



The Effectiveness of Medical Therapy for Severe Carotid Stenosis in Reducing Large-Vessel Embolic Stroke: Open Question or Question Answered?

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Conflicts of Interest

- **Consultant**

- Abbott Vascular
- Arsenal Medical
- Atheromed
- Baxter, Incorporated
- Becker Venture Services Group
- Harvard Clinical Research Institute
- I.C.Sciences, Incorporated
- Micell, Incorporated
- Nexeon Medical Systems
- Takeda Pharmaceuticals

- **Equity**

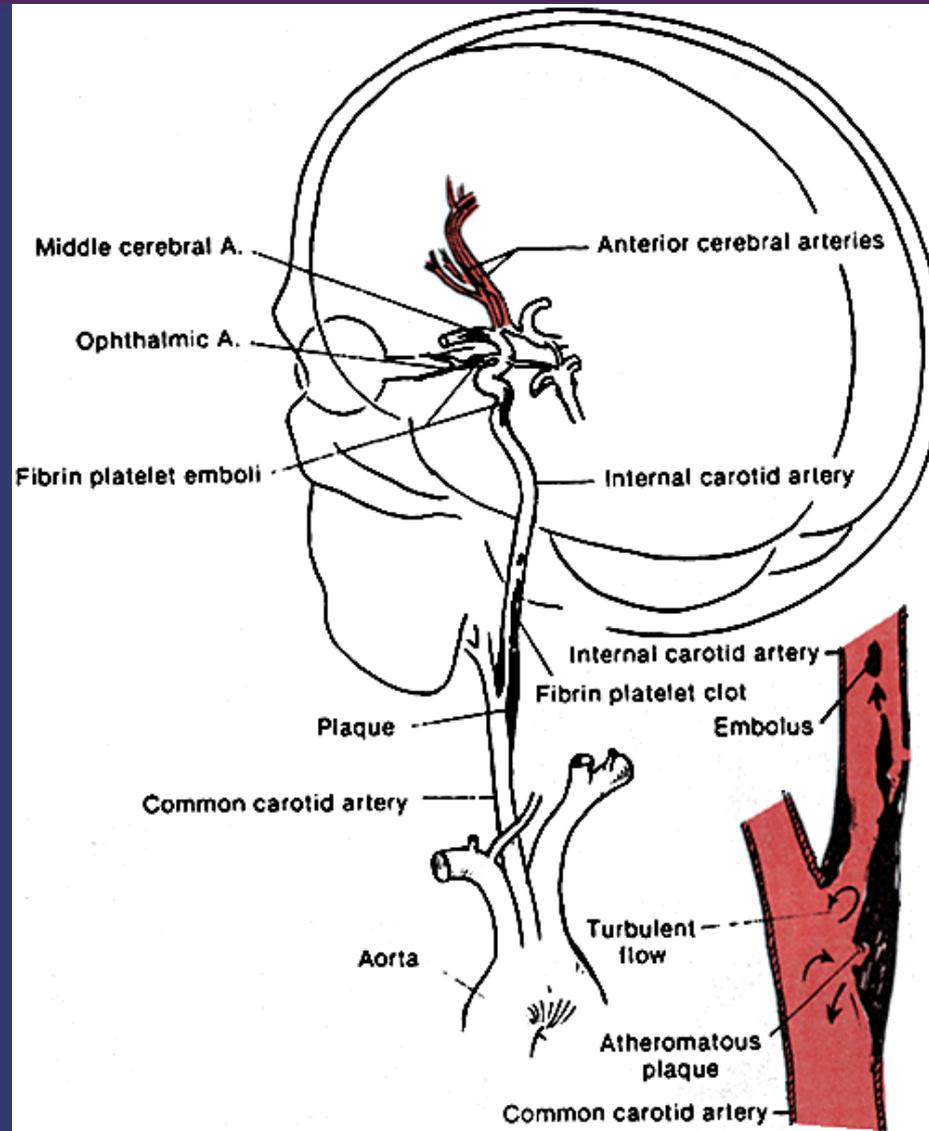
- Access Closure, Inc
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Can Medical Therapy Prevent This???



The Differences in Opinion Regarding the Same Literature Has Boxed Us Into a Corner...



There Has Been a Great Deal of Excitement Around Carotid Revascularization Lately...

- Carotid Endarterectomy
- Carotid Stent with Embolic Protection
 - Proximal
 - Distal



Annual Percentage Rate of Vascular Events

696 patients with asymptomatic carotid artery disease followed for a mean of 43 months

<u>Stenosis</u>	<u>TIA</u>	<u>Stroke</u>	<u>Cardiac Event</u>	<u>Death</u>
<50%	1.0	1.3	2.7	1.8
50-75%	3.0	1.3	6.6	3.3
>75%	7.2	3.3	8.3	6.5

Asymptomatic Carotid Artery Study

- Multicenter trial of carotid endarterectomy in patients with asymptomatic carotid artery stenosis >60% in diameter
- 1662 patients randomized to CEA or no CEA
- Primary outcome: Ipsilateral stroke or perioperative death or stroke
- Median follow-up = 2.7 years



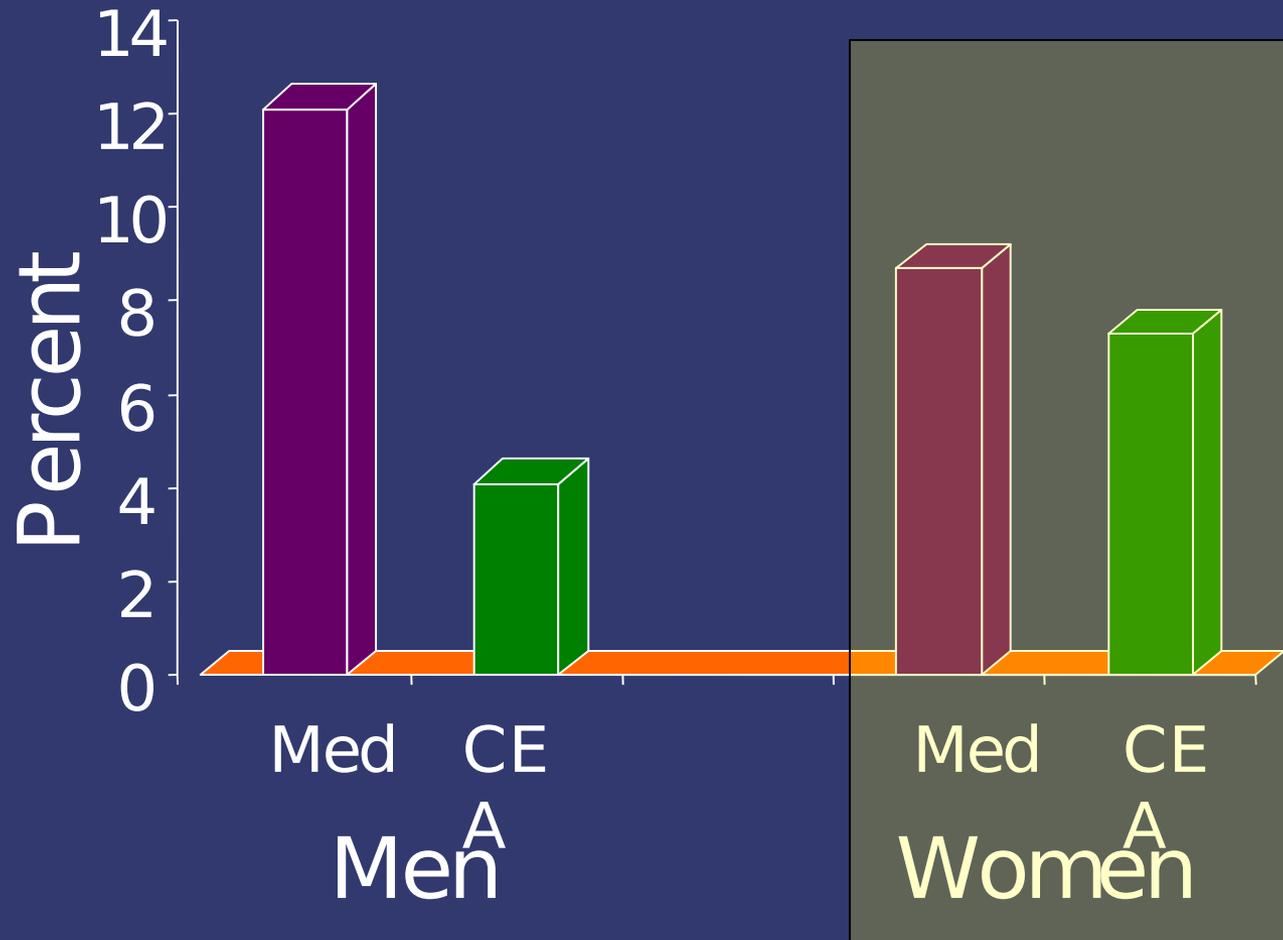
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Executive Committee for ACAS . J.A.M.A., 1995



