

Letters

RESEARCH LETTER

Screening for Asymptomatic Carotid Artery Stenosis in the General Population: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

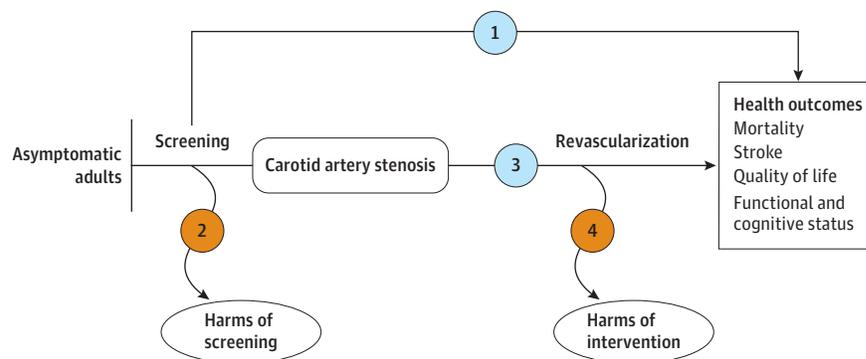
Carotid artery stenosis is a known stroke risk factor and a cardiovascular disease marker. No population-based screening trials for carotid artery stenosis have been conducted. Optimal treatment for clinically significant asymptomatic carotid artery stenosis remains uncertain. Options include best medical therapy alone or in combination with revascularization (carotid endarterectomy or carotid artery stenting) to prevent stroke. Revascularization has been associated with small long-term benefits compared with best medical therapy alone in historic trials but can result in surgical harms.¹

Since 2007, the US Preventive Services Task Force (USPSTF) has maintained a D recommendation against screening for

asymptomatic carotid artery stenosis in the general adult population. This recommendation was based on a low prevalence of stroke attributable to asymptomatic carotid artery stenosis in the general population, the small benefit of surgery compared with medical therapy in older trials, and the potential for small to moderate surgical harms. This brief evidence update aimed to identify studies published since the previous 2014 review¹ to inform an updated USPSTF recommendation.

Methods | A literature search of MEDLINE, PubMed publisher-supplied records, and the Cochrane Central Register of Controlled Trials was conducted from January 1, 2014, to February 18, 2020. Ongoing surveillance in targeted publications was conducted through November 20, 2020. Two investigators independently evaluated articles that met inclusion criteria and summarized the data. The most recent comprehensive publication from each US national database or surgical registry reporting procedural harms was selected for review. The scope of this rapid review was limited to screening in the general population and did not address high-risk subpopulations. The results are limited to studies published since the previous review to support the 2014 recommendation.² An analytic framework and 4 key questions (KQs) guided the evidence update (Figure). Detailed methods and results of this systematic review are available in the full evidence report.⁴

Figure. Analytic Framework: Screening for Asymptomatic Carotid Artery Stenosis in the General Population



Key questions

- 1 Is there direct evidence that screening asymptomatic adults for carotid artery stenosis with duplex ultrasonography improves health outcomes?
- 2 What are the harms associated with screening or confirmatory testing for asymptomatic carotid stenosis?
- 3 For asymptomatic persons with carotid artery stenosis, does revascularization provide incremental benefit beyond current medical treatment?
- 4 What are the harms associated with revascularization of asymptomatic carotid artery stenosis?

Evidence reviews for the US Preventive Services Task Force (USPSTF) use an analytic framework to visually display the key questions that the review will address to allow the USPSTF to evaluate the effectiveness and safety of a preventive service. The questions are depicted by linkages that relate to interventions and outcomes. Further details are available from the USPSTF procedure manual.³

Table. Comparison of Foundational and New Evidence: Screening for Asymptomatic Carotid Artery Stenosis in the General Population

