

Contrasting Outlooks On the Future of Carotid Stenting and Endarterectomy: Will CAS replace CEA?



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Presenter Disclosure Information

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Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization listed below.

Nothing to Disclose



Introduction

- It is essential to critically evaluate therapies as they are introduced to manage extracranial carotid disease
- Rarely has any form of therapy been subject to the rigorous evaluation as has CEA and CAS



Emotional Response

- **No other therapy in modern medical practice has evoked the type of emotional response and parochialism that has occurred comparing CEA to CAS**



Epidemiology: Stroke in the U.S.

- Each year, 750,000 people suffer a stroke in the U.S.
- Stroke is the leading cause of adult long-term disability in North America and the 3rd leading cause of death in the U.S.
- Direct and indirect costs are estimated to approach 40 billion dollars

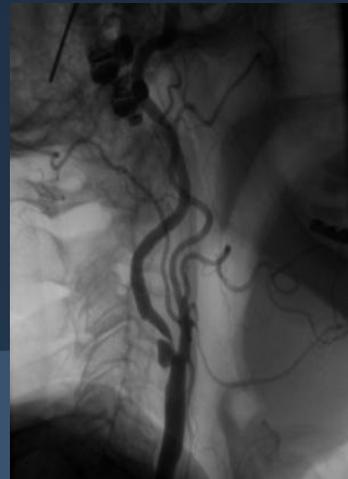
Carotid Disease as a Cause of Stroke

- No general consensus, however a number of studies including a population based study from the Mayo Clinic suggested that carotid stenosis or occlusion as a cause of stroke occurs in 18% of all 1st ischemic strokes



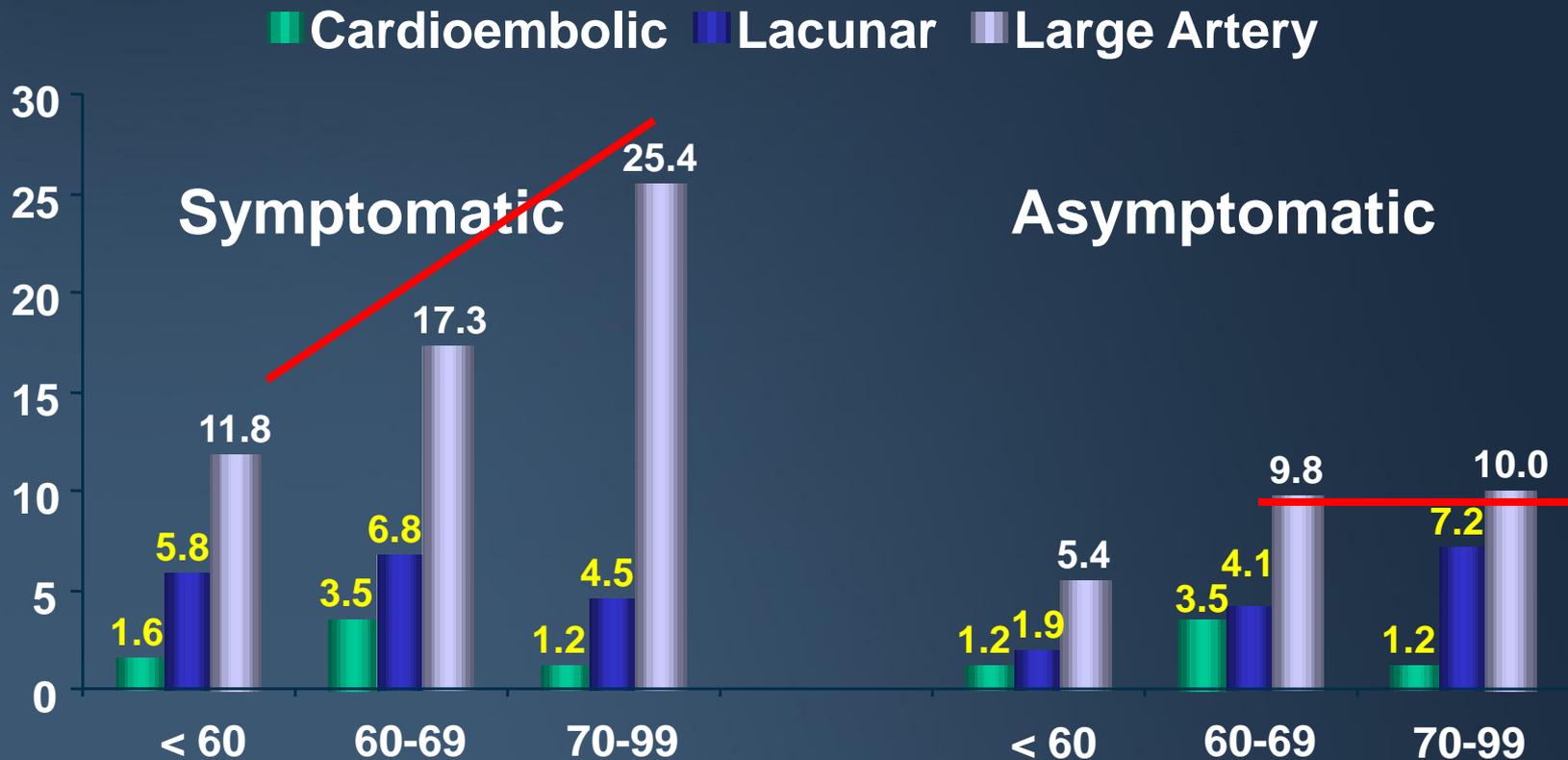
Role of Carotid Revascularization in Stroke Prevention

