Updates in the Management of Carotid Disease

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Ochsner Regional Neuroscience Symposium

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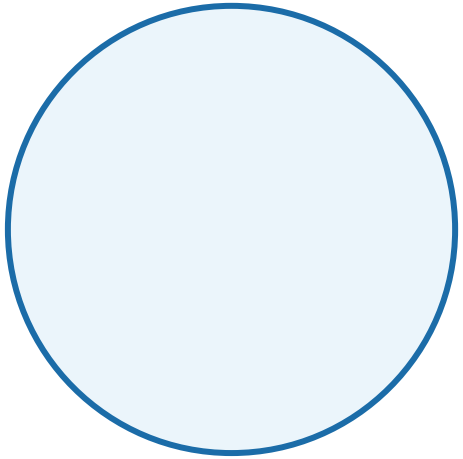
Disclosures

Relevant Financial Relationships



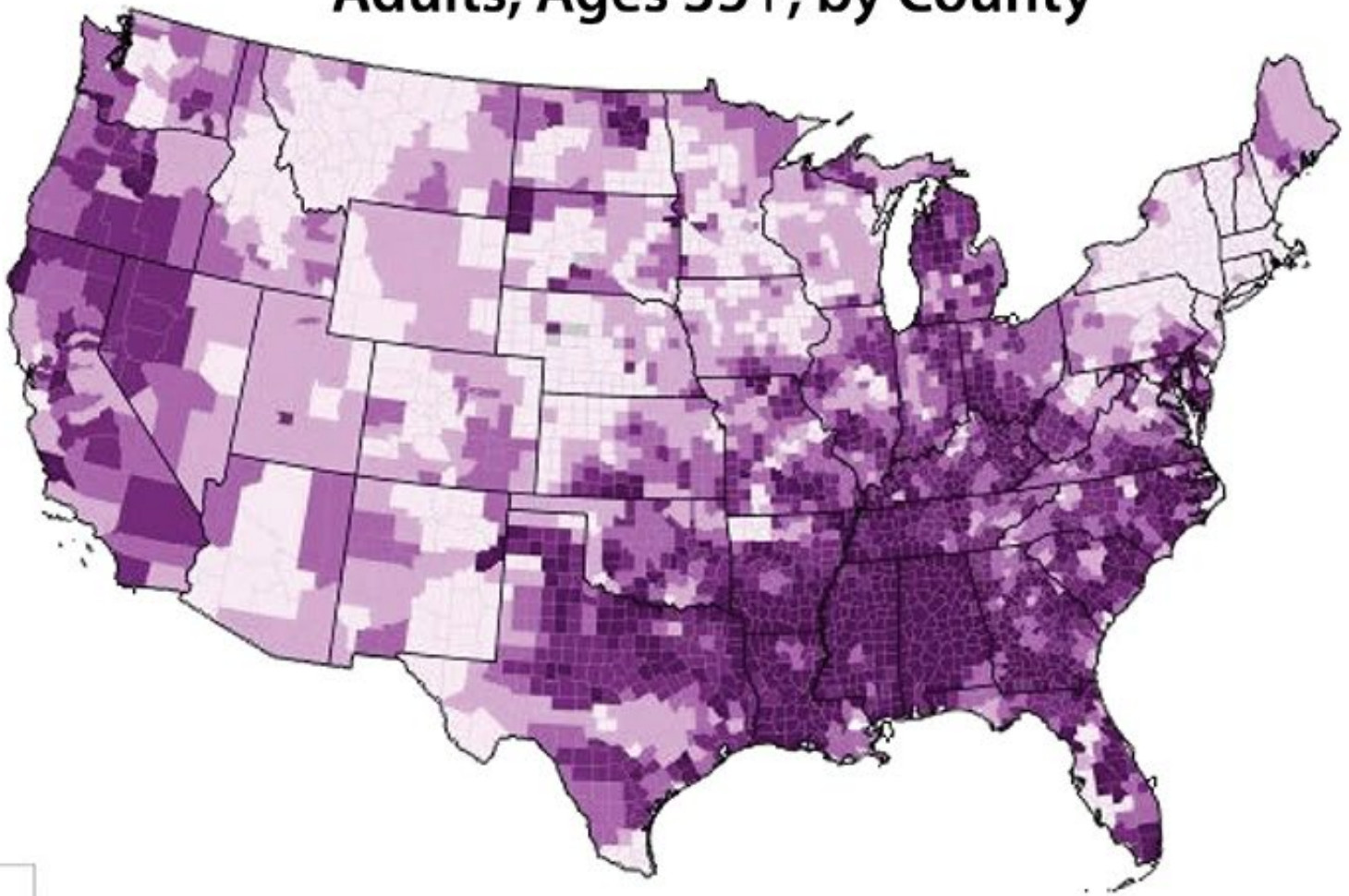
No Financial Relationships to Disclose

The presenter has no relevant financial relationships with ineligible companies to disclose in relation to the content of this CME activity.

Objectives

- Understand the epidemiology and natural history of asymptomatic carotid stenosis (aCAS)
- Summarize the key historical randomized trials that shaped current practice (ACAS, ACST-1, ACST-2, CREST-1)
- Review the results from the recent CREST 2 trials and its impact on current carotid disease management.
- Discuss future directions

Stroke Death Rates, 2018-2020
Adults, Ages 35+, by County



Age-Adjusted Prevalence (%)

