# Why the Carotid RCTs Fail to Support the Recent CMS Expansion of Reimbursement for CAS to Treat Asymptomatic Disease (ACS): Do the 5-Year SPACE-2 Results Suggest that Such Expanded Reimbursement be Delayed Until CREST-2 Data is In

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Veith Symposium 2024

## Disclosures

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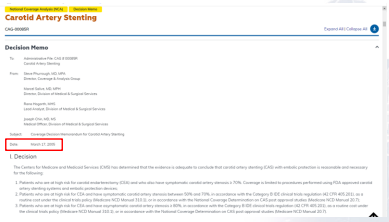
  - American College of Surgeons
  - NIH/NIDDK
  - Society for Vascular Surgery

## History of Carotid Artery Stenting NCD


Carotid Artery Stenting

CAG-00085N

Decision Memo

I. Decision

## CAS NCD: 2005

**Patients at high risk for carotid endarterectomy who have:**

- Symptomatic carotid artery stenosis ≥70%
  - FDA-approved stent + EPD
- Symptomatic carotid artery stenosis 50-70% in a clinical trial
  - Includes post-market approval studies
- Asymptomatic carotid artery stenosis ≥80% in a clinical trial

- Congestive heart failure (CHF) class III/IV;
- Left ventricular ejection fraction (LVEF) < 30%;
- Unstable angina;
- Contralateral carotid occlusion;
- Recent myocardial infarction (MI);
- Previous CEA with recurrent stenosis ;
- Prior radiation treatment to the neck; and
- Other conditions that were used to determine patients at high risk for CEA in the prior carotid artery stenting trials and studies, such as ARCHER, CABERNET, SAPPHIRE, BEACH, and MAVERIC II

## CAS NCD: 2005

- In addition, CMS has determined that CAS with embolic protection is reasonable and necessary only if performed in facilities that have been determined to be competent in performing the evaluation, procedure and follow-up necessary to ensure optimal patient outcomes
- List of 5 minimum standards modeled in part on professional society statements on competency
- Burden of documentation on the facility

## CAS NCD Reconsiderations


Carotid Artery Stenting

CAG-00085N

History of Considerations

2001 Original Consideration — Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting — CAG-00085N — View

2005 First reconsideration — Carotid Artery Stenting — CAG-00085R — You are here

2006 Second reconsideration — Intracranial Stenting and Angioplasty — CAG-00085S2 — View

2007 Third reconsideration — Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting — CAG-00085R3 — View

2008 Fourth reconsideration — Percutaneous Transluminal Angioplasty (PTA) and Stenting of the Renal Arteries — CAG-00085R4 — View

2008 Fifth reconsideration — Intracranial Stenting and Angioplasty — CAG-00085R5 — View

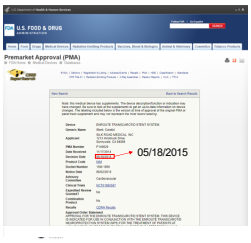
2008 Sixth reconsideration — Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting — CAG-00085R6 — View

2009 Seventh reconsideration — Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting — CAG-00085R7 — View

2023 Eighth reconsideration — Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting — CAG-00085R8 — View

TCAR

## Initial TCAR Approval




**ONE risk factor qualifies patient for CMS high surgical risk status**

- Age ≥75
- Prior head/neck surgery or irradiation
- Restenosis post CEA
- Contralateral occlusion
- Surgically inaccessible lesion
- Severe tandem lesions
- Bilateral stenosis requiring treatment
- Cervical spine immobility
- Uncontrolled diabetes
- LVEF <35%
- Chronic renal insufficiency (Creatinine ≥2.5 mg/dl)
- Need for open heart surgery
- MI >72hr & <6 weeks prior to procedure
- Permanent contralateral cranial nerve injury
- Severe pulmonary disease
- >2-diseased coronaries with ≥70% stenosis
- CHF with NYHA Class III or IV
- Need for major surgery (including vascular)
- Unstable angina
- Abnormal stress test
- Laryngeal palsy or laryngectomy

1. HSR, Symptomatic >50% stenosis
2. HSR, Asymptomatic ≥80% stenosis

→ Covered through TCAR Surveillance Project (TSP)

## TCAR Approved for Standard Risk Patients

Transcarotid artery revascularization is associated with similar outcomes to carotid endarterectomy regardless of patient risk status