- We now know patients with a stroke or TIA secondary to a carotid stenosis have a high risk of another cerebrovascular event and that revascularization has benefit
- The role for revascularization in asymptomatic carotid disease is less clear



Carotid Artery Disease: Causes of Stroke by Lesion Severity

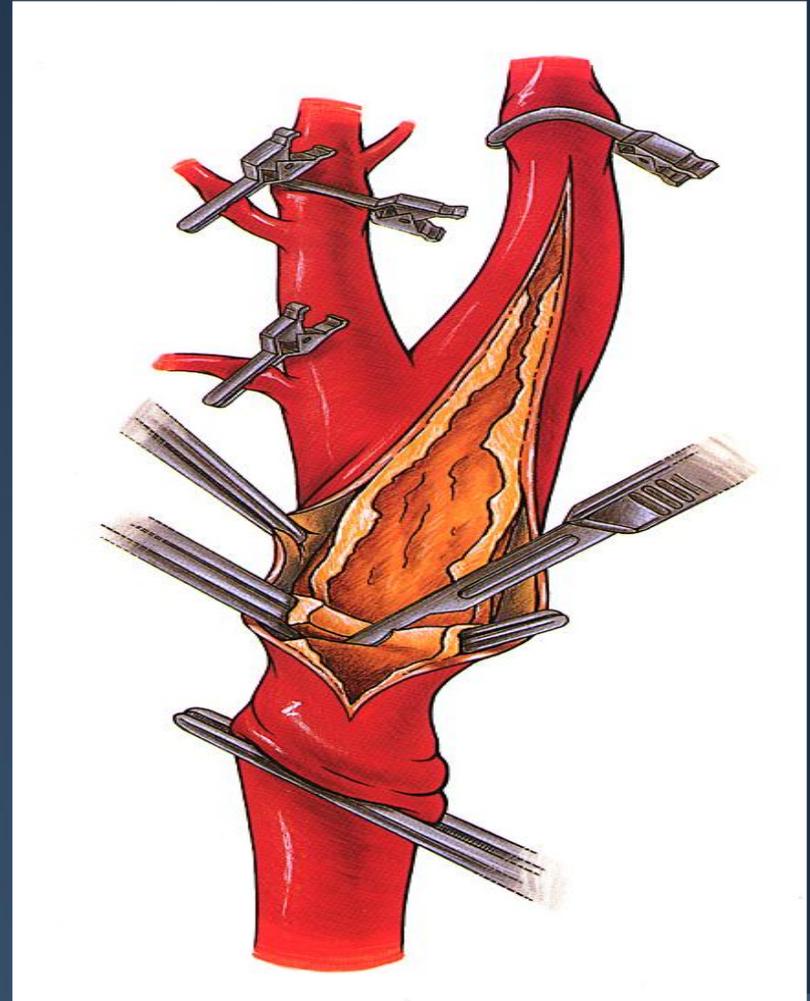
NASCET Trial – Medically Treated Patients, 5-year Risk



Barnett HJM, et al. *JAMA*. 2000;283:1429-1436.

Carotid Endarterectomy (CEA)

- **Most common vascular surgical procedure (250,000/year)**
- **Performed by vascular surgeons (80%) and some cardio-thoracic, general and neurosurgeons**



NASCET: Symptomatic Pts, 70-99%

- Life-table estimate of ipsilateral stroke at 2 years for 659 patients:
 - Medical → 26%
 - Surgical → 9%
 - Absolute RR → 17% (8.5%/yr)
- **Number needed to treat = $100/8.5 = 12$**

