

Carotid Artery Stenting

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I. Description

Carotid artery angioplasty with stenting (CAS) is a treatment for carotid stenosis that is intended to prevent future stroke. It is an alternative to medical therapy and a less-invasive alternative to carotid endarterectomy (CEA).

For individuals who have carotid artery stenosis who receive carotid artery stenting (CAS), the evidence includes randomized controlled trials (RCTs) and systematic reviews of RCTs. Relevant outcomes are overall survival, morbid events, and treatment-related mortality and morbidity. A substantial body of RCT evidence compares outcomes of CAS with CEA for symptomatic and asymptomatic patients with carotid stenosis. The evidence does not support use of CAS in carotid artery disease for the average-risk patient, because early adverse events are higher with CAS and long-term outcomes are similar between the two procedures. Data from RCTs and large database studies establish that the risk of death or stroke with CAS exceeds the threshold considered acceptable to indicate overall benefit from the procedure. Therefore, for patients with carotid stenosis who are suitable candidates for CEA, CAS does not improve health outcomes. The evidence is sufficient to determine qualitatively that the technology is unlikely to improve the net health outcome.

However, based on limited data, clinical input, an indirect chain of evidence, and unmet medical need, CAS may be considered a reasonable treatment option in recently symptomatic patients when CEA cannot be performed due to anatomic reasons. For this population, CAS may be considered medically necessary. It does not meet payment determination for all other indications, including carotid artery dissection.

Background

Combined with optimal medical management carotid angioplasty with or without stenting has been evaluated as an alternative to CEA. Carotid angioplasty and stenting involves the introduction of coaxial systems of catheters, microcatheters, balloons, and other devices. The procedure is most often performed through the femoral artery, but a transcervical approach can also be used to avoid

traversing the aortic arch. Interventionalists almost uniformly use an embolic protection device (EPD) designed to reduce the risk of stroke caused by thromboembolic material dislodged during CAS. EPDs can be deployed proximally (with flow reversal) or distally (using a filter). Carotid angioplasty rarely is performed without stent placement.

Proposed advantages of CAS over CEA include:

- General anesthesia is not required (although CEA can be performed under local/regional anesthesia).
- Cranial nerve palsies are infrequent sequelae (although almost all following CEA resolve over time).
- Simultaneous procedures may be performed on the coronary and carotid arteries.

REGULATORY STATUS

A number of carotid artery stents and embolic protection devices (EPDs) have been approved by the U.S. Food and Drug Administration (FDA) through the premarket approval (PMA) process. Examples are provided in Table 1.

Table 1. FDA-Approved Carotid Artery Stents and Embolic Protection Devices

Manufacturer	Stents and Devices	PMA/510K Date
Guidant, now Abbott Vascular	Acculink™ and RX Acculink carotid stents	Aug 2004
Guidant, now Abbott Vascular	Accunet™ and RX Accunet cerebral protection filters	Aug 2004
Abbott Vascular	Xact® RX carotid stent system	Sep 2005
Abbott Vascular	Emboshield® embolic protection system	Sep 2005
Cordis Corp.	Precise® nitinol carotid stent system	Sep 2006
Cordis Corp.	AngioGuard XP and RX emboli capture guidewire systems	Sep 2006
EndoTex Interventional Systems	NexStent® carotid stent over-the-wire and monorail delivery systems	Oct 2006
Boston Scientific	FilterWire EZ embolic protection system	Oct 2006
ev3 Inc., Arterial Evolution Technology	Protégé® Rx and SpideRx®	Jan 2007
Boston Scientific	Carotid Wallstent®	Oct 2008
GORE	GORE® Flow Reversal System	Feb 2009
GORE	GORE® Embolic Filter	May 2011
Medtronic/Invatec	Mo.Ma® Ultra Proximal Cerebral Protection Device	Oct 2009
Silk Road Medical	ENROUTE™ Transcarotid Stent System and ENROUTE Transcarotid Neuroprotection System	May 2015

FDA: Food and Drug Administration; PMA: premarket approval.

Each FDA-approved carotid stent is indicated for combined use with an EPD to reduce risk of stroke in patients considered to be at increased risk for periprocedural complications from CEA who are

symptomatic with greater than 50% stenosis, or asymptomatic with greater than 80% stenosis—degree of stenosis being assessed by ultrasound or angiogram with computed tomography (CT) angiography also sometimes used. Patients are considered at increased risk for complications during CEA if affected by any item from a list of anatomic features and comorbid conditions included in each stent system's Information for Prescribers.

The RX Acculink™ Carotid Stent System is also approved for use in conventional risk patients (not considered at increased risk for complications during CEA) with symptoms and $\geq 70\%$ stenosis by ultrasound or $\geq 50\%$ stenosis by angiogram, and asymptomatic patients with $\geq 70\%$ stenosis by ultrasound or $\geq 60\%$ stenosis by angiogram.

FDA-approved stents and EPDs differ in the deployment methods used once they reach the target lesion, with the RX (rapid exchange) devices designed for more rapid stent and filter expansion. The Precise and AngioGuard™ devices were studied in a randomized, controlled trial (RCT) (the SAPPHERE trial; see Rationale section). Other devices were approved based on uncontrolled, single-arm trials or registries and comparison to historical controls. The FDA has mandated postmarketing studies for these devices, including longer follow-up for patients already reported to the FDA and additional registry studies, primarily to compare outcomes as a function of clinician training and (e.g., facility experience. Each manufacturer's system is available in various configurations straight or tapered) and sizes (diameters and lengths) to match the vessel lumen that will receive the stent.

In February 2015, the Enroute Transcarotid NPS (Silk Road Medical, Sunnyvale, CA) was cleared for marketing by FDA through the 510(k) process. The Enroute is a flow-reversal device designed to be placed via direct carotid access. Clearance was based on results of the Roadster trial (NCT01685567), a single-arm phase 3 pivotal trial to evaluate outcomes after CAS with the Enroute device among 283 subjects with symptomatic or asymptomatic carotid stenosis.

FDA product code: NIM (stents) and NTE (EPDs).