- 3.6-61.4
- 61.5-70.6
- 70.7-78.4
- 78.5-89.3
- 89.4-177.5
- Insufficient Data

Guam

Northern Mariana Islands

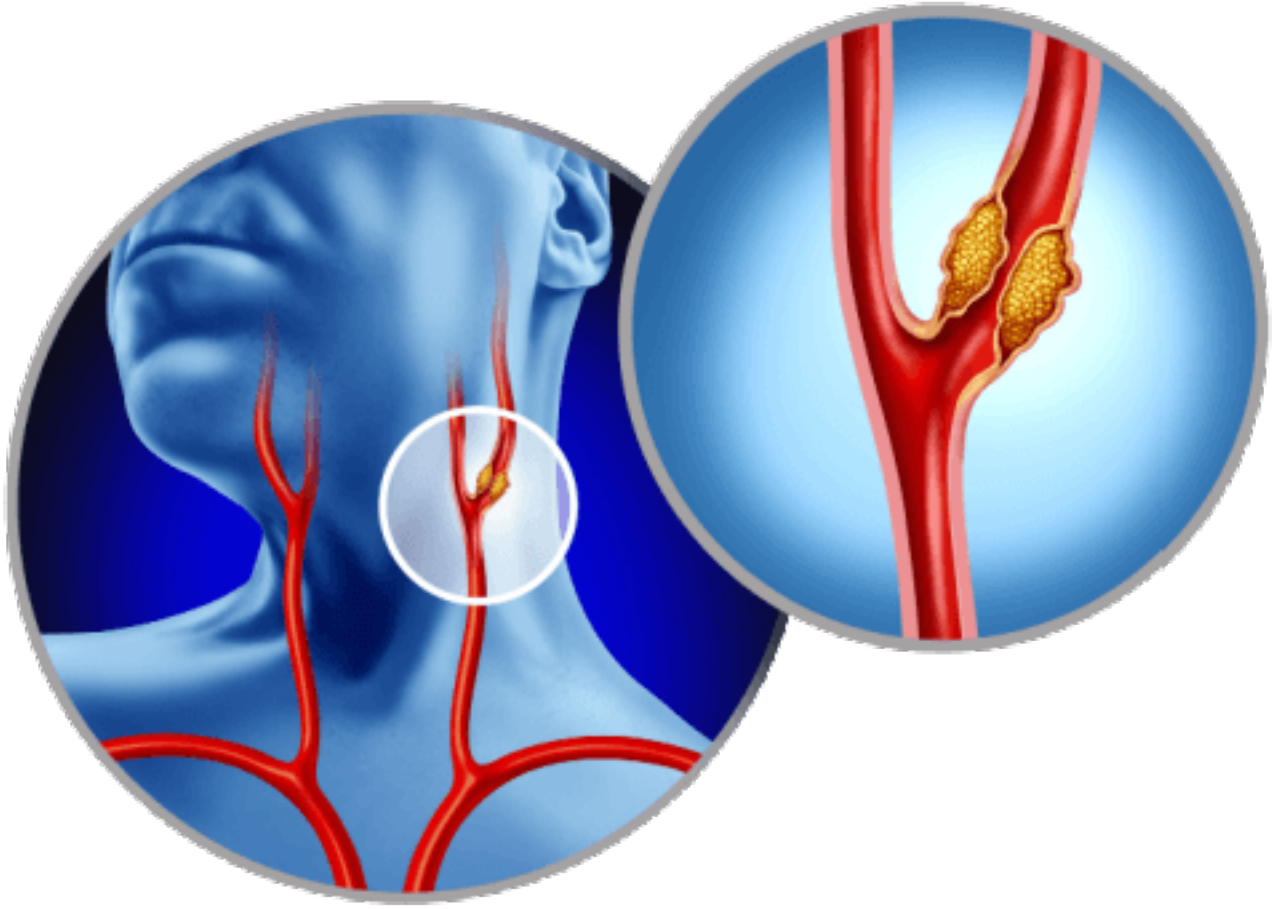
American Samoa

Data source and methodology found at: www.cdc.gov/dhdsp/maps/atlas/statistical-methods

CDC

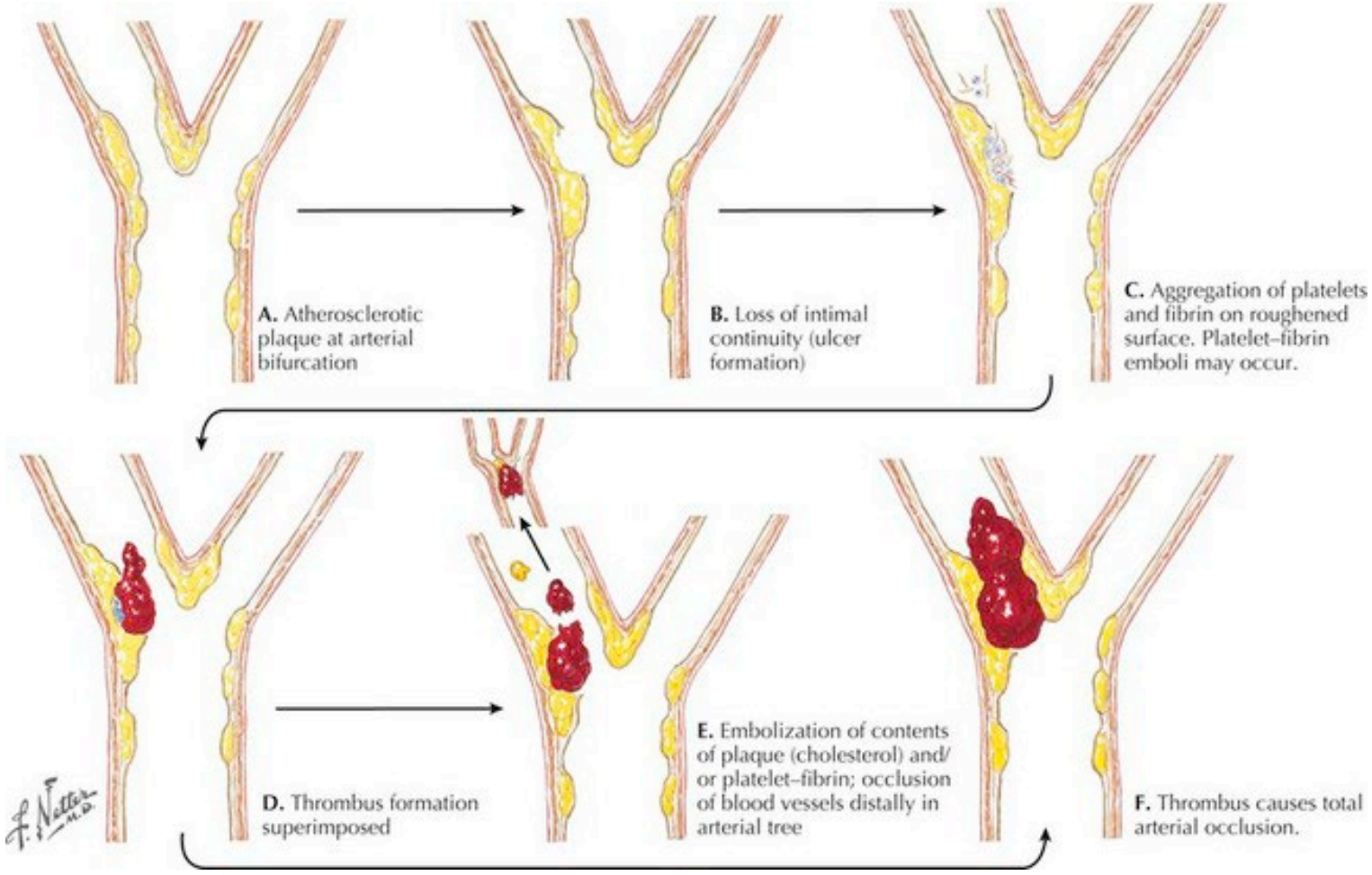
Epidemiology & Natural History of Asymptomatic Carotid Stenosis

~3%	Prevalence of ≥50% stenosis in adults >65 years
~0.5%	Population prevalence of ≥70% stenosis
1–2%/yr	Annual stroke risk with ≥70% stenosis on medical therapy alone
~5–6%	5-year ipsilateral stroke risk (historical, pre-statin era: ~12%)