– *N Engl J Med*
1991;325:445-53



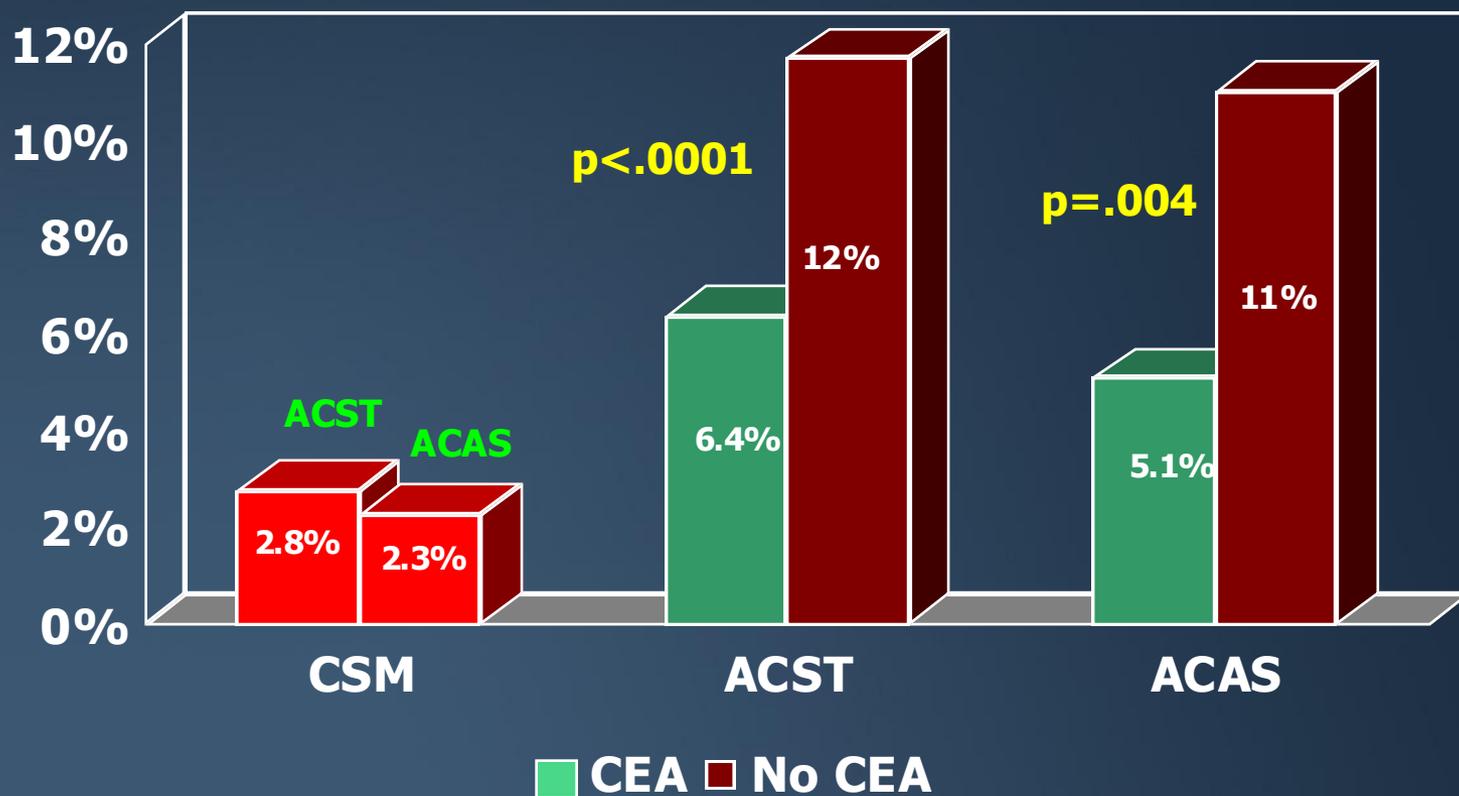
ACAS: Asymptomatic Patients

- 1662 patients with $\geq 60\%$ stenosis
- 5-year ipsilateral stroke rate plus any 30-day perioperative stroke or death:
 - Medical \rightarrow 11%
 - Surgical \rightarrow 5%
 - Absolute RR \rightarrow 6% (1.2%/yr)
- **Number needed to treat = $100 / 1.2 = 83$**

– JAMA 1995;273:1421-8



ACST versus ACAS 5-year Stroke Risks



30-day Stroke and Death Rate for CEA Clinical Trial Data

Symptomatic Disease

	<u>Mortality (%)</u>	<u>Disabling CVA (%)</u>	<u>Minor CVA (%)</u>
NASCET I¹			
(>70% stenosis)	0.6	1.3	3.9
NASCET II²			
(50-69% stenosis)	1.2	1.6	4.0

Asymptomatic Disease

VA Asymptomatic³			
(>50% stenosis)	1.9	1.0	1.4
ACAS⁴			
(>60% stenosis)	0.4*	0.2*	0.5*

*excludes 1.2% risk of stroke after angiography.

1. NEJM 1991; 325:445-453 3. NEJM 1993;328:221-227
2. NEJM 1998;339:1415-1425 4. JAMA 1995;273:1421-1428.



Are NASCET and ACAS Relevant in the Year 2008?

