

Evidence-Based Approach to ***Carotid Artery Stenosis***

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Carotid Artery Stenosis

- Carotid endarterectomy (CEA)
- Carotid artery stenting (CAS)
- Optimal medical therapy

Carotid Artery Disease

RCT's: CAS vs. CEA

completed

ongoing

SAPPHIRE

Symptomatic
High-risk

None

Asymptomatic
High-risk

None

ACST-2

Symptomatic
Standard-risk

EVA3S, SPACE 1, ICSS

Asymptomatic
Standard-risk

ACT 1, SPACE 2

CREST

CEA vs. CAS with Filter

From August 2000 to July 2002

Carotid stenosis with high risk (n=334)

High-risk Sx \geq 50% & ASx \geq 80%

Randomization (1:1)

**Carotid Stenting
with filter device (n=167)**

**Carotid endarterectomy
(n=167)**

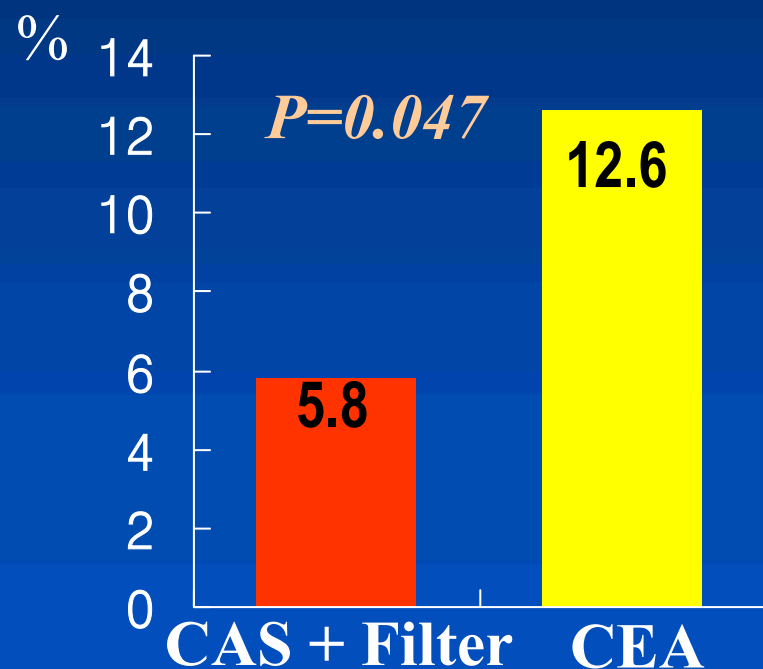
Primary endpoint: composite of death, stroke, or myocardial Infarction within 30 days or death or ipsilateral stroke btw 31days and 1 year

