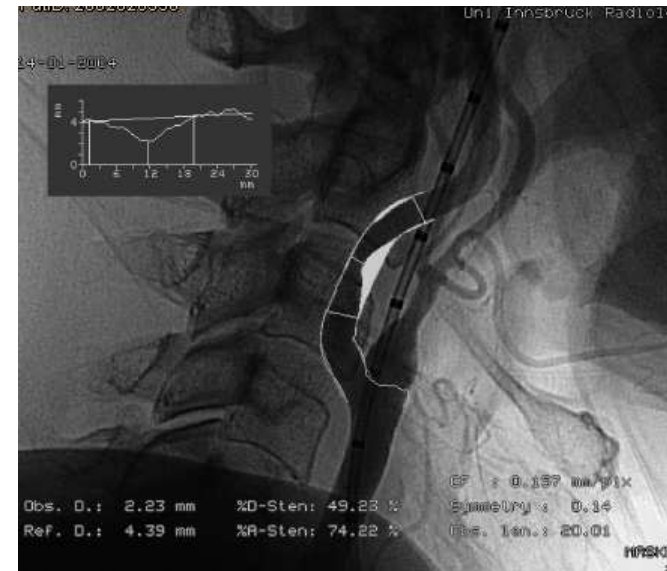
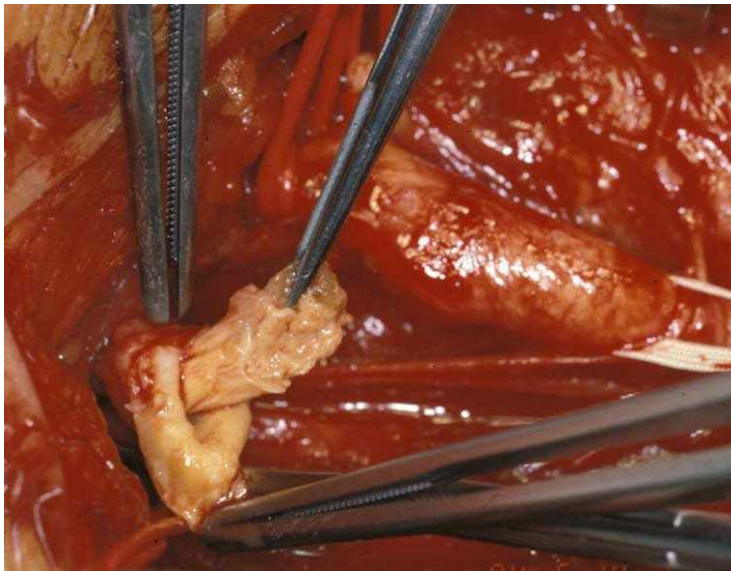




MEDIZINISCHE UNIVERSITÄT
INNSBRUCK



Aktuelle Studienlage CEA versus CAS Current Evidence for CEA versus CAS Stato dell'arte CEA versus CAS



CSTC - Carotid Stenting Trialists' Collaboration

Preplanned meta-analysis of three large randomised European trials of stenting versus endarterectomy for symptomatic carotid stenosis

- Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis trial [EVA-3S]
(*N Engl J Med* 2006;355:1660-1671)
- Stent-Protected Angioplasty versus Carotid Endarterectomy in symptomatic patients trial [SPACE]
(*Lancet* 2006;368:1239-1247)
- International Carotid Stenting Study [ICSS]
(*Lancet* 2010;375:985-997)

Individual data from 3.433 patients (CAS 1.725 & CEA 1.708)



Short-term outcome after stenting versus endarterectomy for symptomatic carotid stenosis: a preplanned meta-analysis of individual patient data