II. Criteria/Guidelines

- A. Carotid angioplasty with associated stenting and embolic protection is covered (subject to Limitations and Administrative Guidelines) for patients with:
 - 1. 50% - 99% stenosis (North American Symptomatic Carotid Endarterectomy Trial [NASCET] measurement); AND
 - 2. Symptoms of focal cerebral ischemia (transient ischemic attack or monocular blindness) in previous 120 days, symptom duration less than 24 hours, or nondisabling stroke; AND
 - 3. Anatomic contraindication for carotid endarterectomy (such as prior radiation treatment or neck surgery, lesions surgically inaccessible, spinal immobility, or tracheostomy)

III. Limitations

- A. Carotid angioplasty with associated stenting and embolic protection is not covered for all other indications, including but not limited to, patients with carotid stenosis who are suitable candidates for CEA and patients with carotid artery dissection.

- B. Carotid angioplasty without associated stenting and embolic protection is not covered for all indications, including but not limited to, patients with carotid stenosis who are suitable candidates for carotid endarterectomy and patients with carotid artery dissection.

IV. Administrative Guidelines

- A. Precertification is not required. HMSA reserves the right to perform retrospective review using the above criteria to validate if services rendered met payment determination criteria.
- B. The following documentation must be kept in the patient's medical records and be made available to HMSA upon request:
1. Clinical notes documenting the patient's symptoms of carotid artery stenosis and any high risk conditions for CEA.
 2. Imaging studies documenting the degree of carotid stenosis as measured by a duplex Doppler ultrasound or carotid artery angiography.
- C. Applicable codes:

CPT Code	Description
37215	Transcatheter placement of intravascular stent(s), cervical carotid artery, open or percutaneous, including angioplasty, when performed, and radiological supervision and interpretation; with distal embolic protection
37217	Transcatheter placement of an intravascular stent(s), intrathoracic common carotid artery or innominate artery by retrograde treatment, via open ipsilateral cervical carotid artery exposure, including angioplasty, when performed, and radiological supervision and interpretation
37218	Transcatheter placement of intravascular stent(s), intrathoracic common carotid artery or innominate artery, open or percutaneous antegrade approach, including angioplasty, when performed, and radiological supervision and interpretation

- D. Code that does not Meet Payment Determination Criteria:

CPT Code	Description
37216	Transcatheter placement of intravascular stent(s), cervical carotid artery, open or percutaneous, including angioplasty, when performed, and radiological supervision and interpretation; without distal embolic protection

V. Scientific Background

This policy has been updated regularly with literature review of the MEDLINE database. The most recent literature update was performed through March 5, 2018.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

RISK-BENEFIT RATIO OF INVASIVE CAROTID PROCEDURES

Endovascular carotid angioplasty and stenting (CAS) or surgical endarterectomy (CEA) for carotid artery disease trades procedure-related harms of stroke and death for the benefit of reduced stroke risk over subsequent years—the balance determines whether either intervention will result in a net clinical benefit. That balance has been scrutinized for CEA although not for CAS; accordingly results from trials of CEA must be extrapolated to CAS.

A series of landmark clinical trials from the late 1980s through the 1990s compared the benefits and harms of CEA to best medical therapies then available in symptomatic and asymptomatic individuals with carotid artery stenosis. The trial results defined the magnitude of risk reduction for stroke, and periprocedural stroke and death rates for 30 days, that must be offset to achieve a net clinical benefit (benefit outweighing harm) less than 3% for asymptomatic (greater than 60% stenosis), and less than 6% for symptomatic patients (50–69% or 70–99% stenosis). Furthermore, because periprocedural harms are immediate but benefit is accrued over time, a net clinical benefit is obtained only in those patients surviving long enough to counterbalance the immediate harms. The necessary life expectancy defined by the trial duration needed to demonstrate benefit, is summarized in the following table.

Table 2. Acceptable Periprocedural Death/Stroke Rate in Clinical Trials of CEA

Symptoms	Stenosis	Acceptable Periprocedural Death/Stroke Rate	Anticipated Life Expectancy, y
No	60%-99%	<3%	5
Yes	50%-69%	<6%	5
	70%-99%	<6%	2

CEA: carotid endarterectomy.

As an example of the fine line between benefit and harm, Arazi et al. performed a decision analysis of benefit for patients with asymptomatic stenosis using a base case derived from the Asymptomatic Carotid Surgery Trial (ACST) (periprocedural death/stroke rate of 1.8%). Over a 5-year time horizon, CEA provided 4 days of stroke-free survival and a net harm when periprocedural death/disabling stroke rates exceeded 2.1%.

Since the landmark trials, there have been considerable improvements in medical care resulting in a substantial decline in stroke rates among patients with asymptomatic carotid disease. Current medical therapies such as aggressive lipid lowering medications were inconsistently used in the landmark trials. Also, surgeons in contemporary clinical trials have achieved CEA periprocedural death and stroke rates lower than those in pivotal trials used to establish the benchmarks. For example, in the Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST), the death/stroke rates for symptomatic patients was 3.2% and for asymptomatic patients was 1.4%. Accordingly, benchmarks established decades ago might no longer be appropriate. A recent consensus document suggests benchmarks of 2.0% for asymptomatic and 4.0% for symptomatic individuals.

Excluded from landmark CEA trials were patients with significant comorbidities such as those judged likely to cause death within 5 years that might also increase periprocedural and anesthetic risk for complications. Therefore, CAS has appeal as a treatment option for patients with potentially higher periprocedural risk due to medical (eg, severe cardiac dysfunction, requirement for combined coronary and carotid revascularization, severe renal or pulmonary dysfunction, and other characteristics associated with increased surgical risk); or anatomic reasons (eg, surgically inaccessible stenosis, prior radiation, prior neck surgery, spinal immobility, prior laryngeal nerve palsy, contralateral occlusion, prior ipsilateral CEA, restenosis after CEA).

Although general anesthetic risk is considered a potential reason to use CAS, CEA can be safely performed under local or regional anesthesia, as confirmed in the 95-center General Anesthesia versus Local Anesthesia (GALA) trial. Investigators randomized 3,526 patients undergoing CEA to general or local anesthesia and found no difference in 30-day death/stroke/myocardial infarction (MI) rates based on anesthetic approach (risk ratio [RR]: 0.94; 95% confidence interval [CI]: 0.70 to 1.3).

Randomized Controlled Trials of CAS versus CEA

SAPPHIRE Trial

The first major RCT of CAS versus CEA was the Stenting and Angioplasty, with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial reported by Yadav et al (2004). The relevant conclusions are summarized as follows:

- SAPPHIRE included few patients with symptomatic stenosis at increased risk for periprocedural complications from CEA (n=96), which resulted in wide confidence intervals; differences between arms in 30-day and 1-year outcomes were not statistically significant.
- For patients with asymptomatic stenosis at increased risk for periprocedural complications from CEA (n=238), differences in 30-day outcomes also had wide confidence intervals and were not statistically significant.