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ACAS: Stroke and Death At 5 Years



MRC Asymptomatic Carotid Surgery Trial (ACST)

- 3120 asymptomatic patients with 60-99% carotid stenosis
- 126 hospitals, 30 nations
- Excluded for poor surgical risk, a cardioembolic possibility
- Follow up was 5 years
- Enrolled from 4/93 to 7/2003
- Report is for first five years of trial



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ACST Collaborative Group. Lancet 2004; 363: 1491

MRC Asymptomatic Carotid Surgery Trial (ACST): Results

Mean Follow Up 3.4 Years

p	Surgery		Medical
	N (%)	N (%)	
<u>Carotid Strokes</u>			
	13 (1)	62 (4)	.0001
	11 (1)	35 (2.2)	.0004
	6 (<1)	8 (<1)	
<u>Other Strokes</u>			
	8 (<1)	8 (<1)	
	4 (<1)	7 (<1)	



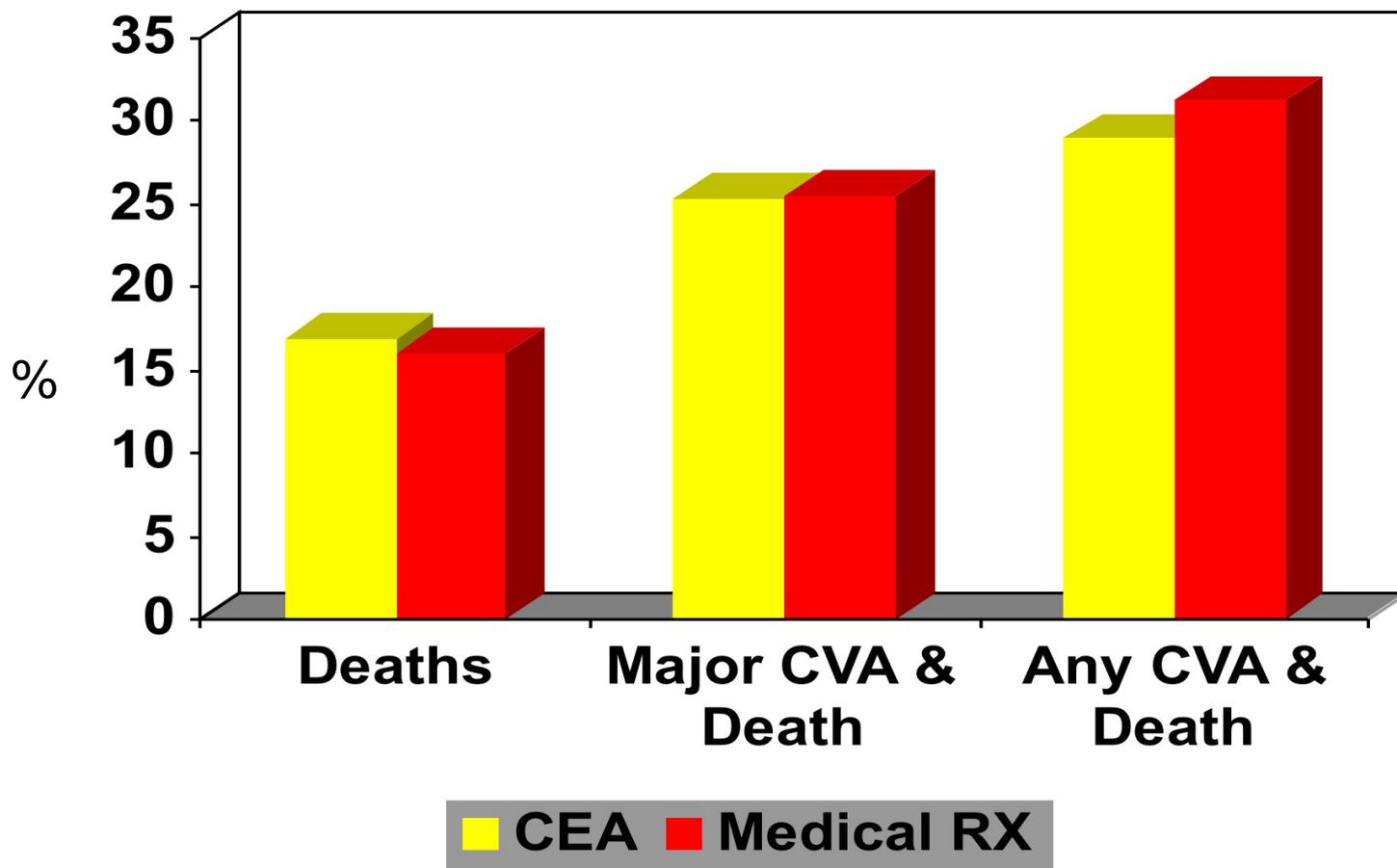
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ACST Collaborative Group. *Lancet* 2004; 363: 1491



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The Real ACST Results



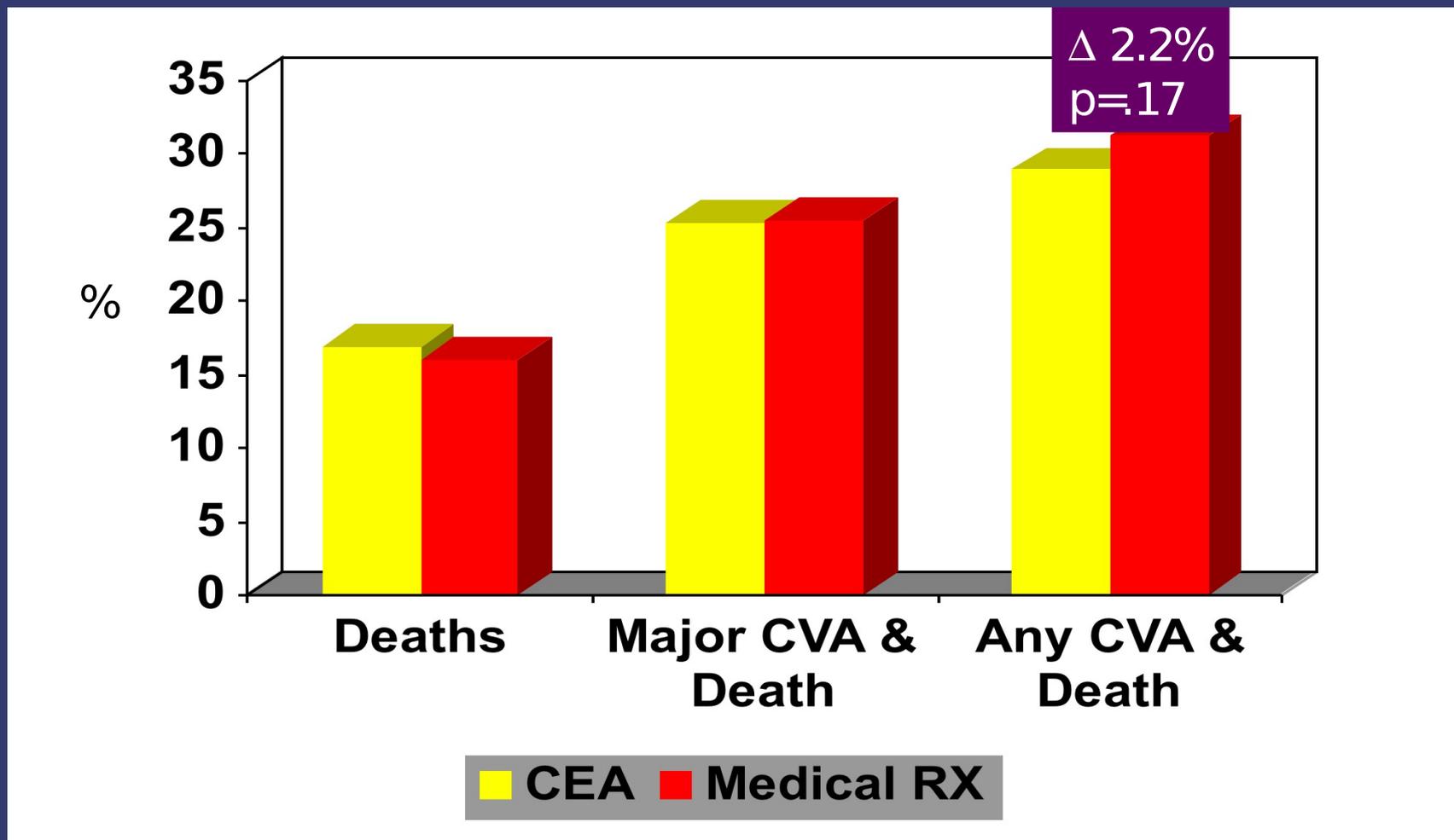
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Primary Prevention of Ischemic Stroke: AHA/ASA 2006 Guidelines