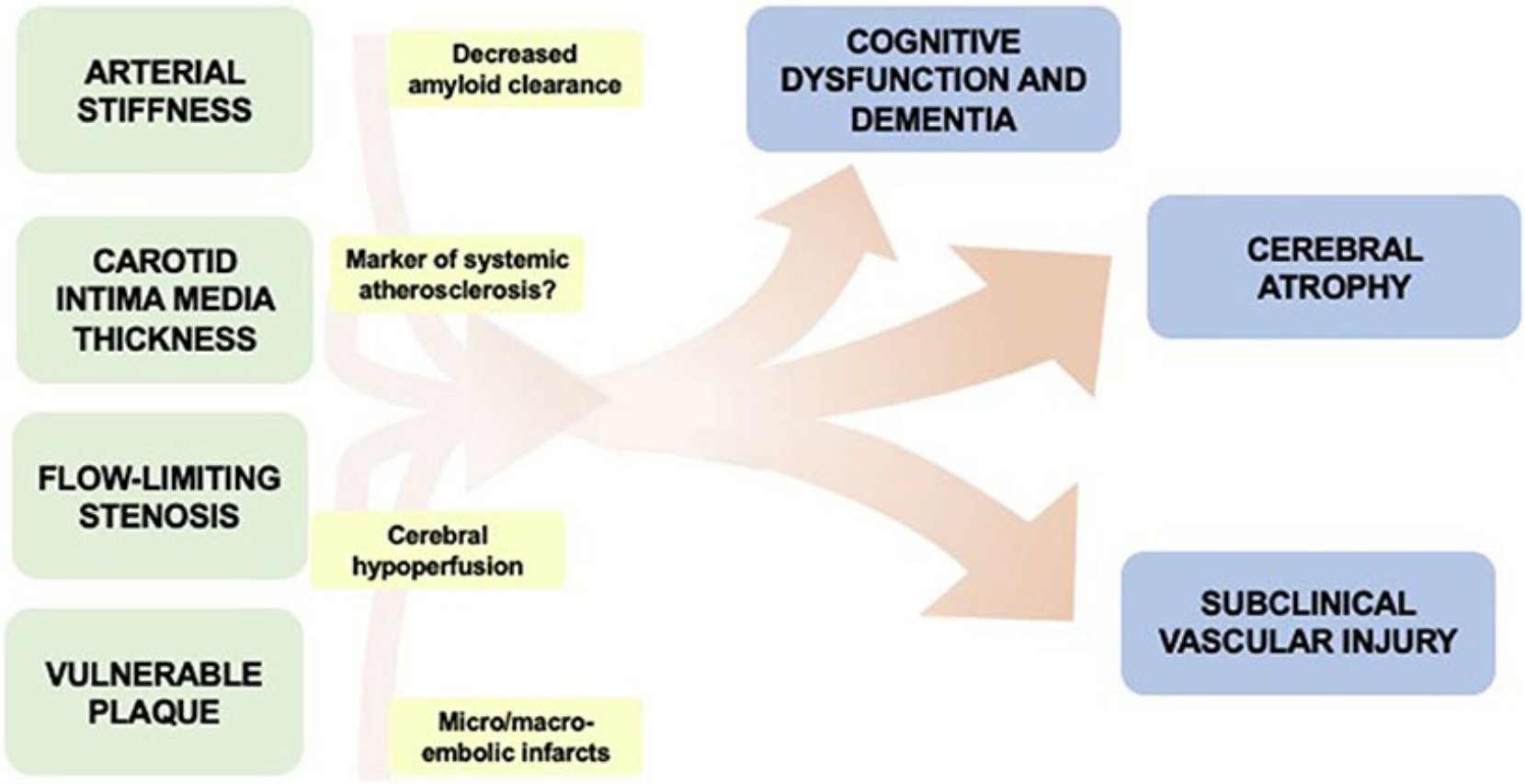


Asymptomatic carotid stenosis (aCAS) is defined as stenosis of the extracranial carotid arteries without a history of ipsilateral ischemic stroke or TIA.

Pathophysiology of Carotid Disease

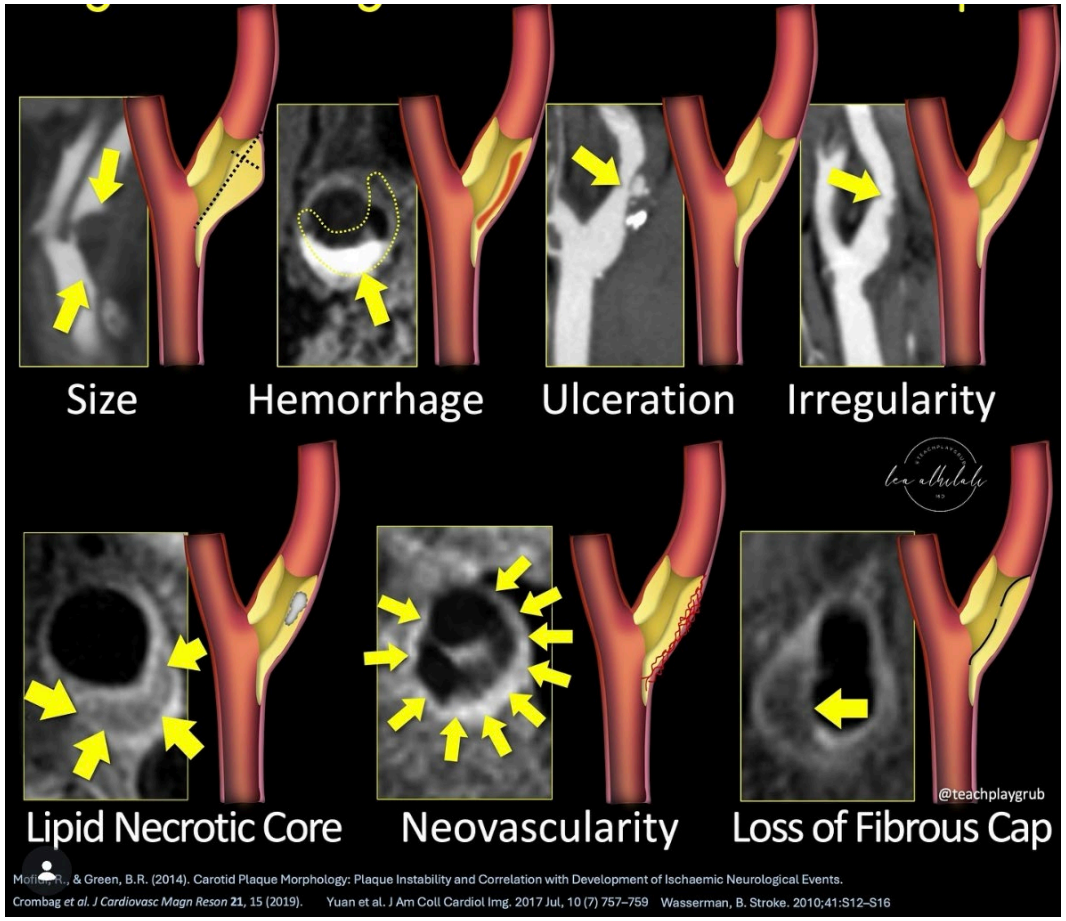


Is asymptomatic carotid disease really asymptomatic?



Baradaran et al., 2021, Frontiers in Neurology

Epidemiology & Natural History of Asymptomatic Carotid Stenosis



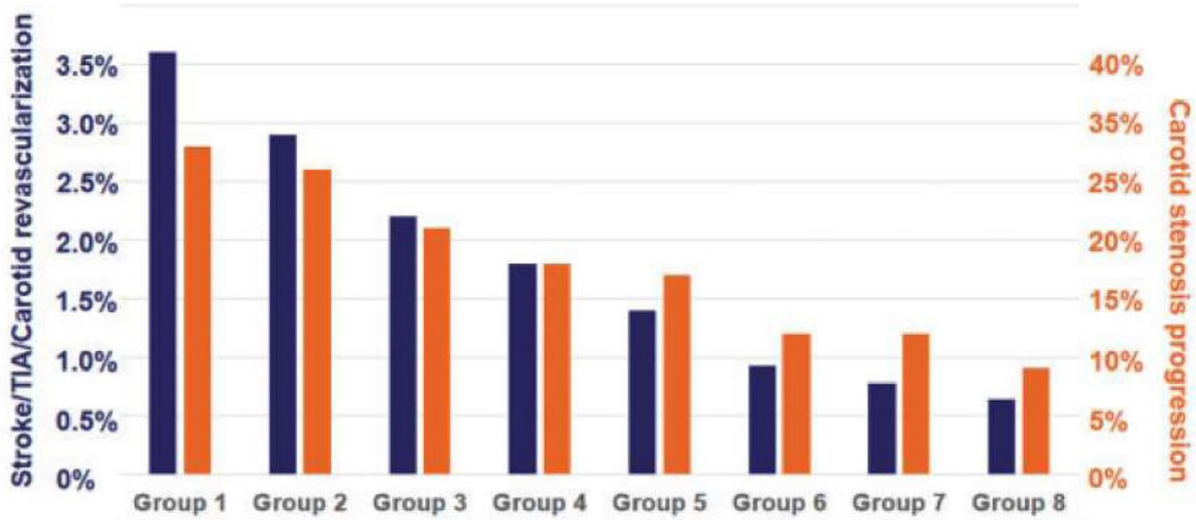
- Higher-grade stenosis (>80%) carries greater stroke risk
- Plaque morphology matters: ulceration, lipid-rich core, intraplaque hemorrhage
- Contralateral occlusion increases ipsilateral risk
- Silent infarcts on MRI are a high-risk marker
- Risk factors: hypertension, diabetes, smoking, hyperlipidemia

