Carotid Artery Stenting
Versus
Carotid Endarterectomy

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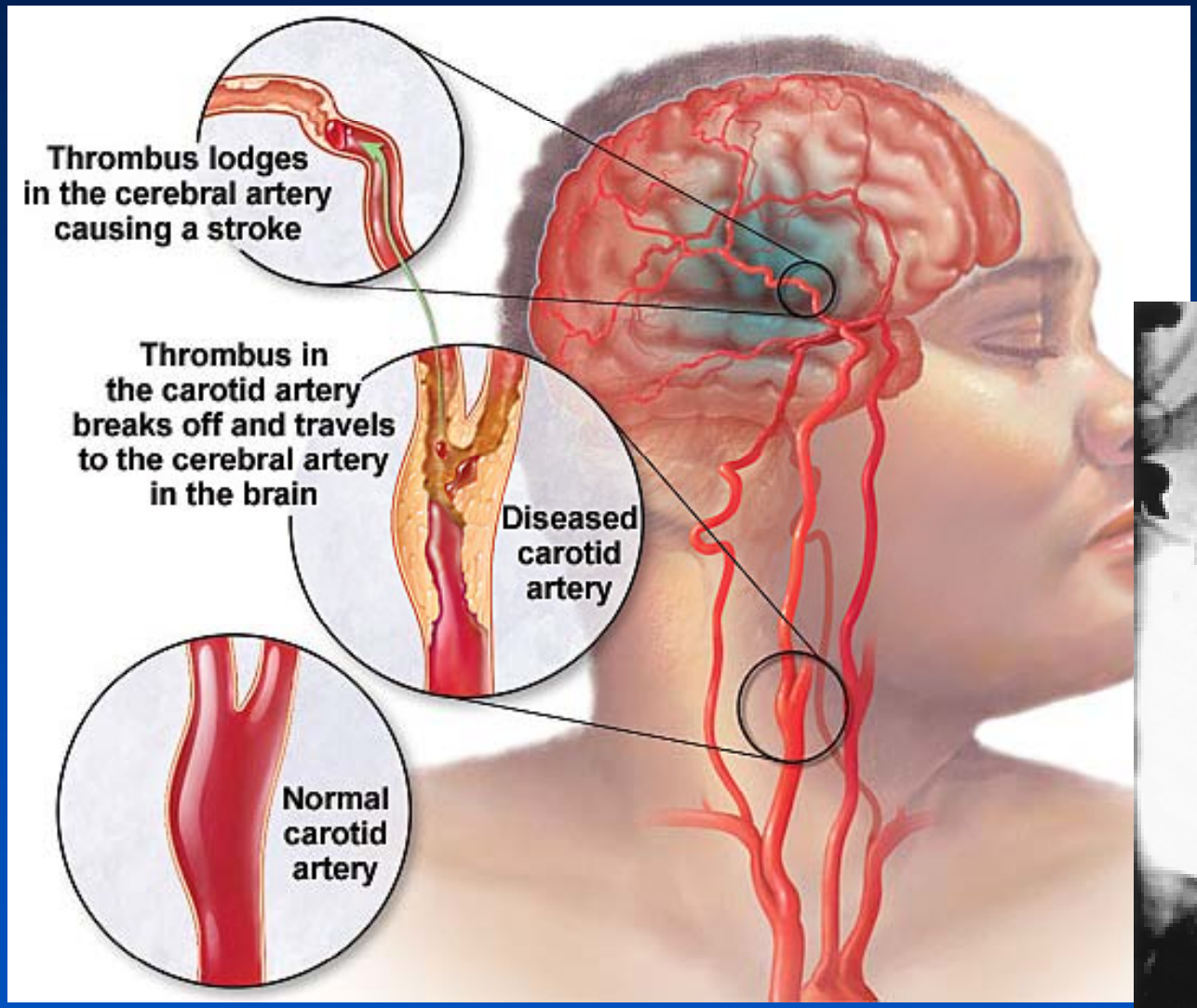
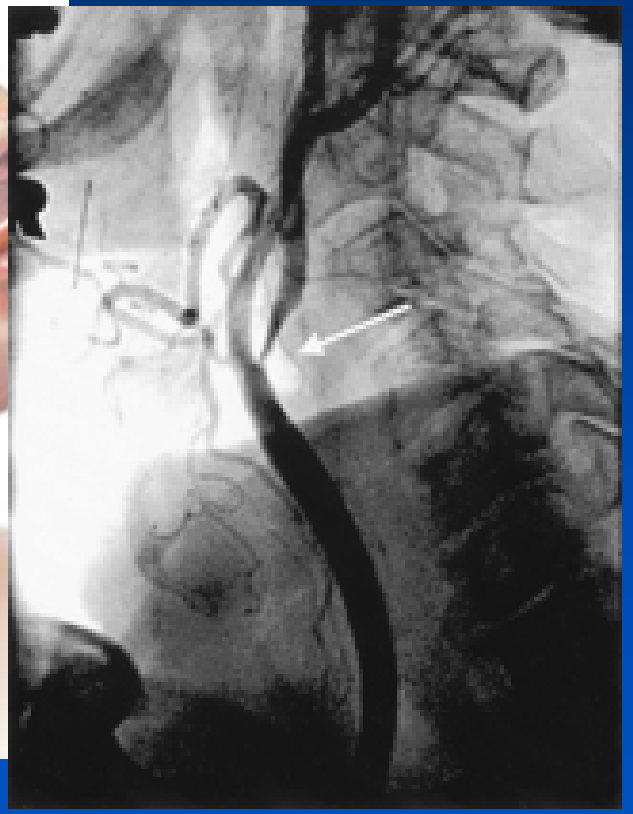
Stroke & Carotid artery stenosis





Stroke & Carotid artery stenosis

- Cerebrovascular disease is one of the leading cause of the death, with an annual stroke rate of approximately 2.4% of the population

- Carotid artery stenosis is responsible for about 25% of stroke

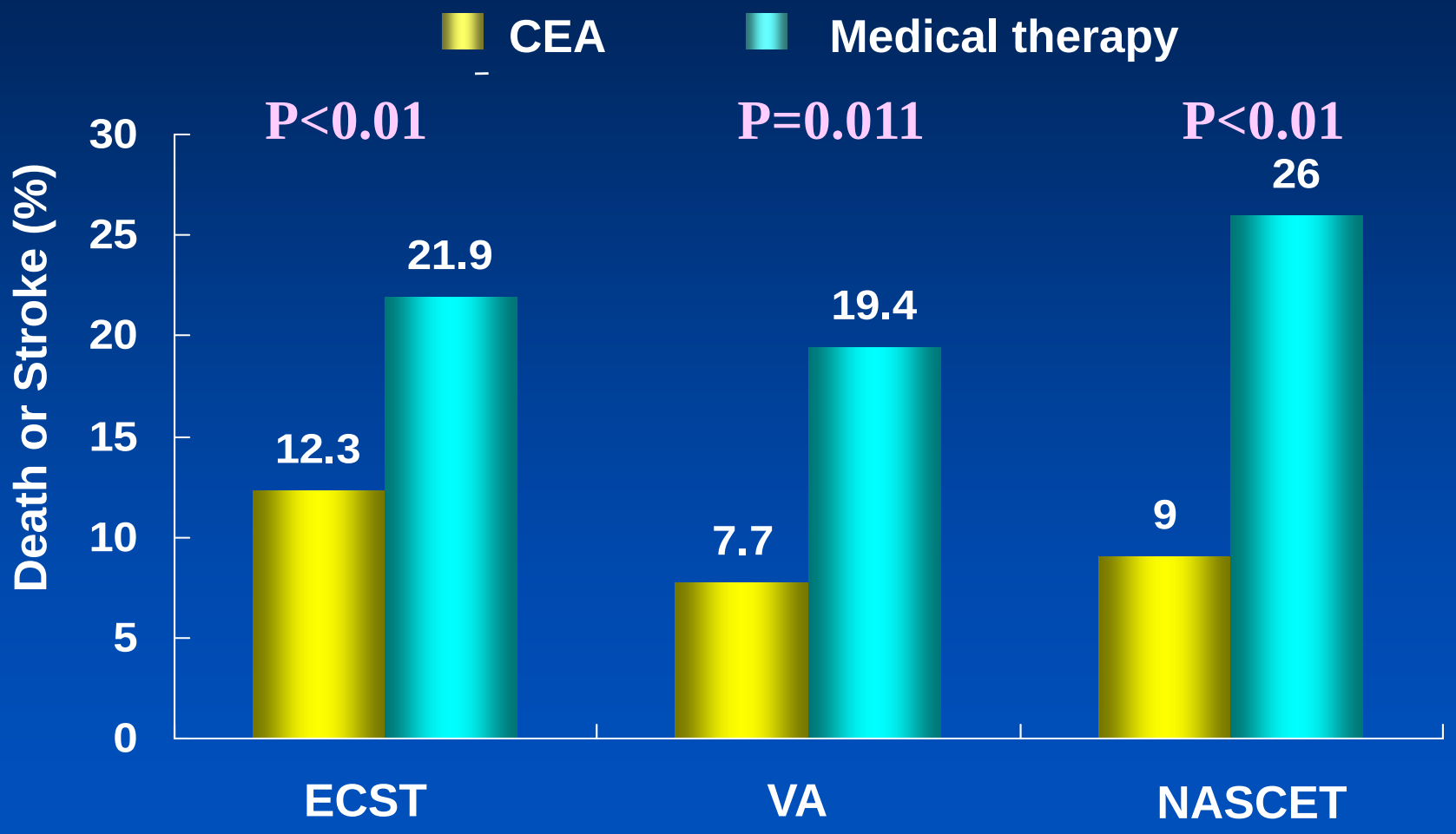
- Population-based studies : carotid stenosis-0.5% in the sixth decade and increased to 10% in persons over 80 years of age. The majority of patients are asymptomatic (70-80%)

Natural Incidence of CVA In Carotid Stenosis

- Asymptomatic >80% carotid stenosis
  - 1.9%/ year (ECST registry)
  - 12% / 5 year (ACAS, ACST)
- Symptomatic >70% carotid stenosis
  - 11% / year
  - 40% / 5 years

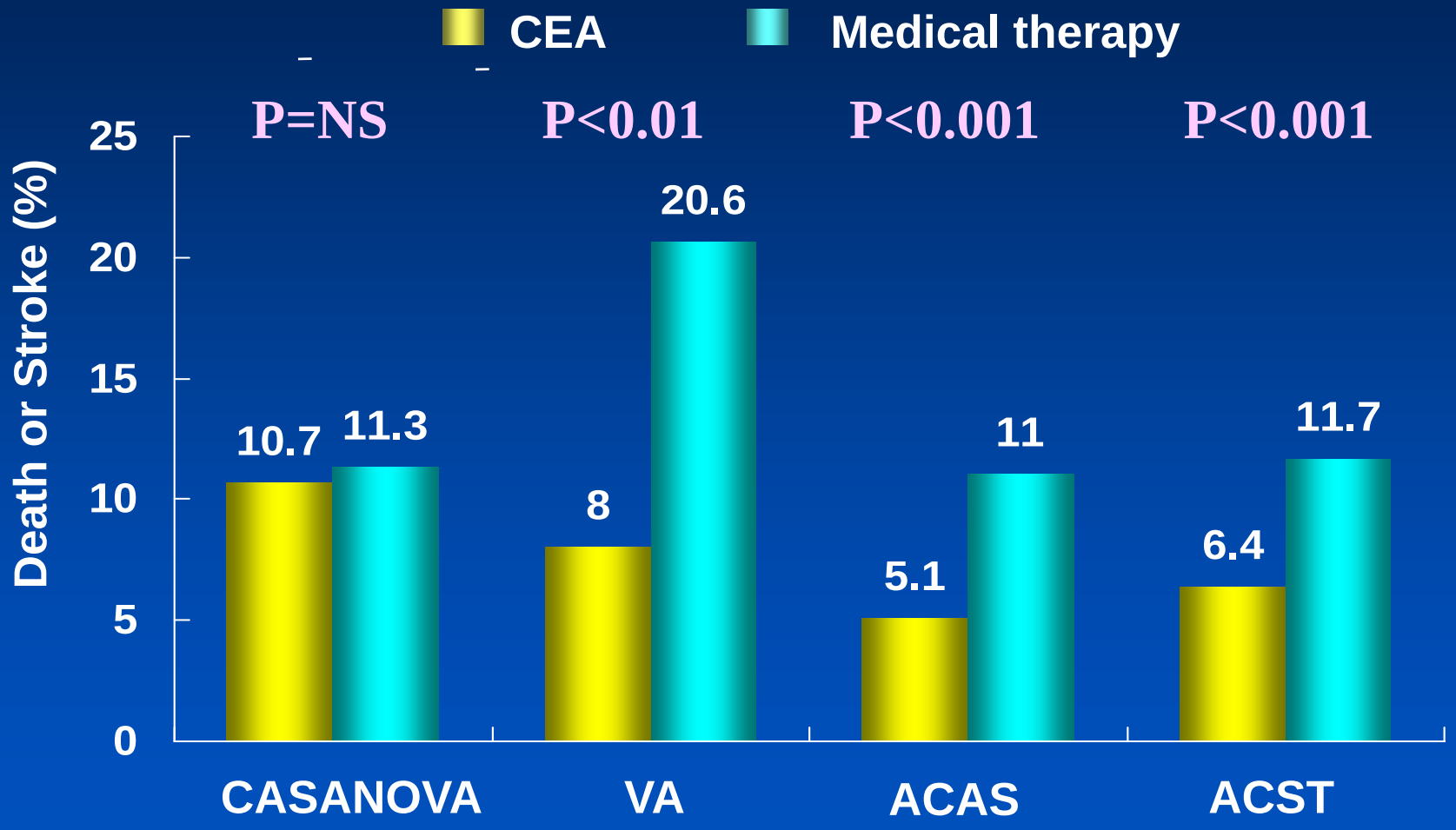
CEA vs. Medical Rx

Symptomatic Patients (DS≥ 70%)

