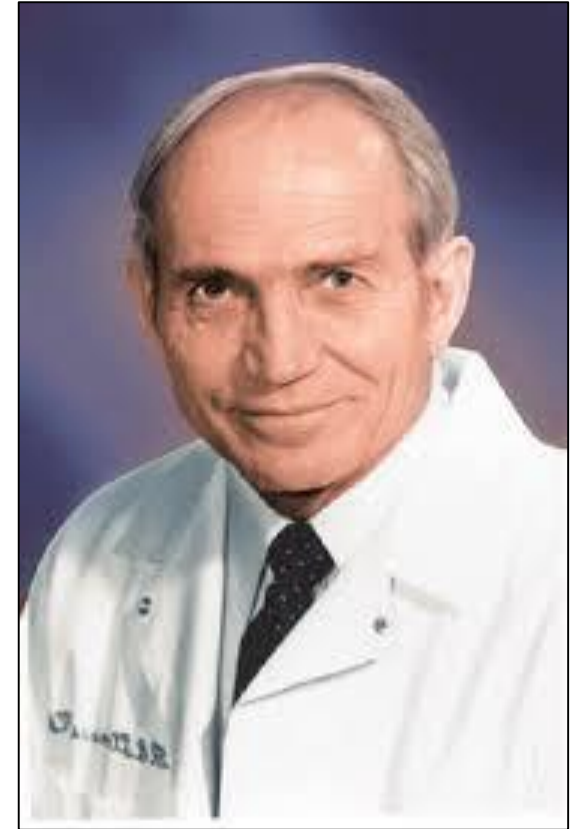


Management of Asymptomatic Carotid Stenosis

The Case For Intervention

Strandness Symposium
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No Disclosures
No Conflicts-of-Interest

Waning Enthusiasm For Intervention For Asymptomatic Carotid Stenosis (ACS)

Why?

- Risk of stroke associated with ACS is relatively low: 1.0-3.5%/Yr
- RCTs of CEA/OMT vs OMT alone: high relative but low absolute RR
- Optimal medical therapy may be improving: statins

Hierarchy of Medical Evidence

Level	Type of evidence
I	At least 1 RCT with proper randomization
II.1	Well designed cohort or case-control study
II.2	Time series comparisons or dramatic results from uncontrolled studies
III	Expert opinions



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Table I. Lifestyle and Medical Measures That Comprise Best Medical Treatment (BMT) for Patients With Asymptomatic and Symptomatic Carotid Artery Stenosis.

Measure	Intervention
Lifestyle measures (+ intervention, if necessary)	
Smoking cessation	Counseling Nicotine replacement therapy Bupropion Varenicline
Obesity	Counseling on caloric restriction Referral to dietician Bariatric surgery in refractory patients with severe obesity ^a
Mediterranean diet	Counseling Provision of a booklet with dietary recommendations/recipes
Exercise	Moderate exercise at least 30 minutes a day, with advice tailored to the patient's disabilities if any
Medical therapy	
Blood pressure control	Individualized therapy directed to the underlying cause of hypertension ^b
Lipid lowering	Highest tolerated statin dose or treat to specific target according to local guidelines Addition of ezetimibe and fibrates/niacin (as needed for low high-density lipoprotein cholesterol [HDL-C]/high triglycerides)
Antiplatelet agents	Low-dose uncoated aspirin (eg, 80-100 mg daily) with probable addition of clopidogrel (see text)
Diabetes	Reinforcement of lifestyle changes, medications

Optimal Medical Therapy

OMT

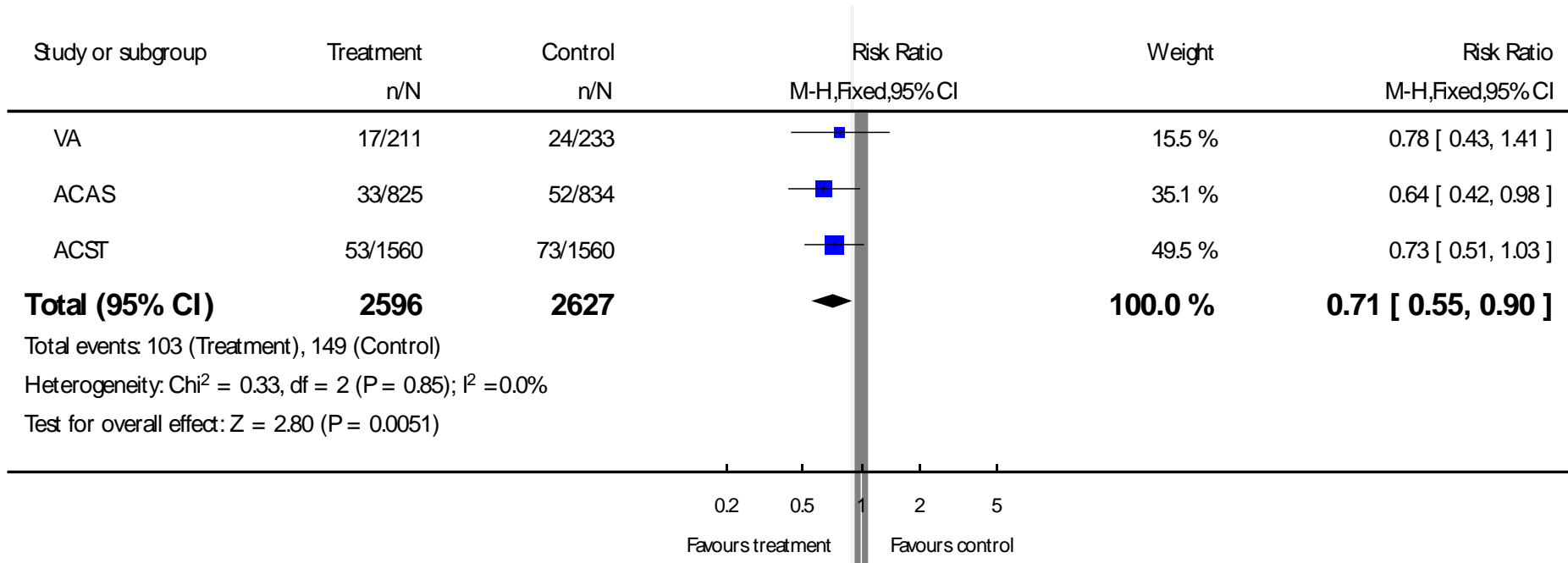
- Moving Target
 - Diet, BP, Antiplatelet Rx
 - Statins
 - Patient's risk profiles