Historical Carotid Stenosis RCTs

Trial	Years	N	Stenosis	Comparison	Key Finding
ACAS	1987–93	1662	≥60%	CEA +BMT vs. BMT	Reduced 5-year risk of ipsilateral stroke, perioperative stroke, or death 5.1% vs 11% ($p < 0.004$).
ACST-1	1993–2003	3120	>60%	CEA vs. Deferred CEA	Reduced 5-year stroke and perioperative events risk 6.4% vs 11.8% ($p<0.0001$). Benefit negated if annual peri-op risk >3.5%. 10-year data increased NNT with CEA from 19 → 22 as medical therapy evolved.
CREST-1	2000–2008	2502 (mixed)	≥50% sx; ≥60% asx	CEA vs. CAS	Similar composite outcomes. CAS: ↑ stroke; CEA: ↑ MI. CAS non-inferior.
ACT I	2005–2013	1453	≥70% asx	CAS vs. CEA	CAS non-inferior to CEA at 5 years (3.8% vs 3.4% composite outcome).
ACST-2	2008–2020	3625	Severe	CAS vs. CEA	Comparable outcomes. ~1% peri-op disabling stroke; ~0.5%/yr thereafter.
SPACE-2	2009–2019	513 (early stop)	≥70%	CEA vs. CAS vs. BMT	Underpowered (early termination). Trend toward benefit with BMT alone.
ECST-2	2012–2023	429 (interim)	≥50% low-risk	Revasc + OMT vs. OMT alone	2-yr interim: No significant benefit of revascularization in low-risk patients.

ACAS=Asymptomatic Carotid Atherosclerosis Study; ACST=Asymptomatic Carotid Surgery Trial; asx=asymptomatic; BMT=best medical therapy; OMT=optimal medical therapy

Risk Factor Management

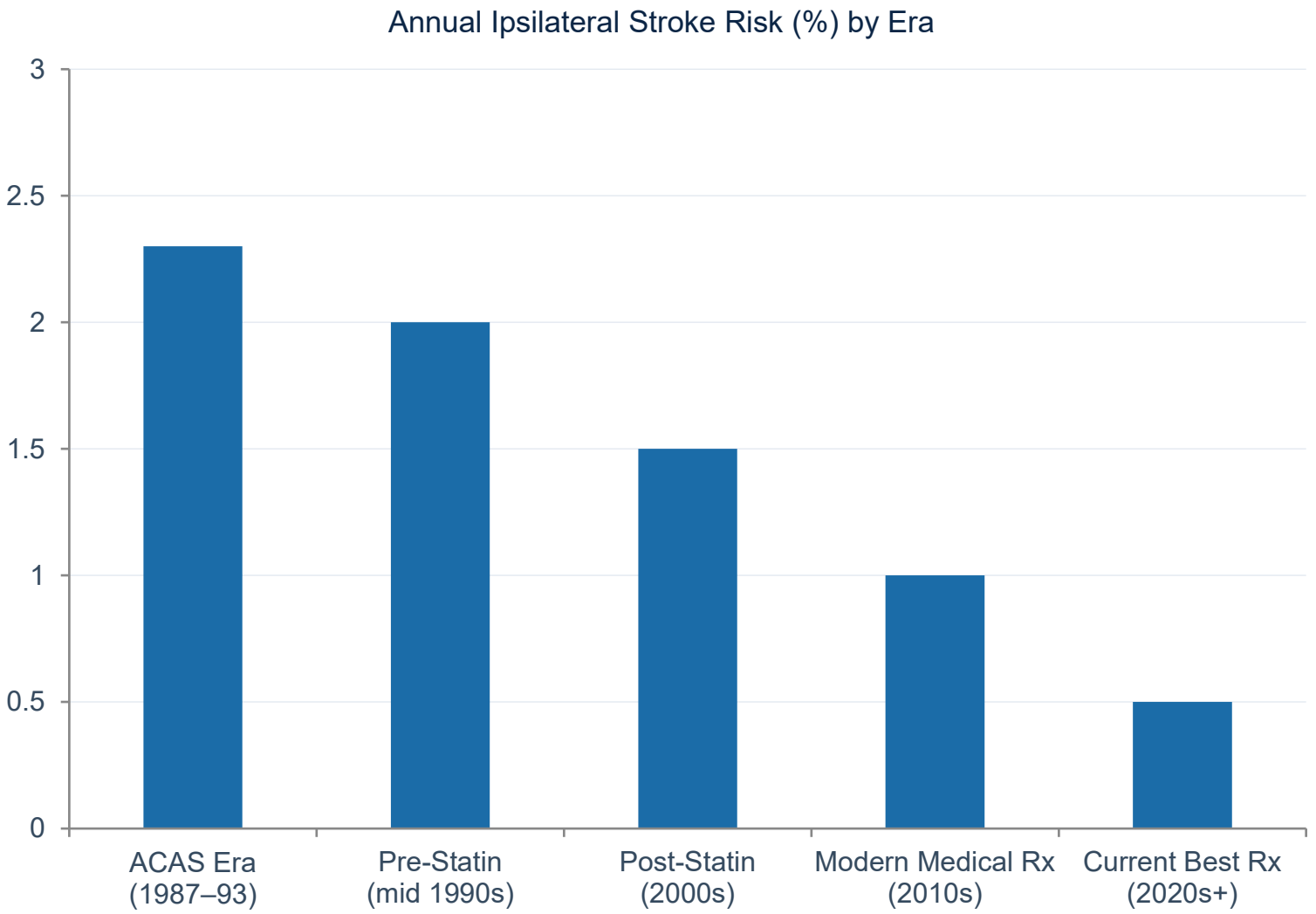


Smoking	YES	YES	YES	YES	YES	YES	YES	NO
BP≥140/90 mmHg	YES	NO	YES	YES	NO	YES	NO	NO
LDL>100 mg/dl	YES	YES	YES	NO	NO	NO	NO	NO
No/low dose statins	YES	YES	NO	YES	YES	NO	NO	NO

1	A	3. In patients with carotid artery stenosis and a TIA or stroke, intensive medical therapy, with antiplatelet therapy, lipid-lowering therapy, and treatment of hypertension, is recommended to reduce stroke risk.[210]

Salameh and Ratchford, Seminars in Vascular Surgery (2026); 2026 AHA / ASA Guidelines