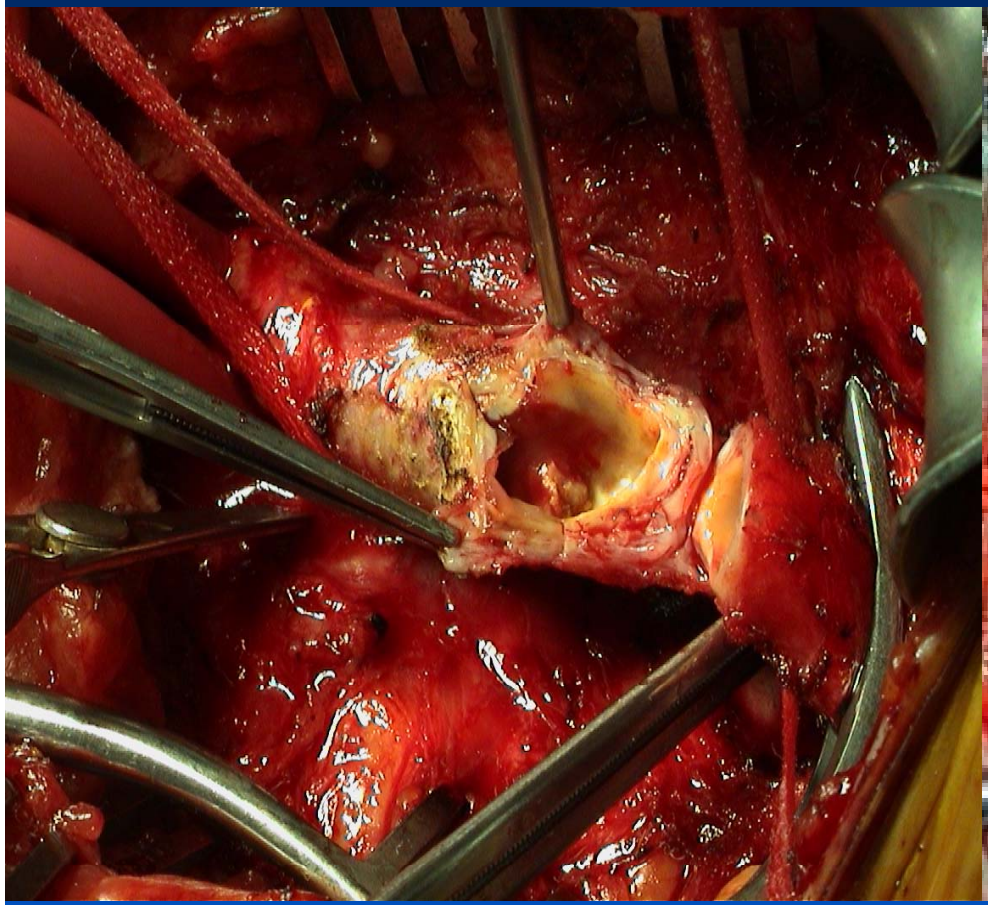


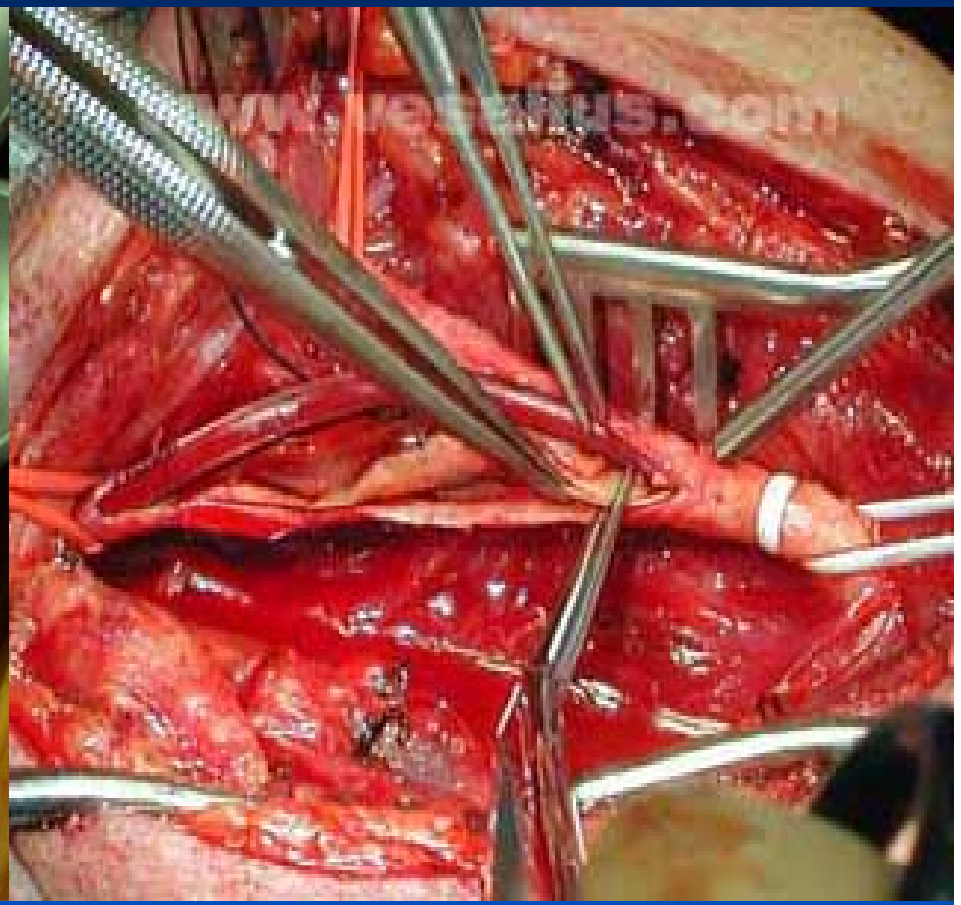
CEA vs. Medical Rx

Asymptomatic Patients (DS > 60%)



*C*arotid *E*nd*A*rterectmy; CEA





Indications for carotid artery revascularization

Indication level	Symptomatic stenosis	Asymptomatic stenosis
Proven	• 70-99% stenosis • Periprocedural complication risk <6%	• > 80% stenosis • Periprocedural complication risk <3% • Life expectancy > 5yrs
Acceptable	• 50-69% stenosis • Periprocedural complication risk <6%	• > 60% stenosis • Periprocedural complication risk <3% • Planned CABG
Unacceptable	• <29% stenosis, or • Periprocedural complication risk > 6%	• < 60% stenosis or • Periprocedural complication risk >3% • No indication for CABG

≥ 70%

≥ 80%

≥ 50%

≥ 60%

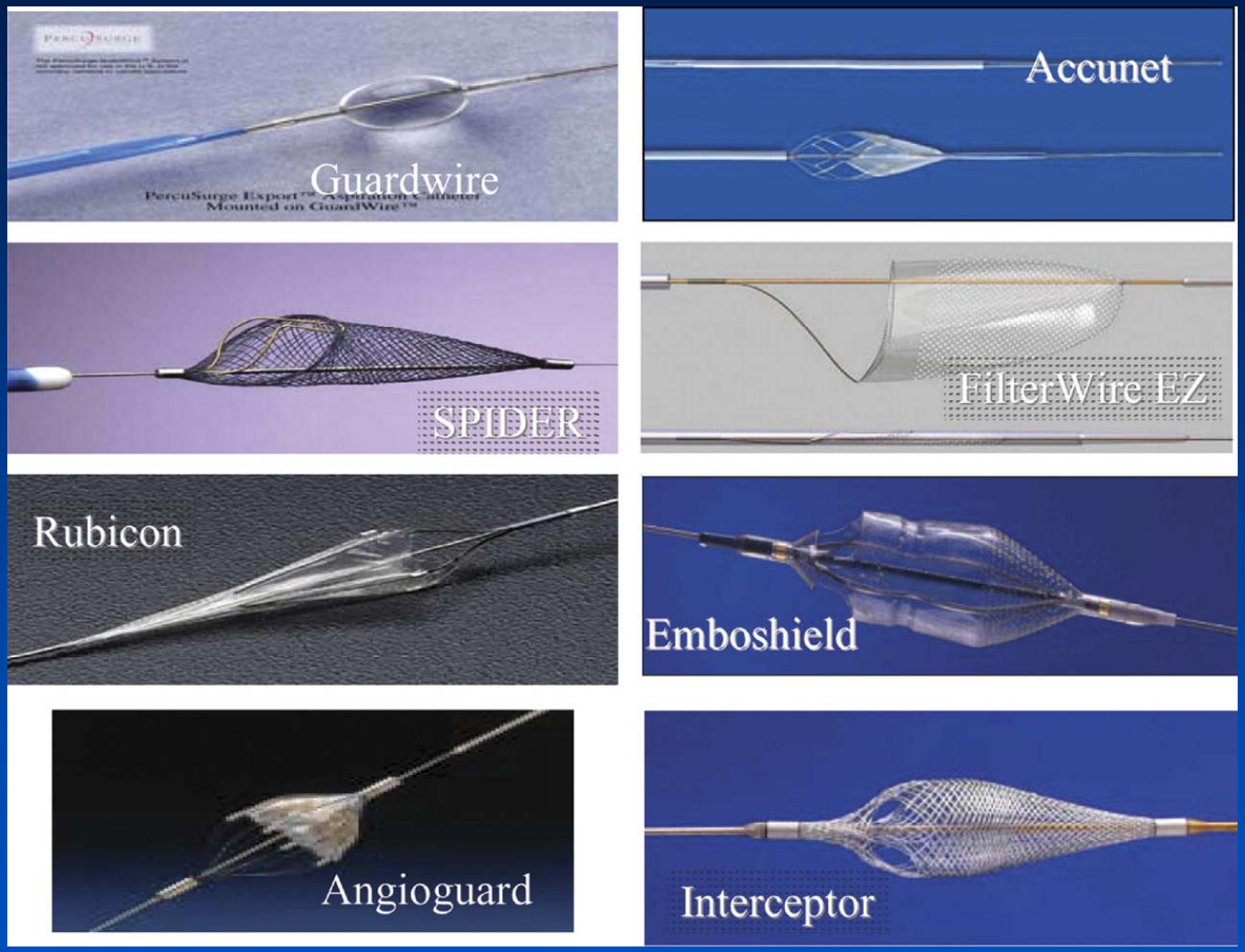
Circulation 2006;113:2021-2030

Carotid Artery Stenting

Current status

Embolic protection device (EPD) is mandatory in CAS

Embolic Protection Devices (EPD)



ACCF/SCAI/SVMB/SIR/ASITN 2007 Clinical Expert Consensus Document on Carotid Stenting J Am Coll Cardiol 2007;49:126–70

Carotid Stent Trial Data

Pre-EPD

- Normal risk/randomized
  - WallStent trial-1999 (223)

Post-EPD

- Normal risk/symptomatic and asymptomatic/randomized
  - CREST, ACT 1
- Normal risk/symptomatic/randomized
  - EVA-3S, SPACE, CAVATAS 2
- Normal risk/non-randomized
  - CARESS-2003 (143)
- High risk/randomized
  - SAPPHIRE-2002 (334)
- High risk/registry
  - SAPPHIRE-2002 (406)
  - ARCHeR-2003 (581)
  - SECuRITY-2003 (305)
  - BEACH-2004 (408)
  - CABERNET-2004 (454)
  - CREATE -2005 (413)

Symptomatic high surgical risk

&

Asymptomatic high surgical risk

CAVATAS

CEA vs. Angioplasty without protection in Low and High Surgical Risk group

	Angioplasty N=251	CEA N=253
30-day death & stroke	6.4%	5.9 %
Cranial neuropathy	0 %	8.7 %
1-year restenosis (>70% DS)*	14 %	4 %
3-year death or disabling stroke	14.3 %	14.2 %