What We Know About Asymptomatic Carotid Stenosis:

- Approximately 1/3rd of all strokes are caused by carotid bifurcation disease.
- The patients we see with a first carotid stroke or TIA had asymptomatic carotid stenosis the day before the event.
- Existing level 1 evidence: CEA plus OMT superior to OMT alone.

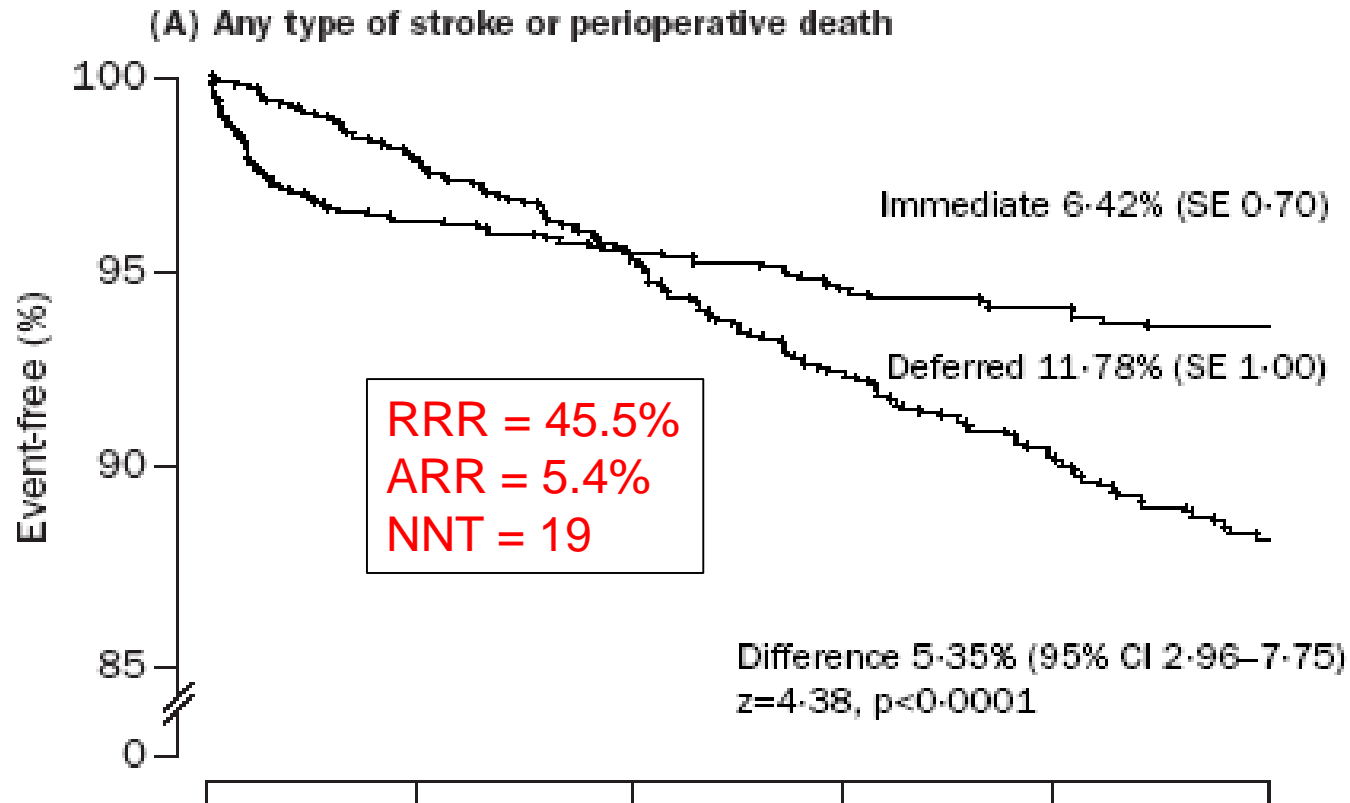
CEA Plus OMT Versus OMT Alone

Three RCTs From The 1990s And Early 2000s



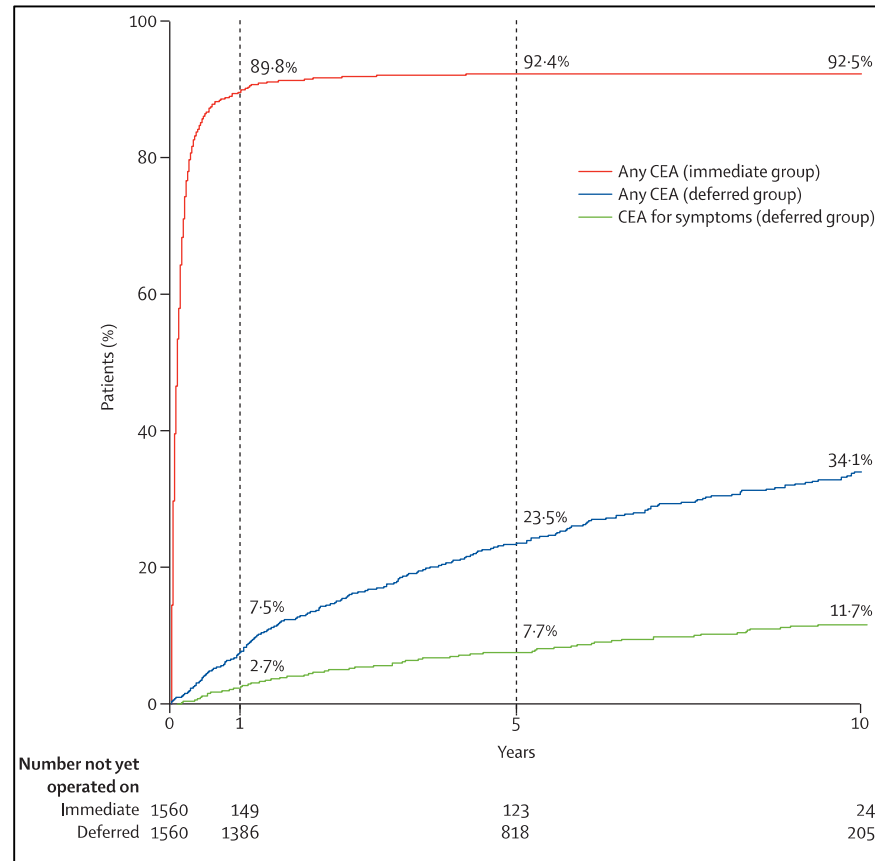
29% relative risk reduction

ACST-1 Results



ACST-1: Immediate Versus Deferred Repair

Total N = 3120

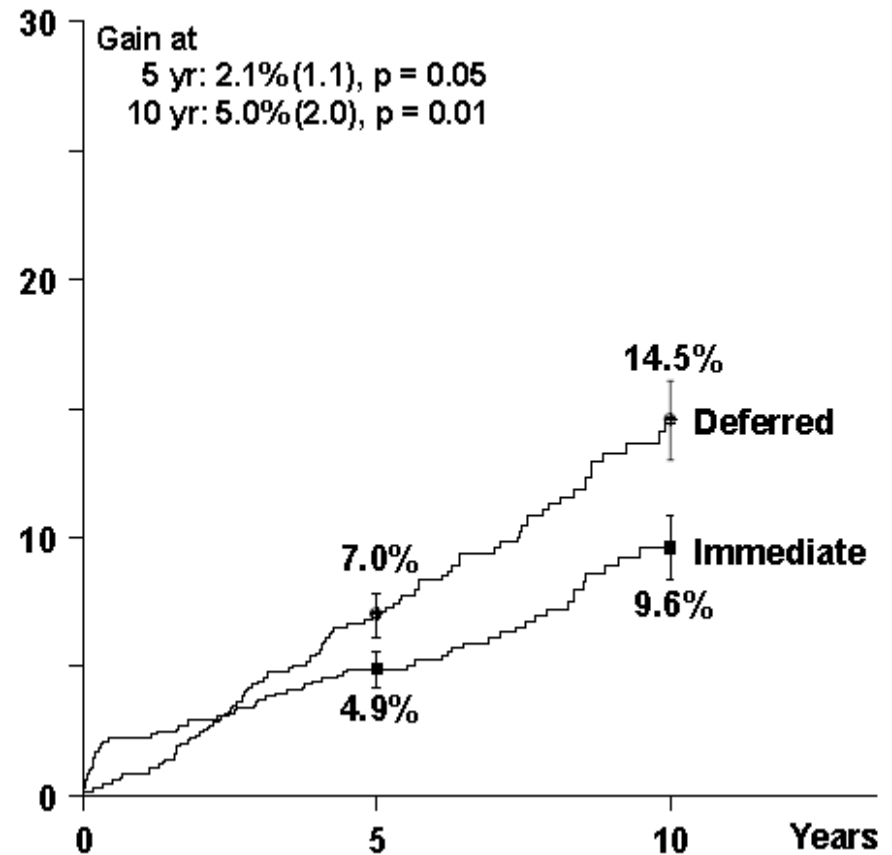
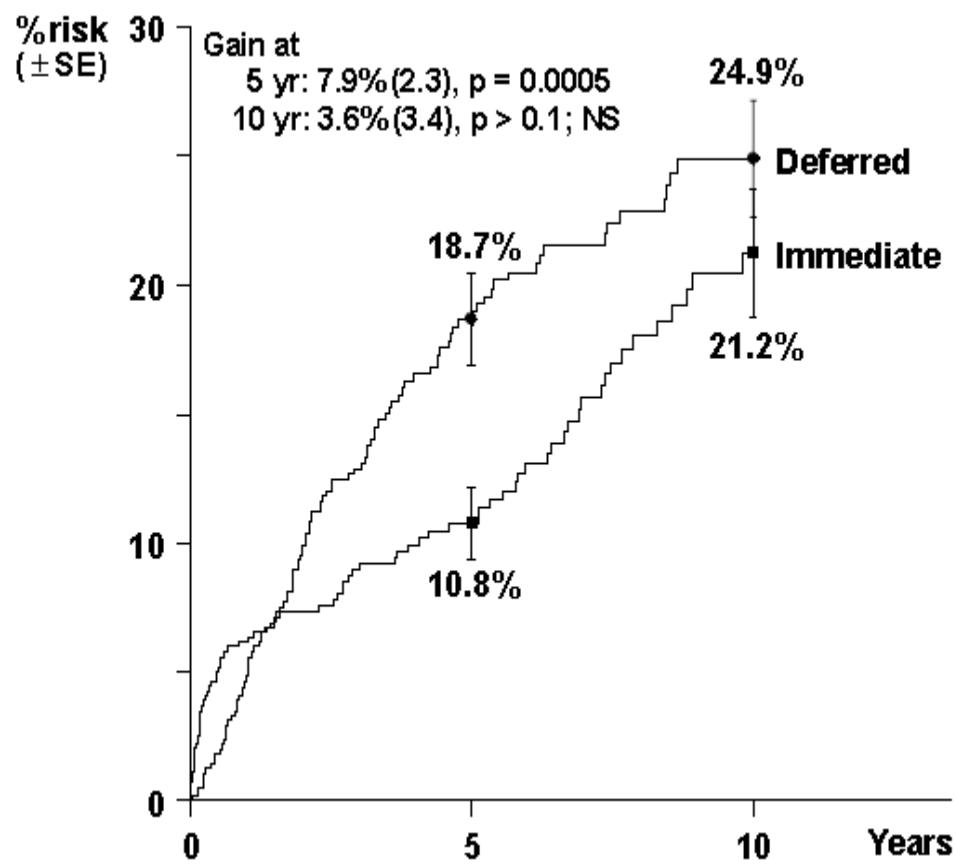


