

Evidence Table 1. Key Randomized Controlled Trials Assessing CAS vs CEA (since the 2009 National Coverage Determination)

Year published (enrollment)	Trial / 1st Author	Study Population				Intervention / Comparator	Outcome (primary)	Time (Duration in years)	Other Events	Results
		Clinical characteristics	Age	Sex	Race					
Foundational RCTs: CEA v OMT										
1998 (1981-94)	ECST / MRC group	<u>N = 3,018</u> • Recently symptomatic (within 6 mos) • Any carotid stenosis	Age, years, mean (SD): 62.3-62.5 (8.0-8.1) across study arms	Male, N (%): 2,168 (72%) Female, N (%): 850 (28%)	Not reported	<u>CEA v OMT</u>	Composite of surgical (procedural) events and all major strokes. Stroke-free life expectancy (time-to-event for major stroke or death, adjusted for age, sex, degree of stenosis).	6	(MIs, Cranial nerve palsies, events other than stroke/death, NR)	CEA superior to OMT if stenosis ≥70-80% ECST criteria (40-60% NASCET criteria); less certainty for women.
1995 (1987-93)	ACAS / Walker	<u>N = 1,662</u> • Asymptomatic. • Stenosis ≥60%.	Age, years, mean: 67 <70: 63-65% ≥70: 36-38% across study arms	Male, %: 66% Female, %: 34%	Race, %: White: 94-95% Black: 3% Other: 2-3% across study arms	<u>CEA v OMT</u>	Aggregate risk over 5 years for ipsilateral stroke and any perioperative stroke or death.	5		CEA superior. Risk for primary outcome: 5.1% CEA, 11.0% OMT (relative difference of 53%; absolute difference of 6%).
1998 (1987-96)	NASCET / Barnett	2nd phase (moderate stenosis only) • <u>N = 2,226</u> • Recently symptomatic (within 6 mos). • Stenosis: low moderate (<50%); high moderate (50-69%). 1st phase (severe stenosis, trial stopped). • Stenosis >70%. • Age <80 yrs.	Age, years, median: 66 <65: 36-41% ≥65: 59-64% across study arms	Male, %: 69-71% across study arms Female, %: 29-31% across study arms	Race, %: White: 93% Black: 3-4% Other: 3-4% across study arms	<u>CEA v OMT</u>	Any ipsilateral stroke (fatal or non-fatal).	5		CEA superior if stenosis >70% NASCET criteria [*trial stopped, at 17% absolute reduction] Rate of death or major stroke 2.1% at 30 days, 6.7% at 8 yrs. CEA slightly superior overall for 50-69%, but depends on patients.
Key RCTs since 2009 NCD										