The Real ACST Results



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Primary Prevention of Ischemic Stroke: AHA/ASA 2006 Guidelines

CEA vs. Med Rx for Stroke Prevention

Recommendation based on Asx RCT's (Level I)

- CEA, *on top of contemporary medical therapy*, is beneficial in selected (“e.g. conventional risk”) patients, ages 40-75 years, who are expected to live for ≥ 5 years, if:
 - Stenosis 60-99% and **physician/hospital stroke/death rate $\leq 3\%$**

-AHA/ASA Guideline; Stroke, Feb 06

Mortality Rate ACST vs ArCHER

Study	Mortality Rate (%)
ACST (3.4 yr)	16.9
ArCHER (3.0 yr)	19.1

Standard Risk

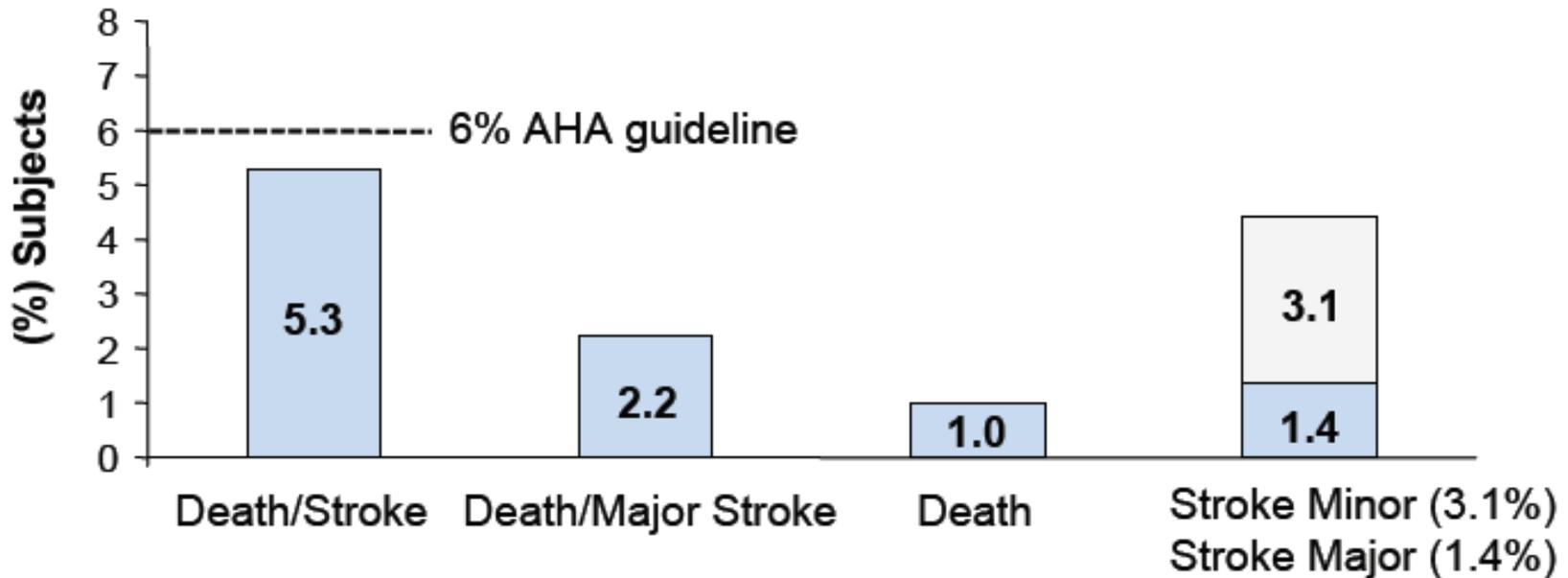
High Risk



30-Day Outcomes from XACT and Capture 2 (N=6320)—All High Risk Patients

Symptomatic Patients <80

N=589



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Circ Cardiovasc Intervent 2009;March 6



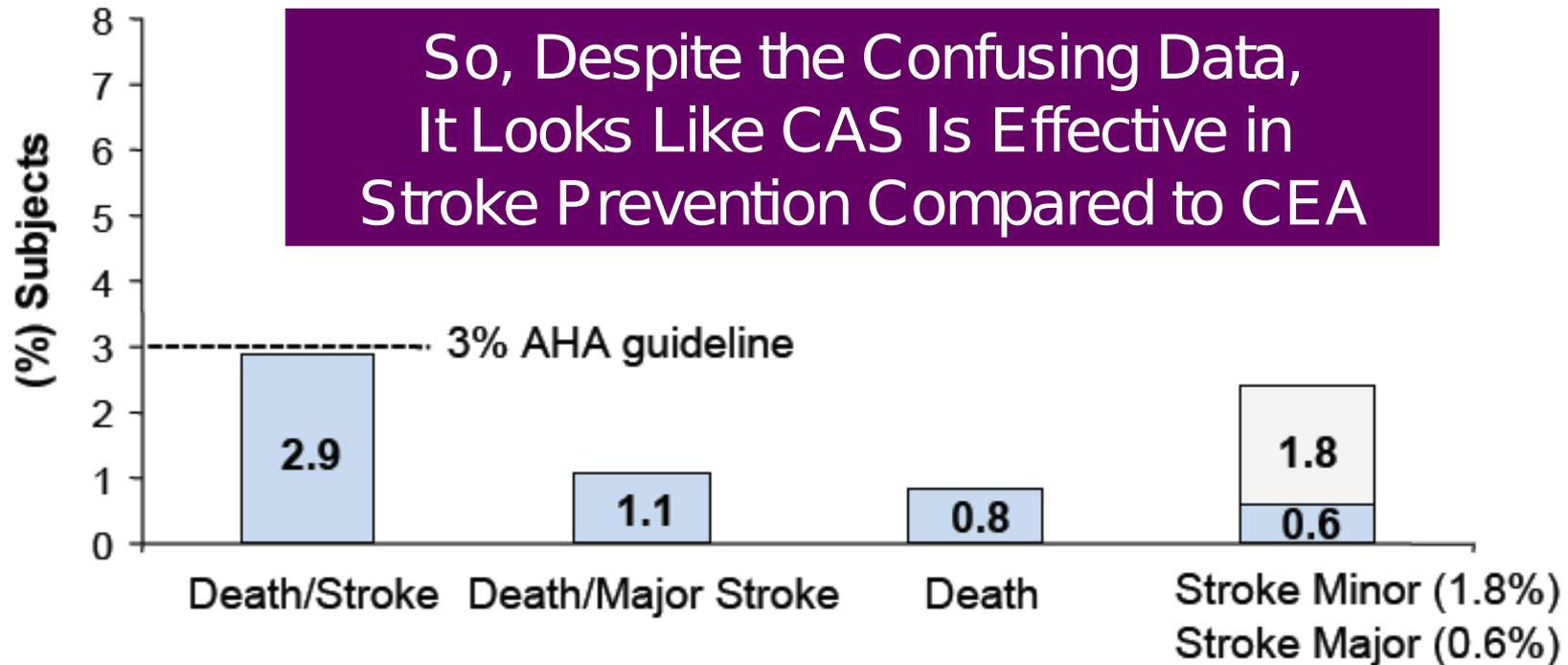
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30-Day Outcomes from XACT and Capture 2 (N=6320)—All High Risk Patients