- Medical arm = aspirin
- Statins didn't exist
- Patients over the age of 80** were not included in the trials

**and other comorbidities



CEA Trial Exclusions

NASCET

- 25 CEA's/yr
- <6% stroke and death
 - <79 years old
 - organ failure
 - CA with <5 yr life exp
 - valve, arrhythmia
 - MI < 6 months
 - uncontrolled HTN, DM
 - **Only 1/3 pts enrolled**

ACAS

- hospital and surgeon <3% CVA and death
 - <79 years old
 - any co-morbidity that increased OR risk
 - any condition that decreased life expectancy
 - **1 patient enrolled for every 25 pts screened**



Ipsilateral Stroke at 3 years

Trial	Medical Risk (%)	Surgical Risk (%)	NNT	Periop CVA/Death (%)	Periop disabling CVA/death (%)
NASCET (70-99%)	25.1	8.9	6	5.8	2.1
NASCET (50-69%)	16.2	11.3	20	7.1	2.1
ECST (70-99%)	16.8	10.3	15	7.5	3.7
CAVATAS (surgery)	18.6	13.9	21	9.9	5.9
CAVATAS (CSSA)	18.6	14.4	24	10.0	6.4

Risks Associated with Revascularization

- **CEA:**
 - **Anesthesia risk- cardiovascular, pulmonary**
 - **Surgical risk- bleeding, cranial nerve palsy, stroke**
 - **Post-op risk-infection, DVT/PE**
 - **6% restenosis rate**



What is the Stroke Risk of Carotid Endarterectomy? Well...It Depends

- **Single Surgeon Experience: 2%**
- **Multiple Surgeon Experience: 5%**
- **Independent Neurologic Oversight: 7%**

Rothwell & Warlow: Stroke, 1996

Introduction of CAS

- **Introduced by Dr. Roubin and associates in the mid 1990's**
- **It was met with cynicism and overt hostility by the vascular community**
- **Subsequent results of several randomized trials and registry studies now support the view that CAS is not inferior to CEA, and in some cases may be superior**

Why Carotid Stenting?

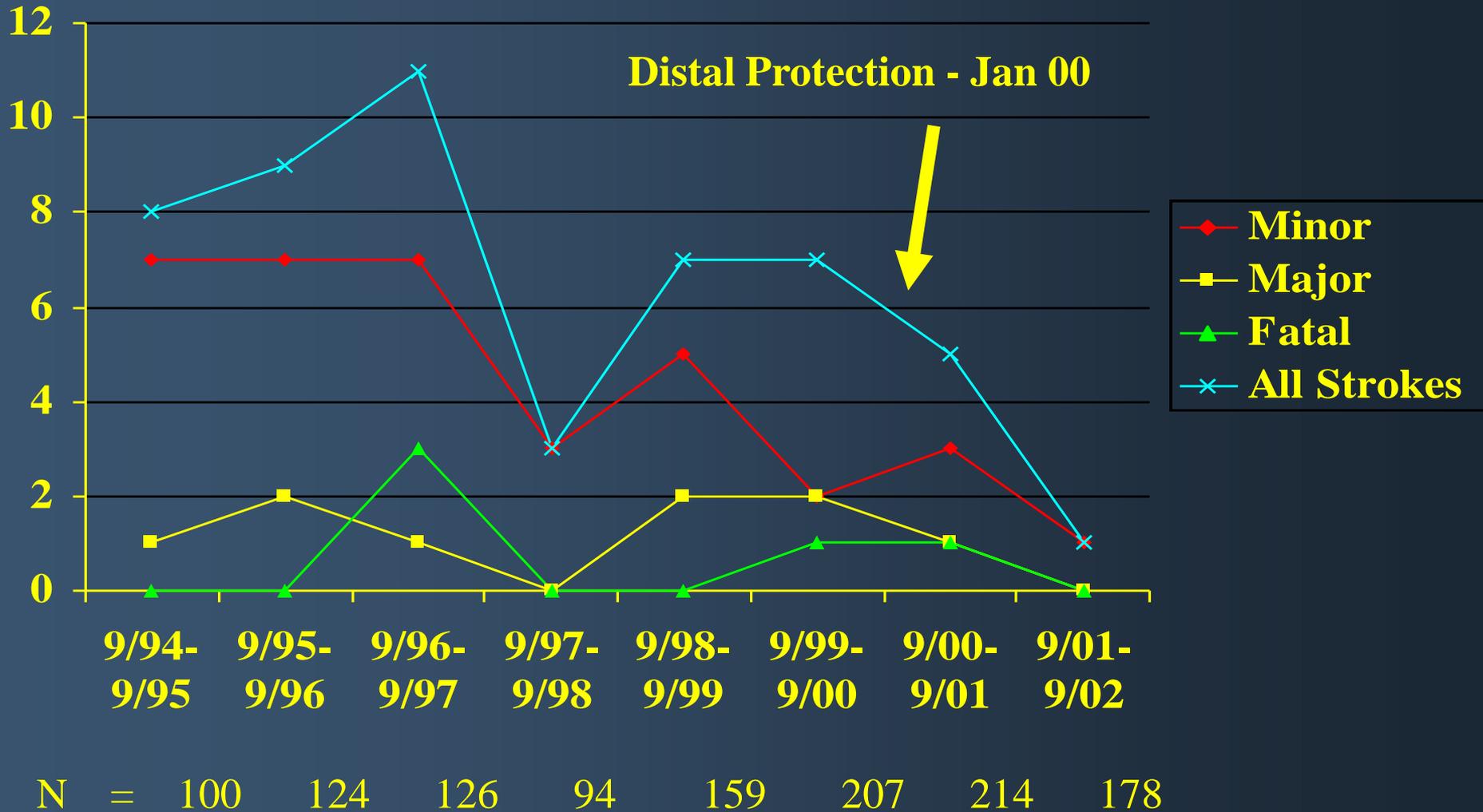
- **Potential Advantages**
 - **Less Invasive Technique**
 - **More Widely Accepted by Patients**
 - **Less Discomfort**
 - **Faster Recovery Time**
 - **Less Expensive?**
 - **Treat Difficult Lesions**
 - **Post Radiation ICA Stenosis**
 - **Restenosis after Endarterectomy**
 - **High Bifurcation Stenosis**
 - **Serious Co-Morbid Medical Conditions**