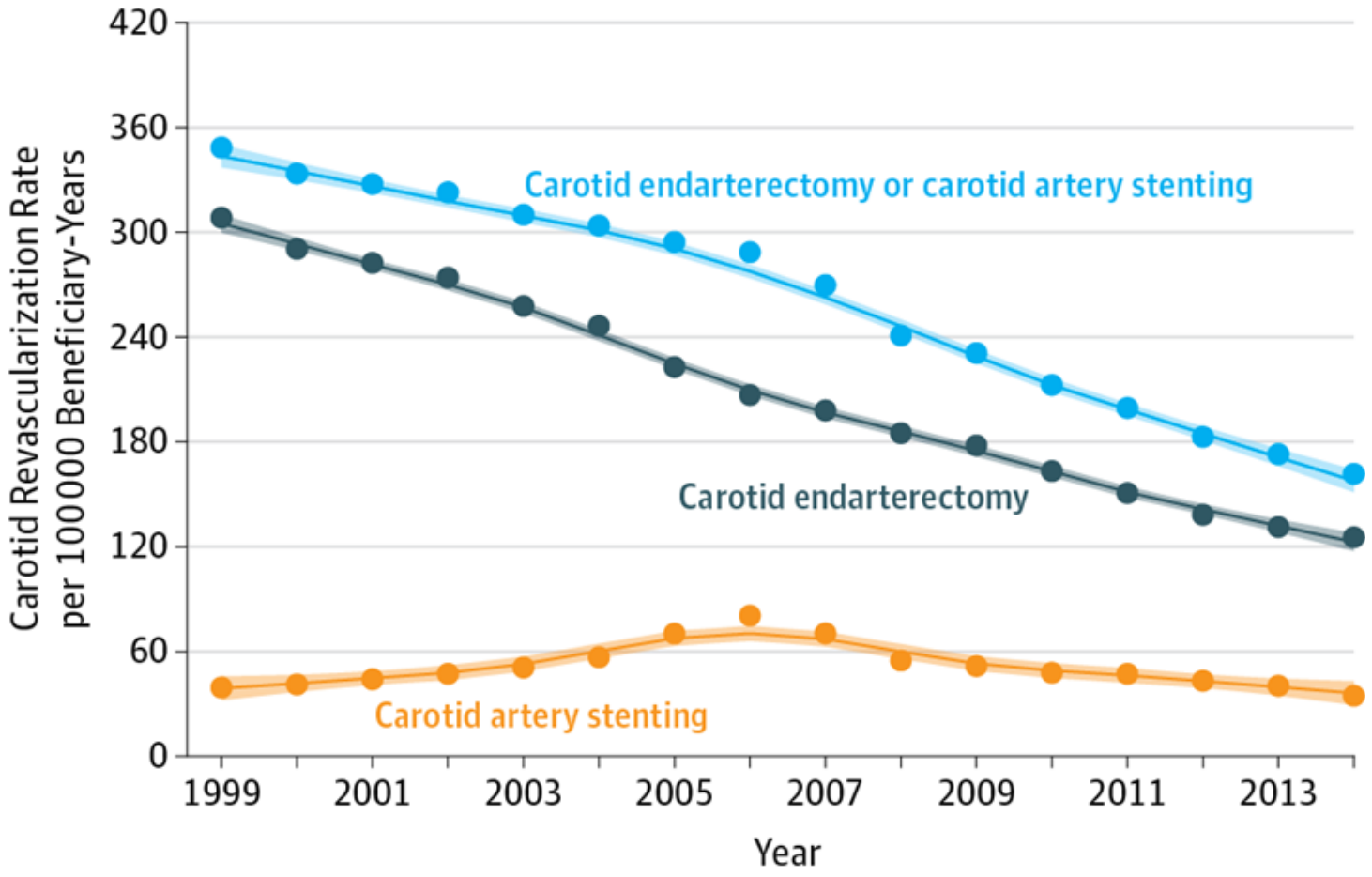
Declining Annual Stroke Risk in Asymptomatic Carotid Stenosis Over Time



Barnett et al.; Naylor et al. Eur J Vasc Endovasc Surg 2018; Abbott et al.

National Carotid Revascularization Rate Among Fee-for-Service Medicare Beneficiaries per 100000 Beneficiary-Years from 1999-2014

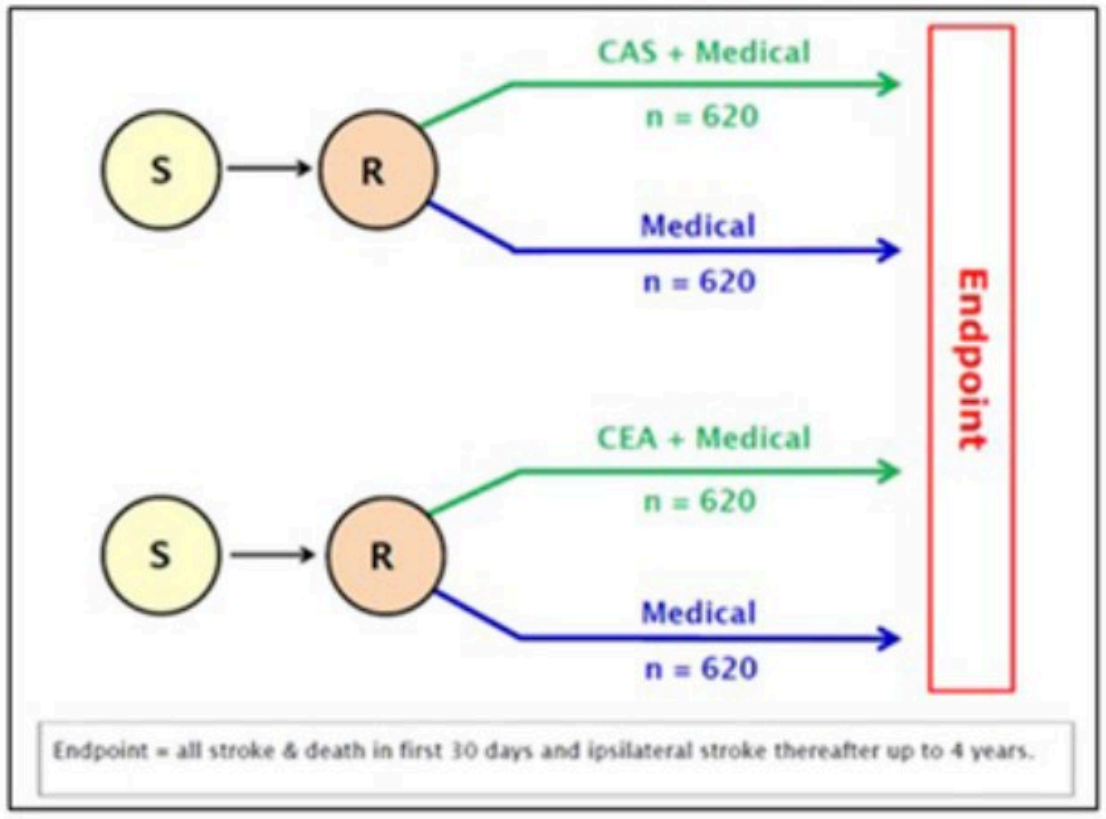
- Carotid endarterectomy rates decreased annually from 1999-2014
- Carotid artery stenting rates increased from 1999-2006 and then decreased from 2007-2014
- Clinical management of vascular risk factors
- Changes in surgical reimbursement policies



CREST 2 (2025)

The Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Study

Health and Hope for Patients at Risk for Stroke



- Two parallel observer-blinded, randomized controlled trials
- ≥ 35 years, ≥ 70% aCAS (no TIA/stroke within 180 days prior to enrollment)
- 155 international centers, 5 countries
- 2485 patients randomized
  - Age ~70 years
  - 63% Male
- Any stroke/death at 44 days
- Ipsilateral ischemic stroke up to 4 years

N Engl J Med. Published November 21, 2025 | doi:10.1056/NEJMoa2508800

CREST-2: Defining 'Intensive Medical Therapy'

Unlike prior trials, CREST-2 standardized and actively monitored optimal medical therapy though a program called INTERVENT in ALL patients.