70.1% : asymptomatic

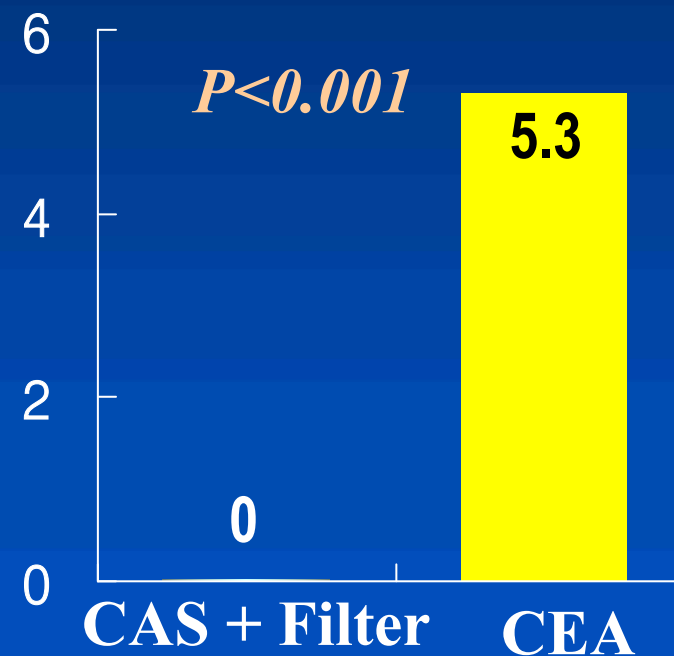
Yadav JS, et al. NEJM 2004;351:1493

30-Day Outcomes

Death /MI /Stroke

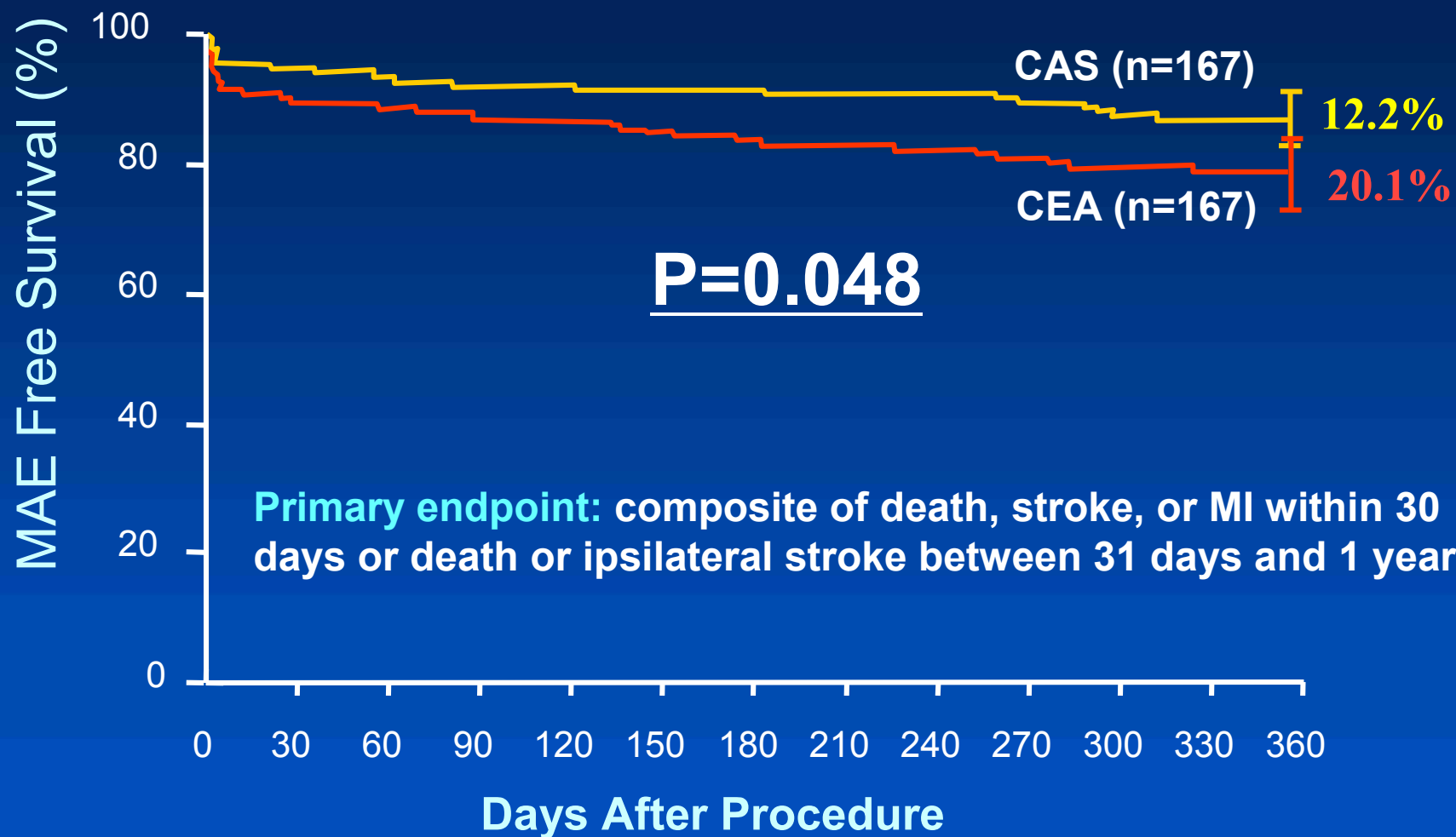


Cranial nerve palsy



Yadav JS, et al. NEJM 2004;351:1493

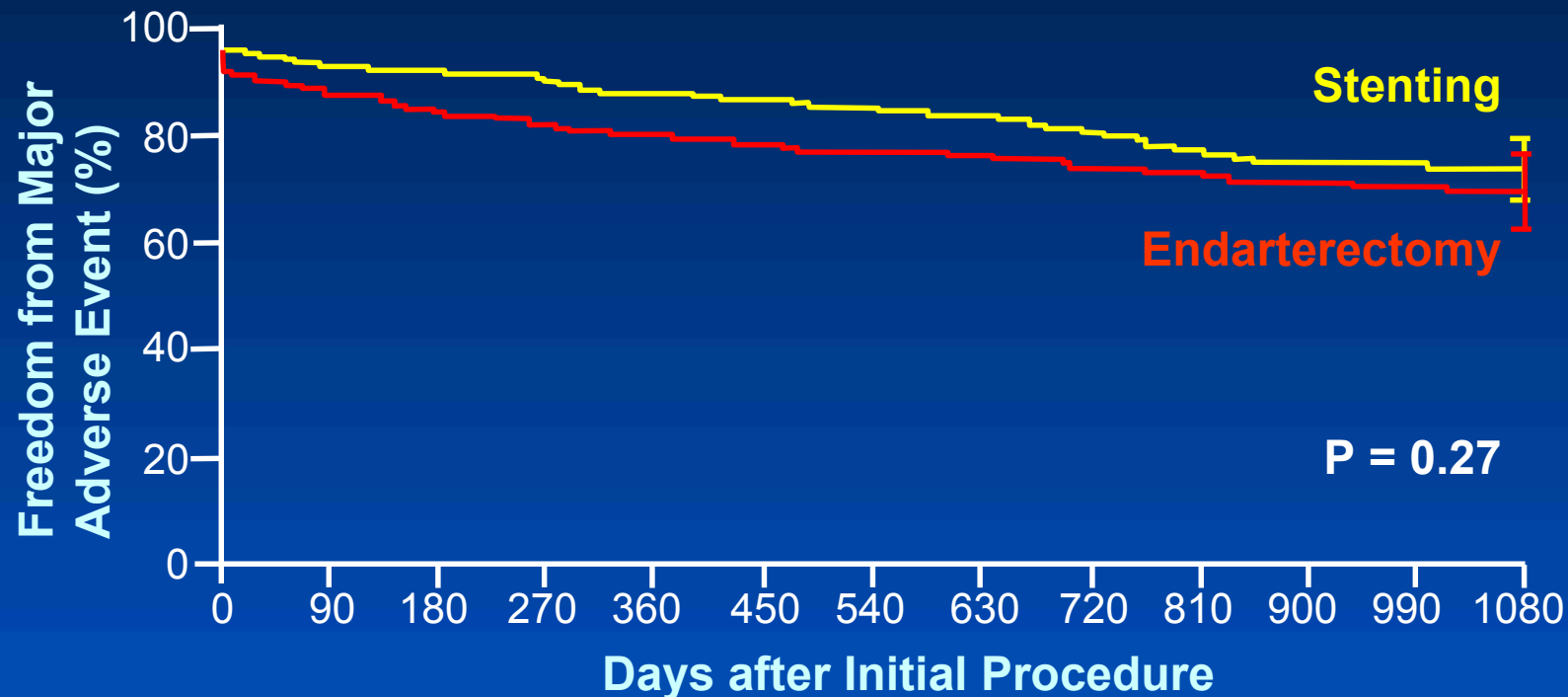
1-Year Clinical Outcomes



Yadav JS, et al. NEJM 2004;351:1493

SAPPHIRE 3-Year Outcomes

Freedom from death, Stroke, MI



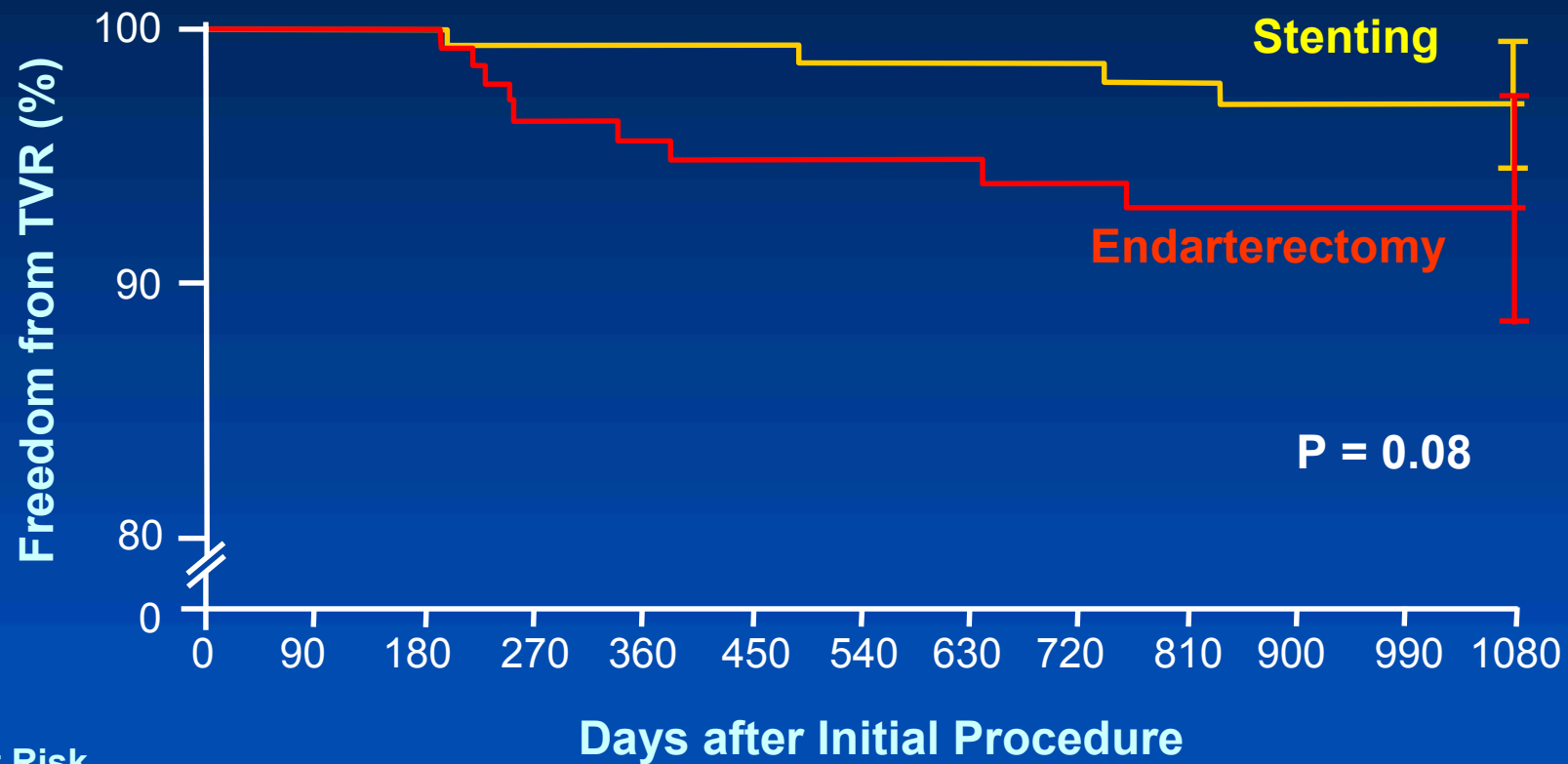
No. at Risk

Stenting	167	155	146	135	129	111	103
Endarterectomy	166	142	123	109	100	85	75

N Engl J Med 2008;358:1572-9

SAPPHIRE 3-Year Outcomes

Freedom from TVR



No. at Risk

Stenting	167	157	151	140	133	116	108
Endarterectomy	166	147	128	112	100	83	74

N Engl J Med 2008;358:1572-9

EVA-3S

EVA-3S

Endarterectomy versus stenting in patients
with symptomatic severe carotid stenosis

872 initially planned

Symptomatic carotid stenosis of 60% or more

N=527: randomization

CEA (n=259)

CAS (n=261)