- Early study closed early due to slow recruitment as nonrandomized stent registries were established, resulting in fewer study patients than planned, which compromised the evaluation of noninferiority.
- Variance in differential complication rates for the two treatments across sites may have influenced results, since 5 of 34 sites contributed 64% of randomized patients, and data were unavailable for comparison.
- Direct comparative evidence was lacking for optimal medical management alone as an alternative to adding CAS with EPD or CEA for patients with increased risk of surgical complications.

Long-term follow-up of SAPPHIRE was reported at 3 years. For asymptomatic and symptomatic patients combined, ipsilateral strokes from day 31 to 1,080 days were observed in 4.4% of patients undergoing CAS and 3.6% with CEA (from digitized figure). Cumulative 3-year repeat target vessel revascularization (a proxy for restenosis) was more common after CEA, but the difference was **not** statistically significant (7.1% vs 3.0%; $p=0.26$).

SPACE Trial

Ringleb et al (2006) published results from the Stent-supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy (SPACE) trial. This trial randomized 1,200 patients within 180 days of neurologic symptoms, transient ischemic attack, or moderate (non-disabling) stroke, and with $\geq 50\%$ stenosis of the ipsilateral carotid artery, to CAS (N=605) with or without EPD (73% of procedures performed without), or CEA (N=595). (18) The analysis (N=1,183) failed to conclude that CAS was noninferior to CEA by a margin of 2.5% for the primary outcome of ipsilateral ischemic stroke or death by 30 days after randomization. Periprocedural (30-day) event rates were 6.8% for the CAS group and 6.3% for the CEA group. The absolute between-group difference favored CEA and was 0.5% (90% CI: -1.9% to 2.9%) by intent-to-treat (ITT) analysis and 1.3% (90% CI: -1.1 to 3.8) in per-protocol analysis.

Editorialists pointed to some methodologic issues raised with SPACE, including the high rate of rejection for potential participating collaborators (approximately 25%, based on their prior outcomes records, but review criteria were not reported), and the lack of a requirement to use an EPD with CAS (although 30-day event rates were 7.3% with vs. 6.7% without EPD).

Long-term follow-up of the SPACE study was reported at 2-years. Approximate annual ipsilateral stroke rates from day 31 through longest follow-up for CAS and CEA were 0.4% in each group. Following the periprocedural period (i.e., 31 days to longest follow-up), stroke risk reduction in symptomatic patients not selected for medical or anatomic comorbidities is similar with either CAS or CEA. Recurrent stenosis greater than 70% was more frequent 2 years following CAS versus CEA (10.7% vs. 4.6%, respectively; $p=0.001$).

EVA-3S Trial

The Endarterectomy Versus Stenting in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) trial was a noninferiority comparison of CAS (with EPD in 92%) versus CEA in symptomatic patients at average risk for complications from CEA with $\geq 60\%$ stenosis of the ipsilateral carotid artery. (21) The trial was terminated prematurely (N=527 enrolled; original target N=872), based on interim analysis of 30-day outcomes. The incidence of any stroke or death through 30 days was

3.9% (95% CI: 2.0% to 7.2%) after CEA and 9.6% (95% CI: 6.4% to 14%) after CAS (RR: 2.5; 95% CI: 1.2% to 5.1%; $p=0.01$).

Over a mean follow-up of 2.1 years, restenosis ($\geq 50\%$) was more frequent following CAS than CEA (12.5% vs 5.0%). Long-term follow-up of EVA-3S was reported at 4 years. Approximate annual ipsilateral stroke rates from day 31 through longest follow-up for CAS and CEA, respectively, were 1.1% and 0.9%. These results support a conclusion that following the periprocedural period (i.e., 31 days to longest follow-up) stroke risk reduction in symptomatic patients not selected for medical or anatomic comorbidities is similar with either CAS or CEA.

Editorialists criticized EVA-3S for recommending but not requiring, antiplatelet premedication (3 days of aspirin plus either ticlopidine or clopidogrel) and for not requiring interventionalists to be adequately experienced with the specific stent and EPD devices they used to treat trial subjects. Participating interventionalists were required to have successfully completed 12 or more CAS procedures, compared with 25 or more CEAs for vascular surgeons. EVA-3S also permitted use of 5 different stents and 7 different EPDs but required only 2 prior procedures with a new device before an investigator could use that device on a patient randomized to CAS.

In 2014, Mas et al published long-term follow up (median 7.2 years) from the EVA-3S trial. Complete follow-up until death or the final telephone interview was obtained in 493 patients (94%). At the 5-year follow-up point, the main composite end point (ipsilateral stroke after randomization or procedural stroke or death) occurred in 29/265 subjects in the CAS group and 16/262 subjects in the CEA group (cumulative probability 11% vs 6.3%; 5-year absolute risk reduction 4.7%). The HR for CAS versus CEA was 1.85 (95% CI, 1.0 to 3.40; $p=0.04$). At the 10-year follow-up point, the HR for the main composite end point for CAS versus CEA was 1.70 (95% CI, 0.95 to 3.06; $p=0.07$).

International Carotid Stenting Study

The International Carotid Stenting Study enrolled 1,713 symptomatic patients at 50 academic medical centers across Europe, Australia, New Zealand, and Canada between May 2001 and October 2008. EPDs were recommended but not required (utilized in 72% of procedures), and a number of different stents and EPD types were used. Based on plausible event rates, a target study sample size of 1,500 was estimated able to define a between-group difference less than 3.3% in disabling stroke or death, but also a 3.0% difference in 30-day stroke, death, or MI. Only interim 30- and 120-day results were included in the initial report. From a per-protocol analysis, the 7.1% periprocedural death/stroke death rates accompanying CAS both exceed the rate established to provide a net clinical benefit and was more than twice that following CEA (3.4%). In a substudy of 231 ICSS participants, new ischemic brain lesions were approximately 3-fold more frequent following CAS protection devices did not appear to mitigate their occurrence. While follow-up of the sample for the primary endpoint is ongoing, interim results are consistent with the accompanying editorialist's conclusion that "routine stenting in symptomatic patients must now be difficult to justify...."