* Stenting = only in 26%

Lancet 2001;357:1729-37

SAPPHIRE

CEA vs. CAS with Filter

From August 2000 to July 2002

Carotid a stenosis with high risk (n=334)

High-risk Sx ≥ 50% & ASx ≥ 80%

Randomization (1:1)

Carotid Stenting with filter device (n=167)

Carotid endarterectomy (n=167)

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

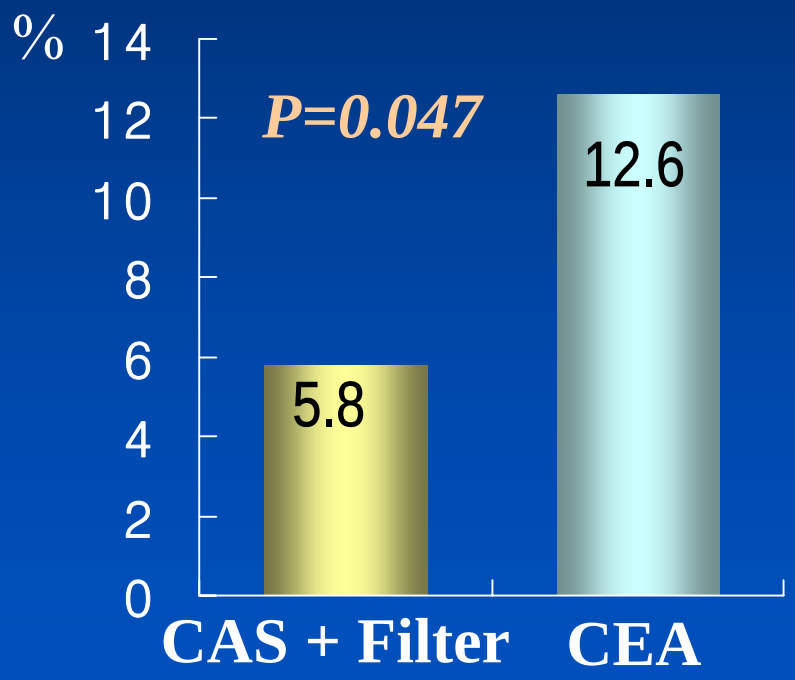
Yadav JS, et al. NEJM 2004;351:1493

CEA vs. CAS with Filter

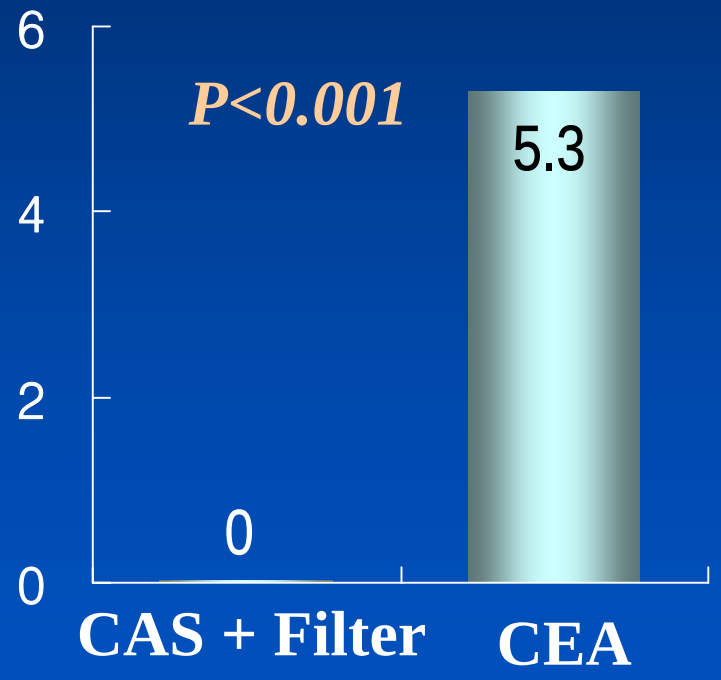
SAPPHIRE

30-Day Outcomes

Death /MI /Stroke



Cranial nerve palsy



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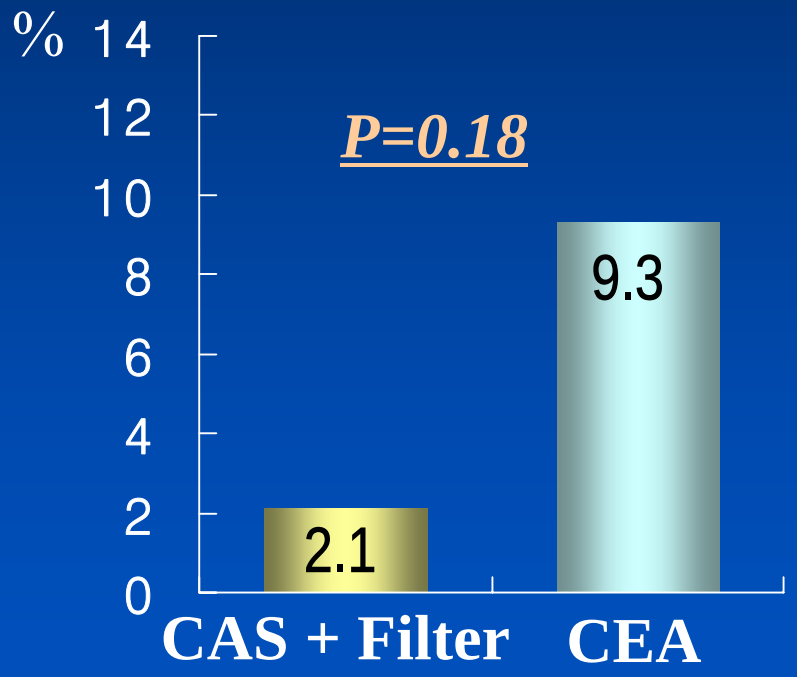
CEA vs. CAS with Filter

30-Day Outcomes

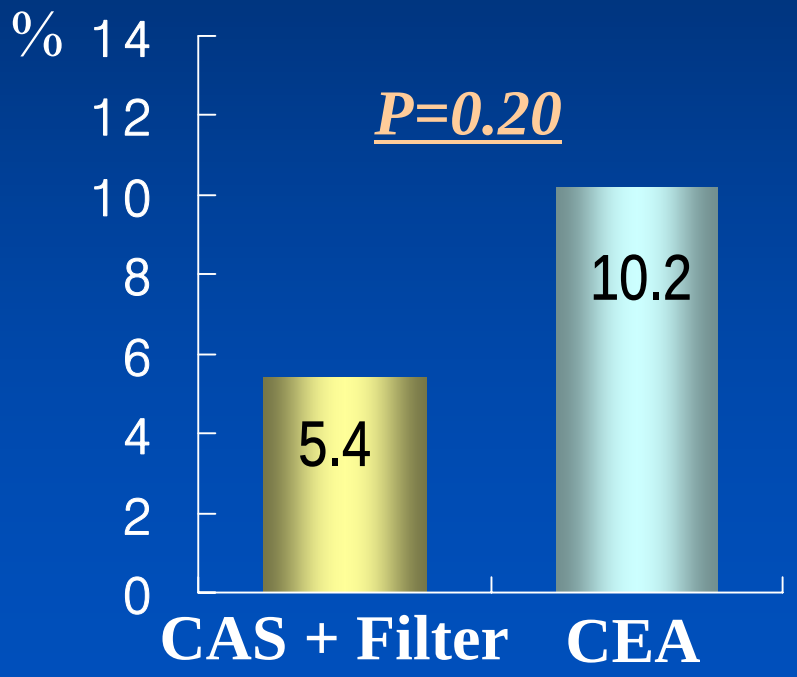
Symptomatic patients

Death /MI /Stroke



Asymptomatic patients

Death /MI /Stroke



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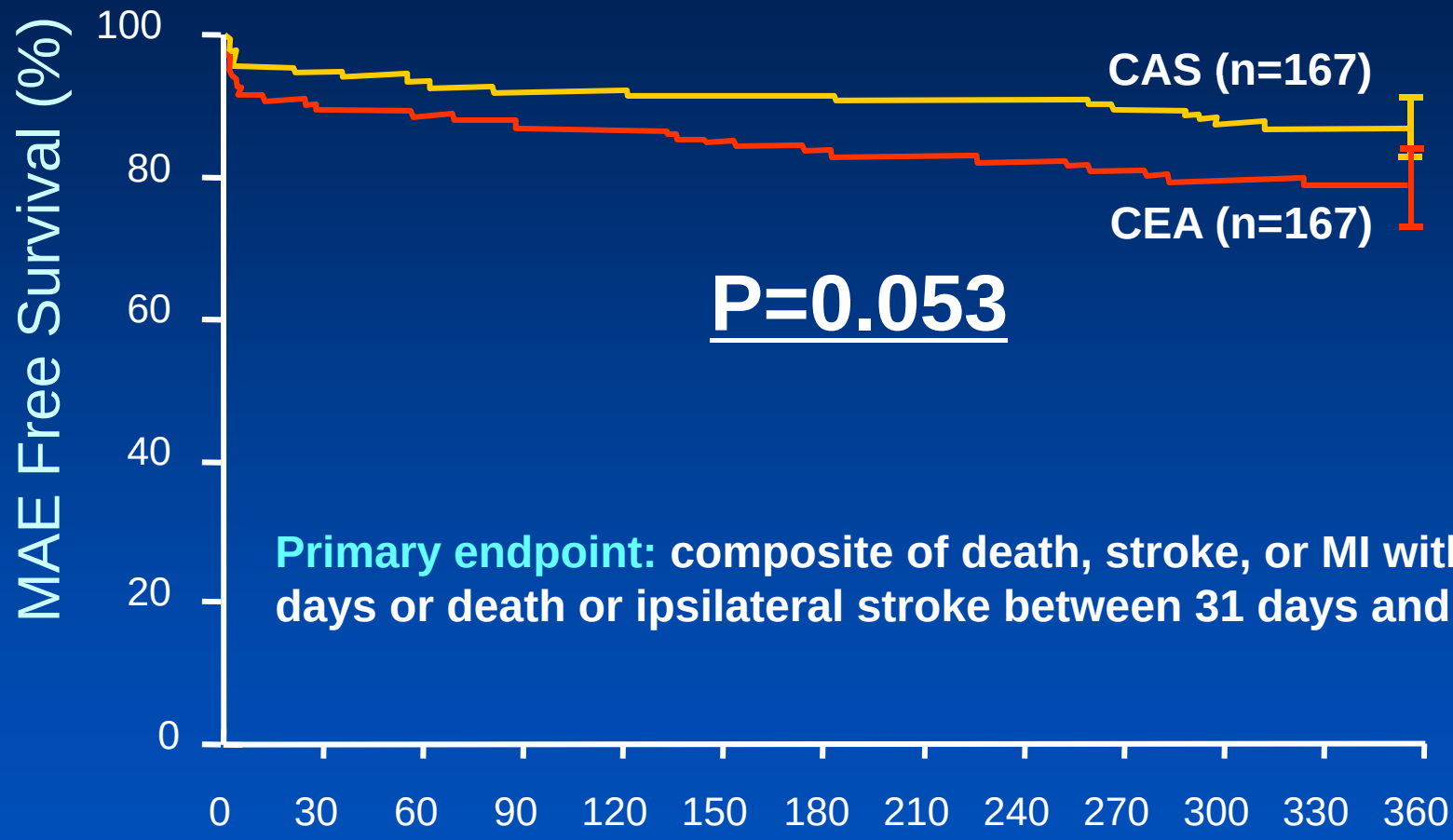
CEA vs. CAS with Filter

SAPPHIRE

1-Year Clinical Outcomes



Primary endpoint: composite of death, stroke, or MI within 30 days or death or ipsilateral stroke between 31 days and 1 year

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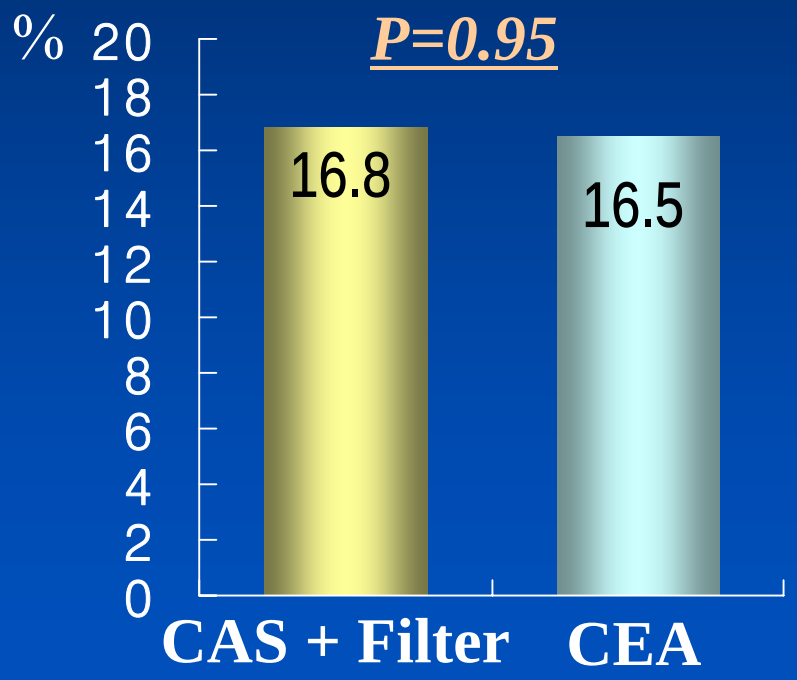
CEA vs. CAS with Filter