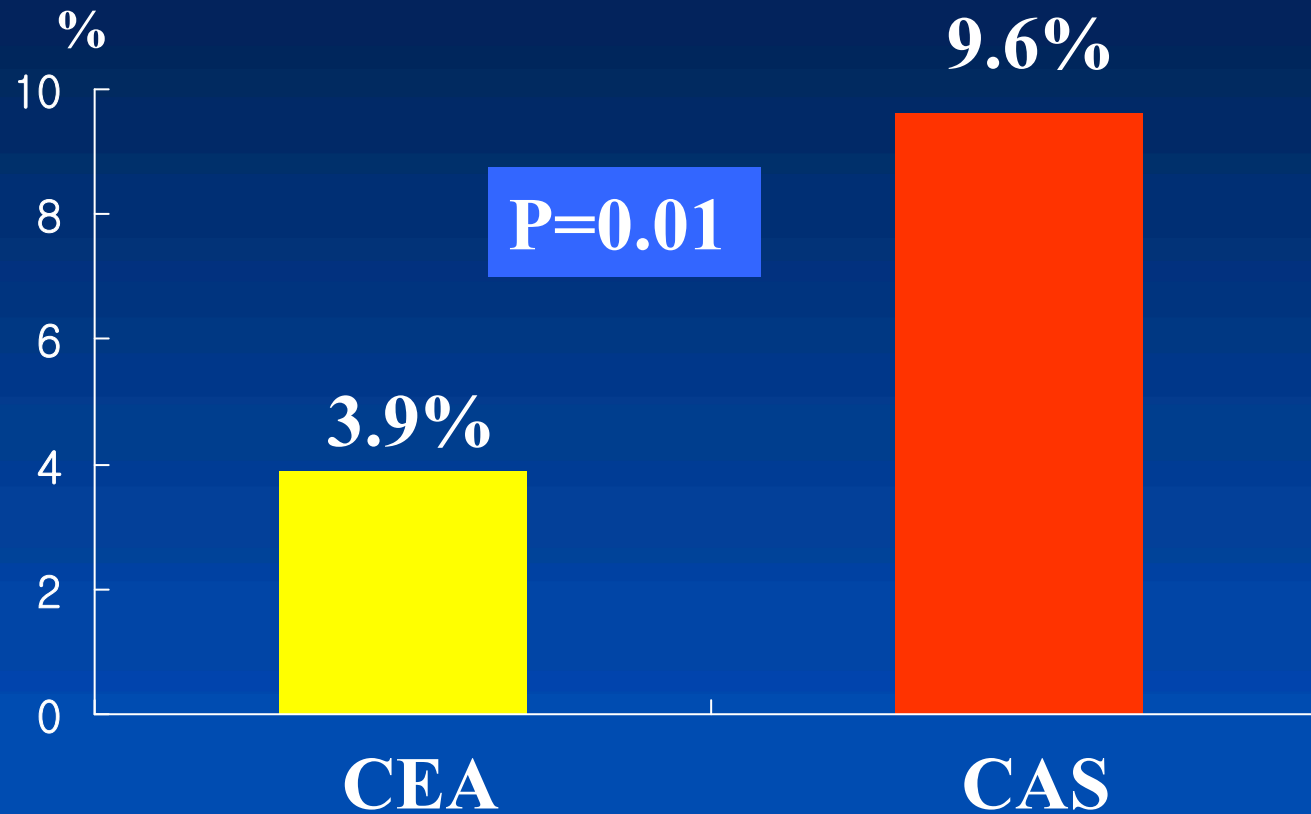
**Primary end point: incidence of any stroke or death
within 30 days after treatment**

Non inferiority design

Hypothesis (stroke+death): 4% CAS vs. 5.6% CEA

NEJM 2006;355:1660-71

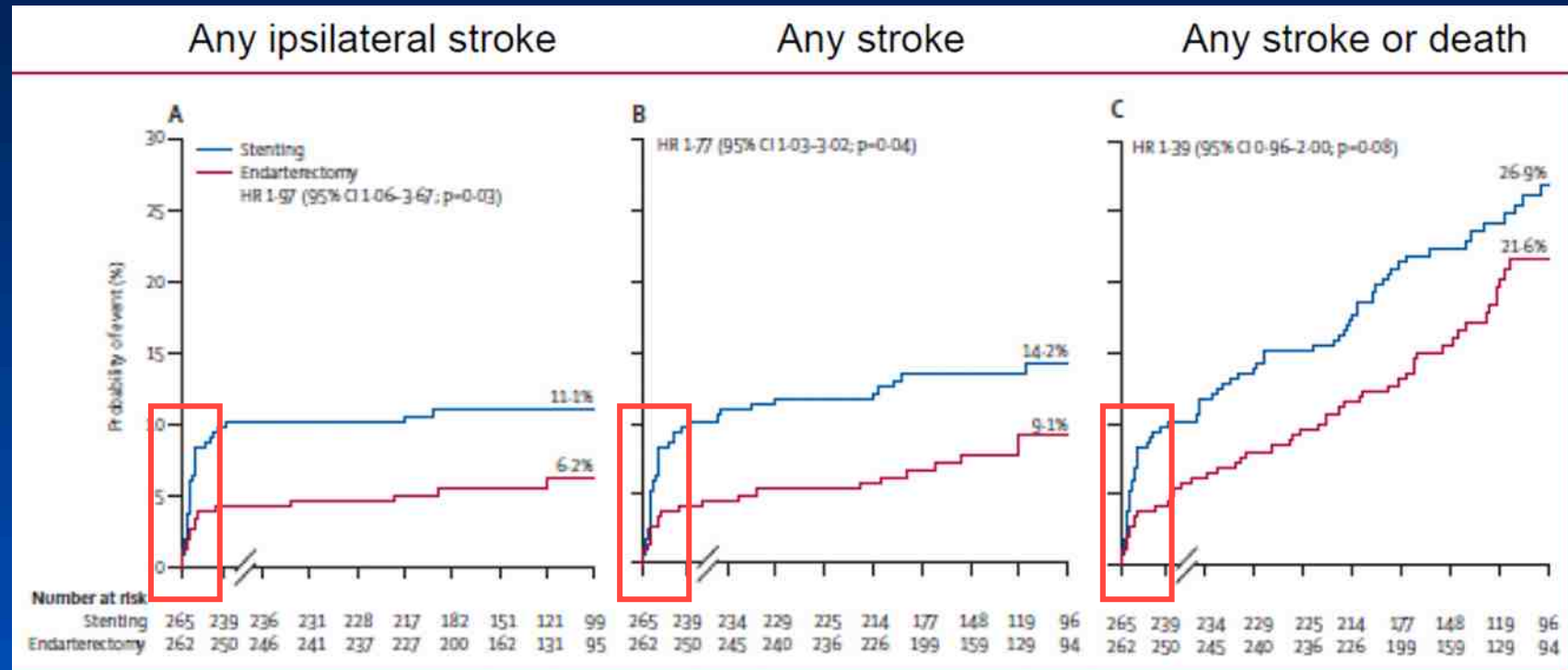
30-Day death or stroke outcomes



Relative risk: 2.5 (95% CI, 1.2 to 5.1)

NEJM 2006;355:1660-71

4-Year Outcome



4 yr risk of non-procedural stroke 4.6% CEA vs 3.7% CAS

Main differences in periprocedural period
 Parallel trend after periprocedural period

30 days results from **SPACE** trial in symptomatic patients

Randomized non-inferiority trial: 1900 initially planned

1200 patients with severe carotid stenosis ($>70\%$)
and recent neurological symptoms (< 180 days)

567 treated with CAS
18 not treated
14 treated with CEA

565 treated with CEA
12 not treated
6 treated with CAS
1 died before Tx.