N=4282

Asymptomatic Patients <80

So, Despite the Confusing Data, It Looks Like CAS Is Effective in Stroke Prevention Compared to CEA



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Medical Treatments That *Did Not Exist* During Revascularization Trials

- **Modulators of Renin Angiotensin System**
 - ACE inhibitors
 - Hope
 - Angiotensin Receptor Blockers
 - Life
- **Statins**
 - HPS
 - CARDS

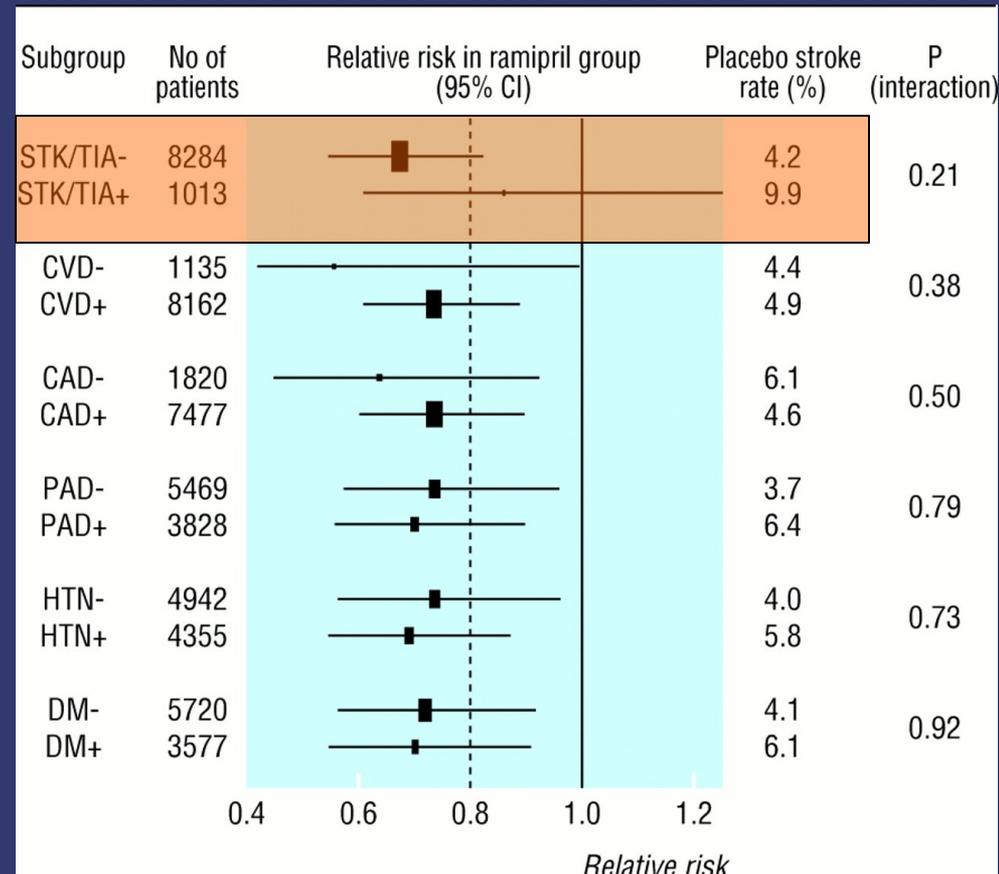


ACE Inhibition Decreases Stroke in a High Risk Population

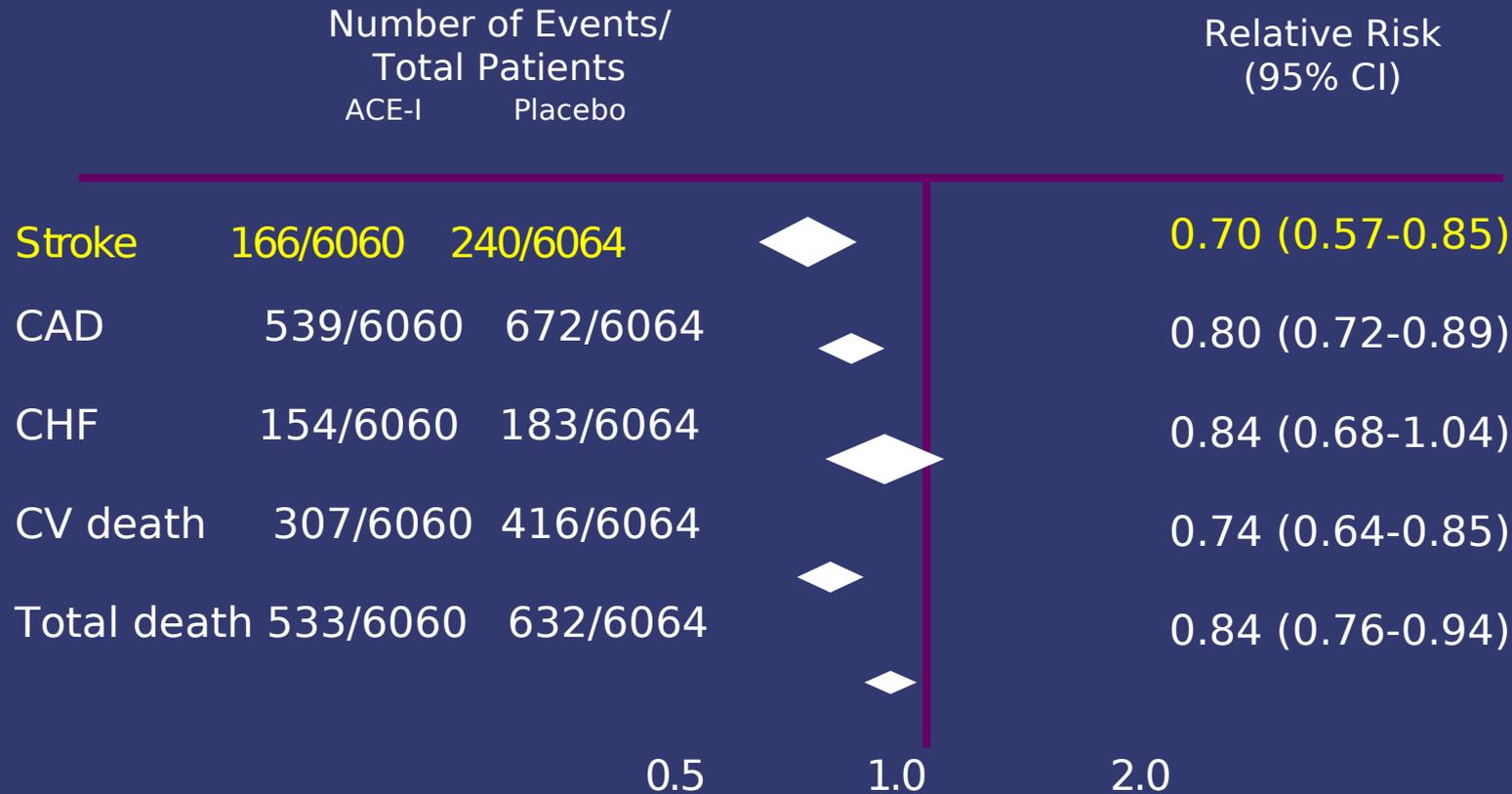
9297 patients with vascular disease or diabetes plus an additional risk factor randomized to ramipril or placebo f/u 4.5 yrs