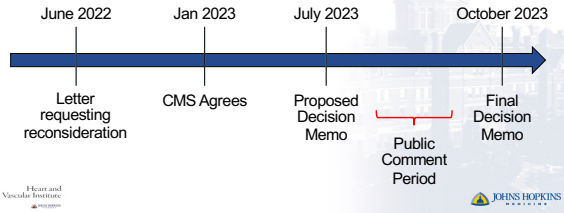
Risk of Stroke, Death, and Myocardial Infarction Following Transcarotid Artery Revascularization vs Carotid Endarterectomy in Patients With Standard Surgical Risk

May, 2022

**Silk Road Medical Announces FDA Approval of Expanded Indications for the ENROUTE® Transcarotid Stent System**

SUNNYVALE, Calif. – May 2, 2022 – Silk Road Medical, Inc. (Nasdaq: SILK), a company focused on reducing the risk of stroke and its devastating impact, today announced that that the U.S. Food and Drug Administration (FDA) approved expanded indications for the ENROUTE stent to include patients at standard risk for adverse events from carotid endarterectomy (CEA). Previously, the stent was approved for use only in patients with anatomic or physiological criteria that put them at high risk of complications from more invasive surgical procedures.

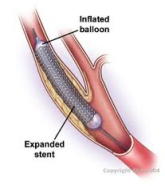
## New Carotid NCD Timeline




## CAS NCD: 2023

- Symptomatic carotid artery stenosis ≥50%
- Asymptomatic carotid artery stenosis ≥70

No High-Risk Criteria Requirements




## CAS NCD 2023 vs. 2025

1. Expands coverage to individuals previously only eligible for coverage in clinical trials;
2. Expands coverage to standard surgical risk individuals by removing the limitation of coverage to only high surgical risk individuals;
3. Removes facility standards and approval requirements;
4. Adds formal shared decision-making with the individual prior to furnishing CAS; and
5. Allows Medicare discretion for all other coverage of PTA of the carotid artery concurrent with stenting not otherwise addressed

Removed Requirement for Outcomes Reporting

## Main Argument in Favor of Expansion

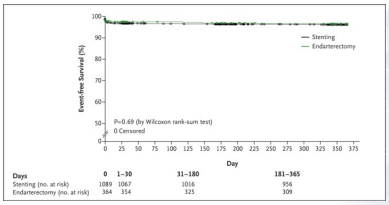
- Contemporary trials show CEA and CAS outcomes are equivalent. But . . .

## CREST Trial

| End Point | CAS (N=1262) no. of patients (% ±SE) | CEA (N=1240) no. of patients (% ±SE) | Periprocedural Period Absolute Treatment Effect of CAS vs. CEA (95% CI) percentage points | Hazard Ratio for CAS vs. CEA (95% CI) | P Value |
|---|---|---|---|---|---|
| Death | 9 (0.7±0.2) | 4 (0.3±0.2) | 0.4 (-0.2 to 1.0) | 2.25 (0.69 to 7.30)† | 0.18† |
| Stroke | | | | | |
| Any | 52 (4.1±0.6) | 29 (2.3±0.4) | 1.8 (0.4 to 3.2) | 1.79 (1.14 to 2.82) | 0.01 |
| Major ipsilateral | 11 (0.9±0.3) | 4 (0.3±0.2) | 0.5 (-0.1 to 1.2) | 2.67 (0.85 to 8.40) | 0.09 |
| Major nonipsilateral‡ | 0 | 4 (0.3±0.2) | NA | NA | NA |
| Minor ipsilateral | 37 (2.9±0.5) | 17 (1.4±0.3) | 1.6 (0.4 to 2.7) | 2.16 (1.22 to 3.83) | 0.009 |
| Minor nonipsilateral | 4 (0.3±0.2) | 4 (0.3±0.2) | 0.0 (-0.4 to 0.4) | 1.02 (0.25 to 4.07) | 0.98‡ |
| Myocardial infarction | 14 (1.1±0.3) | 28 (2.3±0.4) | −1.1 (−2.2 to −0.1) | 0.50 (0.26 to 0.94) | 0.03 |
| Any periprocedural stroke or postprocedural ipsilateral stroke | 52 (4.1±0.6) | 29 (2.3±0.4) | 1.8 (0.4 to 3.2) | 1.79 (1.14 to 2.82) | 0.01 |
| Major stroke | 11 (0.9±0.3) | 8 (0.6±0.2) | 0.2 (-0.5 to 0.9) | 1.35 (0.54 to 3.36) | 0.52 |
| Minor stroke | 41 (3.2±0.5) | 21 (1.7±0.4) | 1.6 (0.3 to 2.8) | 1.95 (1.15 to 3.30) | 0.01 |
| Any periprocedural stroke or death or postprocedural ipsilateral stroke | 55 (4.4±0.6) | 29 (2.3±0.4) | 2.0 (0.6 to 3.4) | 1.90 (1.21 to 2.98) | 0.005 |
| Primary end point (any periprocedural stroke, myocardial infarction, or death or postprocedural ipsilateral stroke) | 66 (5.2±0.6) | 36 (4.5±0.6) | 0.7 (-1.0 to 2.4) | 1.18 (0.82 to 1.68) | 0.38 |