“A lot of repair versus some repair”

ACST-1: Results Stratified By Lipid Lowering Status

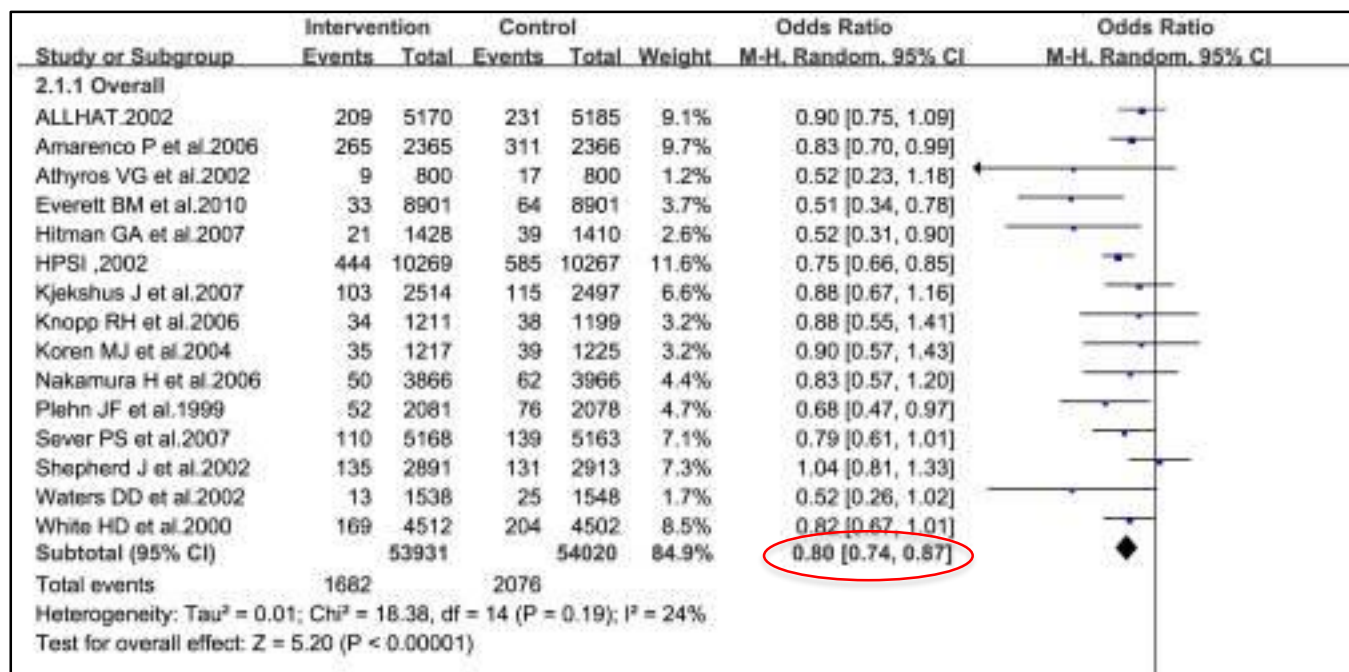
Not on lipid-lowering therapy at entry

On lipid-lowering therapy at entry



Statins And Stroke Risk Reduction

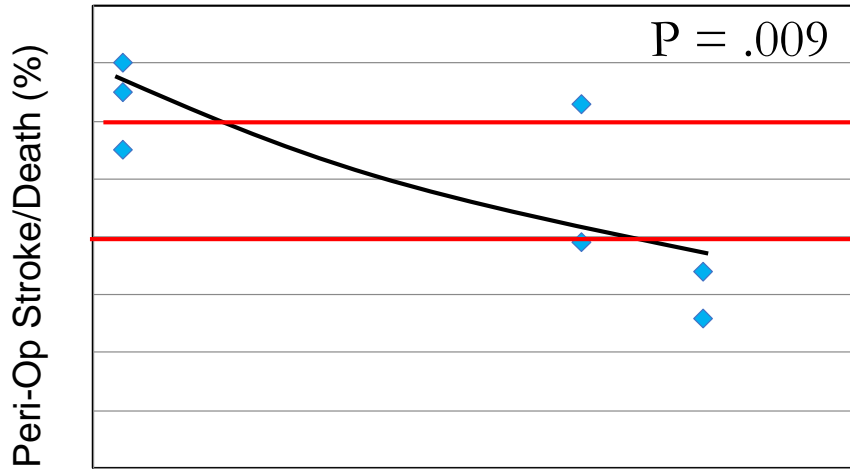
Statin V Placebo, 54K High-Risk Patients