599: Protected -27%

584

1183 randomised patients included on
an intention-to-treat basis for analysis

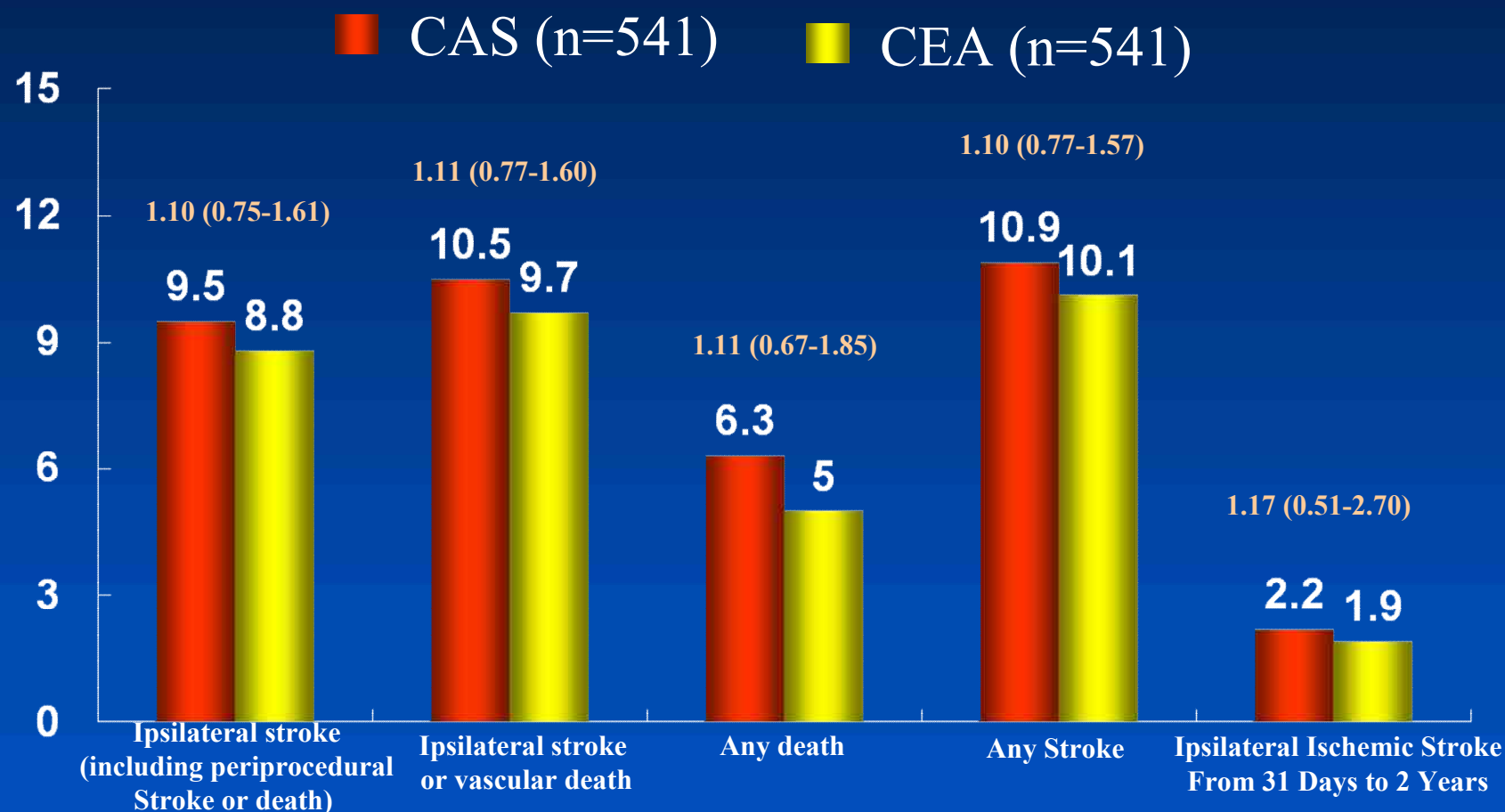
Lancet 2006;368;1239-47

Outcome events up to 30 days

	Number (%)		Absolute diff.	Odds ratio
	CAS (n=599)	CEA (n=584)	CAS-CEA (90% CI)	CAS/CEA (95% CI)
Primary endpoint	41 (6.84%)	37 (6.34%)	0.51* (-2.37 to 3.39)	1.09 (0.69 to 1.72)
Ipsilateral ischemic stroke	39 (6.51%)	30 (5.14%)		1.26 (0.77 to 2.18)
Ipsilateral intra- cerebral bleeding	1 (0.71%)	5 (0.86%)		0.19 (0.004 to 1.74)
Death	4 (0.67%)	5 (0.86%)		0.78 (0.15 to 3.64)

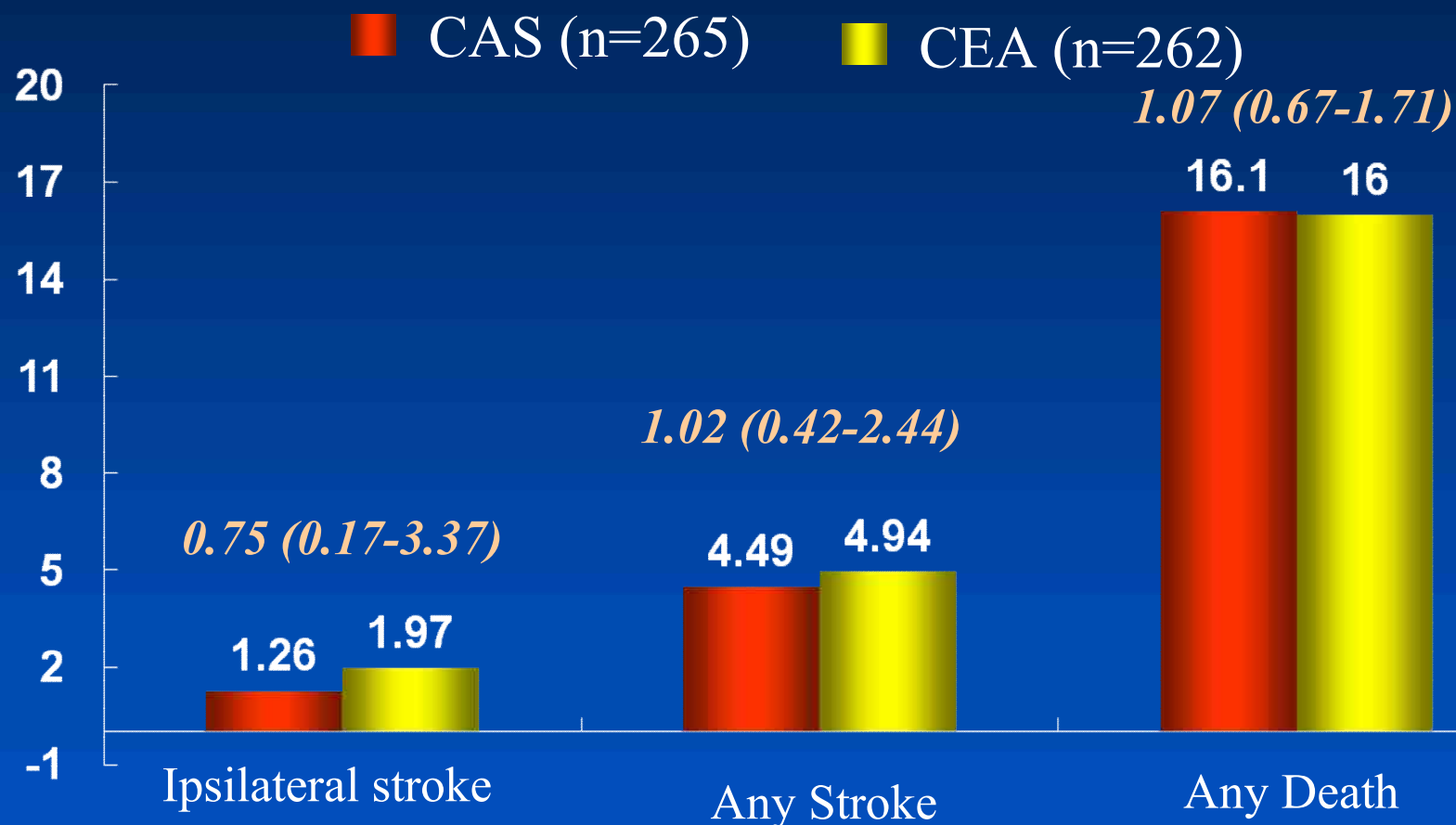
***One-sided p value for non-inferiority is 0.09**

Long-term(2-Year) Data Show Equal Outcomes



Lancet Neurol. 2009;8:135.

Outcomes from 31 Days to 4 Years



Lancet Neurol. 2009;8:135.

ICSS

Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis
(International Carotid Stenting Study)

Symptomatic carotid stenosis of 50% or more

N=1713: randomization

CEA (n=855)

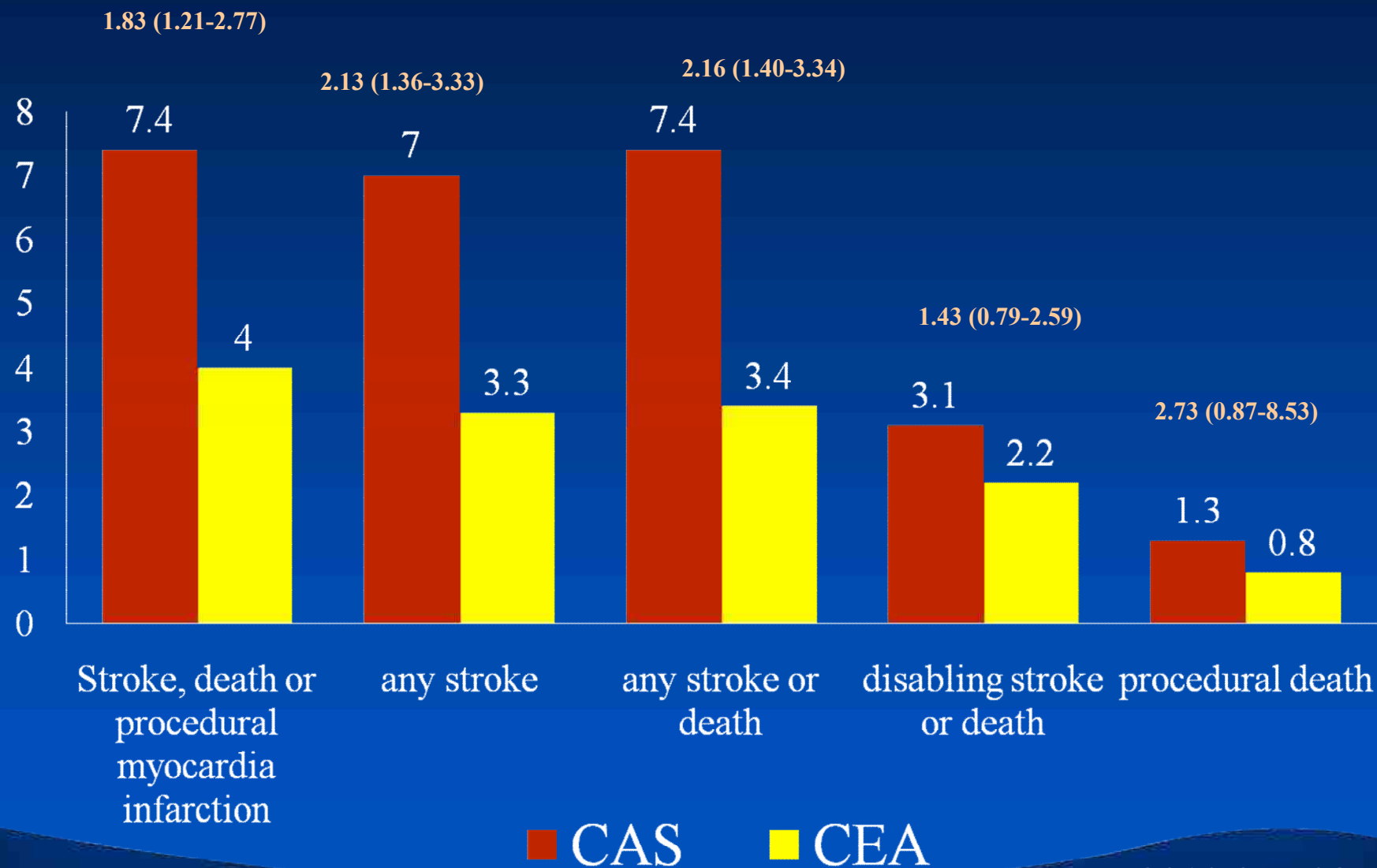
CAS (n=855)