Bonati et al (2015) published longer term follow-up results from the International Carotid Stenting Study (ICSS). The cumulative 5-year risk of fatal or disabling stroke did not differ significantly between the CAS and CEA groups (6.4% for CAS vs 6.5% for CEA; hazard ratio (HR), 1.06; 95% CI,

0.72 to 1.57; $p=0.77$). The risk of any stroke was higher in the CAS group compared with the CEA group (5-year cumulative risk 15.2% vs 9.45; HR, 1.71; 95% CI, 1.28 to 2.3; $p<0.001$). The authors note that the difference between CEA and CAS groups in stroke risk after the procedural period was mainly attributable to strokes occurring in the contralateral carotid or vertebrobasilar territory in the CAS group. Functional outcomes, measured by modified Rankin scale scores, did not differ significantly between groups.

Altinbas et al (2014) reported that periprocedural rates of hemodynamic instability in the ICSS study differed between CEA and CAS groups. Hemodynamic depression occurred more commonly in CAS patients (13.8% vs 7.2%; RR, 1.9; 95% CI, 1.4 to 2.6; $p<0.000$), while hypertension requiring treatment occurred less commonly in CAS patients (RR, 0.2; 95% CI, 0.1 to 0.4; $p<0.000$). Hemodynamic instability was not associated with the ICSS study's primary composite outcome.

Featherstone et al (2016) published a health technology assessment (HTA) on ICSS funded by the U.K.'s National Institute for Health Research Health Technology Assessment program. The HTA reviewed the data presented above, concluding that "the functional outcome after stenting is similar to endarterectomy, but stenting is associated with a small increase in the risk of non-disabling stroke. The choice between stenting and endarterectomy should take into account the procedural risks related to individual patient characteristics."

CREST

The Carotid Revascularization Endarterectomy vs. Stenting Trial was conducted between December 2000 and July 2008, enrolling 2,522 patients at 117 centers across the U.S. and Canada. Of 427 interventionalists who applied to participate in CREST, only 224 (52%) were ultimately approved. Inclusion was initially restricted to recently symptomatic patients; due to slow enrollment, the protocol was amended to include asymptomatic patients. A March 2004 protocol amendment excluded further enrollment of patients 80 years and older due to poor outcomes. Of the 1,271 patients randomized to CAS, 65 underwent CEA and 54 neither procedure; of the 1,251 patients randomized to CEA, 13 underwent CAS and 44 neither procedure. There were 20 patients excluded from one site due to reported data fabrication. A sample size of 2,500 was targeted to detect a 46% reduction in the hazard ratio for the primary endpoint of any stroke, MI, or death during the periprocedural period or ipsilateral stroke within 4 years after randomization.

In the entire sample (symptomatic and asymptomatic patients), investigators reported no difference between CAS and CEA for the primary outcome of any periprocedural stroke, MI, or death or postprocedural ipsilateral stroke. Stroke was more frequent following CAS, MI after CEA. The periprocedural MI rate after CEA (2.3%) was considerably higher in CREST than any comparable trial (e.g., in EVA-3S 0.8%, SPACE 0%, ICSS 0.6%). This may be attributable to a somewhat higher prevalence of coronary artery disease among participants and routine cardiac enzyme assays, but the relative difference was large. Periprocedural CAS death/stroke rates were the lowest reported in any trial. Although participating interventionalists performing CAS were highly selected, periprocedural death/stroke rates following CAS exceeded those for CEA: in symptomatic patients 5.6% versus 2.4%, respectively (the lowest rate for CAS reported in any trial); in asymptomatic patients 2.6% versus 1.4%, respectively. The RR for periprocedural death/stroke in the symptomatic group was 1.89 (95% CI: 1.11 to 3.21) in the asymptomatic group 1.85 (95% CI: 0.79 to

4.34). The trial had limited power to detect a difference between procedures in the asymptomatic group. In CREST, 2-year restenosis (>70%) or reocclusion rates were similar following either CEA (6.3%) or CAS (6.0%)—2-year restenosis alone 5.8% with either procedure.

Brott et al (2016) reported long-term follow-up for CREST. There were no significant differences in the primary composite outcome (any periprocedural stroke, MI, death or postprocedural ipsilateral stroke) between the CEA (9.9%) and CAS (11.8%; HR=1.10) groups when measured out to 10 years.³⁴ The second primary end point of post procedural ipsilateral stroke rates were also not significantly different between CEA (5.6%) and CAS (6.9%; HR=0.99).

Interventionalists in CREST were the most carefully selected in any trial, and the lack of similar careful selection has been a critique expressed concerning the other trials. However, analyses of CAS in Medicare patients between 2005 and 2007 found that few CAS operators had the experience of CREST investigators. Among the 11,846 procedures where operator experience was documented, 68% were performed by operators having performed fewer than 12 procedures.

In a follow-up analysis of the CREST trial data, Gonzalez et al reported no differences in efficacy and safety outcomes for subjects based on receiving treatment in high-, medium-, or low-volume centers.

Asymptomatic Carotid Trial The Asymptomatic Carotid Trial (ACT) I was a noninferiority trial of CAS versus CEA in asymptomatic individuals who were not at high risk for surgical complications.³⁸ Enrollment began in 2005 with a target of 1658 participants, but, because of slow enrollment the trial was halted in 2013 with 1453 participants. The primary composite end point of death, stroke, or MI within 30 days or ipsilateral stroke within 1 year was obtained in 3.8% of CAS and 3.4% of CEA patients, while the cumulative 5-year rate of stroke-free survival was 93.1% with CAS and 94.7% with CEA (p=0.44). This study does not answer the question of how best to treat asymptomatic patients, since it does not include a medical therapy arm. Patients who are treated with current best medical therapy may have an ipsilateral stroke rate of only 0.5% to 1% per year.

Additional RCTs

Several additional smaller trials have compared CEA with CAS. Li et al (2014) published a study that reported to randomize 130 subjects at high risk of stroke due to angiographically confirmed carotid stenosis ($\geq 50\%$) to CEA (n=65) or CAS (n=65). The authors report a 3-month post-operative risk of mortality of 1.5% with CAS, compared with 9.2% with CEA. However, “existence of complete follow-up data” is an inclusion criterion, and insufficient details are provided about enrollment and randomization procedures to allow conclusions to be drawn about the study.

Kuliha et al (2015) published results of an RCT which randomized 150 subjects with at least 70% ICA stenosis to CEA (n=73) or CAS (n=77). New infarctions on magnetic resonance imaging (MRI) were found more frequently after CAS (49% vs 25%; p=0.002).

