without a history of stroke or neurologic signs or symptoms of a transient ischemic attack.
What's new?	This recommendation is consistent with the 2014 USPSTF recommendation. The USPSTF continues to recommend against screening for carotid artery stenosis in asymptomatic adults.
How to implement this recommendation?	<b>Do not screen.</b> The USPSTF found that the harms of screening for asymptomatic carotid artery stenosis outweigh the benefits. Clinicians should remain alert to the signs and/or symptoms of carotid artery stenosis and evaluate as appropriate.
What are other relevant USPSTF recommendations?	The USPSTF has made other recommendations related to stroke prevention and cardiovascular health. These include <ul style="list-style-type: none"> <li>• Screening for high blood pressure in adults</li> <li>• Screening for abdominal aortic aneurysm</li> <li>• Interventions for tobacco smoking cessation in adults, including pregnant persons</li> <li>• Interventions to promote a healthy diet and physical activity for the prevention of cardiovascular disease:                         <ul style="list-style-type: none"> <li>◦ In adults with cardiovascular risk factors</li> <li>◦ In adults without known cardiovascular risk factors</li> </ul> </li> <li>• Aspirin use to prevent cardiovascular disease and colorectal cancer</li> <li>• Statin use for the primary prevention of cardiovascular disease in adults</li> </ul> These recommendations are available at <a href="https://www.uspreventiveservicestaskforce.org">https://www.uspreventiveservicestaskforce.org</a>
Where to read the full recommendation statement?	Visit the USPSTF website to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

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.

Table. Summary of USPSTF Rationale: Screening for Asymptomatic Carotid Artery Stenosis

Rationale	General adult population
Detection	<ul style="list-style-type: none"> <li>• Adequate evidence that duplex ultrasonography has reasonable sensitivity and specificity for detecting clinically relevant carotid artery stenosis. However, duplex ultrasonography yields many false-positive results when screening the general population.</li> <li>• Adequate evidence that auscultating the neck for carotid bruits has poor accuracy for detecting clinically relevant carotid artery stenosis.</li> </ul>
Benefits of early detection, intervention and treatment	<ul style="list-style-type: none"> <li>• Inadequate direct evidence that screening for asymptomatic carotid artery stenosis reduces adverse health outcomes such as stroke or mortality.</li> <li>• Adequate evidence that treating asymptomatic patients with carotid artery stenosis using CEA or CAS provides no to small benefit in reducing adverse health outcomes, including stroke, myocardial infarction, or mortality, compared with current medical therapy.</li> </ul>
Harms of early detection and intervention and treatment	<ul style="list-style-type: none"> <li>• Inadequate direct evidence that screening for asymptomatic carotid artery stenosis can cause harms. However, there are known harms associated with confirmatory testing and interventions.</li> <li>• Adequate direct evidence that treating asymptomatic patients with carotid artery stenosis using CEA or CAS can cause harms, including stroke or death.</li> <li>• The overall magnitude of harms of screening for and treatment of asymptomatic carotid artery stenosis is small to moderate.</li> </ul>
USPSTF assessment	Using a reaffirmation process, the USPSTF concludes with moderate certainty that screening for asymptomatic carotid artery stenosis in the general population has no benefit and may be harmful.

Abbreviations: CAS, carotid artery angioplasty and stenting; CEA, carotid endarterectomy; USPSTF, US Preventive Services Task Force.

## Practice Considerations

### Patient Population Under Consideration

This recommendation applies to adults without a history of transient ischemic attack, stroke, or other neurologic signs or symptoms referable to the carotid arteries.

### Assessment of Risk

Although screening for asymptomatic carotid artery stenosis is not recommended for the general adult population, several factors increase risk for carotid artery stenosis, including older age,

male sex, hypertension, smoking, hypercholesterolemia, diabetes, and heart disease.<sup>6</sup> However, there are no externally validated, reliable methods to determine who is at increased risk for carotid artery stenosis or who is at increased risk of stroke when carotid artery stenosis is present.<sup>7-9</sup>

### Screening Tests

Several modalities are proposed for screening for carotid artery stenosis, including carotid duplex ultrasonography (DUS), magnetic resonance angiography, and computed tomography angiography. Auscultation for carotid bruits has been found to have poor accuracy for detecting carotid stenosis or stroke and is

not considered a reasonable screening approach.<sup>7</sup> The USPSTF does not recommend screening adults without a history of transient ischemic attack, stroke, or other neurologic signs or symptoms referable to the carotid arteries.