	Rationale and foundational evidence ¹	New evidence findings	Limitations of new evidence	Consistency of new evidence with foundational evidence and current understanding
Benefits of screening	No direct evidence	No new evidence	NA	NA
Harms of screening	No studies examined direct harms of screening Stroke after angiography: 0.4% and 1.2%	No new evidence	NA	NA
Incremental benefit of revascularization	CEA: 3 RCTs (n = 5226); 3.5% (95% CI, 1.8%-5.1%) absolute reduction in stroke/death at ≈5 y compared with best medical treatment (in 1990s) CAS: no studies	CEA: AMTEC trial (n = 55) reported a lower composite stroke/death risk after CEA at 3.3 median y (HR, 0.20 [95% CI, 0.06-0.65]) CAS: SPACE-2 trial (n = 316) reported no difference in stroke/death at 1 y (HR, 3.50 [95% CI, 0.42-29.11])	Underpowered, prematurely terminated trials	New trials have mixed results and do not definitively change previous conclusions
Harms of revascularization	CEA: Pooled estimates of 30-d postoperative stroke or death after CEA ranged from 2.41% in trials (n = 3436) to 3.32% in cohorts (n = 16 967) CAS: Estimates of 30-d postoperative stroke or death after CAS ranged from 3.1% in trials (n = 6152) to 3.8% in a credentialing cohort (n = 1151)	CEA: Estimates of 30-d postoperative stroke or death after CEA ranged from 1.4% to 3.5% (n = 1 903 761) CAS: Estimates of 30-d postoperative stroke or death after CAS ranged from 2.6% to 5.1% (n = 332 103)	Concerns of bias in harms estimates of registries and administrative data	Very large increase in sample size Similar or higher complication rates reported in contemporary observational and trial data

Abbreviations: AMTEC, Aggressive Medical Treatment Evaluation for Asymptomatic Carotid Artery Stenosis; CAS, carotid artery stenting; CEA, carotid endarterectomy; HR, hazard ratio; NA, not applicable;

RCT, randomized clinical trial; SPACE-2, Stent Protected Angioplasty vs Carotid Endarterectomy.

Results | We screened 2373 titles and abstracts and 144 full-text articles. No eligible studies were identified that directly examined the benefits or harms of screening for asymptomatic carotid artery stenosis (KQ1, KQ2). Two limited, prematurely terminated trials reported mixed results for the comparative effectiveness of carotid revascularization plus best medical therapy compared with best medical therapy alone (KQ3). The SPACE-2 trial⁵ (n = 316) reported no significant difference in composite outcome of stroke or death (30 days) or ipsilateral ischemic stroke (1 year) after carotid endarterectomy (unadjusted hazard ratio [HR], 2.82 [95% CI, 0.33-24.07]) or carotid artery stenting (unadjusted HR, 3.50 [95% CI, 0.42-29.11]) compared with best medical therapy at 1 year. The smaller AMTEC trial⁶ (n = 55) reported a statistically significantly lower composite risk of nonfatal ipsilateral stroke or death among the carotid endarterectomy group at a median of 3.3 years (calculated unadjusted HR, 0.20 [95% CI, 0.06-0.65]). The 2 trials, 2 national data sets, and 3 surgical registries reported procedural harms associated with carotid endarterectomy (n = 1 903 761) or carotid artery stenting (n = 332 103) (KQ4). These data estimated that postoperative 30-day rates of stroke or death varied from 1.4% to 3.5% for carotid endarterectomy and from 2.6% to 5.1% for carotid artery stenting.

Discussion | The conclusions of this review are consistent with those of the previous review (Table).¹ There was no direct evidence examining the benefits or harms of screening. The 2 new trials added little to the evidence base on effectiveness of revascularization compared with best medical therapy. New evidence related to procedural harms from contemporary national databases and surgical registries reported complication rates; however, their selection and measurement biases re-

main serious concerns. The reported wide variation in complication rates may be attributable to patient and surgeon/operator selection.

While there were few new trials examining the comparative effectiveness of revascularization compared with contemporary best medical treatment alone, the ongoing CREST-2 (NCT02089217, estimated completion date of December 2022), ECST-2 (ISRCTN97744893, estimated completion date of March 2022), and ACTRIS (NCT02841098, estimated completion date of December 2025) trials will add to this treatment evidence base for asymptomatic carotid artery stenosis in the future.

Janelle M. Guirguis-Blake, MD
Elizabeth M. Webber, MS
Erin L. Coppola, MPH

Author Affiliations: Department of Family Medicine, University of Washington, Tacoma (Guirguis-Blake); Kaiser Permanente Evidence-based Practice Center, Kaiser Permanente Center for Health Research, Portland, Oregon (Webber, Coppola).