Brott et al. N Engl J Med. 2010 Jul 1;363(1):11-23

## ACT-1




**Composite Endpoint:** Death, stroke, or myocardial infarction within 30 days after the procedure or ipsilateral stroke within 1 year

Rosenfield et al. N Engl J Med. 2016 Mar 17;374(11):1011-20

## ACT-1

**Underpowered?**
Enrolled = 1453
Intended = 1658

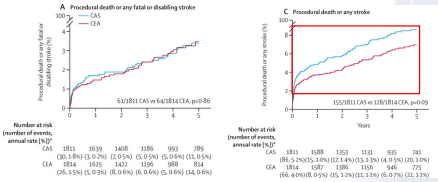
Table 2. Death, Stroke, or Myocardial Infarction and Composite Measure of Complications within 30 Days after Index Procedure.*

| Outcome | Stenting (N=1089) no. of patients/total no. (%) | Endarterectomy (N=364) no. of patients/total no. (%) | P Value† |
|---|---|---|---|
| Death, stroke, or myocardial infarction | 35/1072 (3.3) | 9/348 (2.6) | 0.60 |
| Death or stroke | 31/1072 (2.9) | 6/348 (1.7) | 0.33 |
| Death or major stroke | 6/1072 (0.6) | 2/348 (0.6) | 1.00 |
| Death | 1/1072 (0.1) | 1/348 (0.3) | 0.43 |
| All stroke | 30/1072 (2.8) | 5/348 (1.4) | 0.23 |
| Major stroke | 5/1072 (0.5) | 1/348 (0.3) | 1.00 |
| Ipsilateral | 4/1072 (0.4) | 1/348 (0.3) | 1.00 |
| Nonipsilateral | 1/1072 (0.1) | 0/348 | 1.00 |
| Minor stroke | 26/1072 (2.4) | 4/348 (1.1) | 0.20 |
| Ipsilateral | 22/1072 (2.1) | 4/348 (1.1) | 0.36 |
| Nonipsilateral | 4/1072 (0.4) | 0/348 | 0.58 |
| Myocardial infarction | 5/1072 (0.5) | 3/348 (0.9) | 0.41 |
| Composite measure of complications | 31/1089 (2.8) | 17/364 (4.7) | 0.13 |
| Cranial-nerve injury | 1/1089 (0.1)‡ | 4/364 (1.1) | 0.02 |
| Peripheral-nerve injury | 0/1089 | 0/364 | NA |
| Vascular injury | 8/1089 (0.7) | 3/364 (0.8) | 1.00 |
| Noncerebral bleeding | 21/1089 (1.9) | 6/364 (1.6) | 0.83 |
| Endarterectomy incision or puncture-site bleeding | 3/1089 (0.3) | 4/364 (1.1) | 0.07 |
| Other complications | 0/1089 | 0/364 | NA |