### Treatment

Medical and surgical options are available for treatment of carotid artery stenosis. In general, treatment of asymptomatic carotid artery stenosis is directed at systemic atherosclerotic disease and often includes statins, antiplatelet medications, management of hypertension and diabetes, and lifestyle modification interventions. Surgical procedures designed to improve carotid artery blood flow include carotid endarterectomy (CEA), carotid artery angioplasty and stenting (CAS), or transartery revascularization. Medical therapy can be used alone or with revascularization procedures.<sup>7</sup> For patients with asymptomatic disease, the harms of surgical interventions compared with appropriate medical therapy appear to outweigh the benefits.

### Other Related USPSTF Recommendations

The USPSTF has issued other recommendation statements related to stroke prevention and cardiovascular health. These include

- Screening for high blood pressure in adults<sup>10</sup>
- Screening for abdominal aortic aneurysm<sup>11</sup>
- Interventions for tobacco smoking cessation in adults, including pregnant persons<sup>12</sup>
- Interventions to promote a healthy diet and physical activity for the prevention of cardiovascular disease:
  - In adults with cardiovascular risk factors<sup>13</sup>
  - In adults without known cardiovascular risk factors<sup>14</sup>
- Aspirin use to prevent cardiovascular disease and colorectal cancer<sup>15</sup>
- Statin use for the primary prevention of cardiovascular disease in adults<sup>16</sup>

## Update of the Previous Recommendation

This recommendation statement is a reaffirmation of the 2014 D recommendation for screening for asymptomatic carotid artery stenosis.<sup>4</sup> The USPSTF issued the D recommendation based on evidence that the harms of screening for carotid artery stenosis in asymptomatic adults outweigh the benefits.<sup>4</sup> The USPSTF found no new substantial evidence that could change its recommendation and therefore reaffirms its recommendation.

## Supporting Evidence

### Scope of Review

To reaffirm its recommendation, the USPSTF commissioned a reaffirmation evidence review to update the 2014 review.<sup>7,9</sup> The aim of the evidence update that supports the reaffirmation process is to identify new and substantial evidence sufficient enough to change the prior recommendation.<sup>5</sup> The reaffirmation update focused on the targeted key questions on the potential benefits and harms of screening and interventions, including revascular-

ization procedures designed to improve carotid artery blood flow, in persons with asymptomatic carotid artery stenosis.

### Accuracy of Screening Tests and Risk Assessment

The accuracy of screening tests for carotid artery stenosis was evaluated in the 2014 systematic review for the USPSTF,<sup>8</sup> which found 1 good-quality meta-analysis assessing the accuracy of DUS in detecting carotid artery stenosis.<sup>7</sup> It reported that the sensitivity and specificity of DUS for detecting 70% or greater stenosis were 90% (95% CI, 84%-94%) and 94% (95% CI, 88%-97%), respectively, compared with a reference standard of digital subtraction angiography. However, this evidence from 2014 was limited by lack of information on the proportion of patients who were asymptomatic and by clinically important variation in DUS measurement by patient population, equipment, technique, and other factors.<sup>8</sup> For auscultating the neck for carotid bruits, the 2014 evidence review found a wide range in sensitivity (46%-77%) and specificity (71%-98%) for detecting carotid artery stenosis. Of the 4 included studies, none used angiography as a reference standard and only 2 enrolled patients from the general population.<sup>8</sup>

The USPSTF found no externally validated risk stratification tools that could reliably distinguish between asymptomatic persons who have clinically important carotid artery stenosis and persons who do not, or the risk of stroke related to carotid artery stenosis.<sup>7,9</sup>

### Benefits of Early Detection and Treatment

The USPSTF found no studies that directly examined the health benefits of screening with DUS.<sup>7-9</sup>