1.5% Absolute Reduction

34% Relative Reduction



Effect of ACE-Inhibitor Therapy vs. Placebo on Cardiovascular Endpoints



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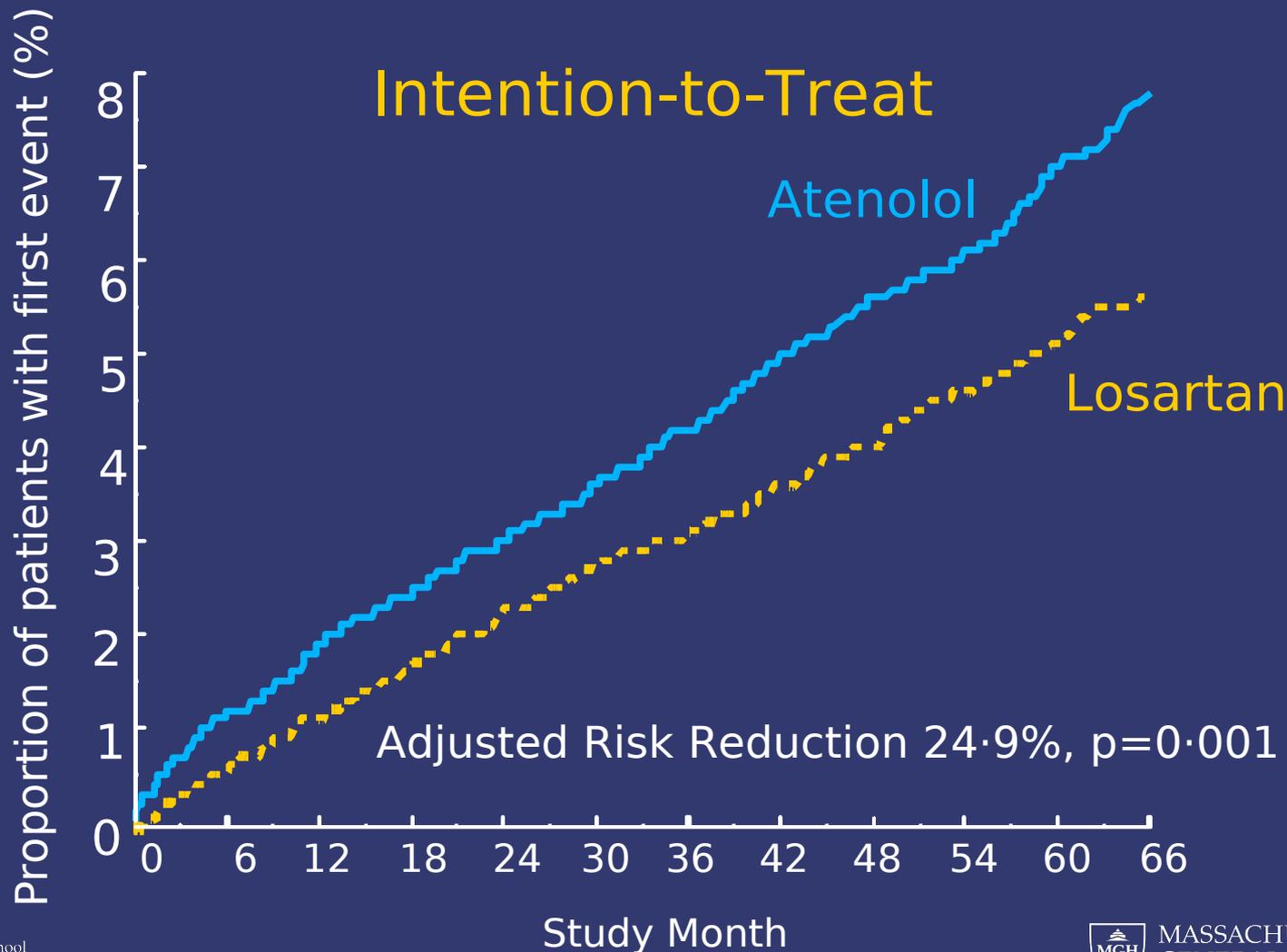
*Blood Pressure Lowering Treatment Trialists' Collaboration
Lancet, 2000; 355: 1955-64; HOPE, PART2; QUIET, SCAT*



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ARBs Decrease Risk of Stroke in High Risk Patients

LIFE: Fatal/Nonfatal Stroke



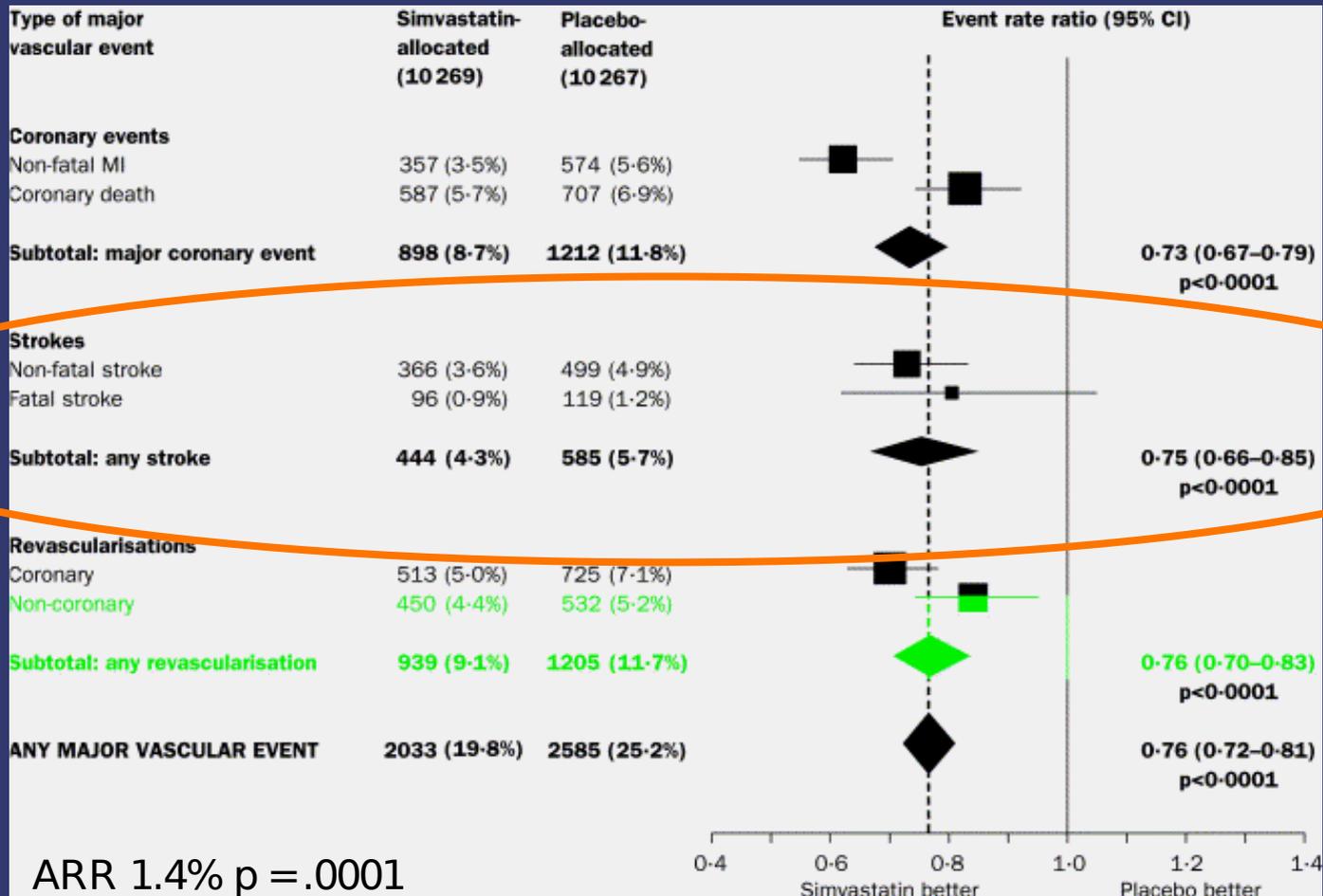
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B Dahlof et al. Lancet 2002;359:995-1003



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Statins Decrease the Risk of Stroke in High Risk Patients: *Heart Protection Study*



A 50% reduction in CEA or angioplasty (ARR .4% P=0.0003).