Primary end point: any stroke, death, or procedural myocardial infarction.

Embolic protection in 72%

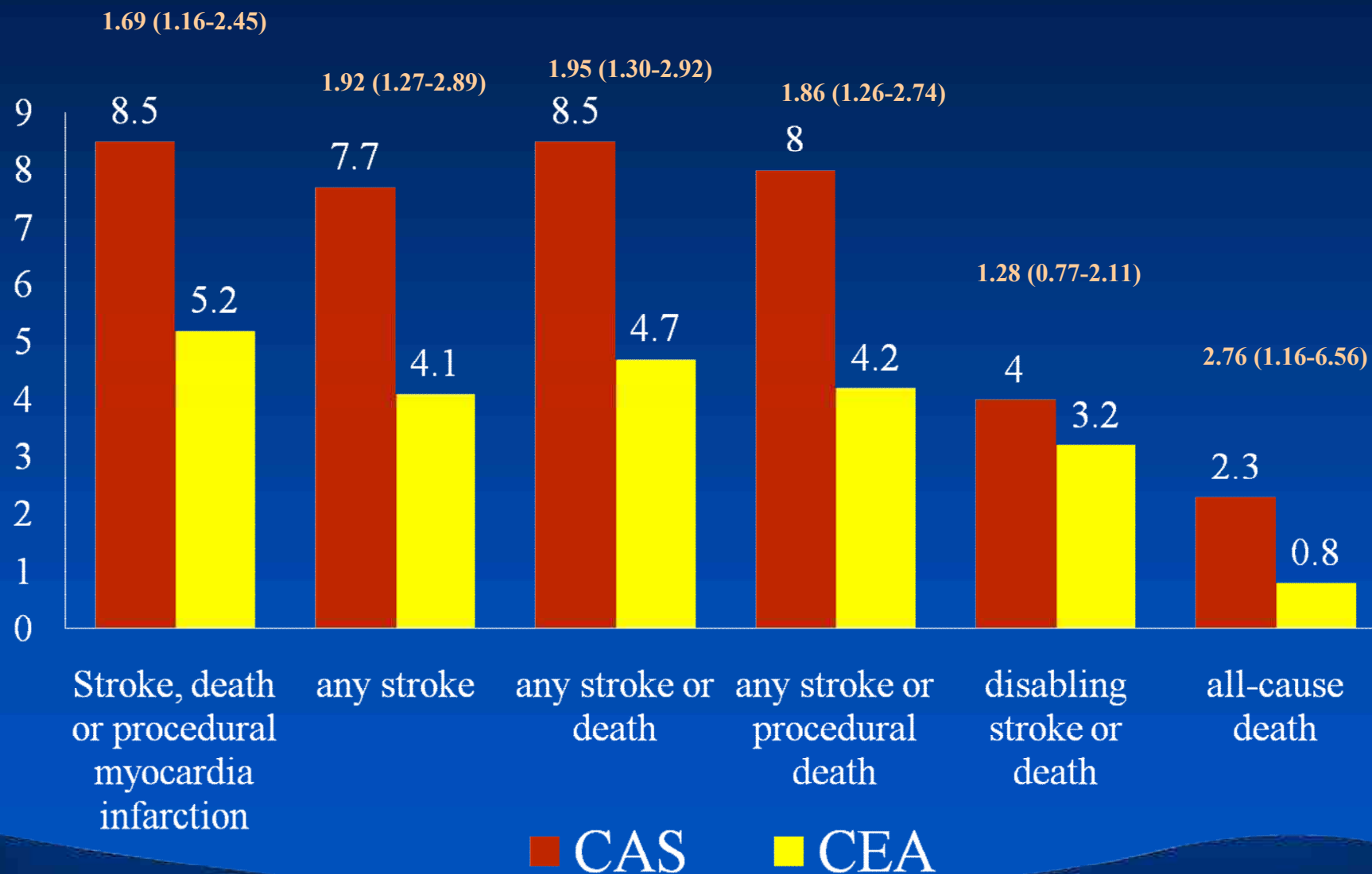
Followed for up to 120 days after randomization

30-day outcome



Lancet 2010;375:985-97

120-day outcome



Brain MRI Sub-study of ICSS

DWI (after procedure)	CAS	CEA	OR (95% CI)	P value
New lesion (≥ 1)	62 (50%)	18 (17%)	Unadjusted 4.94 (2.67-9.16)	<0.0001
			Adjusted 5.21 (2.78-9.79)	<0.0001
Single lesion	18 (15%)	9 (8%)		
Multiple lesions	44 (35%)	9 (8%)		

Brain MR after procedure

- About three times more patients in the CAS versus CEA group had new ischemic lesions on DWI on post-treatment scans.
- The difference in clinical stroke risk in ICSS is therefore unlikely to have been caused by ascertainment bias.
- Protection filter devices did not seem to be effective in preventing cerebral ischemia during stenting.
- DWI might serve as a surrogate outcome measure in future trials of carotid interventions

CREST Trial

Carotid Revascularization Endarterectomy versus Stenting Trial

Carotid Stenosis (N=2502)