Section Summary: RCTs of CAS Versus CEA

RCTs comparing CEA with CAS enrolled a mix of symptomatic and asymptomatic patients and employed different selection criteria for participating centers. Periprocedural stroke and death rates following CAS exceeded those after CEA. Following the early perioperative period (≥ 31 days), the rate of ipsilateral and/or transient ischemic attack (TIA) appears to be similar for the 2

procedures. While some trials found higher restenosis rates after CAS (SAPPHIRE, SPACE, EVA-3S), restenosis in CREST occurred with similar frequency following either procedure. The rates of early complications in these trials exceed the threshold that has been set to denote overall benefit. There is some variability in the results of these trials. For example, results from CREST were more favorable for CAS than those reported from the SPACE, EVA-3S, or ICSS. Periprocedural death/stroke rates with CAS were lower than 6% in symptomatic and 3% in asymptomatic patients. Interventionalists in CREST were the most carefully selected in any trial and the criteria used to credential in other trials has been a focus of criticisms, along with the inconsistent use of embolic protection devices.

No RCTs have compared CAS with medical therapy. Therefore, it is not possible to determine whether CAS is superior to medical therapy. Since the pivotal CEA vs medical therapy trials, there has been a marked improvement in medical therapy and declining stroke rates in asymptomatic patients with carotid stenosis. In 1993, the ACST trial⁴ reported that the annual ipsilateral stroke rate was approximately 2.0% with medical therapy. A meta-analysis of studies completing enrollment between 2000 and 2010 found a pooled estimate for annual ipsilateral stroke incidence of 1.13%. This decrease in stroke risk has been used to argue that medical therapy in asymptomatic patients is preferable to surgical intervention.

Systematic Reviews

Several TEC Assessments and meta-analyses have been published all reporting similar findings. In average risk symptomatic patients the body of evidence demonstrates worse periprocedural outcomes with CAS compared to CEA. While data show secular improvement in periprocedural outcomes following CAS there is evidence of a net harm compared to CEA. The individual patient data meta-analysis of SPACE, EVA-3S, and ICSS indicates some uncertainty in comparative periprocedural death/stroke rates for younger symptomatic patients. Still, that subgroup result must be considered carefully given the larger body of evidence, lack of stratified randomization, as well as the evidence on restenosis. Meta-analyses have generally found that restenosis is more common following CAS than CEA. In a meta-analysis of 13 trials, among those reporting restenosis rates, Bangalore et al. reported pooled relative odds for restenosis following CAS compared to CEA of 2.8 (95% CI: 2.0 to 4.0; $I^2=0\%$). Of note was the individual patient data meta-analysis (n=3,433) of SPACE, EVA-3S and ICSS. In these symptomatic patients the 30-day death/stroke risk (per-protocol analyses) with CAS was 7.7% versus 4.4% following CEA (RR 1.74; 95% CI: 1.32 to 2.30).

The Carotid Stenting Trialists' Collaboration (2016) published an individual patient data meta-analysis (N=4754) of SPACE, EVA-3S ICSS, and symptomatic patients from CREST to evaluate the association between age and risk of stroke or death with CEA and CAS. The periprocedural period was defined as 120 days, which is considerably longer than the conventional 30-day periprocedural definition. For symptomatic patients assigned to CEA, there was no increase in periprocedural or post-procedural risk of death/stroke for patients older than 65 compared to patients younger than 60. In contrast, for patients assigned to CAS, the risk of peri-procedural events increased with age, from about a 2.1% risk for patients younger than 60 years, increasing to about 11% for patients older than 70 years. This analyses found increased periprocedural stroke risk for CAS versus CEA in patients approximately 65 years of age and older, but not among those younger patients (a possible age threshold was not clear). Age was not significantly associated with the

post-procedural stroke risk. The results suggest that the risk-benefit profile of CAS for symptomatic patients enrolled in these trials could be modified by age, but there was considerable imprecision in the age-specific CAS versus CEA comparisons for periprocedural risk. For example, among patients aged 60 to 64 the HR comparing CAS to CEA for the periprocedural risk of stroke or death was 1.07 (95% CI: 0.56 to 2.01).

Paraskavas et al conducted a systematic review of studies comparing cognitive outcomes after CEA with those after CAS. Thirteen studies were included, with heterogeneity in the types of cognitive outcome measures reported. In qualitative analysis, the authors report that most studies did not report a significant difference between CEA and CAS in terms of cognitive outcomes but that the heterogeneity in outcomes reported precluded more definitive conclusions.

Galyfos et al reported results of a systematic review that included 9 trials (n=5959) with a focus on risk of periprocedural symptomatic or asymptomatic myocardial ischemia or MI. Four studies did not report their definition used for myocardial ischemia, and other studies varied in their definitions. In pooled analysis, compared with CEA, CAS was associated with decreased risk for cardiac damage (pooled RR, 0.37; 95% CI, 0.22 to 0.61; $p < 0.000$). However, the study provides incomplete information about selection of studies for inclusion, which limits conclusions that can be drawn.

Vincent et al (2015) conducted a meta-analysis of 8 RCTs (total N=7091 patients).⁵⁴ Studies were selected that compared CAS to CEA, enrolled more than 50 patients, and reported periprocedural or long-term outcomes. Included were the CREST, ICSS, SPACE, EVA-3S, CAVATAS, and SAPPHERE trials described above. CAS was associated with an increased rate of any type of periprocedural stroke (relative risk, 1.49; 95% CI, 1.11 to 2.01), a similar risk of a disabling or major stroke, and a decreased risk of periprocedural myocardial infarction (relative risk, 0.47; 95% CI, 0.29 to 0.78) compared with CEA. However, in long-term follow-up (range, 2 to 10 years), stenting was associated with an increased risk of stroke (relative risk 1.36; 95% CI 1.16 to 1.61) and an increased risk of a composite end point of ipsilateral stroke, periprocedural stroke, or periprocedural death (relative risk, 1.45; 95% CI, 1.20 to 1.75) compared with CEA. This analysis supports the conclusion that CEA remains the treatment of choice for most patients due to the increase in adverse events with CAS.

Section Summary: Systematic Reviews

The systematic reviews corroborate the results of individual RCTs in reporting that early adverse events are higher with CAS compared to CEA that long-term stroke rates following the perioperative period are similar, and that restenosis is higher with CAS. These data indicate that for the average risk patient with carotid stenosis, CAS is associated with a net harm compared to CEA.