SAPPHIRE

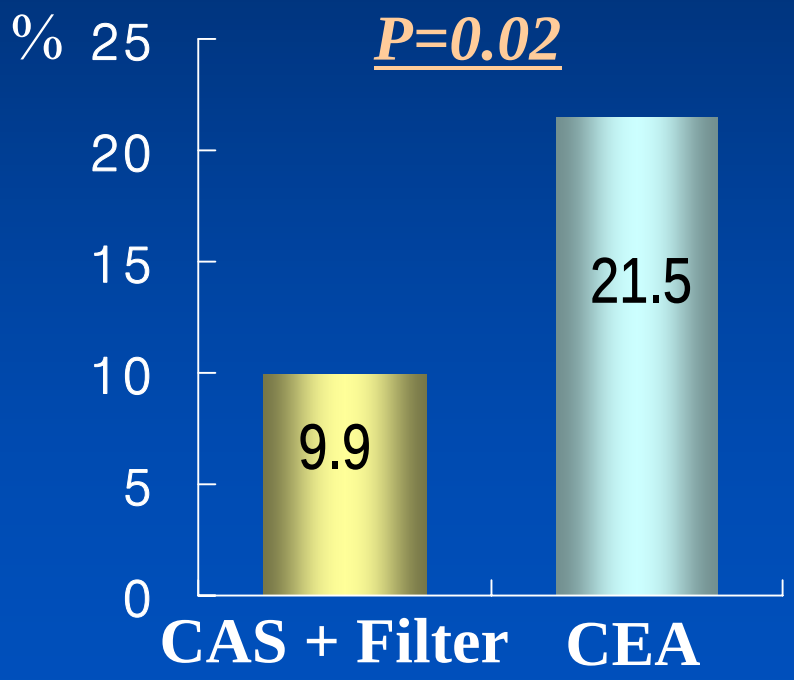
1-Year Clinical Outcomes

Primary endpoint: composite of death, stroke, or MI within 30 days or death or ipsilateral stroke between 31 days and 1 year

Symptomatic patients



Asymptomatic patients



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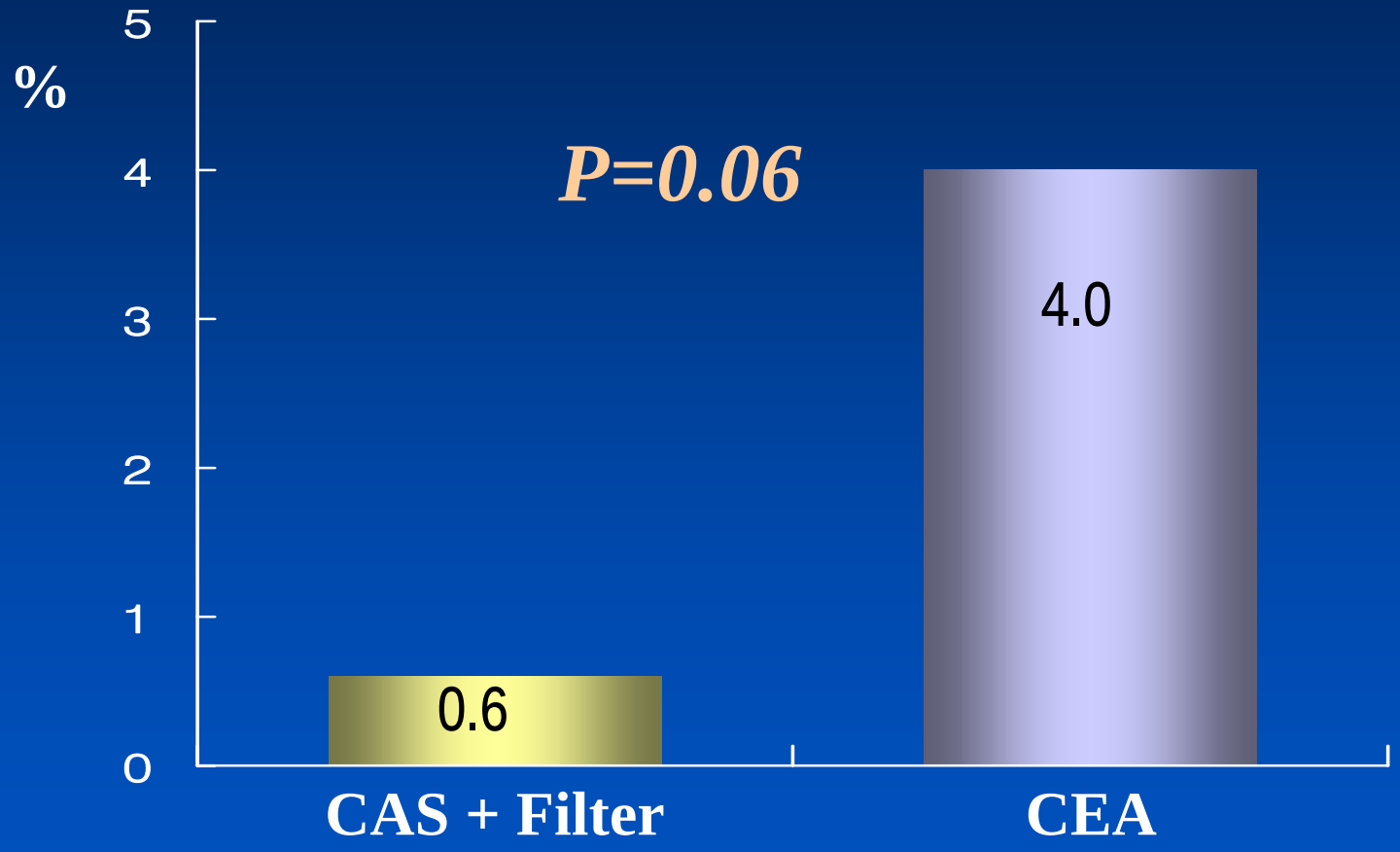
1-Year repeat revascularization



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Conclusion

- Among patients with severe carotid-artery stenosis in high risk group, carotid artery stenting (CAS) with the use of an emboli-protection device is not inferior to carotid endarterectomy (CEA).

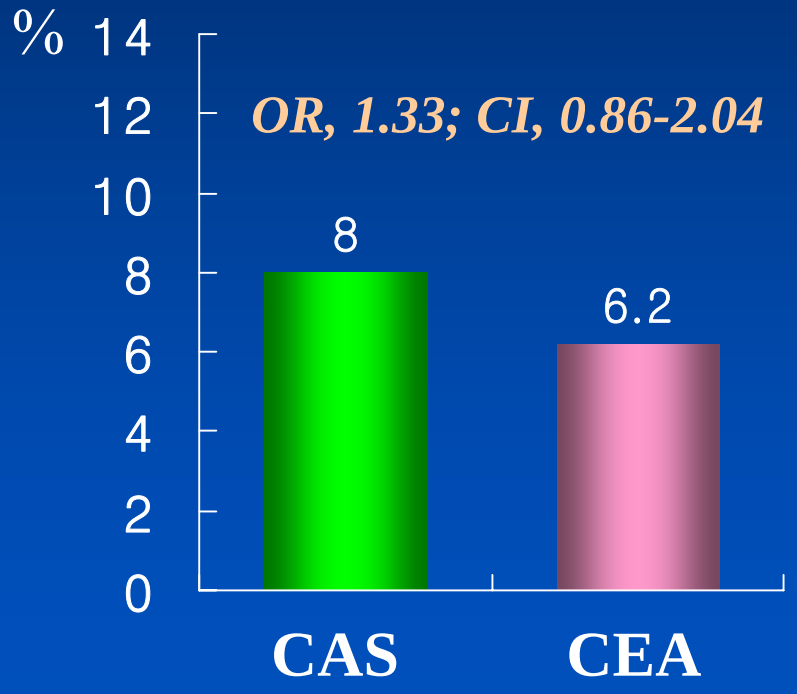
Yadav JS, et al. NEJM 2004;351:1493

CEA vs. CAS with or without EPD

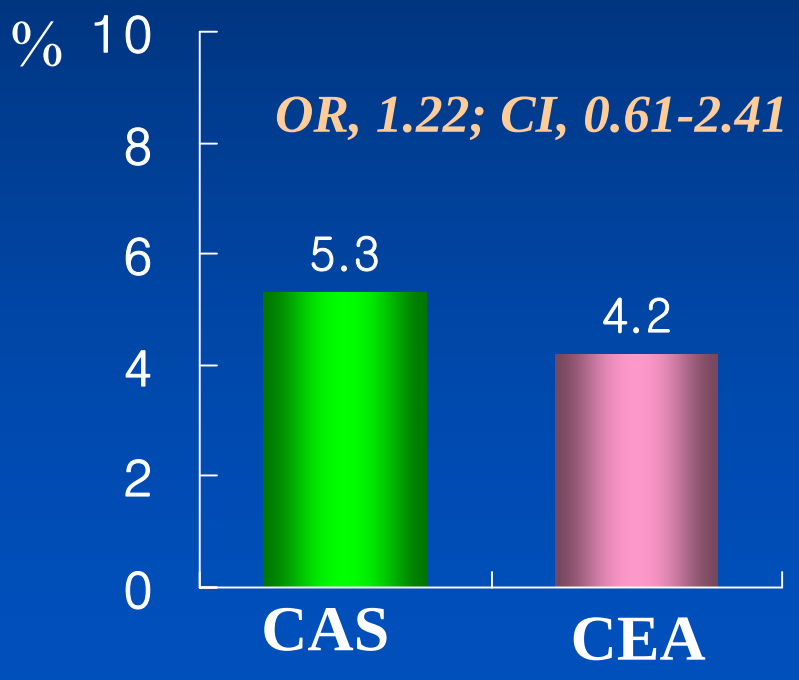
30 days outcomes from 5 RCT (n=1269)

(CAVATAS, Kentucky A&B, Leicester, WALL STENT, SAPPHIRE)

Death / any stroke



Death / disabling stroke



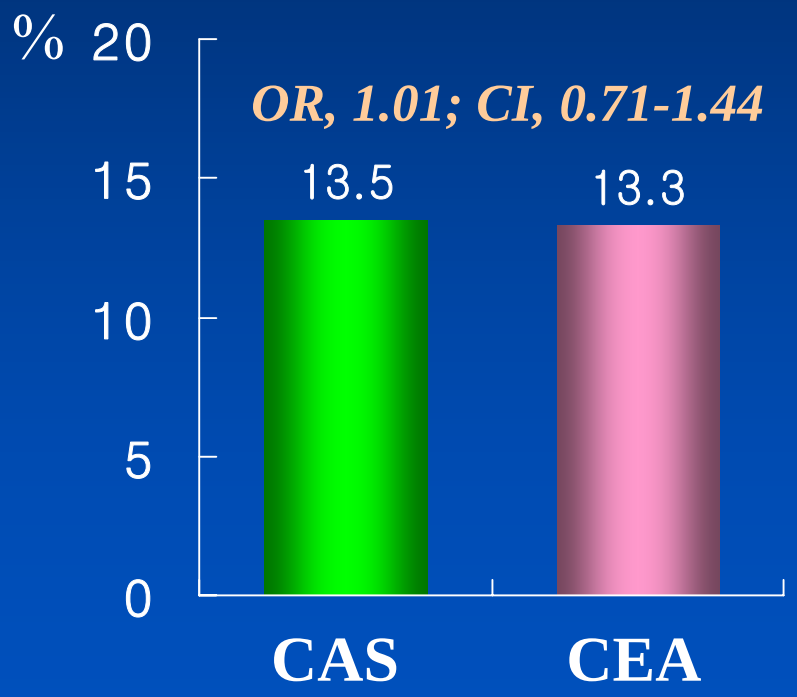
Coward LJ, et al. Stroke 2005;36:905-911