Broad risk

Symptomatic >50%, n=1,321

Asymptomatic >70%, n=1,181

Carotid Stenting

Carotid endarterectomy

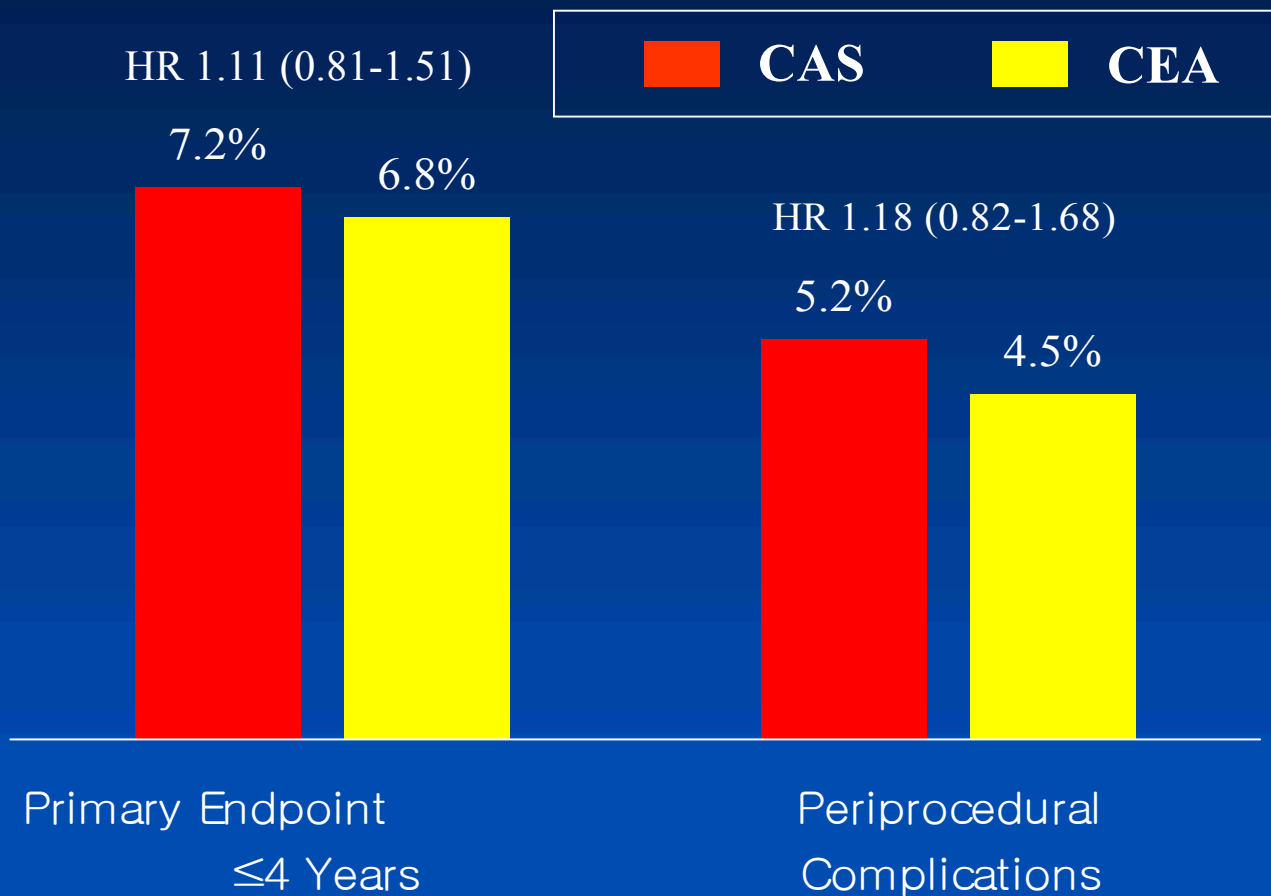
Primary Endpoint

: any stroke, MI, or death within 30 days plus subsequent ipsilateral stroke

Follow-up was out to 4 years (median 2.5).

Presented in Feb.2010. ASA

4-Year Outcome



Primary Endpoint : any stroke, MI, or death within 30 days plus subsequent ipsilateral stroke
Periprocedural Complications : any procedural stroke, MI, or death

Periprocedural Complications

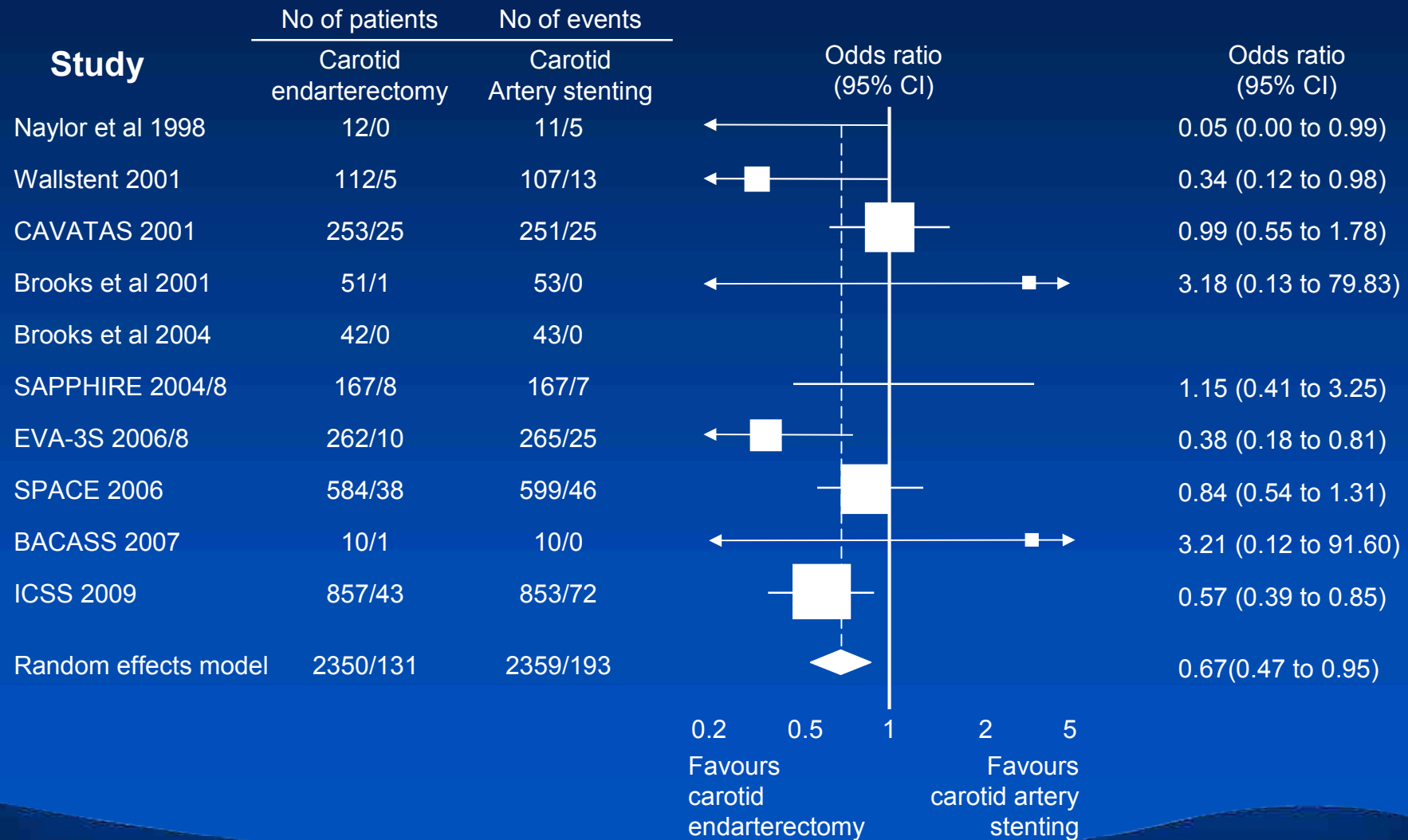
	CEA	CAS	HR (95% CI)	P Value
Stroke	2.3%	4.1%	1.79(1.14-2.82)	0.01
Major	0.8%	1.4%		
Minor	1.4%	2.7%		
MI	2.3%	1.1%	0.50(0.26-0.94)	0.03

Overall death rate : 0.6%

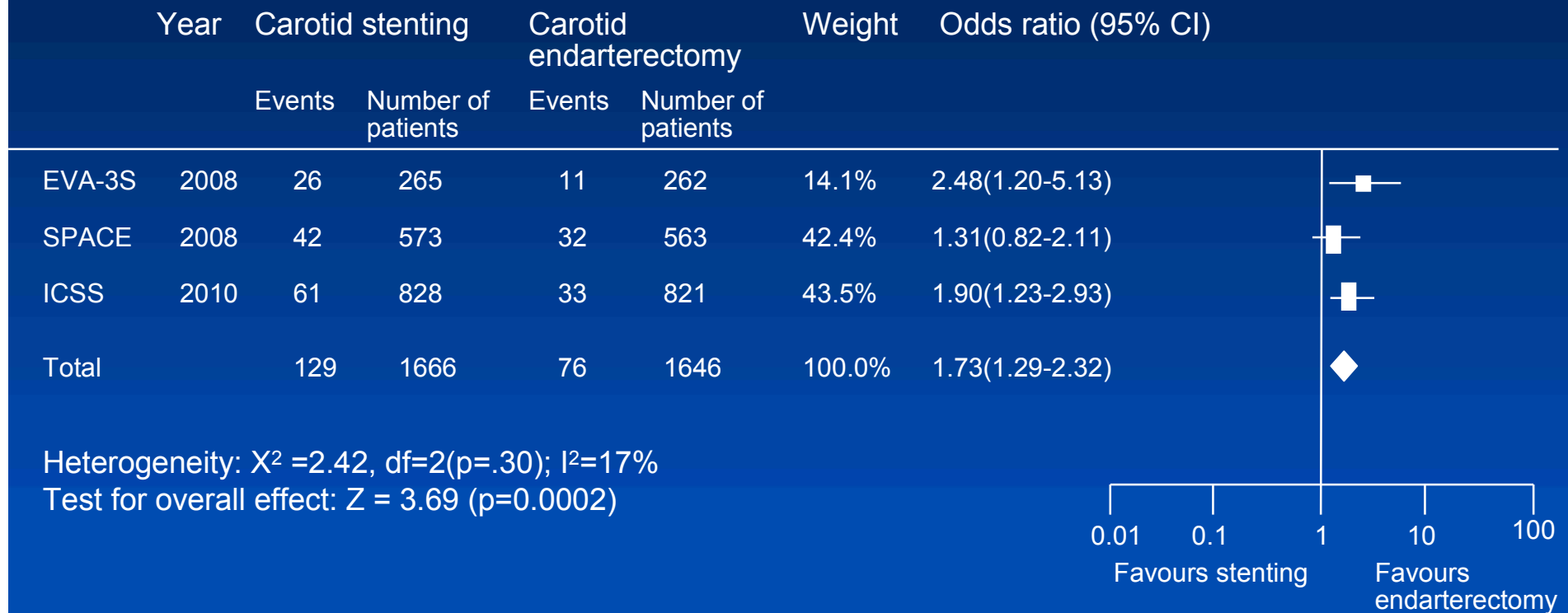
Lowest reported in any randomized trials