Hostile Neck Situation...



Improving Results of Carotid Stenting



Studies Showing Advantage to Embolic Protection

- **SAPPHIRE¹** MAE w CAS 4.8%, CEA 9.8%
- **EVA-3S²** CAS w/o EPD arm terminated 12/03 b/c 3.9-fold increased MAE rate
- **CREST³ (lead-in)** Trend towards decreased stroke rates with EPD (n=413)
- **Meta-analysis⁴** Review of single center studies. Combined CVA and death rate 1.8% for CAS+EPD vs 5.5% for CAS w/o EPD

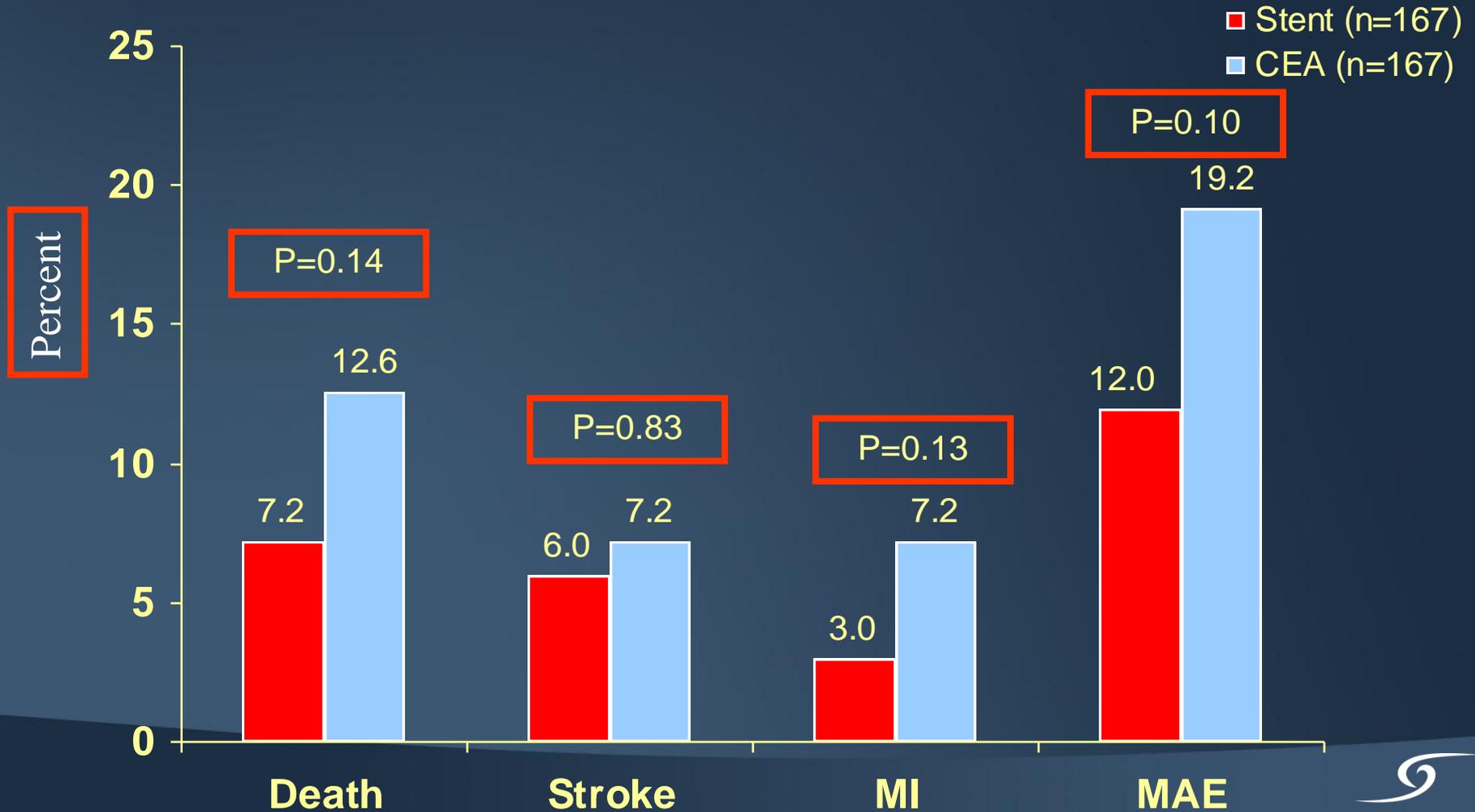
1. Yadav JS et al. NEJM 2004;351:1493-1501; 2. Mas J et al. *Stroke*. 2004; e18-20; 3. Roubin GS et al. *Circulation* 2003; 108:IV6874. Kastrup A et al. *Stroke*. 2003; 34: 813-819

Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE)

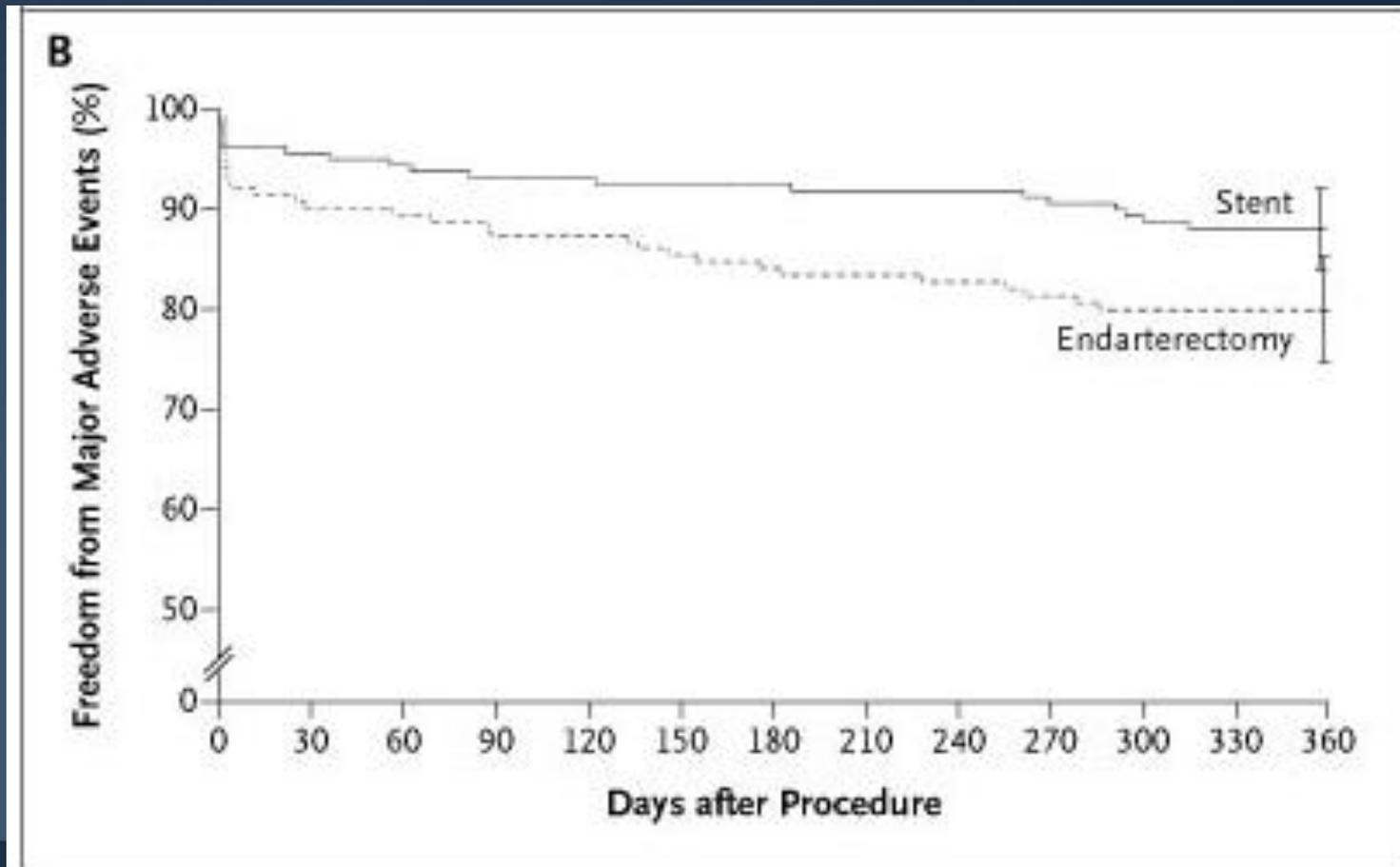
- Inclusion criteria:
 - Asymptomatic with $\geq 80\%$ stenosis by ultrasound
 - OR
 - Symptomatic with $\geq 50\%$ stenosis
 - At least 1 high-risk feature:
 - age > 80 , CHF, severe COPD, previous CEA with restenosis, contralateral carotid occlusion, contralateral laryngeal-nerve palsy, previous radiation therapy or radical neck surgery