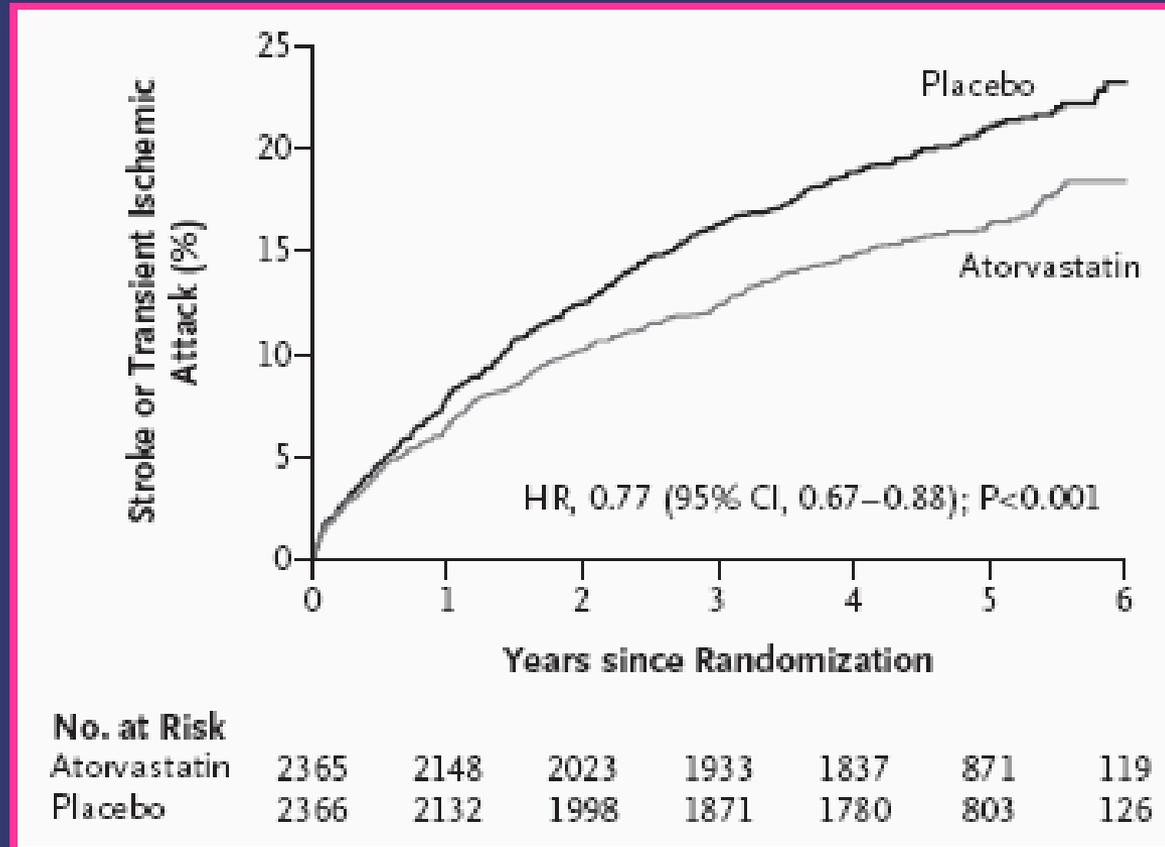
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SPARCL: High Dose Atorvastatin vs Placebo In Patients with Prior CVA/TIA



Stroke or TIA



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N Engl J Med 2006;355:549-559



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Atorvastatin Reduces the Risk of Cardiovascular Events in Patients With Carotid Atherosclerosis

A Secondary Analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial

- 1007 patients with carotid stenosis (not requiring revascularization) at baseline
 - 3271 patients had no carotid stenosis at baseline
- All patients had stroke/TIA within 6 months of randomization
 - Randomized to Atorvastatin 80 mg/d vs Placebo
 - No known CHD
 - LDL Cholesterol between 100-190 mg/dL



Atorvastatin Reduces the Risk of Cardiovascular Events in Patients With Carotid Atherosclerosis

A Secondary Analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial

- Of those patients with carotid artery stenosis at baseline...
 - Atorvastatin lowered any stroke risk by 33%
 - Atorvastatin lowered any CHD event by 43%
 - **Later carotid revascularization was reduced by 56%!**



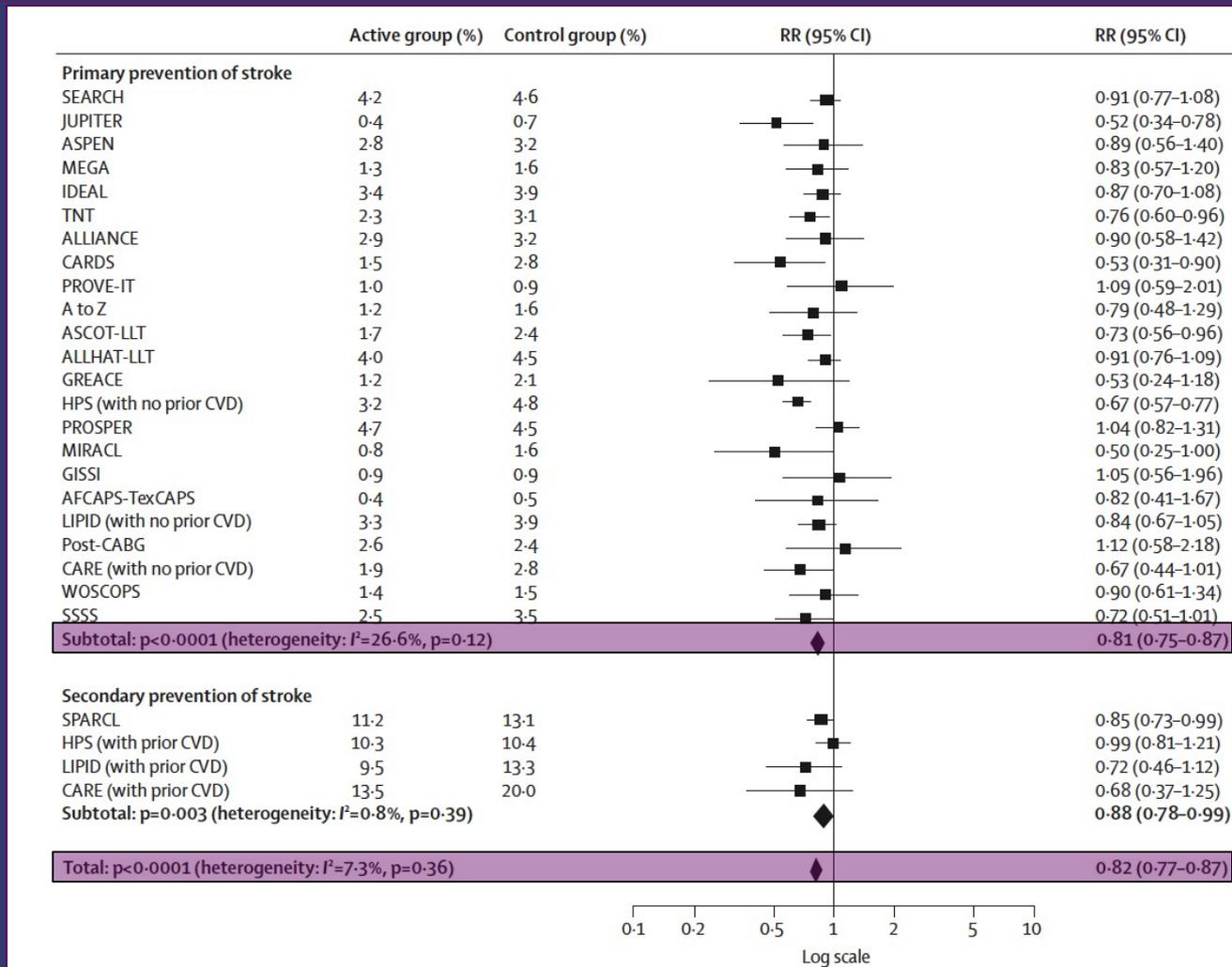
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Stroke 2009;40



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Stroke Prevention with Statin Therapy