Rosenfield et al. N Engl J Med. 2016 Mar 17;374(11):1011-20

## Asymptomatic Carotid Surgery Trial (ACST-2)

NIHR HTA/BUPA Foundation/University of Oxford




**Underpowered**
Enrolled = 3625
Intended = 5000

Halliday et al. 2021 Sep 18;398(10305):1065-1073

## SPACE-2

| | CEA (n=203) | CAS (n=197) | BMT (n=113) | p value* |
|---|---|---|---|---|
| Primary endpoint event | 5 (2·5% [1·0–5·8]) | 8 (4·4% [2·2–8·6]) | 3 (3·1% [1·0–9·4]) | 0·62 |
| Secondary outcome events | | | | |
| Ipsilateral ischaemic stroke | 4 (2·0% [0·7–5·2]) | 8 (4·4% [2·2–8·6]) | 3 (3·1% [1·0–9·4]) | 0·45 |
| Any ischaemic or haemorrhagic stroke | 10 (5·3% [2·9–9·6]) | 17 (9·8% [6·2–15·3]) | 6 (6·5% [2·9–13·9]) | 0·28 |
| Death from any cause | 13 (7·6% [4·5–12·8]) | 15 (9·3% [5·7–15·0]) | 8 (8·0% [4·1–15·4]) | 0·88 |
| Any ischaemic stroke | 10 (5·3% [2·9–9·6]) | 16 (9·2% [5·7–14·7]) | 5 (5·5% [2·3–12·7]) | 0·29 |
| Any disabling stroke† | 2 (1·0% [0·3–4·0]) | 3 (1·7% [0·6–5·2]) | 2 (2·0% [0·5–7·6]) | 0·82 |
| Ipsilateral disabling stroke | 0 | 1 (0·5% [0·1–3·9]) | 2 (2·0% [0·5–7·6]) | 0·14 |
| Any ischaemic stroke or vascular death‡ | 15 (8·1% [4·9–13·1]) | 24 (14·1% [9·7–20·4]) | 9 (9·4% [5·0–17·4]) | 0·23 |
| Re-stenosis ≥70%¶ | 6 (3·2% [1·5–7·1]) | 18 (10·2% [6·6–15·8]) | - | 0·0092 |
| Re-stenosis and progressive stenosis‖** | 6 (3·2% [1·5–7·1]) | 18 (10·2% [6·6–15·8]) | 14 (14·6% [8·9–23·5]) | 0·0050 |
| Vascular death | 5 (2·9% [1·2–6·8]) | 9 (5·6% [3·0–10·6]) | 4 (4·2% [1·6–10·8]) | 0·52 |
| Myocardial infarction | 10 (6·3% [3·4–11·3]) | 8 (5·1% [2·6–10·0]) | 2 (2·7% [0·7–10·4]) | 0·42 |
| Any transient ischaemic attack†† | 10 (5·7% [3·1–10·4]) | 10 (5·5% [3·0–9·9]) | 8 (8·2% [4·1–15·8]) | 0·67 |
| Ipsilateral transient ischaemic attack†† | 2 (1·0% [0·3–3·9]) | 8 (4·3% [2·2–8·4]) | 8 (8·2% [4·1–15·8]) | 0·0168 |

**Composite Endpoint:** Any stroke or death from any cause within 30 days or any ipsilateral ischemic stroke within 5 years

Reiff et al. Lancet Neurol. 2022 Oct;21(10):877-888.

## SPACE-2

| | CEA (n=203) | CAS (n=197) | BMT (n=113) | p value* |
|---|---|---|---|---|
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| Any ischaemic stroke | 10 (5·3% [2·9–9·6]) | 16 (9·2% [5·7–14·7]) | 5 (5·5% [2·3–12·7]) | 0·29 |
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| Ipsilateral disabling stroke | 0 | 1 (0·5% [0·1–3·9]) | 2 (2·0% [0·5–7·6]) | 0·14 |
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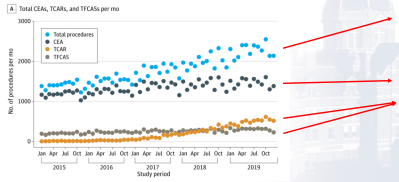
| Ipsilateral transient ischaemic attack†† | 2 (1·0% [0·3–3·9]) | 8 (4·3% [2·2–8·4]) | 8 (8·2% [4·1–15·8]) | 0·0168 |

**Underpowered!**
Enrolled = 513
Intended = 3640

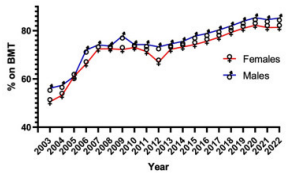
Reiff et al. Lancet Neurol. 2022 Oct;21(10):877-888.

## What Does The 2023 NCD Mean for CAS?




Stonko et al., JAMA Netw Open. 2022 Sep 1;5(9):e2231944

## Medical Management Might Win



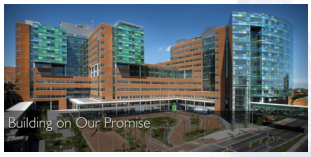

CREST-2

Bose et al. J Vasc Surg. 2023 Mar;77(3):786-794.e2

## Conclusions

- The Carotid Artery Stenting National Coverage Decision has opened up carotid revascularization procedures across the board
- The role of carotid revascularization in asymptomatic disease is not clear
- The future of carotid revascularization (trends, outcomes, appropriateness of treatment) will need close evaluation

## Thank You

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