Antiplatelet

Aspirin 81–325 mg/day (preferred)
or clopidogrel 75 mg/day

Statin Therapy

High-intensity statin (atorvastatin 40–80 mg or rosuvastatin 20–40 mg)

LDL target <70 mg/dL

Blood Pressure

Target <140/90 mmHg
(<130/80 mmHg in 2018 after guideline changes)

Lifestyle Coaching

Third-party health coaching
Smoking cessation, diet, exercise

Compliance Monitoring

Regular biochemical monitoring with 70–80% of patients at goal for LDL and BP throughout the trial

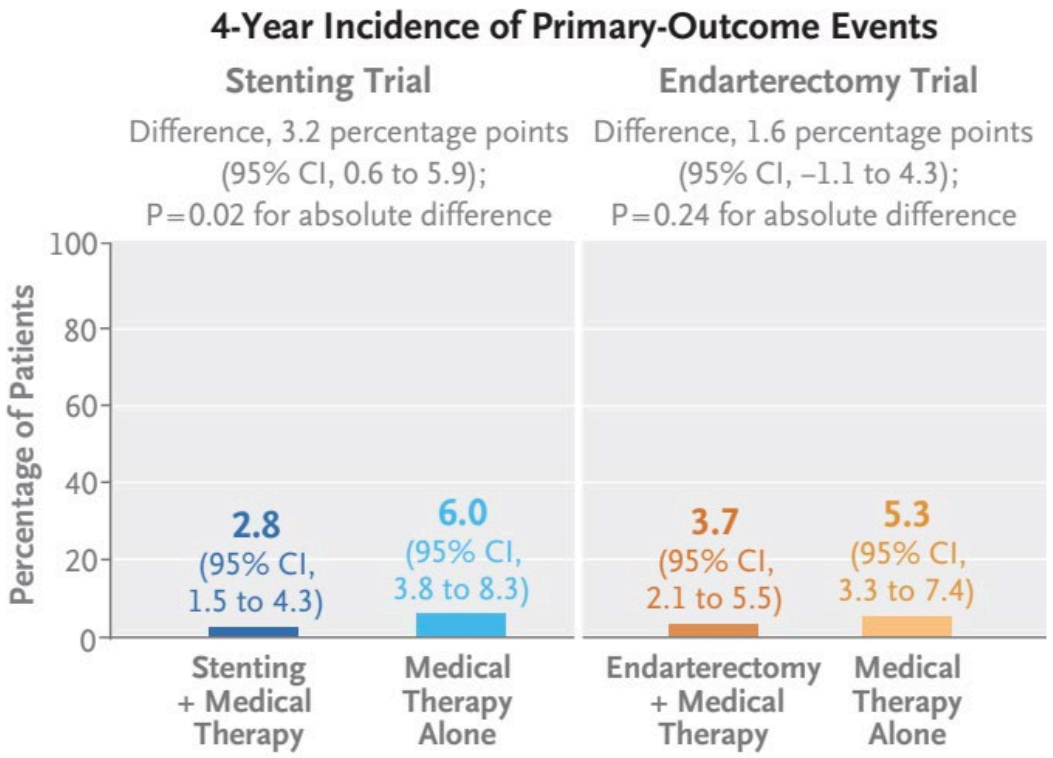
Diabetes Management

HbA1c target <7%
Optimized glycemic control

CREST-2 Results: CAS + Medical Therapy vs. Medical Therapy Alone

✓ POSITIVE TRIAL — CAS Significantly Reduced Stroke Risk

Primary outcome: 2.8% (CAS + Med Rx) vs. 6.0% (Med Rx alone) | p = 0.02 | ARR = 3.2% | RR = 2.13



Key Statistics

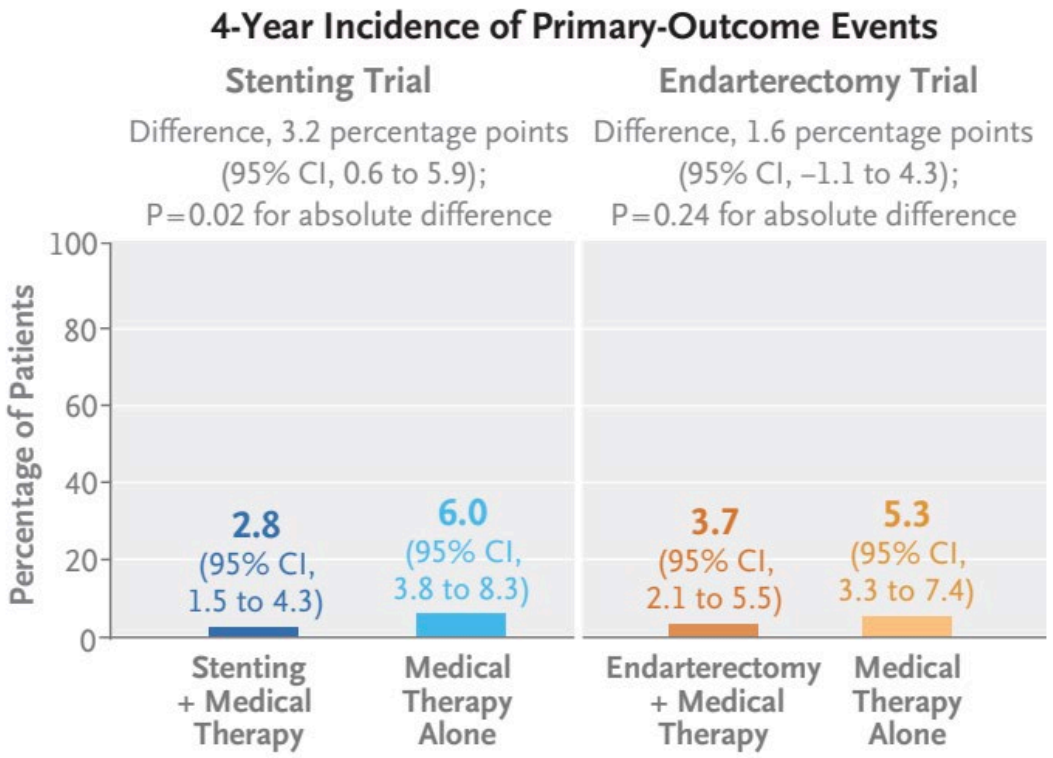
ARR:	**3.2%**	*(95% CI: 0.6–5.9%)*
Relative Risk:	**2.13**	*(95% CI: 1.15–4.39)*
NNT at 4 years:	**31**	*patients to prevent 1 stroke*
Annual stroke risk post-CAS:	**0.4%/yr**	*(vs. 1.7%/yr on med Rx alone)*
Peri-op stroke/death:	**1.3%**	*(only 7 actual periprocedural strokes)*

Brott TG et al. NEJM 2025. Composite endpoint: stroke or death ≤44 days OR ipsilateral ischemic stroke through 4 years.