CEA vs. CAS with or without EPD

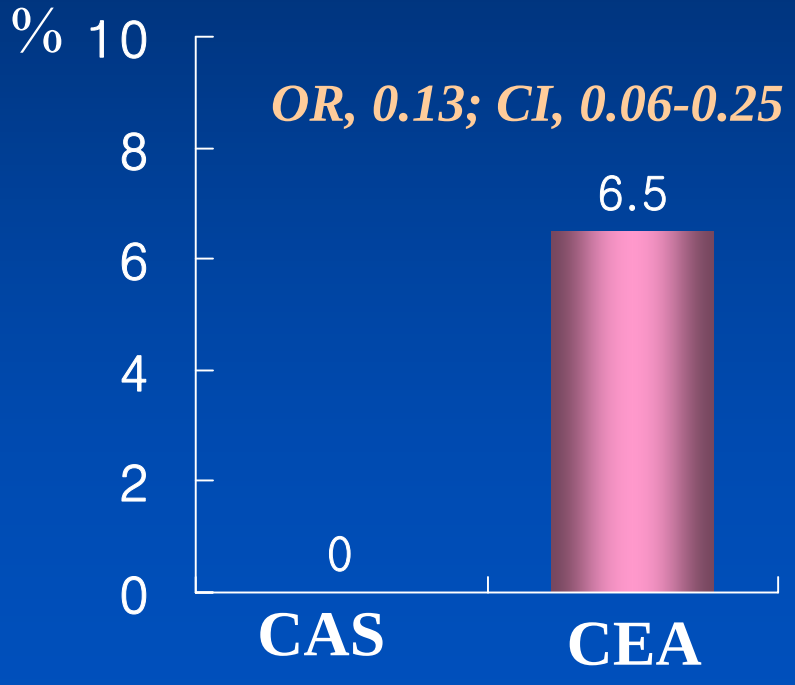
Outcomes from 5 RCT (n=1269)

(CAVATAS, Kentucky A&B, Leicester, WALL STENT, SAPPHIRE)

Death /any stroke @ 1 year



Cranial nerve palsy



Coward LJ, et al. Stroke 2005;36:905-911

CES vs. CAS with Accunet

Multicenter, prospective, nonrandomized

Carotid stenosis (n=581)

High-risk Sx & Asx patients

Carotid Stenting with Accunet (n=581)

Carotid endarterectomy (Historical control)

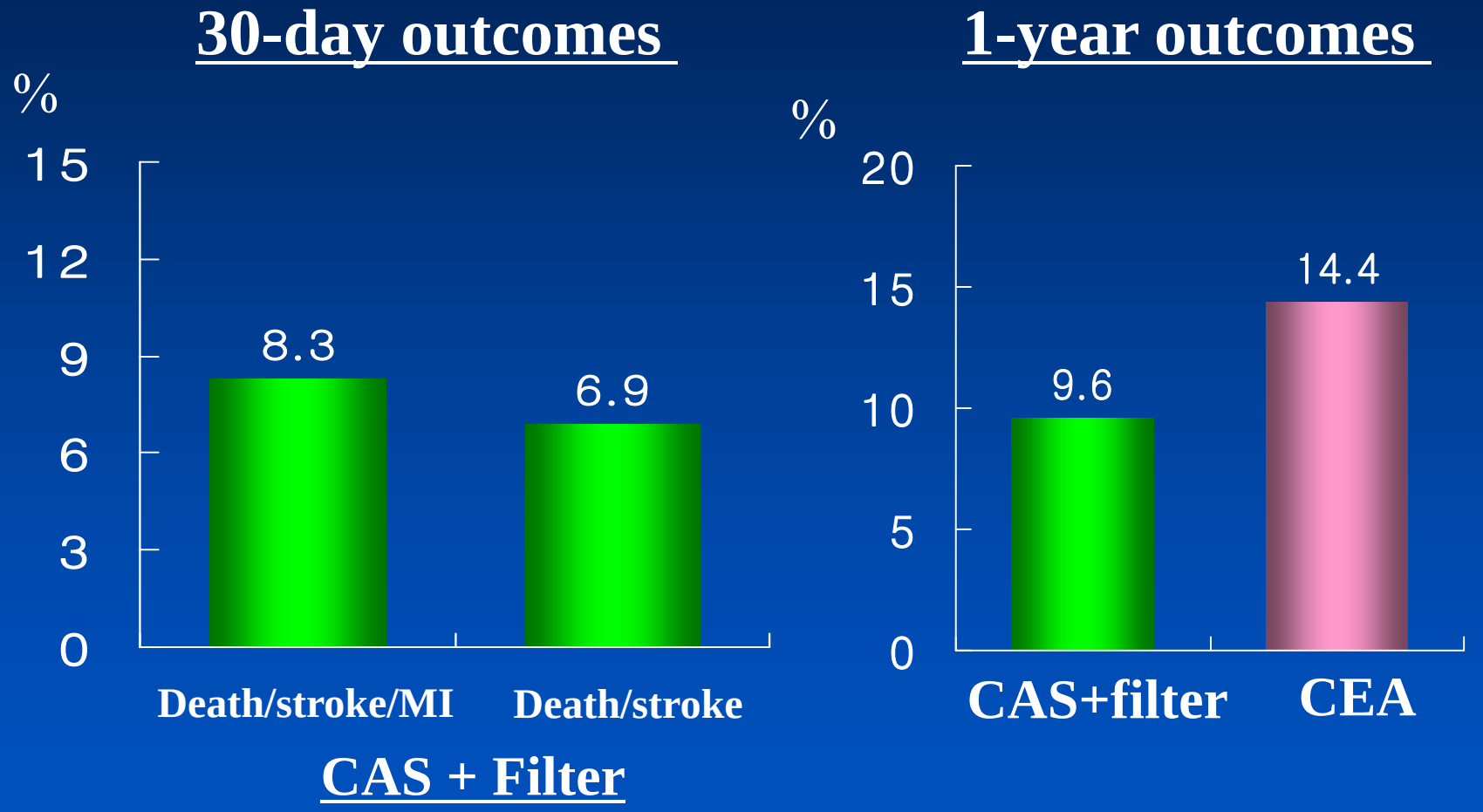
Primary endpint: composite of periprocedural death, stroke, or myocardial Infarction within 30 days, plus ipsilateral stroke btw 31days and 1 year

Gray WA, et al. J Vasc Surg 2006;44:258-69

ARCHeR

CEA vs. CAS with Accunet

30-Day and 1-year Outcomes



Gray WA, et al. J Vasc Surg 2006;44:258-69

Symptomatic normal risk

&

Asymptomatic normal risk

CaRESS

CES vs. CAS with GuardWire

Multicenter, prospective, nonrandomized 1:2 ratio

Carotid a stenosis (n=397)

Normal-risk Sx & Asx patients

Carotid Stenting with GuardWire (n=143)

Carotid endarterectomy (n=254)

Primary endpint: death and stroke at 30 days and a composite of death, stroke, or myocardial Infarction within 30 days and death or stroke btw 31days and 1 year

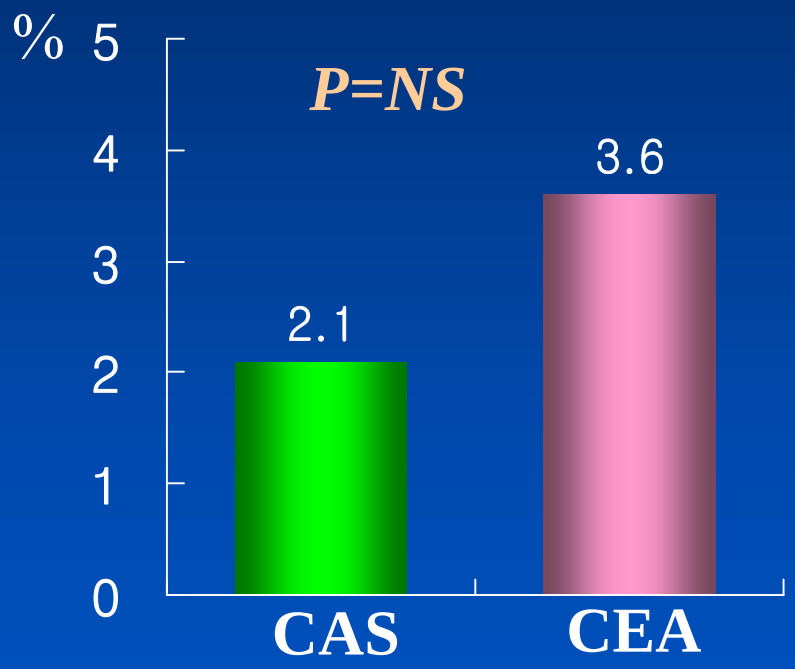
J Vasc Surg 2005;42:213-9

CaRESS

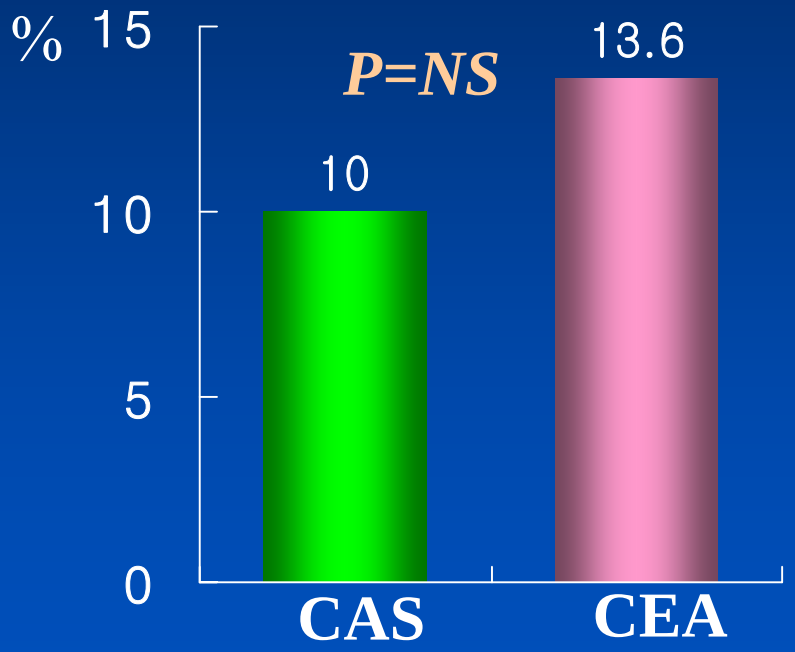
CEA vs. CAS with GuardWire

30-Day and 1-year Outcomes

Death / stroke at 30 days



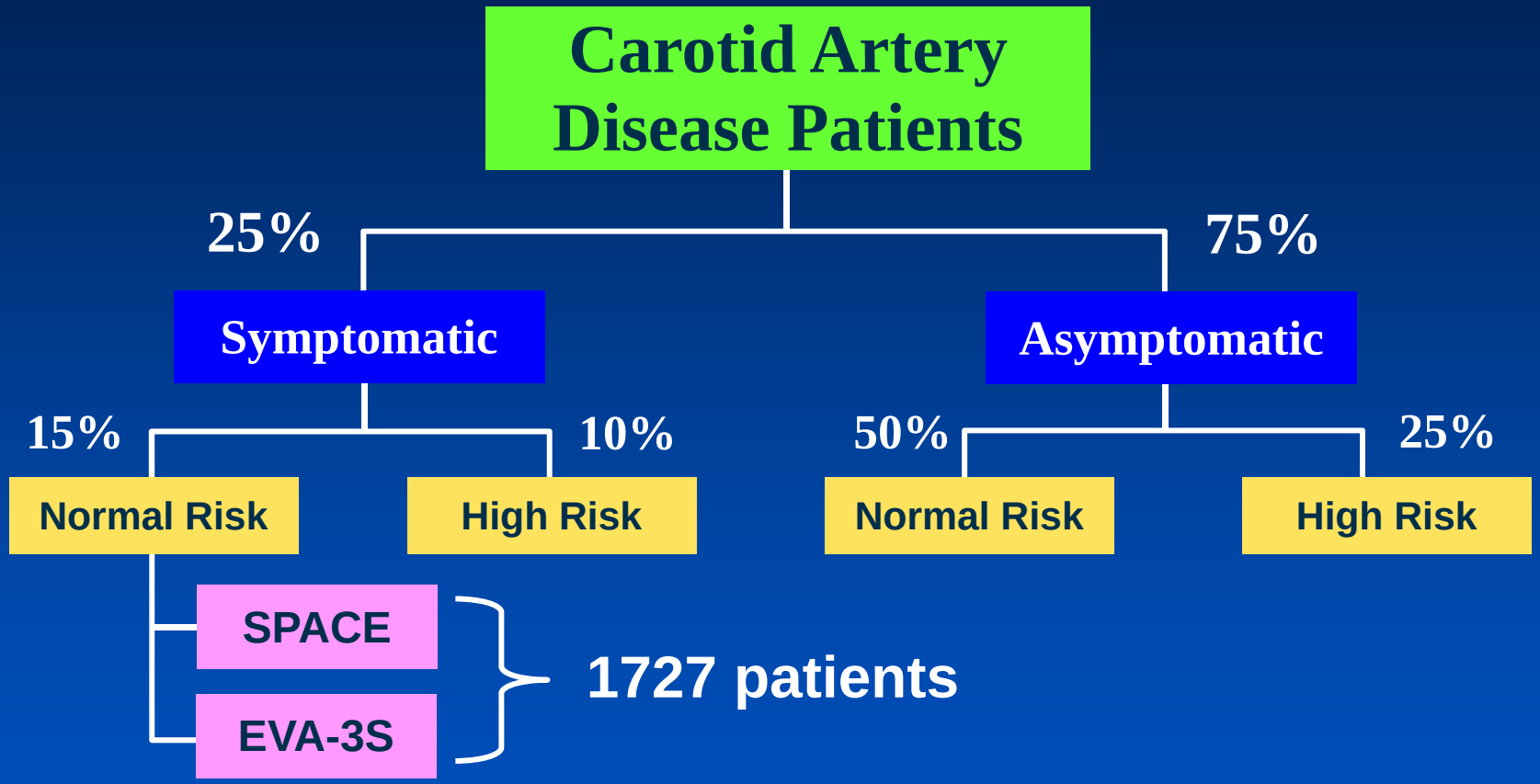
Death / stroke at 1 year



J Vasc Surg 2005;42:213-9

Carotid Stenting

Clinical trials for normal risk



Recent NEGATIVE RCT's ???