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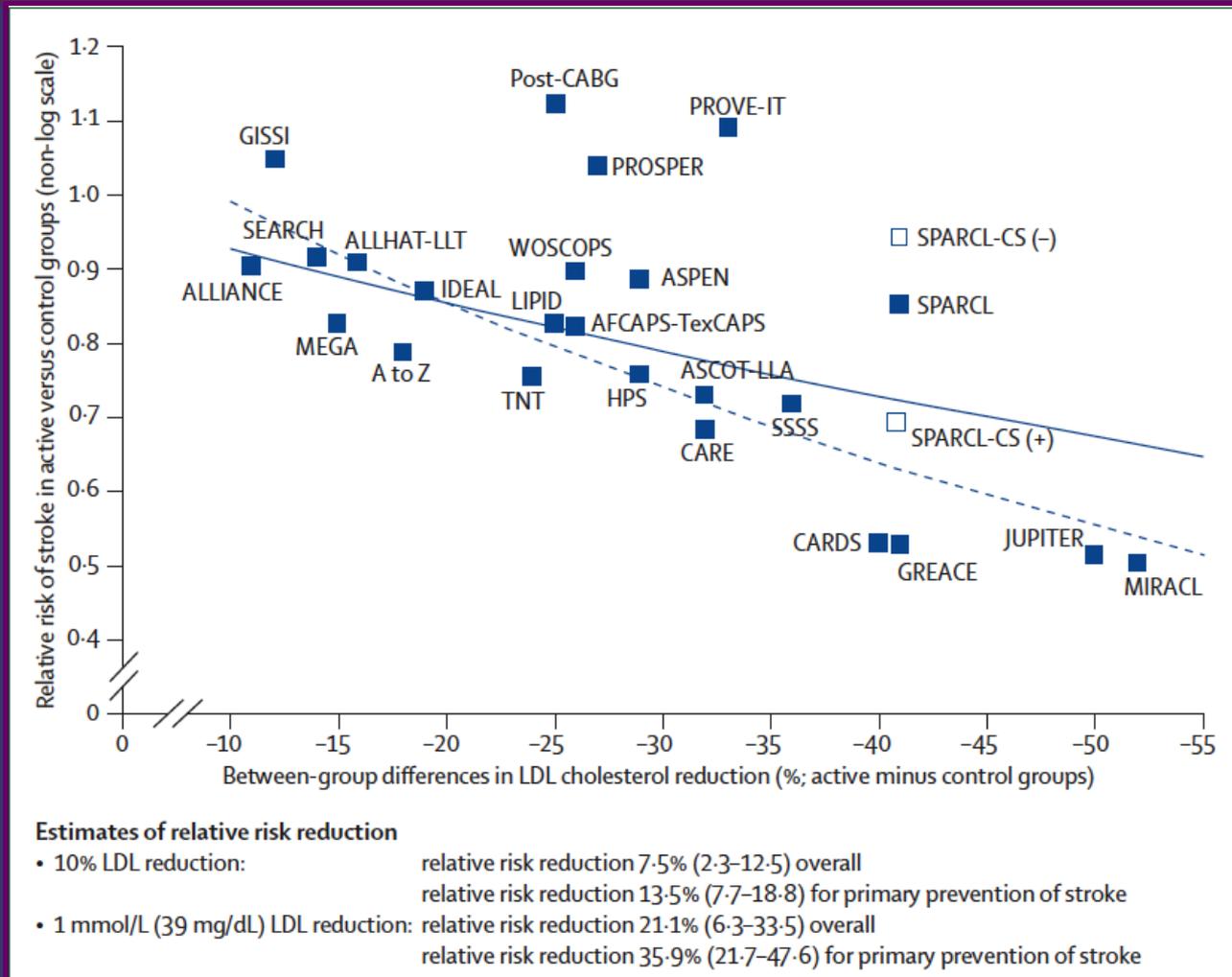


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Lancet Neurol 2009;8:453-63

Stroke Prevention with Statin Therapy



Medical (Nonsurgical) Intervention Alone Is Now Best for Prevention of Stroke Associated With Asymptomatic Severe Carotid Stenosis

Results of a Systematic Review and Analysis

Anne L. Abbott, PhD, MBBS, FRACP

Abstract—Significant advances in vascular disease medical intervention since large randomized trials for asymptomatic severe carotid stenosis were conducted (1983–2003) have prompted doubt over current expectations of a surgical benefit. In this systematic review and analysis of published data it was found that rates of ipsilateral and any-territory stroke (+/–TIA), with medical intervention alone, have fallen significantly since the mid-1980s, with recent estimates overlapping those of operated patients in randomized trials. However, current medical intervention alone was estimated at least 3 to 8 times more cost-effective. In conclusion, current vascular disease medical intervention alone is now best for stroke prevention associated with asymptomatic severe carotid stenosis given this new evidence, other cardiovascular benefits, and because high-risk patients who benefit from additional carotid surgery or angioplasty/stenting cannot be identified. (*Stroke*. 2009;40:00-00.)

Key Words: asymptomatic carotid stenosis ■ carotid endarterectomy ■ endovascular treatment ■ health policy
■ stroke prevention

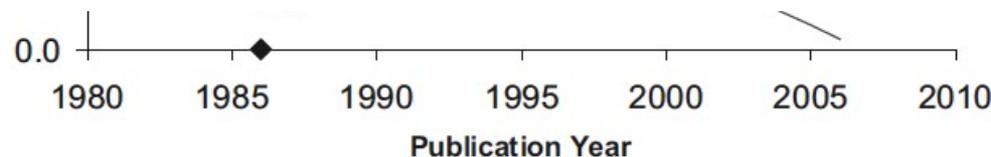


Medical (Nonsurgical) Intervention Alone Is Now Best for Prevention of Stroke Associated With Asymptomatic Severe Carotid Stenosis

Results of a Systematic Review and Analysis

Ipsilateral Stroke Risk

associated with asymptomatic severe carotid stenosis. It is no longer appropriate to refer to vascular disease medical intervention as “conservative,” “control,” or “natural history” therapy, as has been done in the past.^{12,71,72,96,97} It is also inappropriate to reserve more effective sounding terminology, like “intervention,” “revascularization,” and “repair,” to surgery, angioplasty, or stenting.^{39,98–100} The appropriate referral path for patients identified with asymptomatic severe carotid stenosis is to an enthusiastic clinician expert in current best practice vascular disease medical intervention.



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Stroke 2009;40.



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TCD Microembolus Detection

319 ACS patients
between 2000 and 2004

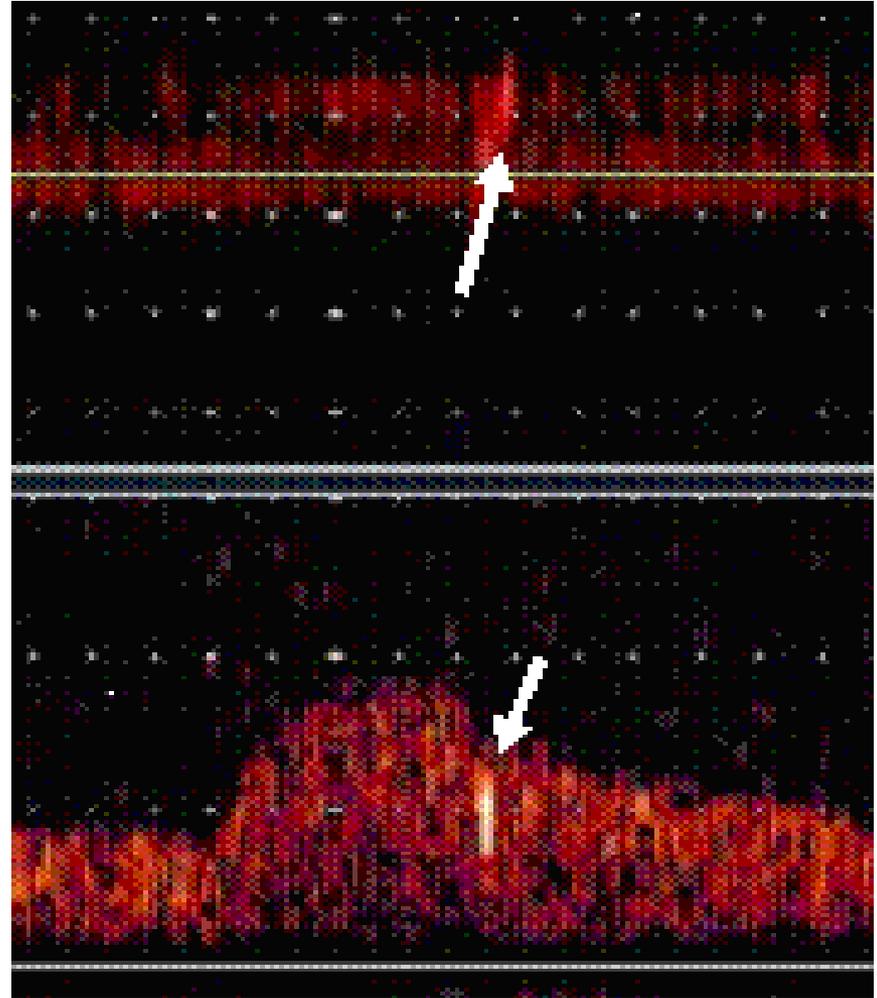
10% had microemboli

1-year Risk	Stroke
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No Emboli	Emboli
1%	15.6%