CREST-2 Results: CEA + Medical Therapy vs. Medical Therapy Alone

✗ NEGATIVE TRIAL — CEA Did Not Significantly Reduce Stroke Risk

Primary outcome: 3.7% (CEA + Med Rx) vs. 5.3% (Med Rx alone) | p = 0.24 | ARR = 1.6% | Not significant

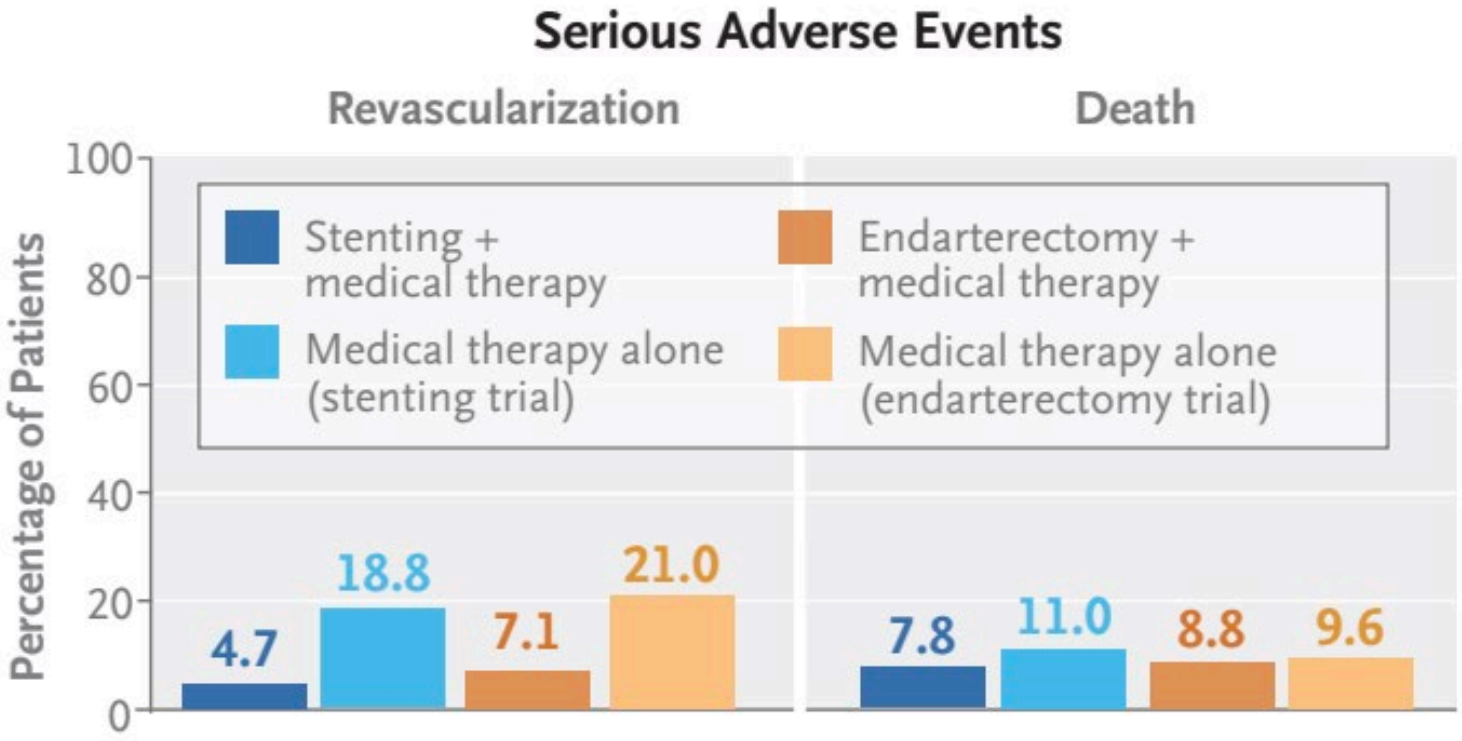


Key Statistics

ARR:	**1.6%**	*Not statistically significant*
Peri-op stroke/death:	**~1.4%**	*CEA arm*
Annual stroke risk (CEA):	**~0.8%/yr**	*post-procedure*
Annual stroke risk (Med):	**~1.4%/yr**	*medical therapy alone*

Brott TG et al. NEJM 2025. Composite endpoint: stroke or death ≤44 days OR ipsilateral ischemic stroke through 4 years.

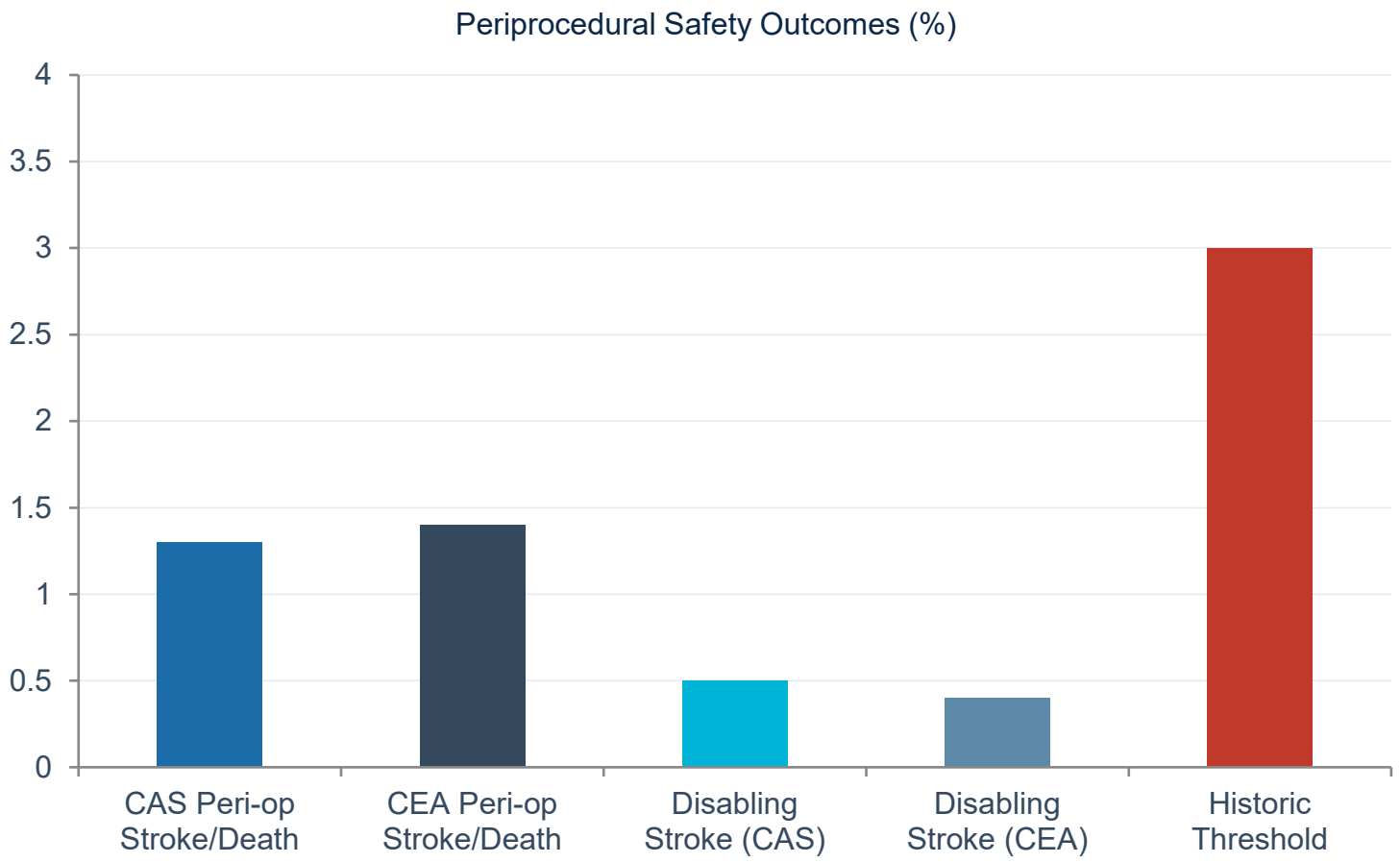
CREST-2 Results: Serious Adverse Events



Brott TG et al. NEJM 2025

CREST-2: Periprocedural Safety — A Landmark Achievement

All groups maintained periprocedural stroke/death rates well below the 3% threshold historically required to justify prophylactic intervention



Safety Highlights

- Only 7 actual periprocedural strokes in entire CAS trial
- Disabling stroke rates <0.5% for both procedures
- Operator qualification: min. 3 prior cases; 86% of applicants accepted
- 45% of CAS operators were interventional cardiologists
- Results transferable to general practice (not just elite centers)
- No excess MI in CAS arm (unlike CREST-1)

CREST-2 operator qualification was intentionally broad to reflect real-world practice.