The 2014 review found 3 randomized clinical trials (n = 5226) that assessed the benefits of treating asymptomatic carotid artery stenosis (defined as stenosis  $\geq$ 50%) with CEA compared with medical therapy alone over 2.7 to 9 years. These studies included participants with cardiovascular disease risk factors such as diabetes, hypertension, hypercholesterolemia, and coronary artery disease. Pooled analyses found that, compared with patients receiving medical therapy alone, 2.0% fewer patients treated with CEA had perioperative stroke or death and subsequent ipsilateral stroke (combined outcome) and 3.5% fewer patients treated with CEA had perioperative stroke or death and any subsequent stroke (combined outcome).<sup>8</sup> However, none of the trials focused on exclusively asymptomatic populations identified by primary care screening. Between 20% and 32% of trial patients reported a history of contralateral artery transient ischemic attack, stroke, or CEA at baseline.<sup>8</sup> Additionally, requirements for asymptomatic status differed slightly across the trials. For example, 1 study enrolled participants with no transient ischemic attack or stroke attributable to the ipsilateral artery for the past 6 months, while another enrolled participants with no history of cerebrovascular events in the distribution of the ipsilateral carotid artery and no symptoms referable to the contralateral artery for the past 45 days. Medical therapy varied by trial and may not reflect contemporary aggressive risk factor modification, and operators (eg, surgeons and interventionists) were highly selected based on their low morbidity and mortality rates.<sup>8</sup> Because of these limitations, the USPSTF concluded that the magnitude of any benefit would be smaller in asymptomatic persons in the general population than among patients in the trials.<sup>4</sup>

The current review found 2 new fair-quality studies conducted in Europe that were prematurely terminated because of low recruitment or interim analysis showing that patients randomized to best medical therapy had unexpectedly higher rates of ipsilateral stroke or death than patients randomized to CEA.<sup>7,9</sup> Results from comparative effectiveness studies of CEA plus best medical therapy compared with best medical therapy alone were mixed. The Stent-Protected Angioplasty in Asymptomatic Carotid Artery Stenosis vs Endarterectomy 2 (SPACE-2) trial (n = 316) found no difference between groups in the composite outcome of stroke or death at 30 days of follow-up or ipsilateral ischemic stroke at 1 year of follow-up (unadjusted hazard ratio [HR], 2.82 [95% CI, 0.33-24.07]).<sup>17</sup> The Aggressive Medical Treatment Evaluation for Asymptomatic Carotid Artery Stenosis (AMTEC) trial (n = 55) found that patients who underwent CEA had a significantly lower composite risk of nonfatal ipsilateral stroke or death at 3.3 median years of follow-up than patients who received best medical therapy alone (calculated unadjusted HR, 0.20 [95% CI, 0.06-0.65]).<sup>7,18</sup>

The 2014 review found no studies that compared CAS with medical therapy.<sup>8</sup> The current review<sup>7</sup> identified 1 trial that compared CAS with best medical therapy; in this trial, there were no significant differences between groups in the composite outcome of stroke or death at 30 days of follow-up or in ipsilateral ischemic stroke at 1 year of follow-up (unadjusted HR, 3.50 [95% CI, 0.42-29.11]).<sup>17</sup>

### Harms of Early Detection and Treatment

The USPSTF found no studies that directly examined the harms of screening using DUS.<sup>8</sup>

The 2014 review found that DUS leads to many false-positive results when screening the general population, which has a low prevalence of carotid artery stenosis (0.5%-1%).<sup>8</sup> The 2014 review found 2 studies of angiography, a confirmatory testing method that is less commonly used today than noninvasive magnetic resonance angiography or computed tomography angiography. Of patients who had angiography, 0.4% to 1.2% had strokes as a result.<sup>8</sup> The current review found no new studies on the harms of confirmatory testing methods.<sup>7</sup>