Recurrent event rates 2.0% for CAS versus 2.4% for CEA

Meta-analysis 30-day stroke or death



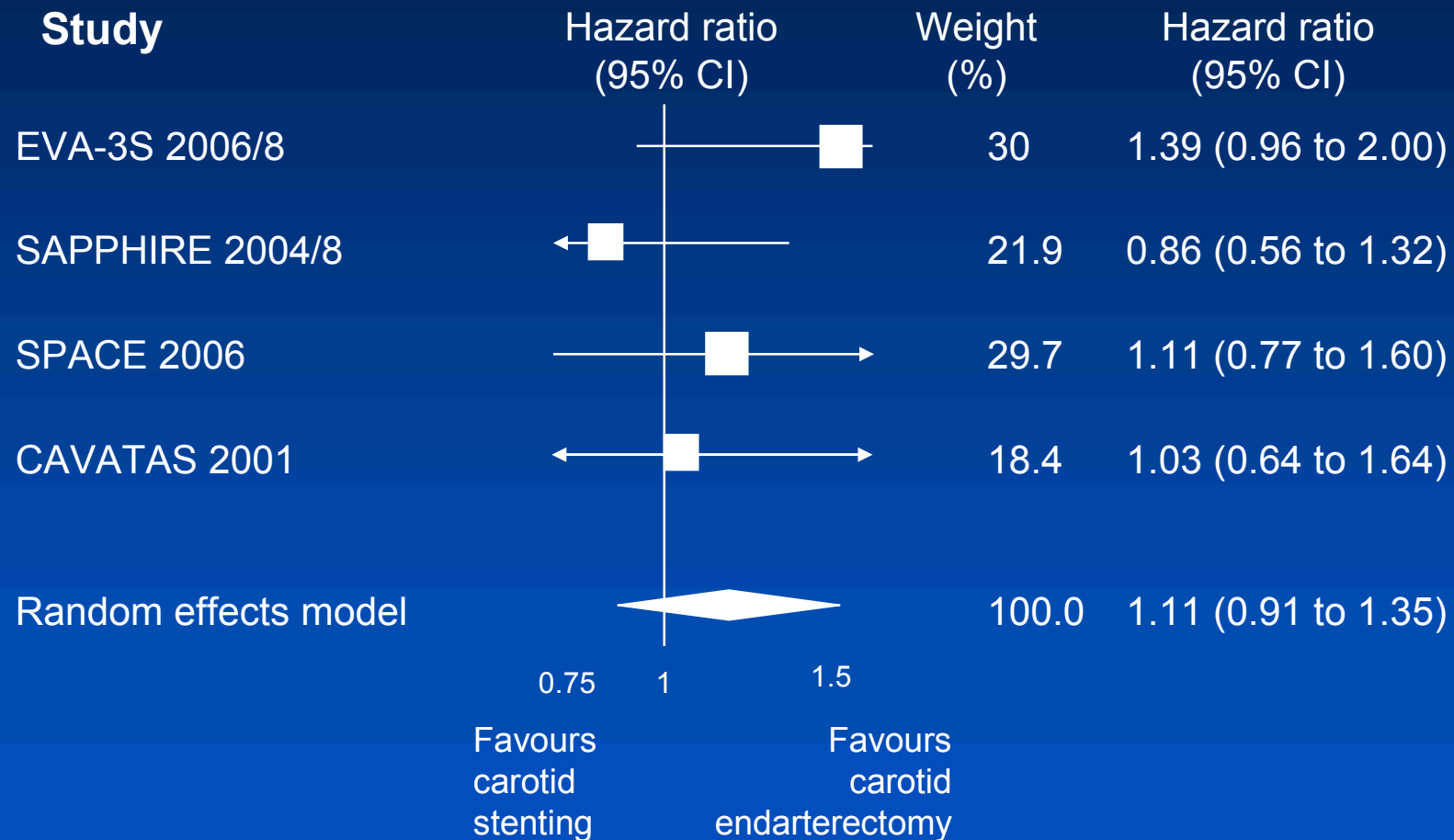
Meta-analysis including ICSS trial



After including ICSS trial, CEA is superior to CAS

Meta-analysis

Intermediate-term risk of stroke or death



CEA vs. CAS

- Several randomized controlled trials showed favorable short-term results with CEA in symptomatic patients.
- Meta-analysis also showed CEA was superior to CAS for short term outcomes. But, there was no difference in intermediate-term outcomes.
- However, long-term results showed equivalent clinical outcomes between CAS vs. CEA.

Intensive Medical Therapy for Patients with Carotid Stenosis

Intensive Medical Therapy for Patients with Carotid Stenosis

- Antiplatelet agents
- High dose statin, other lipid lowering agents
- Antihypertensive agents: ACEI, ARB
- Tight glycemic control
- Life style modification: cessation of smoking, exercise, diet control

Intensive Medical Therapy

Contemporary Results of Carotid Endarterectomy for Asymptomatic Carotid Stenosis

Karen Woo, MD; Joy Garg, MD; Robert J. Hye, MD; Ralph B. Dilley, MD

- 5,009 CEA for asymptomatic stenosis from the 2005, 2006, and 2007 NSQIP (National Surgical Quality Improvement Program) database.
- **30-day stroke**, death, and MI rate: **0.96%**, 0.56%, 0.22% respectively.
- If the 0.96% of perioperative stroke rate is combined with the 5-year stroke risk after CEA of 3.8% from ACST (Asymptomatic Carotid Surgery Trial), **the average annual stroke rate is 1%, comparable to the stroke rate of 0.8% for the best medical management from the SMART** (Second Manifestations of Arterial Disease Study trial).
- Stroke rates with CEA and best medical management for asymptomatic stenosis are similar

Intensive Medical Therapy

Effects of Intensive Medical Therapy on Microemboli and Cardiovascular Risk in Asymptomatic Carotid Stenosis

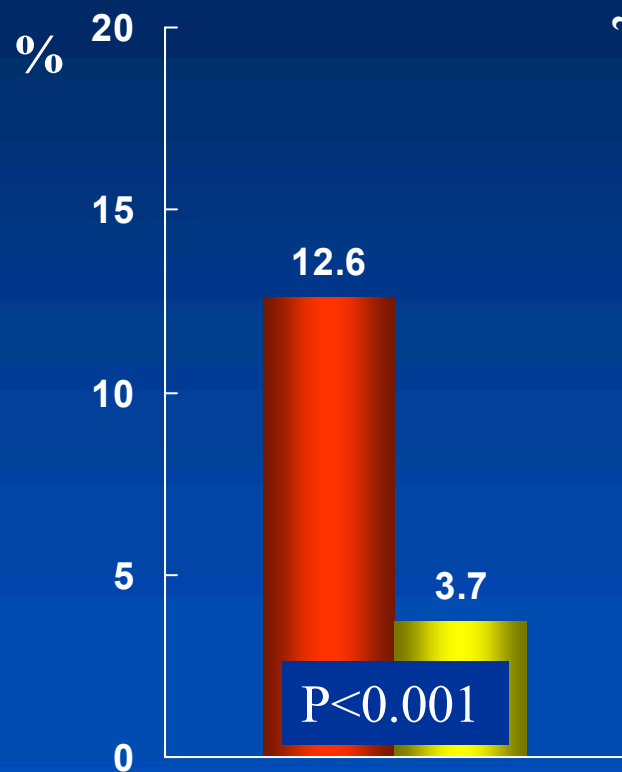
ARCHIVES EXPRESS

J. David Spence, MD; Victoria Coates, BA, HBSc; Hector Li, MD; Arturo Tamayo, MD; Claudio Muñoz, MD, PhD; Daniel G. Hackam, MD, PhD; Maria DiCicco, RVT; Janine DesRoches, RVT; Chrysi Bogiatzi, MD; Jonathan Klein, MD; Joaquim Madrenas, MD, PhD; Robert A. Hegele, MD