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

Major eligibility Criteria

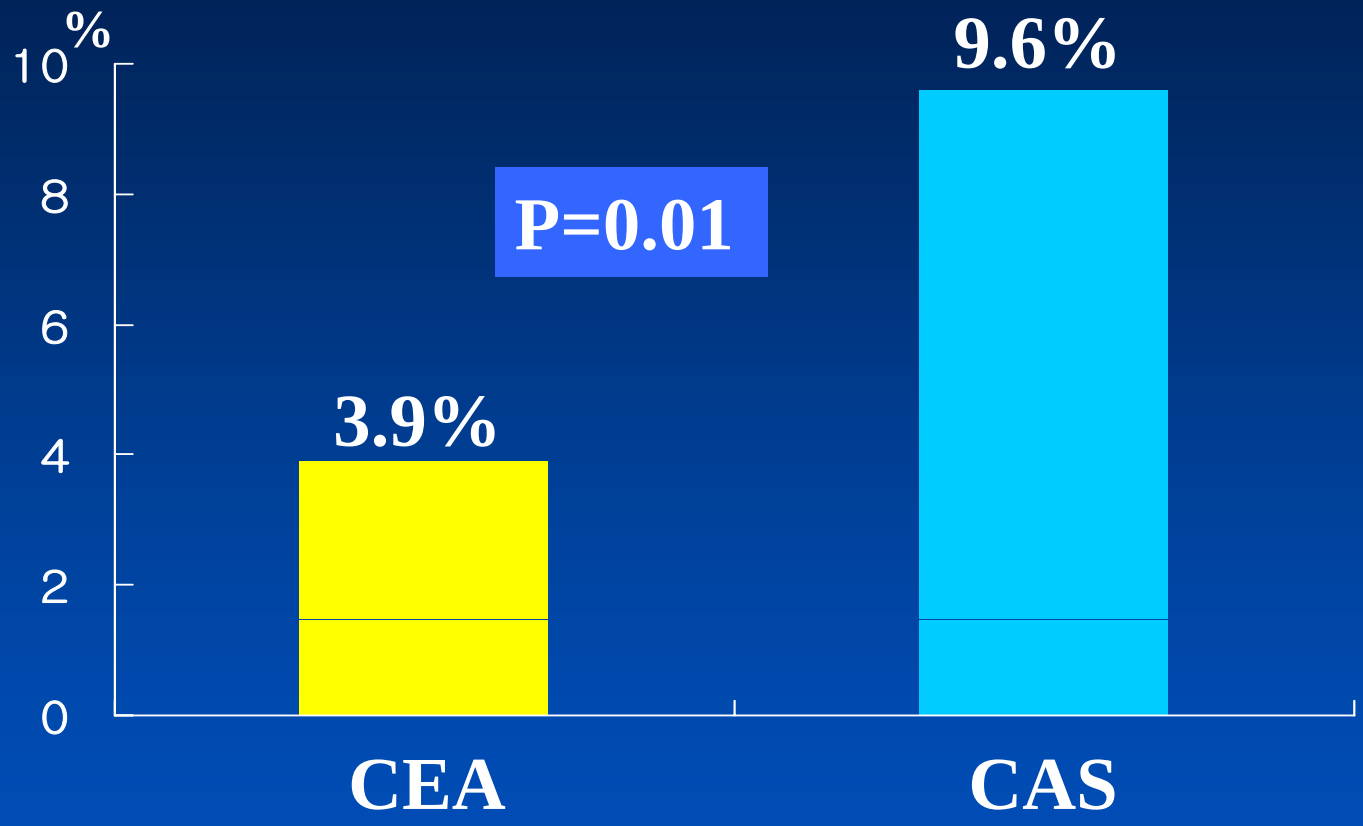
Inclusion criteria

- Age ≥18yrs
- Hemispheric or retinal transient ischemic attack or nondisabling stroke (or retinal infarct) within 120 days before enrollment
- Stenosis ≥ 60%
  in symptomatic carotid artery

Exclusion criteria

- Modified Rankin S ≥ 3
- Severe tandem lesion
- Previous Hx. (CEA,CAS)
- Uncontrolled HT or DM
- Unstable angina
- Contra-Ix. of heparin, clopidogrel
- Hx. of bleeding disorder
- Life expectancy < 2yr

30-Day Outcomes

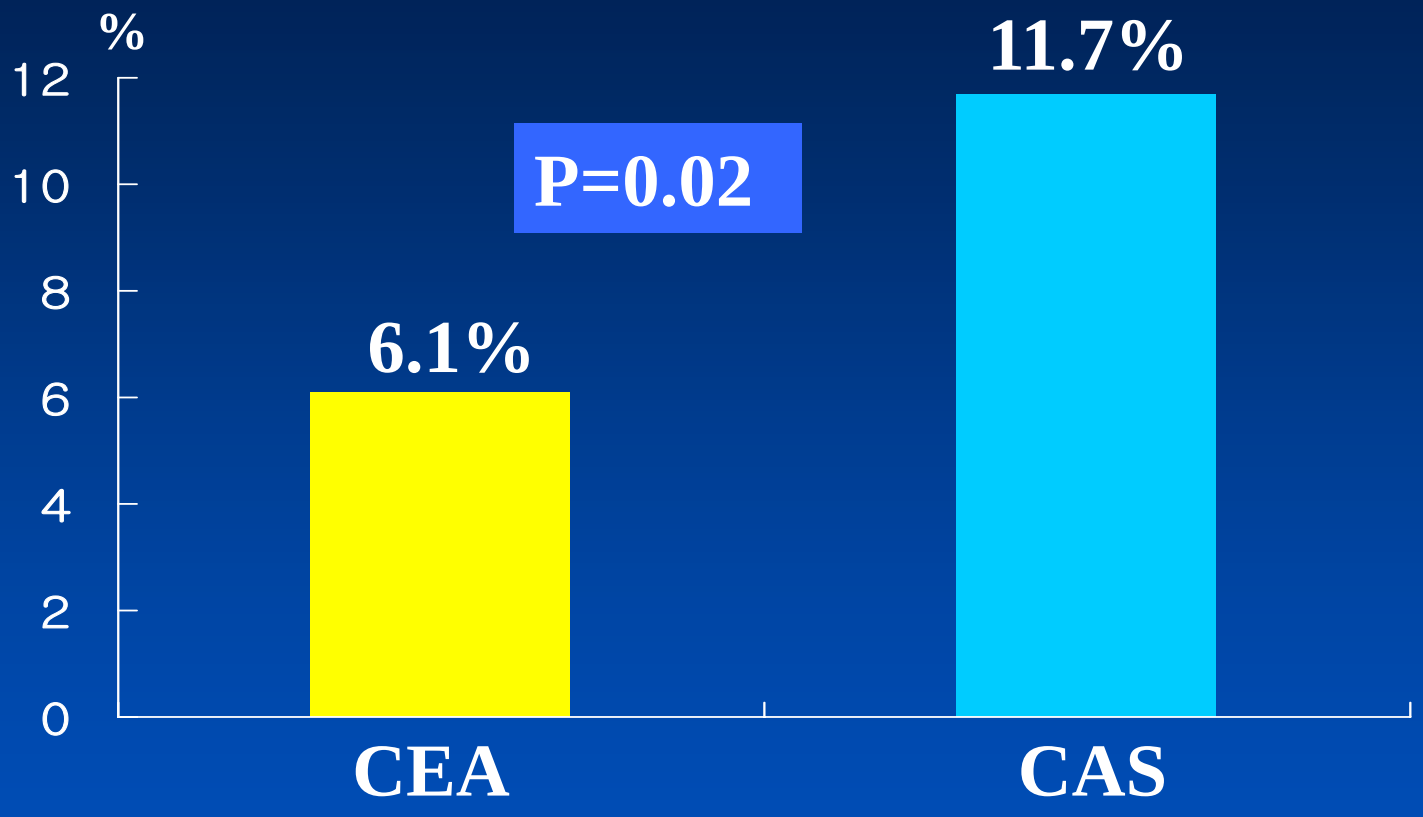


Relative risk: 2.5 (95% CI, 1.2 to 5.1)

NEJM 2006;355:1660-71

EVA-3S

6 Months Events



Events: any stroke or death after treatment

NEJM 2006;355:1660-71

Conclusion

In patients with symptomatic carotid stenosis of 60% or more, the rates of death and stroke at 1 and 6 months were lower with endarterectomy than with stenting

NEJM 2006;355:1660-71

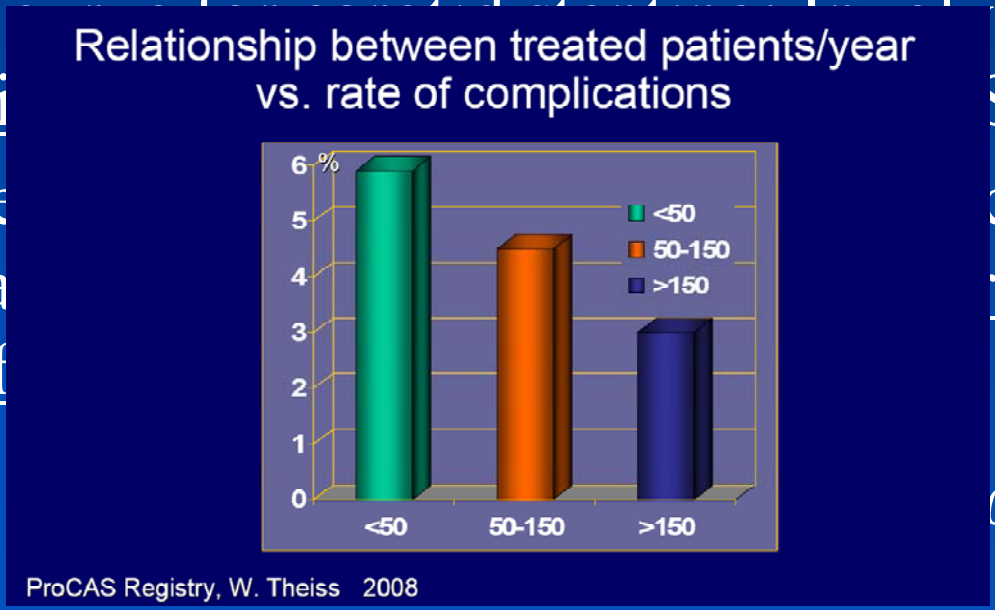
Limitation

EVA-3S

- E… ism w… ting, a… -P… st…
- Learning … ed center had a vari… S.