The 2014 review found 3 trials that reported on harms of CEA or CAS, most of which were conducted during the 1990s.<sup>8</sup> Many study participants had hypertension, coronary artery disease, or diabetes. Pooled analysis of data from 6 trials (n = 3435) found that 2.4% (95% CI, 1.7%-3.1%) of patients died or had a stroke within the 30 days after CEA. A meta-analysis of 3 trials (n = 5223) found that 1.9% (95% CI, 1.2%-2.6%) more participants treated with CEA had perioperative (30-day) stroke or death than participants treated with medical therapy. A meta-analysis of 2 trials (n = 6152) found that 3.1% (95% CI, 2.7%-3.6%) of patients died or had a stroke after CAS. Pooled data from 7 cohort studies found that 3.3% (95% CI, 2.7%-3.9%) of patients died or had a stroke within 30 days after CEA.<sup>8</sup> One cohort study found that 3.8% (95% CI, 2.9%-5.1%) of patients had a stroke or died within 30 days after CAS.<sup>19</sup>

The current review found 2 fair-quality trials that assessed perioperative harms.<sup>7,9</sup> In the SPACE-2 trial, 2.5% of patients who underwent CAS or CEA died or had a stroke within 30 days after their procedure.<sup>17</sup> The AMTEC trial reported 1 patient (3.2%) who had a fatal postoperative stroke after CEA.<sup>18</sup> The current review

identified several large national databases and surgical registries that measured postoperative outcomes associated with CEA (n = 1903761) or CAS (n = 332103).<sup>7,9</sup> The proportion of patients experiencing 30-day postoperative stroke or death after CEA ranged from 1.4% in the Vascular Quality Initiative<sup>20</sup> to 3.5% in a large Medicare database.<sup>21</sup> The proportion that experienced 30-day postoperative stroke or death after CAS ranged from 2.6%<sup>20</sup> to 5.1% (Medicare database).<sup>21</sup>

### Response to Public Comments

A draft version of this recommendation statement was posted for public comment on the USPSTF website from August 4, 2020, to August 31, 2020. Several comments noted that the term "general adult population" includes patients who may be at increased risk for carotid artery stenosis or stroke and noted that other organizations recommend screening in these higher-risk individuals. Several risk factors for developing carotid artery stenosis are noted in the recommendation, including hypertension, diabetes, smoking, and hypercholesterolemia. The studies included in the review included participants with these risk factors, and the USPSTF found no benefit in screening asymptomatic populations. The USPSTF added language to clarify this point. No reliable tools are available to determine which individuals are at increased risk for carotid artery stenosis or are at increased risk of stroke when carotid artery stenosis is present. Respondents questioned the USPSTF's conclusions regarding the harms associated with surgical interventions and the comparative benefit of best medical therapy vs CEA. Comments pointed to several studies that demonstrate the benefits of CEA over best medical therapy to reduce stroke risk in asymptomatic persons. Comments also noted that new, safer procedures are now available (ie, transcatheter carotid artery revascularization) that were not reviewed and that may shift the balance of net benefit. The USPSTF reviewed all available evidence and concluded that the magnitude of benefit would be smaller in truly asymptomatic persons in the general population than among selected patients in trials. The USPSTF added language about the new studies it considered. The review found no studies that examined the benefits and harms of transcatheter carotid artery revascularization.

### Research Needs and Gaps

More research is needed to evaluate the benefits and harms of screening for asymptomatic carotid artery stenosis in the general adult population. Important research would include

- Trials with long-term follow-up (>5 years) that compare CEA or CAS plus contemporary best medical therapy with best medical therapy alone, including completion of ongoing trials.<sup>7</sup>
- Development and validation of tools to determine which persons are at high risk for carotid artery stenosis and for stroke due to carotid artery stenosis and who might experience harm from treatment with CEA or CAS.

### Recommendations of Others

US guidelines differ regarding the role of DUS screening in patients without a history of transient ischemic attack, stroke,

or other neurologic signs or symptoms referable to the carotid arteries. The American Heart Association and the American Stroke Association jointly recommend against routine screening for carotid artery stenosis in asymptomatic patients using DUS.<sup>6</sup> Joint guidelines from multiple US professional societies<sup>22</sup> conclude that DUS screening is indicated (or reason-

able) for asymptomatic patients with a carotid bruit. The Society for Vascular Surgery<sup>23</sup> and joint guidelines from multiple US professional societies<sup>22</sup> recommend consideration of DUS screening in patients with multiple risk factors for stroke and in those with known peripheral artery disease or other cardiovascular disease.

## ARTICLE INFORMATION

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