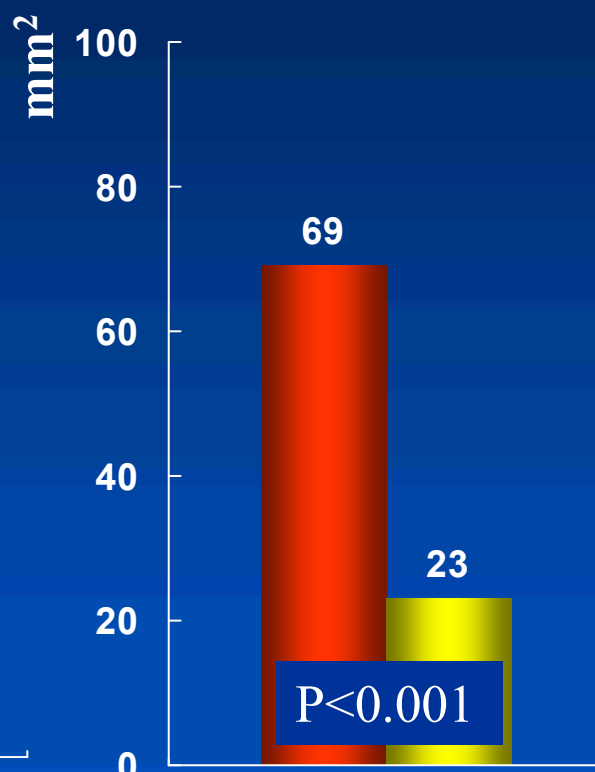
- Asymptomatic carotid stenosis (>60%)
- 199 patients, between Jan 2000 and Dec 2002
- 269 patients, between Jan 2003 and July 2007
(Intensive medical therapy)
- Outcome values
 1. Micro-emboli on TCD
 2. Cardiovascular events
 3. Rate of plaque progression
 4. Baseline medical therapy, before and since 2003

Clinical outcomes

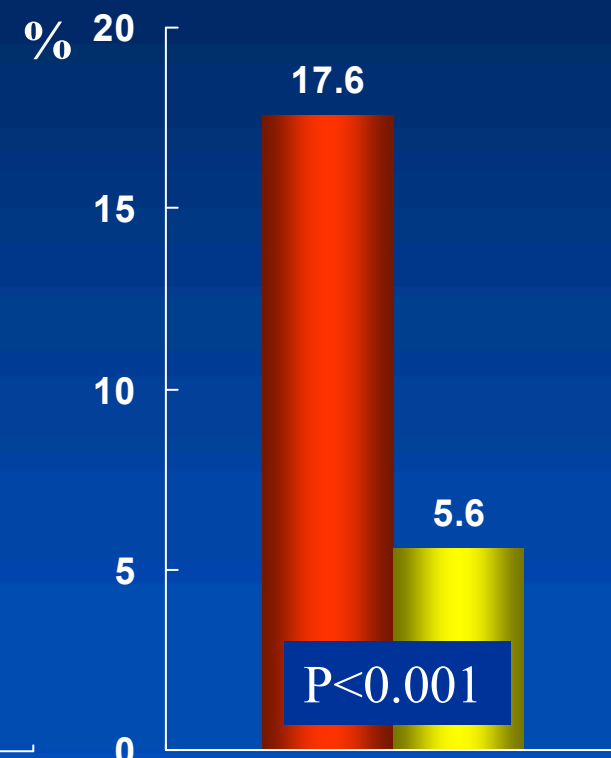
Before 2003 Since 2003



Microemboli on TCD



Plaque progression/yr

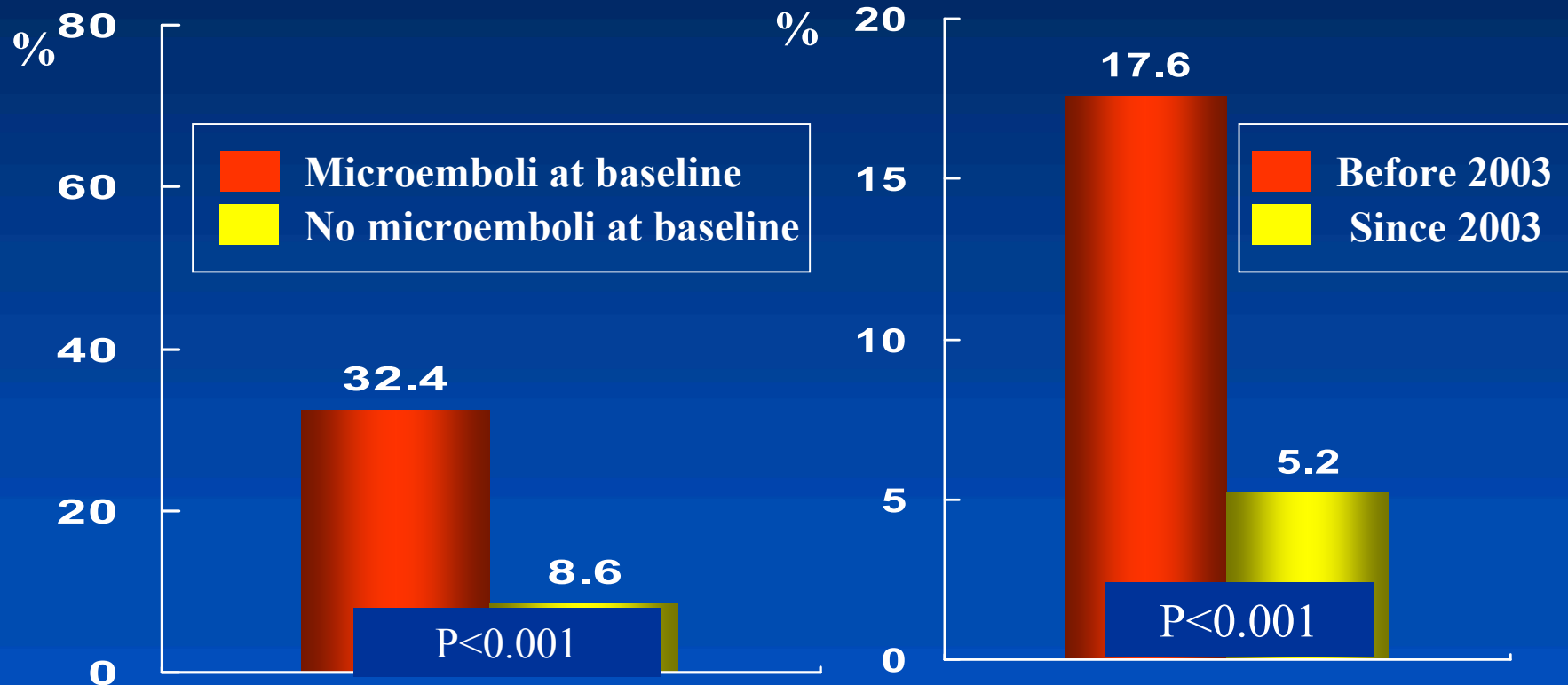


Primary endpoint for 2 years

Primary endpoint: stroke, death, MI, or carotid endarterectomy upon symptom development.

Clinical outcomes for 2 years

Primary endpoint: stroke, death, MI, or carotid endarterectomy upon symptom development.



- Less than 5% of Asymptomatic Carotid Stenosis patients can benefit from revascularization
- Only those with microemboli should be considered for endarterectomy or stenting

CEA vs. Intensive Medical Tx. In Asymptomatic Stenosis

- Contemporary intensive medical therapy may reduce event rate significantly, compared with conventional medical therapy.
- The randomized, prospective trials comparing revascularization and best medical management for asymptomatic stenosis (SPACE 2, TACIT) will answer these issues.

(TACIT : Transatlantic Asymptomatic Carotid Intervention Trial, optimal medical therapy alone, OMT plus stenting and OMT plus CEA in asymptomatic patients)

Current guidelines: CEA

1. CEA is indicated in symptomatic patients with $>50\%$ (NASCET) stenosis (A). The perioperative stroke/death rate should be $<6\%$. CEA is contraindicated for symptomatic patients with less than 50% stenosis (A).
2. CEA should be performed within 2 weeks of the patients' last symptoms (A).
3. CEA can be recommended for asymptomatic men below 75 years old with $70-99\%$ stenosis if the perioperative stroke/death risk is $<3\%$ (A)
4. The benefit from CEA in asymptomatic women is significantly less than in men (A). CEA should therefore be considered only in younger, fit women (A)

Eur J Vasc Endovasc Surg. 2009 Apr;37(4 Suppl):1-19
European Society for Vascular Surgery 2009 guidelines

Current guidelines: CAS

1. CAS should be offered to symptomatic patients, if they are at high risk for CEA, in high-volume centers with documented low peri-procedural stroke and death rates or inside a randomized controlled trial (C).
2. It is advisable to offer CAS in asymptomatic patients only in high-volume centers with documented low peri-procedural stroke and death rates or within well-conducted clinical trials (C).
3. CAS should not be offered to asymptomatic “high risk” patients if the peri-intervention complication rate is $>3\%$ (C).

Eur J Vasc Endovasc Surg. 2009 Apr;37(4 Suppl):1-19
European Society for Vascular Surgery 2009 guidelines