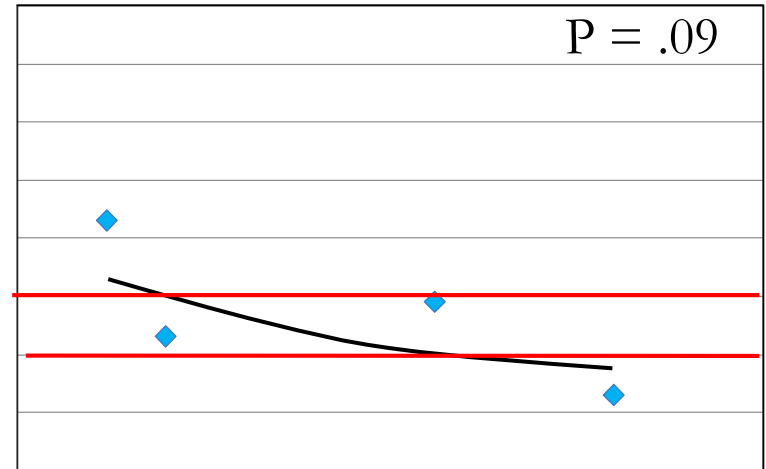
20% relative risk reduction

Temporal Trends In Perioperative Stroke/Death Rate Following CEA

Symptomatic



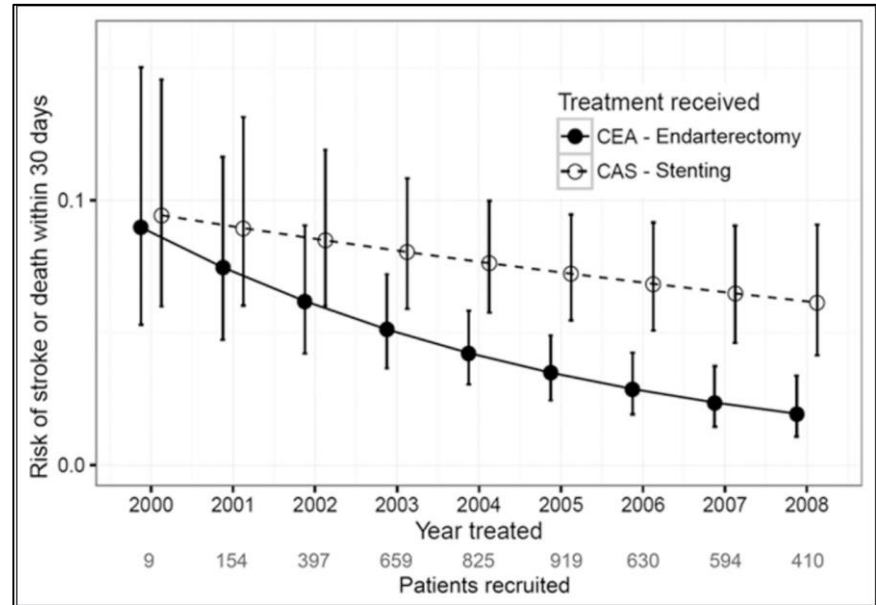
Asymptomatic



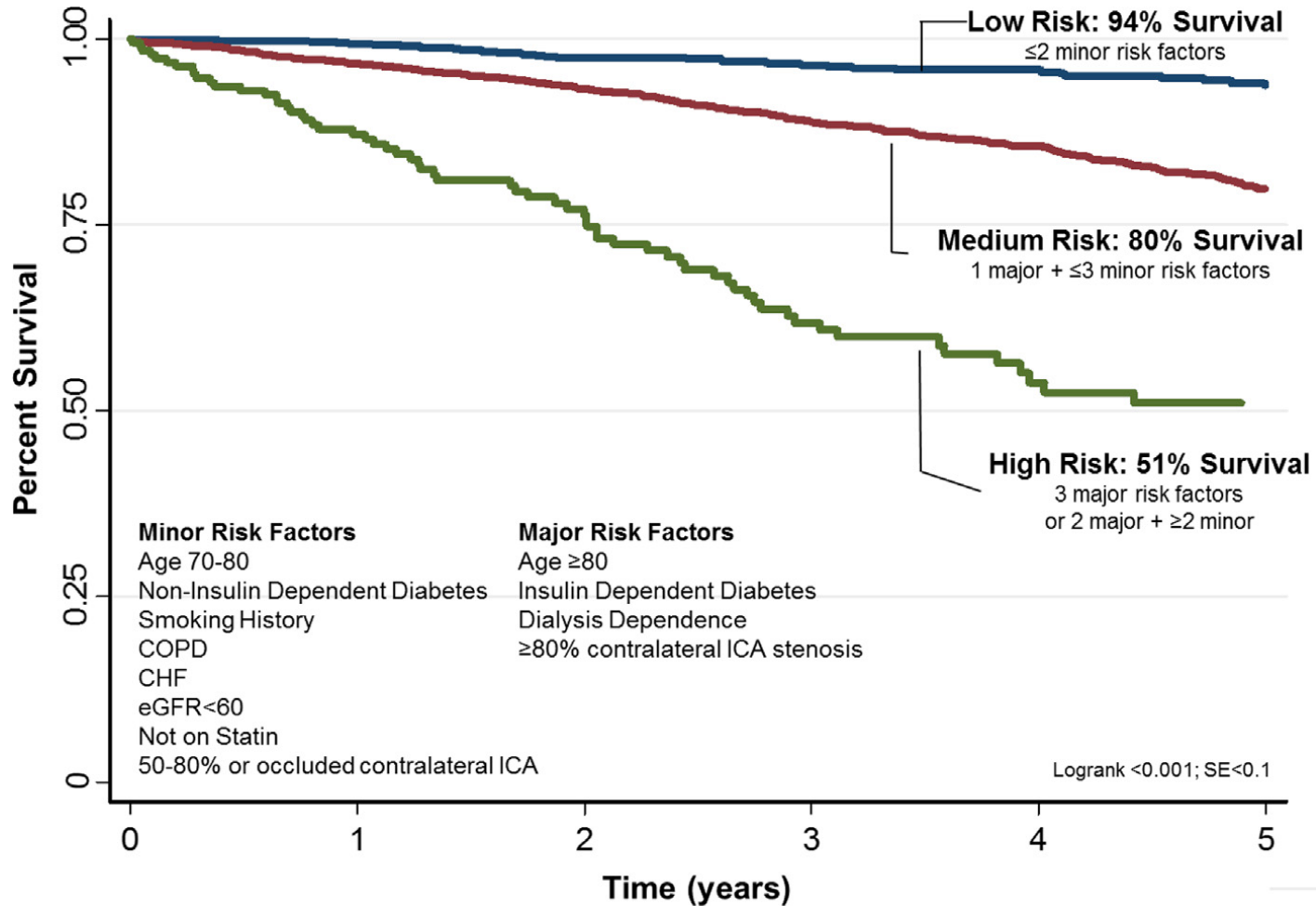
Year of Trial Publication

Improving Results Of CEA and Stenting

- Meta-analysis of 4 RCTs
- 4597 patients
- Peri-procedural S/D
- CEA > CAS



Life Expectancy in Patients With ACS



Stroke Risk Posed by Asymptomatic Carotid Stenosis?

High risk factor	Annual stroke risk	Reference
Silent brain infarct	4.6%	Kakkos et al. J Vasc Surg 2009 49:902
Progression	13.7%	Conrad et al. J Vasc Surg 2013;58:128
JBA >10 mm by duplex	5%	Kakkos et al. J Vasc Surg 2013;57:609
Intraplaque hemorrhage by MRI	8.4%	Hellings et al. Circulation 2010;121:1941
Evidence of embolization (TCD)	7-10%	Spence et al. Stroke 2005;36:2373 Topakian et al. Neurology 2011;77:751

Cognitive Decline And ACS?

Issue	Study	Ref
Cognitive impairment	>50% carotid stenosis, Bilateral or severe unilateral carotid stenosis Comparative study: 49% of asx carotid stenosis patients impaired in at least 2 cognitive function tests	Chang et al. Neurosci Behav Rev 2013;37:1493 Buratti et al. Stroke 2014;45:2072 Lal et al J Vasc Surg 2017;66:1083
Improved function after repair	In comparison to pre-op and controls Repair stops decline	Baracchini et al. Surgery 2012;151:99 Dempsey et al. Neurosurg 2017;epub
Alzheimer's disease and dementia	Microembolization identified in 40% of Alzheimer's and 37% of dementia patients vs 15% of controls	Purandare et al BMJ 2006;332:1119
Significant loss of cortical gray matter volume	>70% unilateral stenosis or bilateral moderate stenosis, MRI follow up at a mean of 3.8 years	Muller et al. Ann Neurol 2011;70:237

Cognitive Impairment AND Statins

- **FDA announcement (2012):** statins may cause reversible cognitive impairment (10%-15%)
- Large RCTs
 - Lead-in phase excludes up to 30% of patients with “statin intolerance”