Periprocedural Death/Stroke Rates following CAS

Systematic Reviews

Questions of periprocedural death/stroke rates were assessed in the 2009 TEC Assessment. Given that CAS (like CEA) trades procedure-related risk of stroke and death for a reduced risk of stroke over subsequent years, and limits for periprocedural stroke and death rates that can be traded to achieve a net clinical benefit outlined in current guidelines are less than 3% for asymptomatic and

less than 6% for symptomatic patients, the Assessment sought evidence to address the following questions:

1. Is the periprocedural death/stroke rate with CAS less than 3% for asymptomatic and less than 6% for symptomatic patients?

Eighteen multicenter prospective registries collectively enrolling 20,194 patients were identified. Eleven enrolled patients in accordance with FDA labeling and 30-day outcomes were available for analysis according to symptomatic status (13,783 asymptomatic and 3,353 symptomatic). For 9 registries, 30-day death/stroke rates were either reported or obtained from investigators; in the remaining 2, death/stroke rates were estimated from 30-day death/stroke/MI and MI rates. An independent assessment of neurological outcomes was required in all but one registry. For asymptomatic patients, the pooled periprocedural death/stroke rate was 3.9% (95% CI: 3.3%–4.4%); for symptomatic patients 7.4% (95% CI: 6.0%–9.0%; $I^2=59\%$).

A subsequent systematic review, without consideration to FDA labeling, reported results consistent with the TEC Assessment (pooled periprocedural death/stroke rates in asymptomatic patients of 3.3% [95% CI: 2.6% to 4.1%; 23 studies; 8,504 patients] and in symptomatic patients of 7.6% [95% CI: 6.3% to 9.1%; 42 studies; 4,910 patients]).

2. For those subgroups defined by a) medical comorbidities or b) unfavorable anatomy, are periprocedural death/stroke rates with CAS less than 3% for asymptomatic and less than 6% for symptomatic patients?

Combined data from 2 registries reported periprocedural death/stroke rates for patients with unfavorable anatomy but included only 371 asymptomatic and 60 symptomatic patients. No other registry reported results by symptomatic status for those subgroups.

Since the publication of the 2009 TEC Assessment, some additional evidence has been published related to rates of periprocedural stroke/death following CAS, particularly related to subgroups defined by medical comorbidities. Spangler et al evaluated patients treated with isolated primary CEA (n=11,336) or primary CAS (n=544) at 29 centers between 2003 and 2013 to assess periprocedural mortality and stroke risks for patients considered medically high risk. A Cox proportional hazards model was used to generate predicted 5-year mortality, and patients in the highest risk score quartile were considered high risk. For asymptomatic patients, there were no significant differences between CEA and CAS for major periprocedural outcomes (major or minor stroke, MI, death) for either high- or low-risk patients. Periprocedural death/stroke rates with CAS were 1.1% for low-risk patients and 1.6% for high-risk patients. For symptomatic patients, periprocedural death/stroke rates were higher with CAS than CEA for both low- and high-risk groups. For low-risk symptomatic patients, periprocedural death/stroke rates were 6.0% for CAS, compared with 2.2% for CEA ($p<0.01$). For high-risk symptomatic patients, periprocedural death/stroke rates were 9.3% for CAS, compared with 2.5% for CEA ($p<0.01$).

Retrospective Analyses

Salzler et al (2017) conducted a large retrospective analysis of the increased use of CAS since the Centers for Medicare & Medicaid guidelines recommended CAS for high-risk patients needing

carotid revascularization.⁶⁰ Data from the Nationwide Inpatient Sample were searched for patients undergoing carotid revascularization. From 2005 (when the guidelines were published) to 2011, 20,079 CEAs and 3447 CASs were performed on high-risk patients. During the study period, CAS utilization increased significantly among all high-risk patients. A subgroup analysis of symptomatic high-risk patients did not show an increase in CAS use, indicating that the increase in CAS was primarily in asymptomatic high-risk patients. The odds of in-hospital mortality (odds ratio, 2.6; 95% CI, 1.2 to 5.6) and postoperative in-hospital stroke (odds ratio, 1.5; 95% CI, 1.1 to 3.7) were independently and significantly higher in patients undergoing CAS compared with CEA in the overall sample of high-risk patients.

CAS for Carotid Dissection

Carotid dissection is uncommon (incidence approximately 2 per 100,000/year) and occurs generally in younger individuals. With a frequently favorable prognosis, conservative therapy with anticoagulants to restore blood flow is typically employed while surgical intervention reserved for patients whose symptoms fail to respond to conservative care. Some have described CAS as a potential treatment in those instances however, there are no clinical trials comparing alternative strategies and interventions. Current guidelines (detailed below) rate CAS in for this indication as a class IIb (Level of Evidence: C) recommendation.

SUMMARY OF EVIDENCE

For individuals who have carotid artery stenosis who receive carotid artery stenting, the evidence includes randomized controlled trials (RCTs) and systematic reviews of RCTs. Relevant outcomes are overall survival, morbid events, treatment-related mortality, and treatment-related morbidity. A substantial body of RCT evidence compares outcomes of carotid artery stenting (CAS) with CEA for symptomatic and asymptomatic patients with carotid stenosis. The evidence does not support use of CAS in carotid artery disease for the average-risk patient, because early adverse events are higher with CAS and long-term outcomes are similar between the two procedures. Data from RCTs and large database studies establish that the risk of death or stroke with CAS exceeds the threshold considered acceptable to indicate overall benefit from the procedure. Therefore, for patients with carotid stenosis who are suitable candidates for CEA, CAS does not improve health outcomes. The evidence is sufficient to determine qualitatively that the technology is unlikely to improve the net health outcome.

SUPPLEMENTAL INFORMATION

CLINICAL INPUT FROM PHYSICIAN SPECIALTY SOCIETIES AND ACADEMIC MEDICAL CENTERS

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received through 4 physician specialty societies (6 reviewers) and 4 academic medical centers while this policy was under review in 2009. (In addition, 1

unsolicited response from a specialty society was also received.) This clinical input strongly supported use of carotid artery stenting in recently symptomatic patients where carotid surgical endarterectomy cannot be performed due to anatomic reasons, although acknowledging the limited evidence pertaining to this subgroup. The lack of alternative treatments for recently symptomatic patients and the established increased risk of stroke were factors supporting this opinion.