95% CI (1.01 -1.36)
(4.1-79)

$p < 0.0001$



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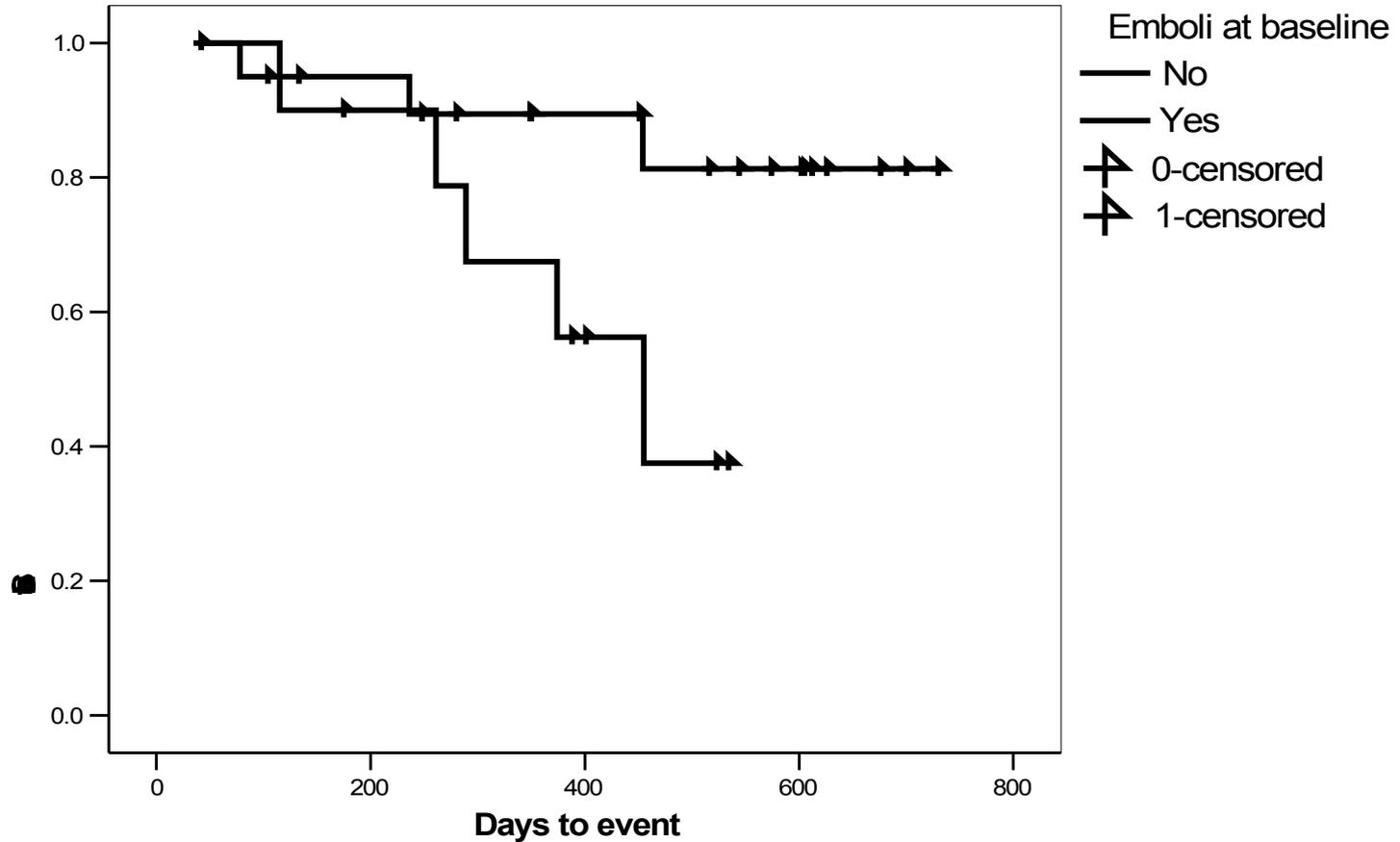
Spence JD et al. Stroke 2005; 36:2373-2378.



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Stroke risk over 2 years by Baseline Microemboli Status



Decline in Events in Asymptomatic Patients with More Intensive Medical Therapy

	No emboli	Micro-emboli	p	Before 2003	Since 2003	p
Stroke in year 1	1.2%	14.3%	<0.0001	4%	0.8%	0.02
Stroke in year 2	0.5%	0%	0.85	1	0%	0.19
MI in year 1	2.4%	8.6%	0.07	6.5%	0%	0.0001
MI in year 2	1.2%	5.7%	0.096	3.5%	0%	0.003
Death in year 1	2.9%	12.1%	0.027	5.1%	2%	0.12
Death in year 2	1.9%	6.1%	0.17	4%	0%	0.011
CEA year 1	1.4%	5.7%	0.12	2.5%	1.2%	0.23
CEA year 2	0.5%	8.6%	0.004	2.5%	0%	0.016

CEA = carotid endarterectomy



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Data from J . D. Spence, MD



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“At least 95% of Asymptomatic Patients with Carotid Stenosis Should be Treated Medically Only”

- The treatment of choice for ACS should be intensive medical therapy
- Less than 5% of ACS patients can benefit from revascularization
- Only those with microemboli should be considered for endarterectomy or stenting

So, Do We Know that Medical Therapy Is the Best Therapy to Prevent Stroke in Patients with Extracranial Carotid Stenosis?

- Despite what I have shown you....
- **We DO NOT KNOW!**
 - No one takes into account compliance
 - Treatment rates are always better in trial patients compared to non-trial patients
 - No large scale trial has been performed comparing best medical therapy alone vs best medical therapy and revascularization



RCT's: CAS vs. OMT for Stroke Prevention

Symptomatic
High-risk

None

Asymptomatic
High-risk

None

Symptomatic
Standard-risk

None

Asymptomatic
Standard-risk

None

Like It Or Not....WE Need to Do This Trial.....

Or Someone Else Will Tell Us What To Do...



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Funding Highlights:

- Accelerates the adoption of health information technology and utilization of electronic health records.
- Expands research comparing the effectiveness of medical treatments to give patients and physicians better information on what works best.
- Invests over \$6 billion for cancer research at the National Institutes of Health as part of the Administration's multi-year commitment to double cancer research funding.
- Strengthens the Indian health system with sustained investments in health care services for American Indians and Alaska Natives to address persistent health disparities and foster healthy Indian communities.

Expands research comparing the effectiveness of medical treatments to give patients and physicians better information on what works best.

- Strengthens the Medicare program by encouraging high quality and efficient care, and improving program integrity.
- Invests over \$1 billion for Food and Drug Administration food safety efforts to increase and improve inspections, domestic surveillance, laboratory capacity and domestic response to prevent and control foodborne illness.

Proposed Decision Memo for Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085R7) COMMENT

Proposed Decision Memo

TO: Administrative File CAG-00085R7

FROM: Tamara Syrek Jensen, JD
Acting Director, Coverage and Analysis Group

We propose to make no changes in coverage of patient groups for percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting (Medicare National Coverage Determination (NCD) Manual 20.7B4). We
Director, Division of Medical and Surgical Services

Sarah McClain, MHS
Lead Analyst, Division of Medical and Surgical Services

Joseph Chin, MD, MS
Medical Officer, Division of Medical and Surgical Services

SUBJECT: Proposed Coverage Decision Memorandum for Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085R7)

DATE: September 10, 2009



CDC Warning: *DO NOT DO THIS!!!*****



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