-Five diffe… ction devices, a… es was required f…

2. Procedural requirements for competency in all areas
   a. Diagnostic peripheral angiograms—100 cases (50 as primary operator)
   b. Peripheral interventions—50 cases (25 as primary operator)
   c. No fewer than 20 diagnostic/10 interventional cases in each area, excluding extracranial cerebral arteries†
   d. Extracranial cerebral (carotid/vertebral) arteries—30 diagnostic (15 as primary operator)/25 interventional (13 as primary operator)
   e. Percutaneous thrombolysis/thrombectomy—5 cases



06;355:1660-71

Limitation

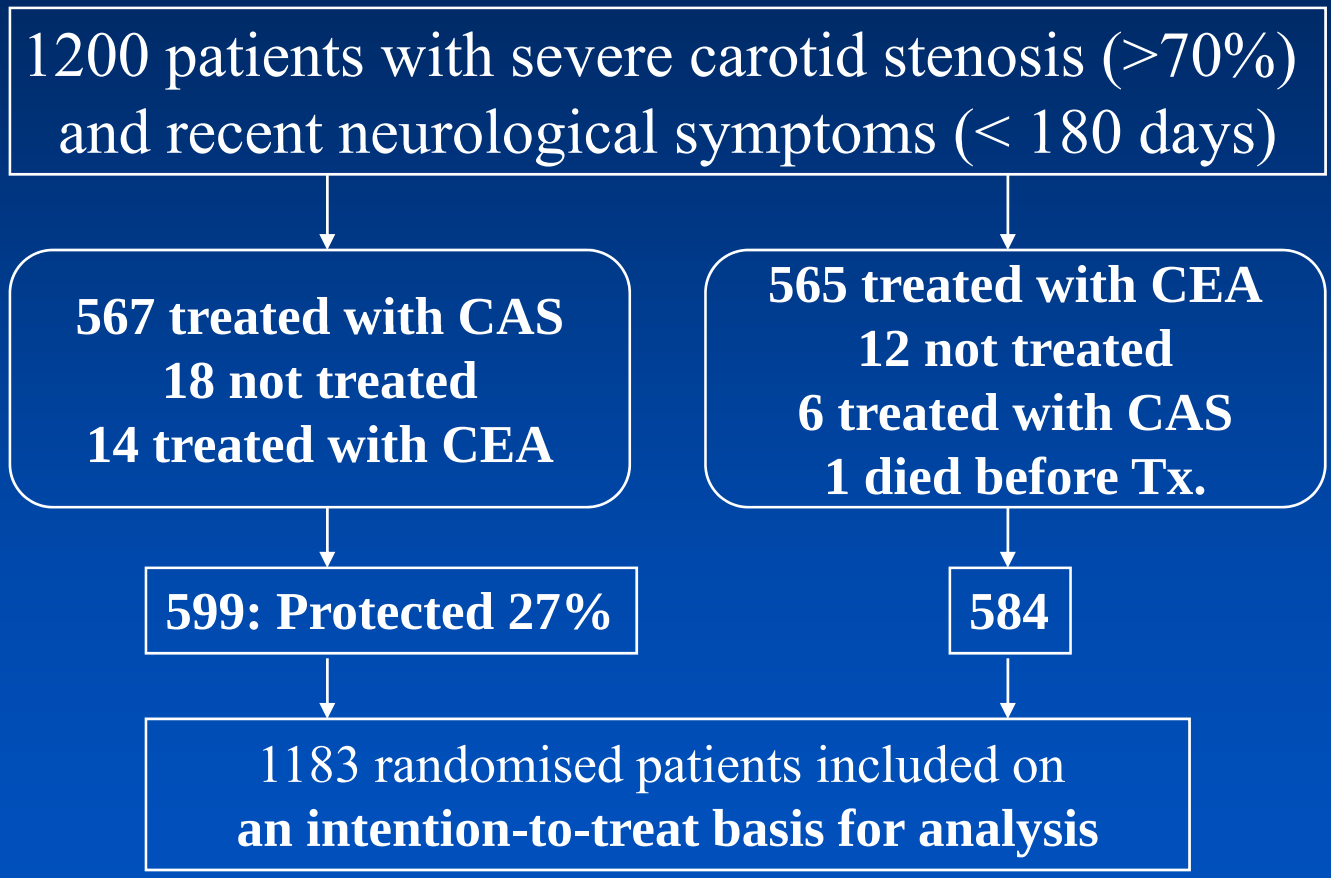
- Although the angiographic appearance of the lesion was not an eligibility criterion, plaque morphology (length, degree of ulceration, and presence or absence of thrombus) could be related to complication rates for stenting.

- 42 and 36 patients who underwent stenting in the EVA-3S trial received only single (unspecified) antiplatelet therapy before and after the procedure, respectively.

NEJM 2006;355:1660-71

30 days results from SPACE trial in symptomatic patients

Randomized non-inferiority trial: 1900 initially planned



Lancet 2006;368;1239-47

Primary endpoint

Ipsilateral stroke (ischemic stroke or intracerebral bleeding or both , with symptoms lasting more than 24 hr) or death of any cause between randomization and 30 days after Treatment.

Null hypothesis

The difference between the events rates in CAS and CEA group was 2.5% or more.

Non-inferiority margin

defined as less than 2.5%

on the basis of an expected event rate 5%

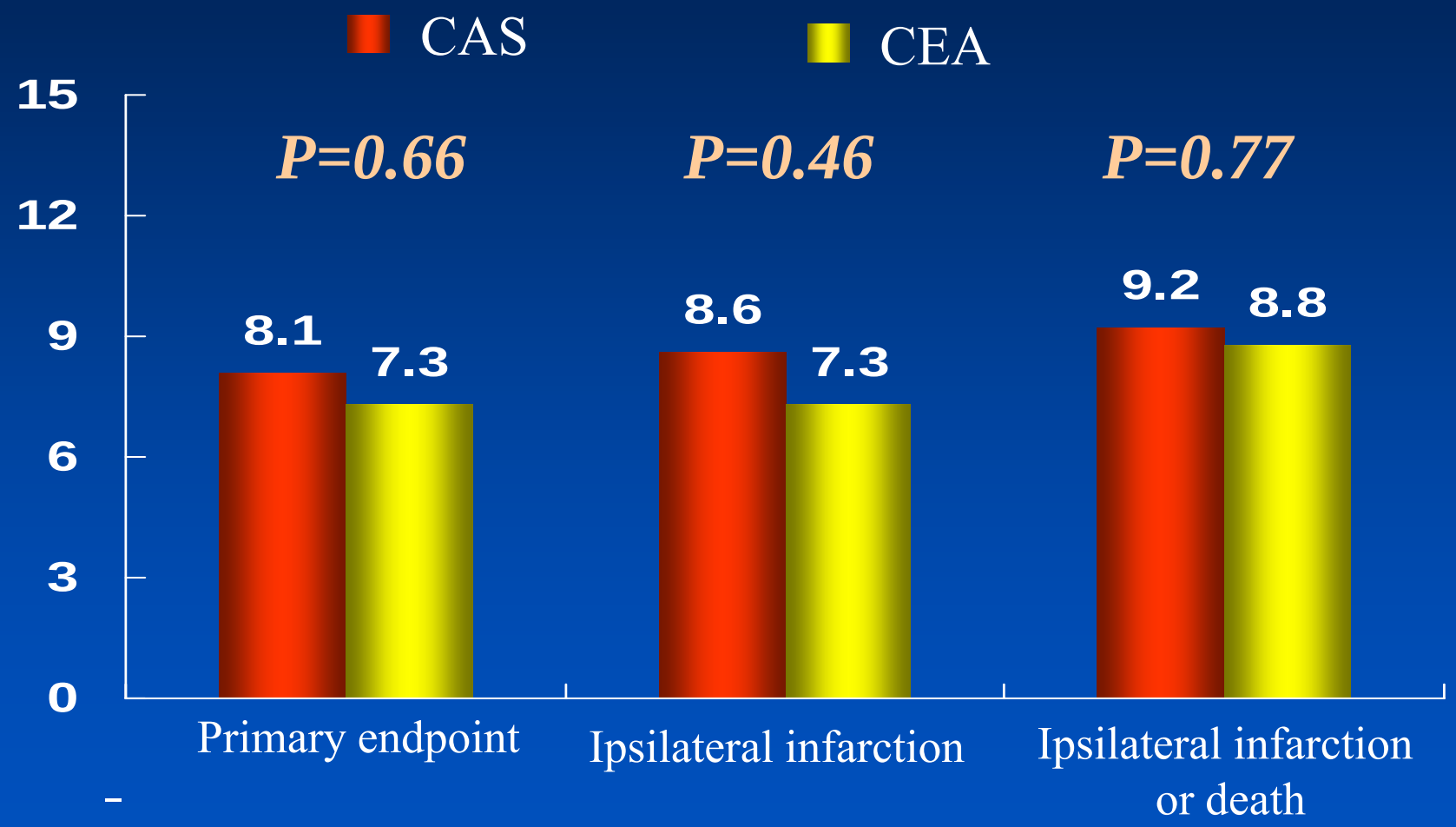
Lancet 2006;368;1239-47

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 (0.18%)	5 (0.86%)		0.19 (0.004 to 1.74)
Death	4 (0.67%)	5 (0.86%)		0.78 (0.15 to 3.64)

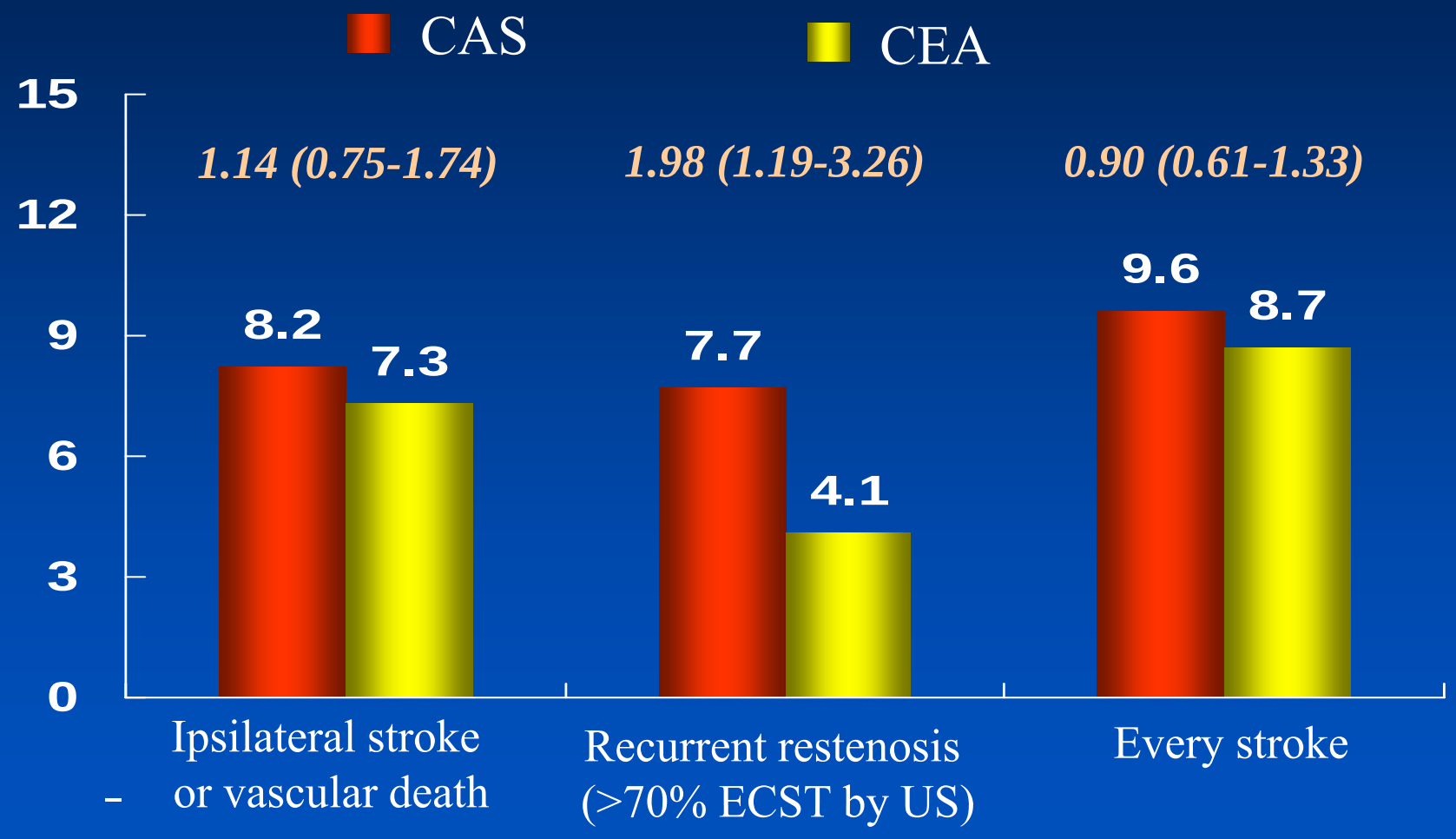
***One-sided p value for non-inferiority is 0.09**

6 Months Results



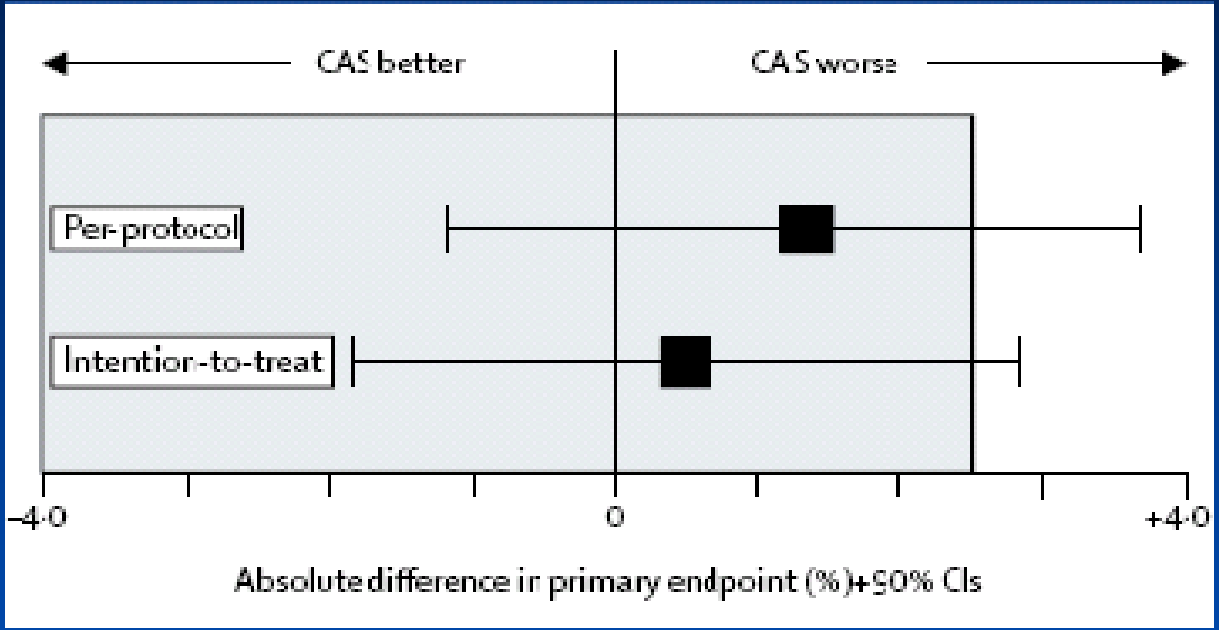
TCT 2007

1 Year Results



TCT 2007

Limitation of SPACE trial



Actual difference (90% CI) for primary endpoint in SPACE.
Because upper CI is more than 2.5, study has failed to show non-inferiority for carotid angioplasty and stenting (CAS). However, because CIs cross zero, difference in primary outcome between carotid endarterectomy and carotid angioplasty and stenting was not statistically significant.