Corresponding Author: Janelle M. Guirguis-Blake, MD, Kaiser Permanente Research Affiliates EPC, Department of Family Medicine, University of Washington, 521 Martin Luther King Jr Way, Tacoma, WA 98405 (jguirgui@u.washington.edu).

Accepted for Publication: September 28, 2020.

Author Contributions: Dr Guirguis-Blake had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: All authors.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: All authors.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Guirguis-Blake.

Administrative, technical, or material support: Webber, Coppola.

Supervision: Guirguis-Blake.

Conflict of Interest Disclosures: None reported.

Funding/Support: This research was funded under HHS2902015000071, Task Order 6, from the Agency for Healthcare Research and Quality (AHRQ), US Department of Health and Human Services, under a contract to support the US Preventive Services Task Force (USPSTF).

Role of the Funder/Sponsor: Investigators worked with USPSTF members and AHRQ staff to develop the scope, analytic framework, and key questions for this review. AHRQ had no role in study selection, quality assessment, or synthesis. AHRQ staff provided project oversight, reviewed the report to ensure that the analysis met methodological standards, and distributed the draft for peer review. Otherwise, AHRQ had no role in the conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript findings. The opinions expressed in this document are those of the authors and do not reflect the official position of AHRQ or the US Department of Health and Human Services.

Additional Contributions: We gratefully acknowledge the following for their contributions to this project: the AHRQ staff; the USPSTF; and Melinda Davies, MAIS, and Katherine Essick, BS (Kaiser Permanente Center for Health Research), for technical and editorial assistance. The USPSTF members, peer reviewers, and federal partner reviewers did not receive financial compensation for their contributions.

Additional Information: A draft version of this evidence report underwent external peer review from 5 content experts (Ethan Halm, MD, MPH [University of Texas Southwestern Medical Center]; James F. Meschia, MD [Mayo Clinic Hospital, Jacksonville, Florida]; John J. Ricotta, MD [George Washington School of Medicine and Health Sciences]; Nicholas J. Swerdlow, MD [Beth Israel Deaconess Medical Center]) and 1 federal partner: National Institutes of Health, National Institute of Neurological Disorders and Stroke. Comments were presented to the USPSTF during its deliberation of the evidence and were considered in preparing the final evidence review.

Editorial Disclaimer: This evidence report is presented as a document in support of the accompanying USPSTF recommendation statement. It did not undergo additional peer review after submission to *JAMA*.

1. Jonas DE, Feltner C, Amick HR, et al. *Screening for Asymptomatic Carotid Artery Stenosis: A Systematic Review and Meta-Analysis for the U.S. Preventive Services Task Force*. Evidence Synthesis No. 111. Agency for Healthcare Research and Quality; 2014.

2. LeFevre ML; US Preventive Services Task Force. Screening for asymptomatic carotid artery stenosis: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014;161(5):356-362. doi:10.7326/M14-1333

3. Procedure manual. US Preventive Services Task Force. Updated 2017. Accessed November 24, 2020. <https://www.uspreventiveservicestaskforce.org/uspstf/procedure-manual>

4. Guirguis-Blake JM, Webber EM, Coppola EL. *Screening for Asymptomatic Carotid Artery Stenosis in the General Population: An Evidence Update for the U.S. Preventive Services Task Force*. Evidence Synthesis No. 199. Agency for Healthcare Research and Quality; 2020. AHRQ publication 20-05268-EF-1.

5. Reiff T, Eckstein HH, Mansmann U, et al. Angioplasty in asymptomatic carotid artery stenosis vs. endarterectomy compared to best medical treatment: one-year interim results of SPACE-2. *Int J Stroke*. 2019;15(6):1747493019833017. doi:10.1177/1747493019833017

6. Kolos I, Troitskiy A, Balakhonova T, et al; Aggressive Medical Treatment Evaluation for Asymptomatic Carotid Artery Stenosis (AMTEC) Study Group. Modern medical treatment with or without carotid endarterectomy for severe asymptomatic carotid atherosclerosis. *J Vasc Surg*. 2015;62(4):914-922. doi:10.1016/j.jvs.2015.05.005