SAPPHIRE STUDY

Primary Endpoint (Stroke, Death, MI) at 360 Days



Actual-Treatment Analysis :SAPPHIRE

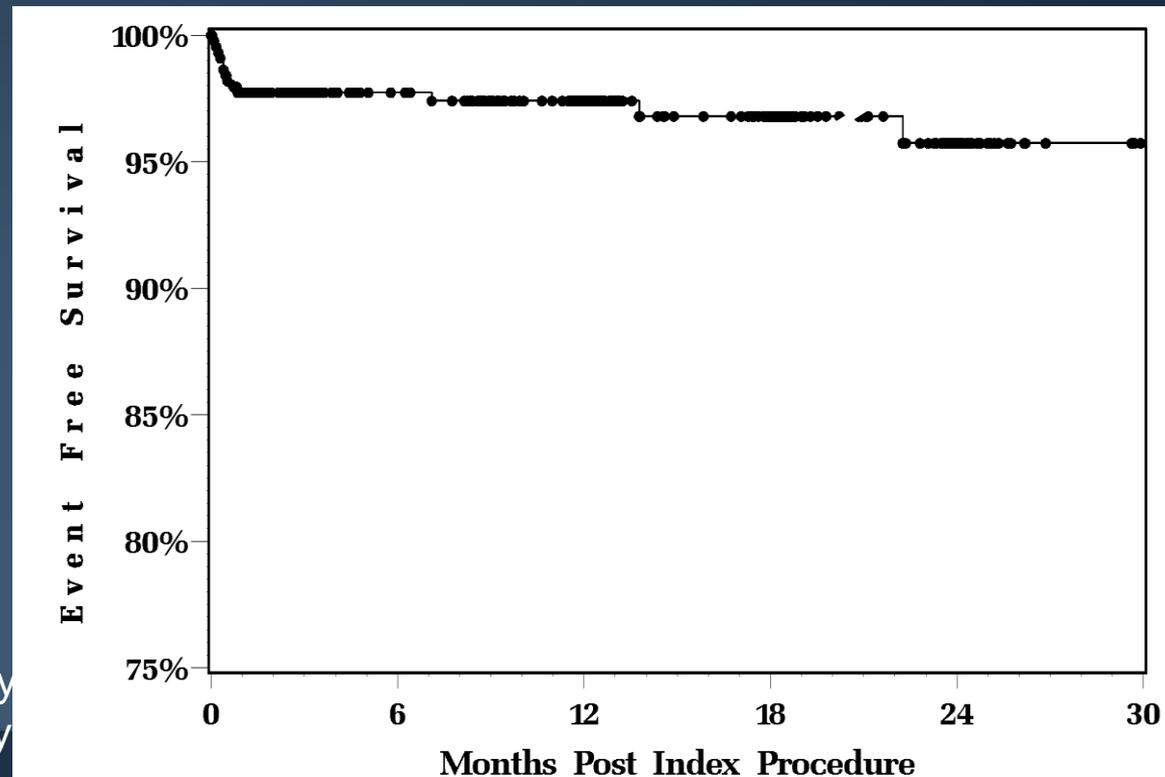


ARChER Trials

- **Patients treated using the Acculink carotid-stent system and the Accunet distal-protection device**
- **In ARChER 1, 1,158 patients received carotid stenting without distal protection**
- **In ARChER 2, the pivotal trial, 278 patients underwent stenting with distal protection**
- **End points: death, stroke, and MI at 30 days plus ipsilateral stroke from 31 days to one year**

Major Adverse Outcomes to 2.5 years Asymptomatic Patients in ARChE R 1, 2 & 3 (N=581)

Freedom from periprocedural death/major stroke and
major ipsilateral stroke 1 month to 2.5 years