Optimal Medical Therapy

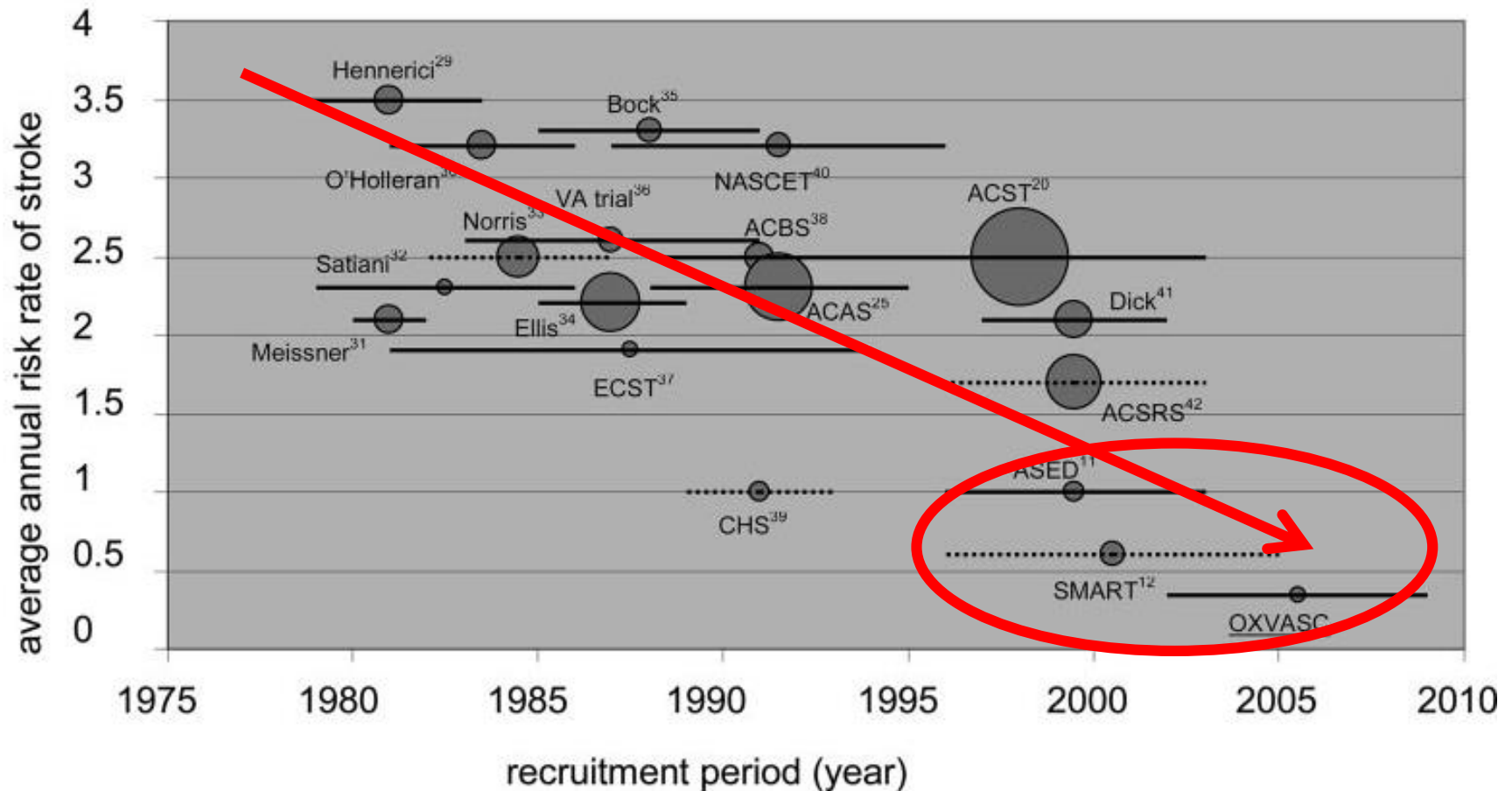
Non-Compliance and Side Effects

- Non-compliance in real-life studies is substantially more than RCTs
 - Non-compliance rates 25% - 40%
 - RCT “lead-in”
- Statin intolerance
 - Myopathy and myositis: 10% - 20%
 - Elevated liver enzymes, nausea/vomiting, rash, flushing, headache
 - Cognitive impairment
- Anti-platelet agents
 - Resistance 20%
 - GI and other bleeding

Ho et al. Circulation 2009;119:3028
Joy et al. Ann Internal Med 2009;150:858
Bosworth et al. Am Hear Journal 2011;162:412
Wang et al. Eur Heart Journal 2006;27:647
Paraskevas et al. Angiology 2016;67:411

Medical Therapy for Asymptomatic Carotid Stenosis

What Is The Annual Stroke Risk?



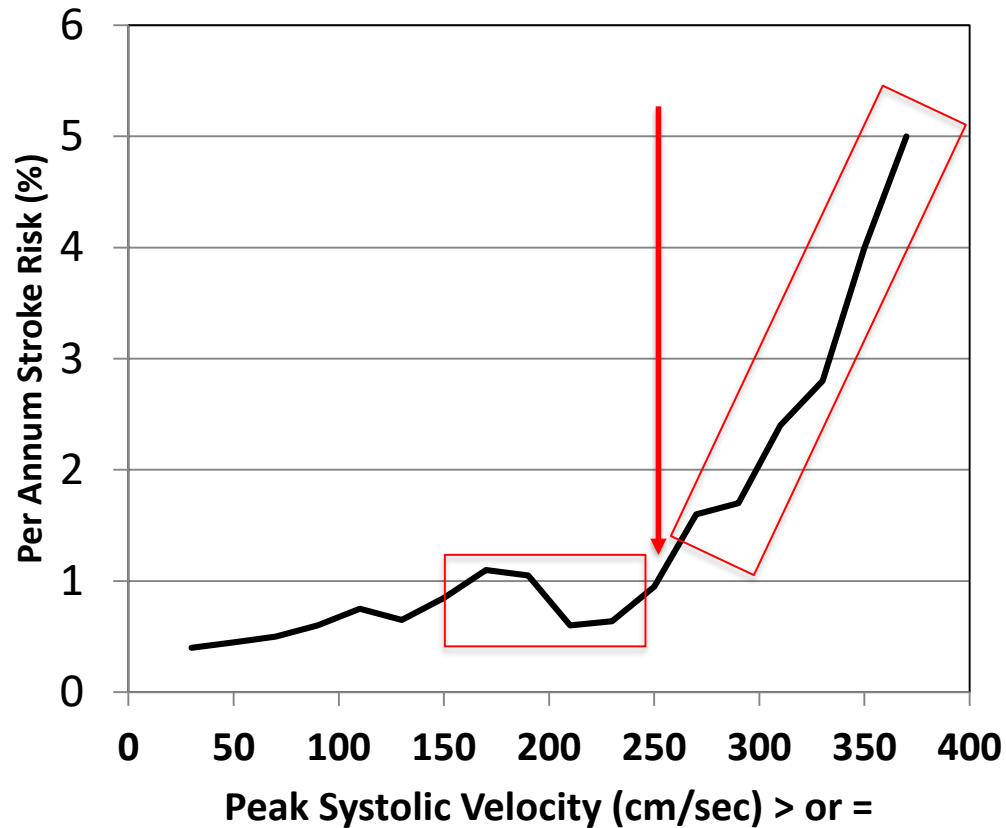
Medical Therapy for Asymptomatic Carotid Stenosis

Annual Stroke Risk <1%?