Lancet 2006;368;1239-47

Limitation of SPACE trial

- Only 27% (n=151) of patients used embolic protection devices

- Study underpowered: with the current event rates, a sample size of >2,500 would be needed

- Running out of funds

- Slow enrollment: 1.200 pts in 4 years

Lancet 2006;368;1239-47

Limitation of SPACE trial

- Despite SPACE being the biggest trial to date, one is left with the unavoidable conclusion that it was stopped prematurely.

- Notwithstanding funding issues, the planned margin of non-inferiority (<2.5%) was based on a power calculation of 1900 patients and this larger sample might have provided much tighter CIs and more robust statistical data.

Lancet 2006;368;1239-47

Conclusion

- Although SPACE failed to prove non-inferiority of CAS compared with CEA for the periprocedural complication rate, which was statistically not significant (p=0.09)
- No statistical difference of primary and secondary end points up to 1 year

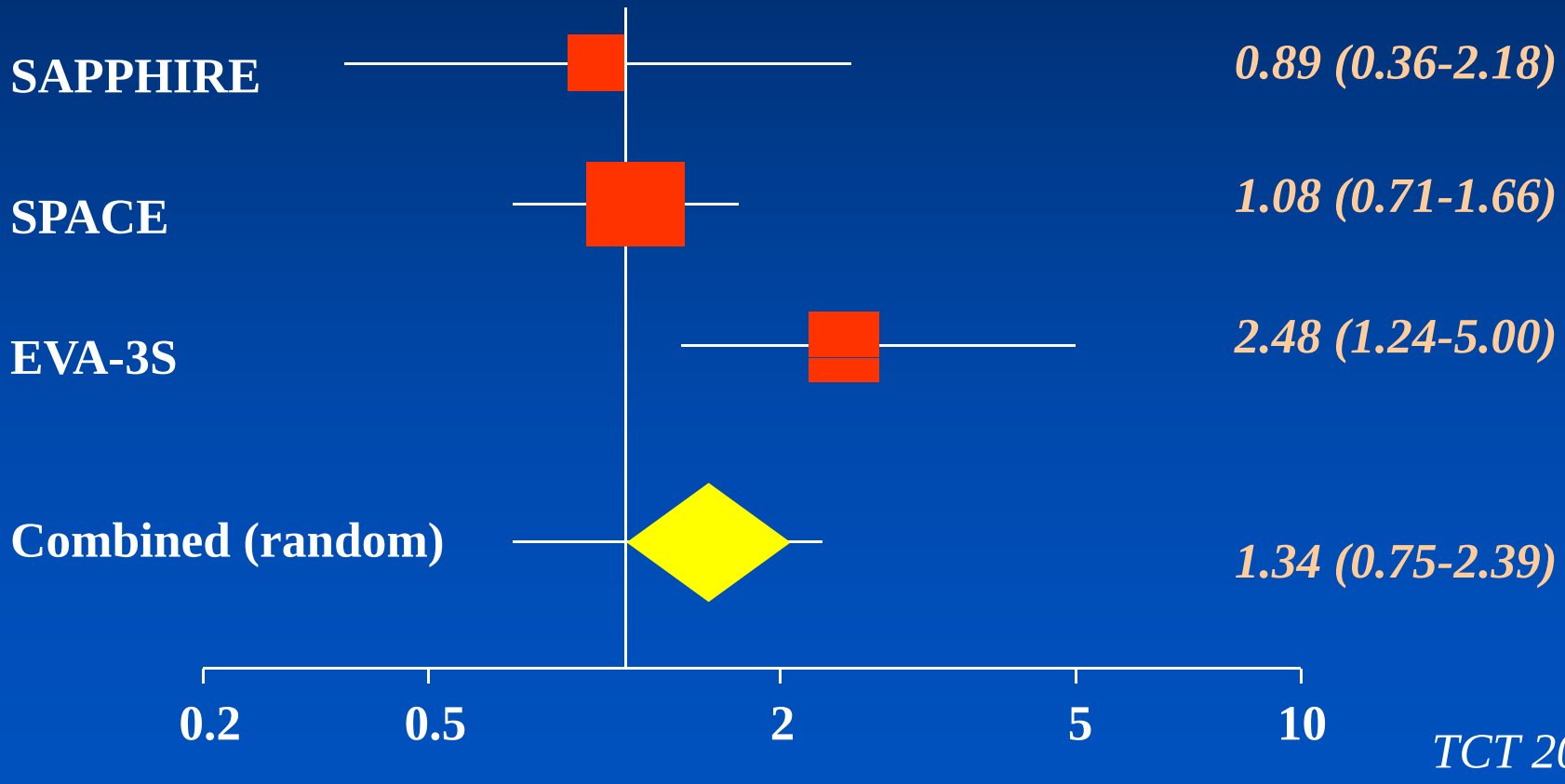
Lancet 2006;368;1239-47

Meta-analysis of randomized trials

Protected CAS vs. CEA

Death & stroke at 30 day

Relative risk meta-analysis (random effect)



TCT 2007

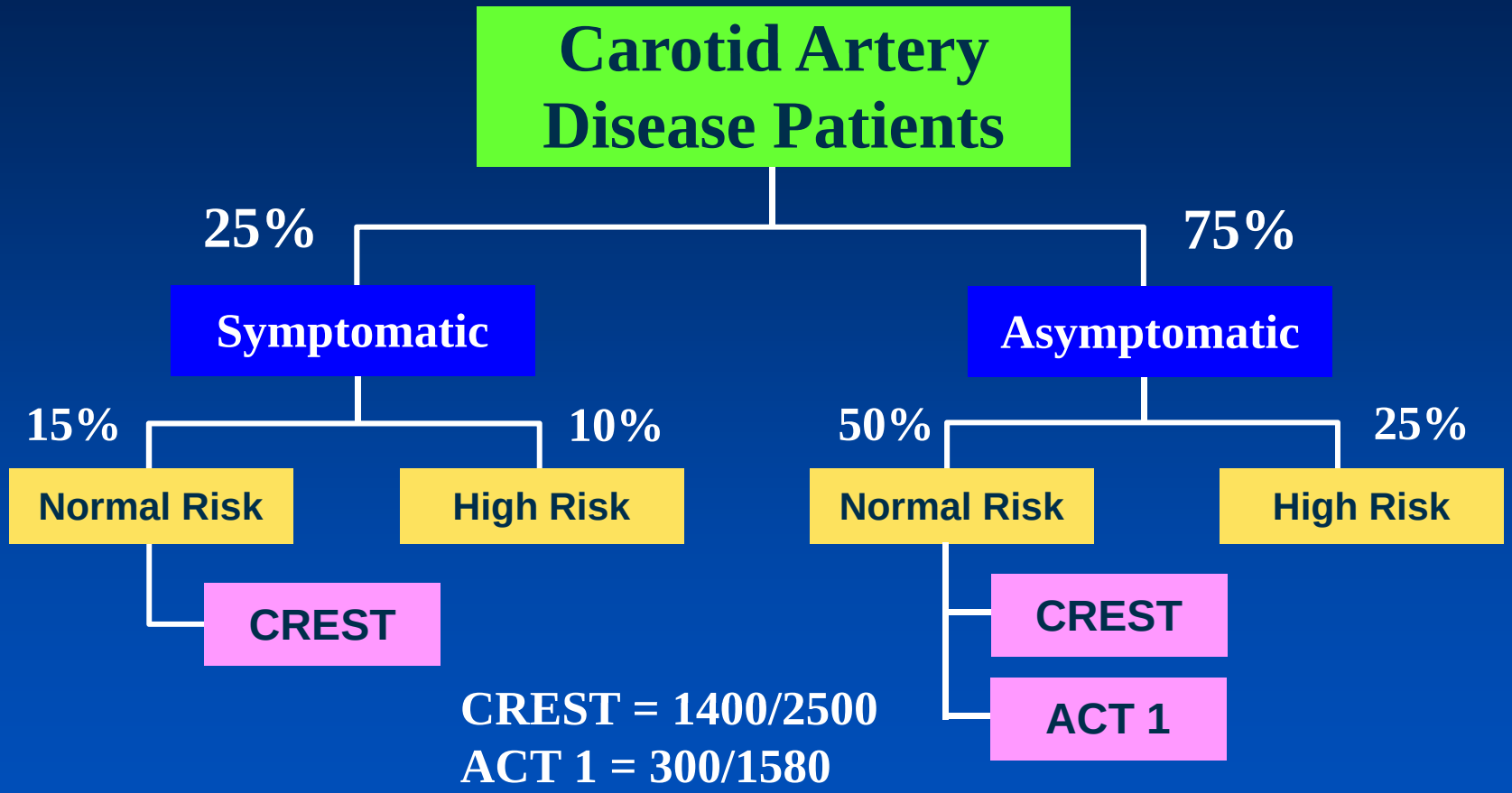
Randomized CAS vs. CEA

Trial	N	Patient Subset	EPD Stent	Primary End Point	Comment
Wallstent (184)	219	Low risk Symptomatic	None Wallstent	1 yr stroke/D	CAS 10.4%, CEA 4.4%; stopped prematurely
SAPPHIRE (160)	334	High risk Symptomatic, Asymptomatic	AngioGuard Precise	30 days MI/stroke/D plus 1 yr ipsilateral stroke/D	CAS 12.2%, CEA 20.1%; stopped prematurely for slow enrollment
CREST	2,500	Low risk Symptomatic, Asymptomatic	Accunet AccuLink	30 days MI/stroke/D and 4 yr ipsilateral stroke	Active enrollment
SPACE (196a)	1,183	Low risk Symptomatic	Various Various	30 days ipsilateral stroke/D	CAS 6.8%, CEA 6.3%; stopped prematurely
EVA-3S (198a)	527	Low risk Symptomatic	Various Various	30 days stroke/D and 4 yr ipsilateral stroke	CAS 9.6%, CEA 3.9%; stopped prematurely
ICSS (CAVATAS II)	1,500	Low risk Symptomatic	Various Various	30 days MI/stroke/D and 3 yr disabling stroke/D	Active enrollment
ACT-1	1,540	Low risk Asymptomatic	Emboshield Xact	30 days MI/stroke/D plus 1 yr ipsilateral stroke	Active enrollment
ACST-2	5,000	Any risk Asymptomatic	Various Various	30 days MI/stroke/D 1 yr stroke/D	Active enrollment

ACCF/SCAI/SVMB/SIR/ASITN 2007 Clinical Expert Consensus Document on Carotid Stenting J Am Coll Cardiol 2007;49:126–70

Carotid Stenting

Clinical trials for normal risk



CREST = 1400/2500
ACT 1 = 300/1580

On going trials ascertain this issues

Vascular Medicine Perspective: CEA versus Stent

- High risk symptomatic patient (>50%)
  – carotid stenting is preferred and reimbursed
- High risk asymptomatic patient (>80%)
  – carotid stenting is preferred and reimbursed
- Normal risk symptomatic patient (>50%)
  :CaRESS, SPACE, EVA-3S
  – More data are needed (CAVATAS-2, CREST)
- Normal risk asymptomatic patient (>80%)
  :CaRESS,
  – More data are needed (CREST, ACT1)