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	Trial / 1st Author	Clinical characteristics	Age	Sex	Race	Outcome (primary)				
2010, 2016 (2000-08)	CREST / Brott	<u>N = 2,502</u> <ul style="list-style-type: none"> Standard surgical Risk. Symptomatic (52.8%), ≥50% stenosis by angio. Asymptomatic (47.2%), ≥60% stenosis. 	Age, years, mean (SD): 69.0 (8.9)	Male, N (%): 1630 (65%) Female, N (%): 872 (35%)	White race, %: 93.2%	<u>CAS v CEA</u> <ul style="list-style-type: none"> Embololic protection in CAS: 96%. Physician criteria. 	<u>30-day</u> : 1° composite of any death, stroke, or MI. <u>Long-term</u> : any ipsilateral stroke 1° composite of any stroke, MI, or death, (at 10yrs).	5, 10	CAS at 10yrs: sig. higher (37%) 30-day stroke or death plus subsequent ipsilateral stroke (due to higher CAS 30-day strokes). Similar rates of restenosis or revascularization.	CAS ≈ CEA at 10yrs for 1° composite outcome, and long-term outcome.
2010, 2015 (2001-08)	ICSS / Bonati	<u>N = 1,710</u> <ul style="list-style-type: none"> Standard surgical Risk. Symptomatic (within 12 mos). Stenosis ≥70% (in 90% of pts), ≥50% (in 10%). 	Age, years, mean (SD): 70 (9) across study arms	Male, N (%): 1,207 (71%) Female, N (%): 503 (29%)	Not reported	<u>CAS v CEA</u> <ul style="list-style-type: none"> Embololic protection in CAS not stated. Physician criteria. 	Fatal or disabling stroke in any territory to end of follow up.	5, 10	CAS with more non-disabling stroke at 30 days and 5 and 10 yrs; CEA, with more cranial nerve palsies (but not more MIs).	CAS ≈ CEA at 5 and 10 yrs for: <ul style="list-style-type: none"> fatal or disabling stroke; ipsilateral stroke and severe restenosis of treated carotid artery.
2016 (2005-13)	ACT-1 / Rosenfield	<u>N = 1,453</u> <ul style="list-style-type: none"> Standard surgical Risk. Asymptomatic, ≥70% stenosis. 	Age, years, mean (SD): 67.7-67.9 (6.9-7.0) across study arms	Male, N (%): 873 (60%) Female, N (%): 1,080 (30%)	White race, N (%): 1,312 (90%)	<u>CAS v CEA</u> <ul style="list-style-type: none"> Embololic protection in CAS: required. No physician criteria. 	Composite of any death, stroke, or MI at 30 days, or any ipsilateral stroke within 1 yr.	1, 5	At 30 days, CAS had more strokes; CEA, more MIs and cranial nerve palsies.	CAS noninferior to CEA (at 3% margin) for 1° composite outcome at 1 yr. At 5 yrs, similar overall survival, and cumulative 5-yr stroke-free survival.
2021 (2008-20)	ACST-2 / Halliday	<u>N = 3,625</u> <ul style="list-style-type: none"> Standard surgical Risk. Asymptomatic, ≥70% stenosis by US (97% of pts). 	Age, years, N (%): <70: 1,802 (50%) ≥70: 1,823 (50%)	Male, N (%): 2,545 (70%) Female, N (%): 1,080 (30%)	Not reported	<u>CAS v CEA</u> <ul style="list-style-type: none"> Embololic protection in CAS: required. Physician criteria: h/o <3% stroke or death for asymptomatic patients. 	<u>30-day</u> : Composite of any disabling stroke or death. <u>Long-term</u> (at "5 or more years"): "prevention of stroke, particularly disabling or fatal stroke".	5, 10	CAS had more procedural and long-term non-disabling strokes; CEA had more procedural MIs and cranial nerve palsies.	CAS ≈ CEA at 30 days for procedural disabling stroke or death (1% each), and 5yr non-procedural fatal or disabling stroke (2.5%).

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2022 (2009-19)	SPACE-2 / Reiff	N = 513 • Asymptomatic, mod-to-severe (≥50%) stenosis by NASCET criteria.	Age, years, median (IQR): 70 (64-75)	Male, N (%): 381 (74%) Female, N (%): 132 (26%)	Not reported	Parallel RCTs: • <u>CAS v OMT</u> • <u>CEA v OMT</u>	Composite of cumulative incidence of any stroke or death at 30 days or any ipsilateral ischemic stroke at 5 yrs.	5		No difference for the 1° composite outcome in either trial. Trial stopped early due to poor enrollment in OMT arm.

ACAS: Asymptomatic Carotid Atherosclerosis Study

ACST-2: Asymptomatic Carotid Surgery Trial-2

ACT-1: Asymptomatic Carotid Trial

CREST: Carotid Revascularization Endarterectomy versus Stent Trial

ECST: European Carotid Surgery Trial

ICSS: International Carotid Stenting Study

MI: Myocardial infarction

NASCET: North American Carotid Endarterectomy Trial

SPACE-2: Stent Protected Angioplasty versus Carotid Endarterectomy-2