Study	Purpose	Reference	Patients	PSV	Details
SMART	Study vascular events at Univ of Utrecht	Goessens Stroke 2007	221 with $\geq 50\%$ stenosis Excluded 996 patients with history of cerebrovascular disease	150 cm/sec	Only 96 pts had PSV ≥ 210 , 7% had carotid repair
Oxford Vascular Study	Study vascular events in Oxford	Marquardt Stroke 2010	101 with $\geq 50\%$ stenosis (Only 32 with $\geq 70\%$)	150 cm/sec	Vascular death in 7.7% (undefined)
ASED	Use TCD to find high risk group	Abbott Stroke 2005	202 with $\geq 50\%$ stenosis	150 cm/sec	10 underwent CEA

Risk of Stroke in CHS

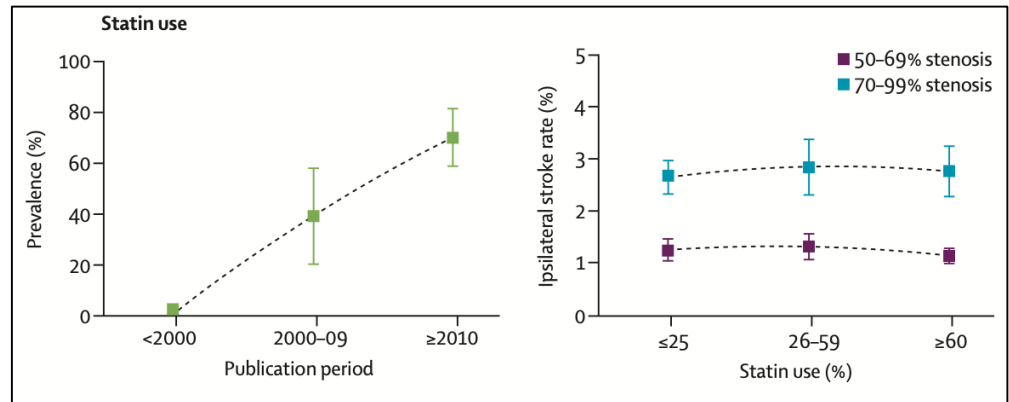
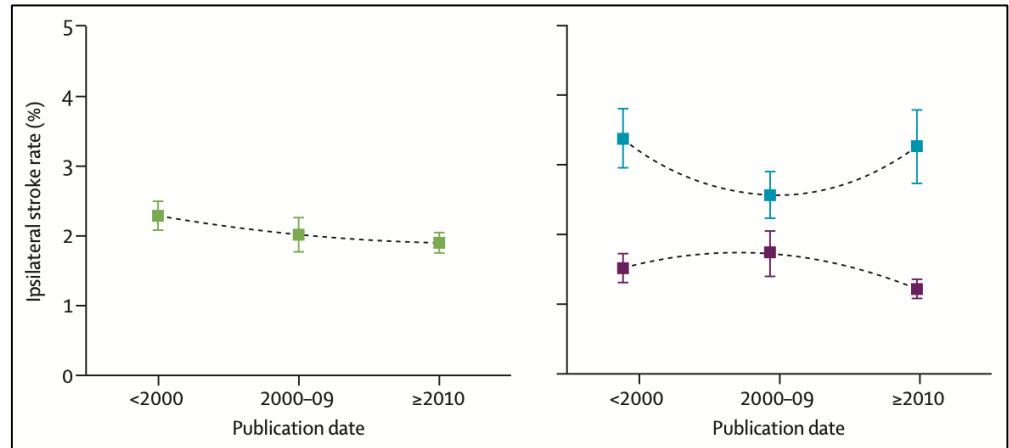
Inflection Point at PSV >250



Asymptomatic Internal Carotid Artery Stenosis Defined by Ultrasound and the Risk of Subsequent Stroke :
The Cardiovascular Health Study. Longstreth et al Stroke 1998;29(11):2371-2376.

Contemporary Association Of Stroke Risk With Degree of Carotid Stenosis

- Meta-Analysis
- 56 studies 13,717 patients
- 30 cohort studies with $\geq 50\%$ stenosis stratified
 - 50-69%
 - 70-99%



New SVS Guidelines Carotid DZ (2022)

- For low surgical risk patients with asymptomatic carotid stenosis of >70%, we recommend CEA with best medical therapy instead of maximal medical therapy alone for the long-term prevention of stroke and death. **Level of recommendation (strong); quality of evidence (moderate).**
- We recommend CEA over TF-CAS in low- and standard-risk patients with >50% symptomatic carotid artery stenosis. **Level of recommendation (strong); quality of evidence: (high)**
- **Remark:** TCAR-CAS and TF-CAS may be reasonable alternatives in selected patients. TCAR-CAS has promising results in non-randomized studies suggesting superiority over TF-CAS. It's role in the treatment of carotid stenosis is being defined.

Ongoing Carotid Intervention Trials

Trial	Patients	Groups	Total N	Centers
CREST-2	$\geq 70\%$ Asx	CEA/CAS/OMT	2418	North America
ECST-2	CAR Score	CEA/CAS/OMT	2000	Europe
SPACE-2	Asx	CEA/CAS/OMT	513*	Europe

*Trial stopped due to slow recruitment

Treatment Of Asymptomatic Carotid Stenosis

Conclusion

- Every patient should be on optimal medical therapy.
- The best evidence we have shows a clear but modest benefit of CEA + OMT over OMT alone
- Statins have likely reduced the risk of stroke in patients with ACS, but
 - Magnitude of benefits are probably overstated
 - Statin intolerance is somewhat common
- Repair should be limited to
 - Those with good life expectancy ($\geq 3-5$ y)
 - Perhaps to those with high-risk lesions only