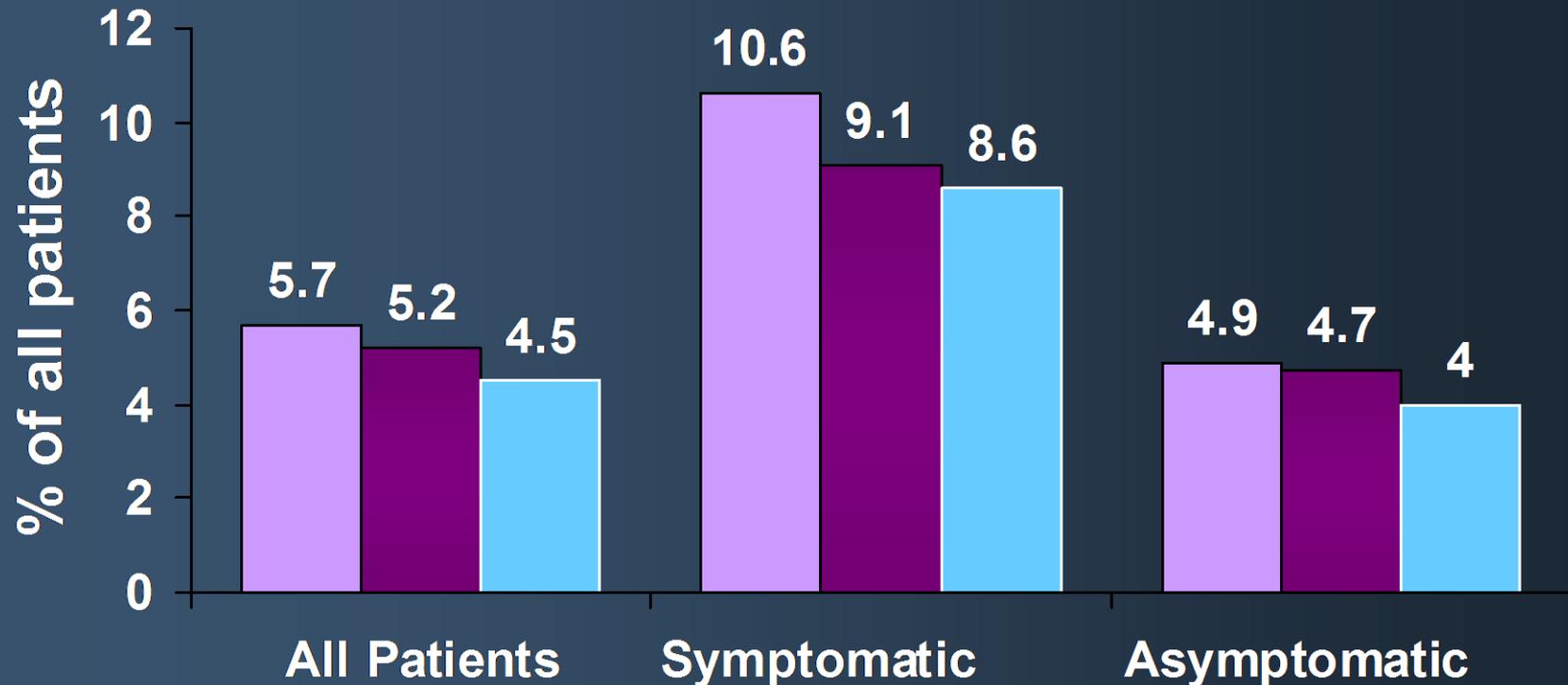
95.7%

Mean follow-up of 391 day
Max follow-up of 1180 day

EXACT & CAPTURE 2 & CAPTURE:

All Patients (combined stroke/death*)

■ CAPTURE (3500) ■ CAPTURE 2 (597) ■ EXACT (1430)



C: n=482; E#: n=139 C2#: n=66

C: n= 3018; E: n=1291; C2: n=531

#Small symptomatic cohorts preclude any comparisons

* Hierarchical Events – Includes only the most serious event for each patient and includes only each patient's first occurrence of each event

Cochrane Review of Randomized Studies: CAS vs CEA

- **Five trials, 1269 patients**
 - **Leicester (1998)**
 - **CAVATAS (2001)**
 - **Kentucky studies (2001, 2004)**
 - **WALLSTENT (2001)**
 - **SAPPHIRE (2004)**
- **No difference in treatment-related CVA + death**
- **No difference in stroke + MI + death**

Risks Associated with Revascularization

- **Carotid Stent:**
 - **Angiography: stroke, dye nephropathy**
 - **Balloon angioplasty: dissection, vessel rupture, stroke**
 - **Stent deployment: stroke, migration of stent or protection device**
 - **Impact on stroke prevention not completely defined**
 - **incidence of restenosis ,stent fx ?**

Clinical Decision Making: How do we apply what we know?

- **Assessment of risk vs benefit**
- **Appropriate patient selection**
- **Recognize the limitations of each therapeutic option**
- **Assess outcomes at your institution, remembering that all results are local**



Primary Questions

- **What is the optimal revascularization strategy?**
- **Will carotid artery stenting virtually replace carotid endarterectomy?**



Role of Cardiologists

- It would be nice to suggest to an audience of cardiologists that CEA will be replaced by carotid stenting and that cardiologists are the best individuals to provide this therapy



What Do We Know?

- The data is imperfect and not complete
- Neither strategy for revascularization is without potential complications and the results of each are imperfect



Factors That Influence Outcomes

- Operator experience
- Patient selection
- Clinical judgment

** All are moving targets not yet defined*



Procedural Aspects That Influence Outcomes for CAS

- These are not fully understood
- How do we deal with symptomatic lesions, severe tortuosity, concentric calcification or significant arch disease
- Aspects of clinical judgment including age and timing of revascularization may also increase the risk of periprocedural stroke or death



Rogues Gallery



Severe arch disease



String Sign



Severe atheroma with filling defect



Complimentary Strategies

- **Certain patients are well suited for CAS with its reduced invasive nature**
- **Alternatively, patients at higher procedural risk may be better served by CEA**



Summary

- **Greater emphasis needs to be placed on the elements of patient selection with improved methods of defining who is likely to do well and who is not**
- **Efforts to define and improve training and the required experience level that is required to perform the procedure is essential in ultimately providing optimal benefit for the patient**