CREST-2: Subgroup Analyses — CAS Trial (Who Benefits Most?)

Subgroup	CAS + Med Rx	Med Rx Alone	Interpretation
Overall	2.8%	6.0%	Significant benefit (p=0.02)
Male sex	~2.5%	~6.5%	Strong benefit
Female sex	~3.2%	~5.2%	Trend toward benefit
Age <70 yrs	~2.4%	~6.1%	Consistent benefit
Age ≥70 yrs	~3.3%	~5.9%	Benefit maintained
Stenosis 70–79%	~2.5%	~5.5%	Benefit present
Stenosis ≥80%	~3.0%	~6.8%	Greater absolute benefit
Contralateral stenosis	~2.9%	~7.2%	Higher baseline risk; greater benefit
Silent infarcts on MRI	~3.0%	~7.5%	High-risk group; clear benefit

Approximate subgroup values based on reported data. Formal interaction p-values not all significant.

Patient Selection: Who Should Be Considered for CAS in 2025+?

A risk-stratified, shared decision-making approach is essential. Not all patients with asymptomatic stenosis ≥70% require or benefit equally from intervention.

Consider CAS/CEA + Medical Rx

- Stenosis ≥70% with good life expectancy (>3–5 yrs)
- Ipsilateral silent cerebral infarcts on MRI
- Contralateral carotid occlusion
- Microemboli detected on TCD
- Rapidly progressive stenosis
- High-risk plaque morphology (intraplaque hemorrhage, ulceration)
- Age <75 years with low surgical/procedural risk
- Patient preference after informed shared decision-making

Intensive Medical Therapy Alone

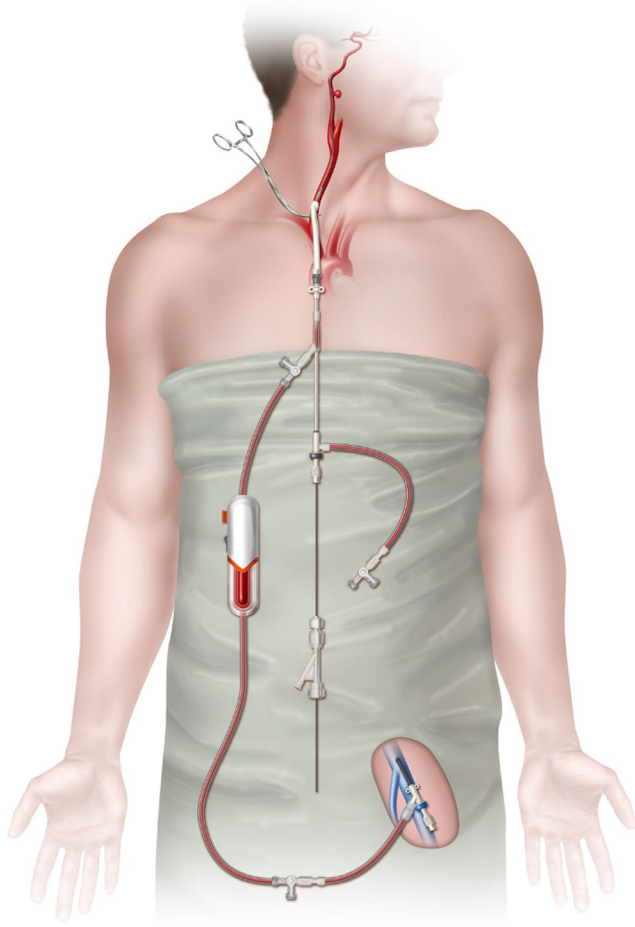
- High surgical/procedural risk (cardiac, renal comorbidities)
- Age >75–80 with multiple comorbidities
- Stenosis 50–69% (below CREST-2 threshold)
- Low-grade plaque risk features on imaging
- Short life expectancy (<3 years)
- Already well-controlled on optimized medical therapy
- Patient preference to avoid procedural risk
- Low-risk patients per Carotid Artery Risk (CAR) score (ECST-2 framework)

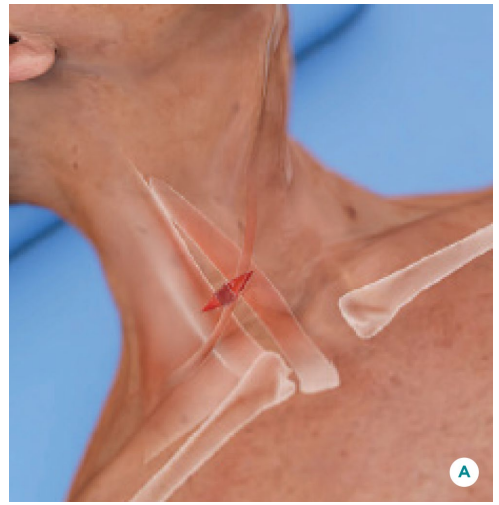
Naylor et al. European Society for Vascular Surgery guidelines 2023; AHA/ASA Stroke Guidelines 2021; SVS 2022.

Beyond TF-CAS: Transcarotid Artery Revascularization (TCAR) & Future Directions

What is TCAR?

- Transcarotid Artery Revascularization is a minimally invasive, hybrid procedure that combines endovascular techniques with surgical exposure.
- Involves placing a stent via a small incision in the neck and uses dynamic flow reversal for embolic protection.
- Lower learning curve than TF-CAS
- Used in patients with hostile aortic arch anatomy
- Not directly studied in CREST-2 — separate ROADSTER / CREST-3 data





ROADSTER trial: TF-CRAS vs TCAR for high-risk anatomy. CREST-3: planned trial of TCAR vs. best medical therapy.

Beyond TF-CAS: Transcarotid Artery Revascularization (TCAR) & Future Directions

- CREST-3: RCT investigating TCAR vs medical therapy
- Biomarker-guided patient selection (intraplaque hemorrhage MRI)
- AI-based plaque risk scoring
- Longer follow-up data from CREST-2
- Comparative effectiveness: TCAR vs. TF-CAS
- Role of PCSK9 inhibitors in further reducing medical management event rates

ROADSTER trial: TF-CRAS vs TCAR for high-risk anatomy. CREST-3: planned trial of TCAR vs. best medical therapy.

Key Takeaways

01 The annual stroke risk in asymptomatic carotid stenosis has fallen significantly since the pre-statin era, fundamentally changing the risk-benefit equation for prophylactic revascularization.

02 CREST-2 demonstrated that CAS + intensive medical therapy significantly reduced 4-year stroke/death rates vs. medical therapy alone (2.8% vs. 6.0%, p=0.02) — the first RCT to show this benefit.

03 CEA did not provide a statistically significant additional benefit over intensive medical therapy alone in CREST-2 (3.7% vs. 5.3%, p=0.24), questioning its routine use in asymptomatic disease.

04 Periprocedural risk was very low (<1.5% stroke/death), suggesting CAS can be performed safely in well-selected patients by appropriately trained operators.

05 Patient selection should be individualized: high-risk features (silent infarcts, plaque morphology, progressive stenosis) favor intervention; low-risk patients may be best managed medically.

06 Guideline updates are anticipated; TCAR remains an important alternative requiring its own randomized evidence (CREST-3 in development).

References & Further Reading

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11. Kernan WN, et al. Guidelines for the prevention of stroke in patients with stroke or TIA. Stroke. 2014;45(7):2160–2236.

Thank You

Questions & Discussion

"The right procedure, for the right patient, at the right time — supported by the best available evidence."