PRACTICE GUIDELINES AND POSITION STATEMENTS

American College of Cardiology Foundation et al

In 2011, the American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) Task Force on Practice Guidelines, American Stroke Association (ASA), American Association of Neuroscience Nurses (AANN), American Association of Neurological Surgeons (AANS), American College of Radiology (ACR), American Society of Neuroradiology (ASNR), Congress of Neurological Surgeons (CNS), Society of Atherosclerosis Imaging and Prevention (SAIP), Society for Cardiovascular Angiography and Interventions (SCAI), Society of Interventional Radiology (SIR), Society of NeuroInterventional Surgery (SNIS), Society for Vascular Medicine (SVM), and Society for Vascular Surgery (SVS) issued guidelines on the management of patients with extracranial carotid and vertebral artery diseases, which are summarized in Table 3.

Table 3. Summary of 2011 Guidelines on the Management of Patients With Extracranial Carotid and Vertebral Artery Disease

Class	LOE ^a
Class I Benefit >>> Risk	
CAS is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery is reduced by >70%, as documented by noninvasive imaging or >50% as documented by catheter angiography and the anticipated rate of periprocedural stroke or mortality is <6% (360)	B
Selection of asymptomatic patients for carotid revascularization should be guided by an assessment of comorbid conditions, life expectancy, and other individual factors and should include a thorough discussion of the risks and benefits of the procedure with an understanding of patient preferences	C
Class IIa Benefit >> Risk	
It is reasonable to choose CEA over CAS when revascularization is indicated in older patients, particularly when arterial pathoanatomy is unfavorable for endovascular intervention	B
It is reasonable to choose CAS over CEA when revascularization is indicated in patients with neck anatomy unfavorable for arterial surgery	B
When revascularization is indicated for patients with TIA or stroke and there are no contraindications to early revascularization, intervention within 2 wk of the index event is reasonable rather than delaying surgery	B
Class IIb Benefit ≥ Risk	
Prophylactic CAS might be considered in highly selected patients with asymptomatic carotid stenosis (minimum 60% by angiography, 70% by validated Doppler ultrasound), but its effectiveness compared with medical therapy alone in this situation is not well established	B
Carotid angioplasty and stenting might be considered when ischemic neurologic symptoms have not responded to antithrombotic therapy after acute carotid dissection	C
Class III: No Benefit	
Except in extraordinary circumstances, carotid revascularization by either CEA or CAS is not recommended when atherosclerosis narrows the lumen by <50%	A

Carotid revascularization is not recommended for patients with chronic total occlusion of the targeted carotid artery	C
Carotid revascularization is not recommended for patients with severe disability caused by cerebral infarction that precludes preservation of useful function	C

CAS: carotid artery angioplasty with stenting; CEA: carotid endarterectomy; LOE: level of evidence. ^a Levels of evidence: A (data derived from multiple randomized controlled trials or meta-analyses; multiple populations evaluated); B (data derived from a single randomized controlled trial or nonrandomized studies; limited populations evaluated); C (only consensus opinion of experts, case studies, or standard of care; very limited populations evaluated).

Society for Vascular Surgery

In 2011, SVS issued updated guidelines for management of extracranial carotid disease, which are summarized in Table 4.

Table 4. Summary of 2011 SVS Guidelines for Extracranial Carotid Disease

Grade	LOE ^a
Grade I "benefit clearly outweighs risk"	
In most patients with carotid stenosis who are candidates for intervention, CEA is preferred to CAS for reduction of all-cause and periprocedural death	B
Grade II "benefits and risks are more closely matched and are more dependent on specific clinical scenarios"	
CAS is preferred over CEA in symptomatic patients with >50% stenosis and tracheal stoma, situations where local tissues are scarred and fibrotic from prior ipsilateral surgery or external beam radiotherapy, prior cranial nerve injury, and lesions that extend proximal to the clavicle or distal to the C2 vertebral body	B
CAS is preferred over CEA in symptomatic patients with >50% stenosis and severe uncorrectable coronary artery disease, congestive heart failure, or chronic obstructive pulmonary disease	C
There are insufficient data to recommend CAS as primary therapy for neurologically asymptomatic patients with 70%-99% diameter stenosis. In properly selected asymptomatic patients, CAS is equivalent to CEA in the hands of experienced interventionalists with a combined stroke and death rate <3%	B

CAS: carotid artery angioplasty with stenting; CEA: carotid endarterectomy; LOE: level of evidence; SVS: Society for Vascular Surgery. ^a Levels of evidence: A (high quality); B (moderate quality); C (low quality).

European Society of Cardiology

The European Society of Cardiology (2018) updated its 2011 guidelines on the diagnosis and treatment of peripheral artery diseases, which included recommendations regarding carotid revascularization, summarized in Table 5.

Table 5. Guidelines for Diagnosing and Treating Carotid Artery Disease

Recommendation	LOE ^a
In asymptomatic patients who have been deemed "high risk for CEA" and who have an asymptomatic 60%-99% stenosis in the presence of clinical and/or imaging characteristics that may be associated with an increased risk of late ipsilateral stroke, CAS should be considered, provided documented perioperative stroke/death rates are <3% and the patient's life expectancy is >5 years	B
In "average surgical risk" patients with an asymptomatic 60-99% stenosis in the presence of clinical and/or imaging characteristics that may be associated with an increased risk of late ipsilateral stroke, CAS may be an alternative to CEA provided documented perioperative stroke/death rates are <3% and the patient's life expectancy is >5 years	B
In recently symptomatic patients with a 50%-99% stenosis who present with adverse anatomical features or medical comorbidities that are considered to make them 'high risk for CEA', CAS should be considered, provided the documented procedural death/stroke rate is <6%	B
When revascularization is indicated in "average surgical risk" patients with symptomatic carotid disease, CAS may be considered as an alternative to surgery, provided the documented procedural death/stroke rate is <6%.	B

CAS: carotid artery angioplasty with stenting; CEA: carotid endarterectomy; ESC: European Society of Cardiology; LOE: level of evidence.

^a Levels of evidence: A (data derived from multiple randomized clinical trials or meta-analyses); B (data derived from a single randomized clinical trial or large nonrandomized studies); C (consensus of opinion of the experts and/or small studies, retrospective studies, registries).

National Institute for Health and Clinical Excellence

The National Institute for Health and Clinical Excellence made the following recommendations about CAS:

“Current evidence on the safety of CAS placement for asymptomatic extracranial carotid stenosis shows well documented risks, in particular, the risk of stroke. The evidence on efficacy is inadequate in quantity..”

Royal Australasian College of Physicians et al

The Royal Australasian College of Physicians, Royal Australasian College of Surgeons, and Royal Australian and New Zealand College of Radiologists issued joint recommendations in 2011 on CAS :

“CAS may be considered as a treatment option for patients with symptomatic severe carotid stenosis who are at high risk of stroke, but are surgically unsuitable for CEA, namely post-radiation therapy, block dissection of the neck, in situ tracheostomy, recurrent stenosis following previous CEA, severe cervical spine arthritis, surgically inaccessible carotid stenosis (e.g., obesity, high carotid bifurcation), contralateral recurrent laryngeal nerve injury, and contralateral internal carotid occlusion.”

“The overall results of randomized controlled trials indicate that CAS is not as safe as CEA for treatment of symptomatic carotid stenosis for prevention of ipsilateral stroke.”

“There is currently no evidence to support CAS as a treatment for asymptomatic carotid stenosis.”

MEDICARE NATIONAL COVERAGE

From March 2001, Medicare’s national coverage policy restricted coverage for carotid angioplasty and stenting to patients participating in a clinical trial with Category B Investigational Device Exemption (IDE) designation from the FDA. Percutaneous transluminal angioplasty (PTA) of the vertebral and cerebral arteries remained noncovered.

When FDA approved the first (Guidant) devices, Medicare coverage under the IDE trial policy was no longer available for that manufacturer’s devices and was not applicable to FDA-required post-approval studies. Thus, on October 12, 2004, Medicare broadened its national coverage policy and “determined that the evidence is adequate to conclude that percutaneous transluminal angioplasty (PTA) with carotid stent placement is reasonable and necessary when performed consistent with FDA approval of the carotid stent device and in an FDA required post-approval study.” For unapproved stents and EPD devices, the prior policy remained in effect and restricted coverage to

patients participating in an FDA-approved Category B IDE trial of stent placement in the cervical carotid artery.

While the Medicare decision differed from the conclusions of this policy, Medicare made a public policy decision “that making available new, effective therapies aimed at addressing treatment and prevention of cerebrovascular disease was important to Medicare beneficiaries.” Medicare also noted that it recognized value in supporting post-approval studies as “the collected data may provide an opportunity for practitioners to determine which patients are most appropriate for carotid artery stenting and to reinforce IDE trial data on health outcomes and adverse events.”

CMS provides a continually updated listing of facilities eligible for Medicare reimbursement that met CMS's minimum facility standards for performing carotid artery stenting for high-risk patients.

On March 17, 2005, CMS determined that CAS with EPD is reasonable and necessary for patients at high risk for CEA who also have symptomatic carotid artery stenosis equal to or greater than 70%. CMS limited coverage for these patients to procedures performed using FDA-approved devices. CMS also limited coverage for patients at high risk for CEA with symptomatic carotid artery stenosis between 50% and 70%, and for patients at high risk for CEA with asymptomatic stenosis equal to or greater than 80%, to FDA-approved Category B IDE clinical trials for unapproved devices, or to FDA-required post-approval studies for approved devices. CMS defined patients at high risk for CEA as having significant comorbidities and/or anatomic risk factors (i.e., recurrent stenosis and/or previous radical neck dissection) who would be poor candidates for CEA in the opinion of a surgeon. The paragraph below provides CMS' reasoning for this change in coverage policy:

“Considering the evidence and clinical situation, there appears to be sufficient evidence to infer that CAS with embolic protection can improve health outcomes for patients with severe symptomatic stenosis >70% who are also at high risk for CEA, if performed with the same expertise and rate of adverse events as demonstrated in the published clinical trials. Since patients with severe symptomatic stenosis \geq 70% are at high risk for stroke, carotid interventions to reduce the risk of stroke should be considered. Although the published studies on CAS have various potential biases, we feel that the need for an alternative treatment to CEA for patients who are truly at high risk for CEA should be factored into the coverage decision, unlike the BCBS TEC report, which did not consider this circumstance. By not covering this group, symptomatic patients who also are at high risk for surgery may be left with no other treatment options. The risk benefit consideration may be similarly influenced. However, having mentioned this situation, the high risk CAS studies compared CAS to CEA and found that CEA can be performed as well as CAS in a group classified as high risk. Therefore, two comparable options exist for patients with symptomatic stenosis \geq 70% who are at high risk.”

On April 30, 2007, a decision memo reaffirmed CMS's previous decision following a request to expand coverage while clarifying that “CAS is only covered when used with an embolic protection device and is, therefore, not covered if deployment of the distal embolic protection device is not technically possible.” On October 14, 2008 in the sixth reconsideration, and on December 9, 2009 in the seventh reconsideration, CMS reaffirmed their prior coverage decisions.

On January 25, 2012 CMS convened a MEDCAC panel to consider “Management of Carotid Atherosclerosis.” Panel members voted on specific questions using a scale of 1 (low confidence) to

5 (high confidence). For symptomatic patients not considered at high-risk, the mean scores to the question of whether CAS is the favored treatment strategy in this population was 1.85 and for CEA 3.6. For asymptomatic patients not considered high-risk the evidence was judged to have not reached a level of certainty to determine a favored treatment.

ONGOING AND UNPUBLISHED CLINICAL TRIALS

Table 6. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02538276	Carotid Endarterectomy and Carotid Artery Stenting in Brazil	500	Jul 2019
NCT00883402	Asymptomatic Carotid Surgery Trial-2 (ACST-2): an International Randomised Trial to Compare Carotid Endarterectomy With Carotid Artery Stenting to Prevent Stroke	3600	Dec 2019
ISRCTN78592017	Stent-protected angioplasty in asymptomatic carotid artery stenosis vs endarterectomy: two two-arm clinical trials (SPACE-2)	5000	Jul 2020
NCT02089217	Carotid revascularization and medical management for asymptomatic carotid stenosis trial (CREST-2)	2480	Dec 2020
ISRCTN97744893	European Carotid Surgery Trial 2 (ECST-2): a randomized controlled trial	2000	Mar 2022

VI. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii's Patients' Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA's determination as to medical necessity in a given case, the physician may request that HMSA consider the application of this Medical Policy to the case at issue.

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