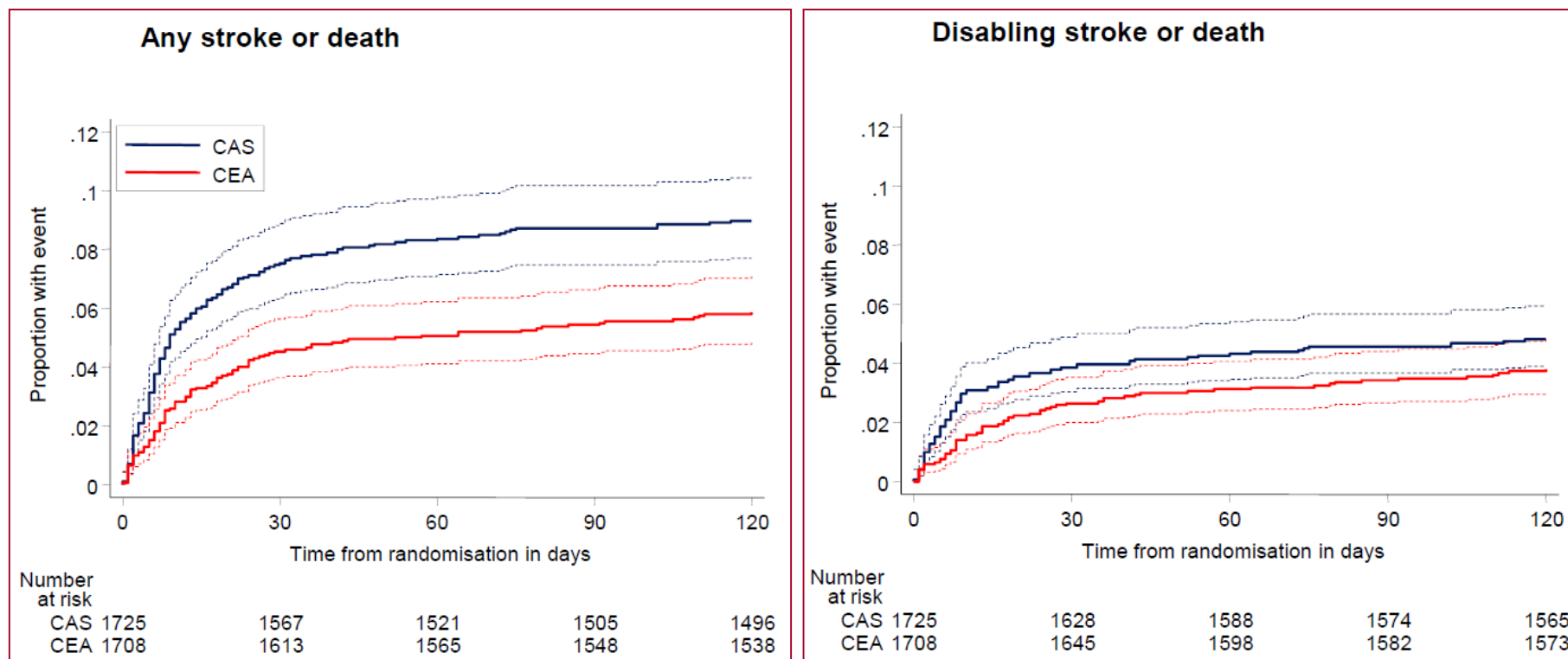
Carotid Stenting Trialists' Collaboration*

Lancet 2010; 376: 1062-73

Baseline characteristics of contributing studies

	EVA-3S		SPACE		ICSS	
	CAS	CEA	CAS	CEA	CAS	CEA
All patients (n)	265	262	607	589	853	857
Excluded from PPA	2 %	2%	3 %	4%	3 %	4 %
Age (yrs)	69.5	70.7	68.1	68.7	70.2	70.1
Male	73 %	78 %	72 %	72 %	70 %	71 %
Retinal ischemia	15 %	16 %	16 %	15 %	21 %	20 %
TIA	37 %	30 %	36 %	37 %	33 %	36 %
Hemispheric stroke	48 %	54 %	48 %	48 %	47 %	45 %
Days event and TX	15.5	17.6	10.3	11.3	15.8	18.9
Stenosis = 70%	94 %	92 %	63 %	61 %	89 %	91 %
Contralateral stenosis	13 %	13 %	10 %	11 %	18 %	17 %

Outcome events within 120 days of randomisation



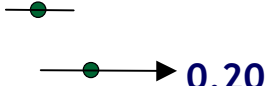
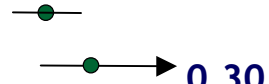
	CAS n=1725	CEA n=1708	Risk ratio (95% CI)	P-value	Risk diff. (95% CI)
Any stroke or death	8.9% (153)	5.8% (99)	1.53	0.0006	3.2 (1.4,4.9)

Outcome events within 120 days of randomisation

	CAS n=1679 n(%)	CEA n=1645 n(%)	Risk ratio [95% CI]	P-value	Risk diff. [95% CI]
Any stroke or death	130 7.7%	73 4.4%	1.74 [1.32-2.30]	0.0001	3.4 [1.8-5.0]
Disabling stroke or death	65 3.9%	43 2.6%	1.48 [1.01-2.15]	0.04	1.2 [0.0-2.4]
All-cause death	19 1.1%	10 0.6%	1.86 [0.87-4.00]	0.10	0.6 [-0.1-1.2]
Any stroke	125 7.4%	70 4.3%	1.74 [1.31-2.32]	0.0001	3.3 [1.7-4.9]

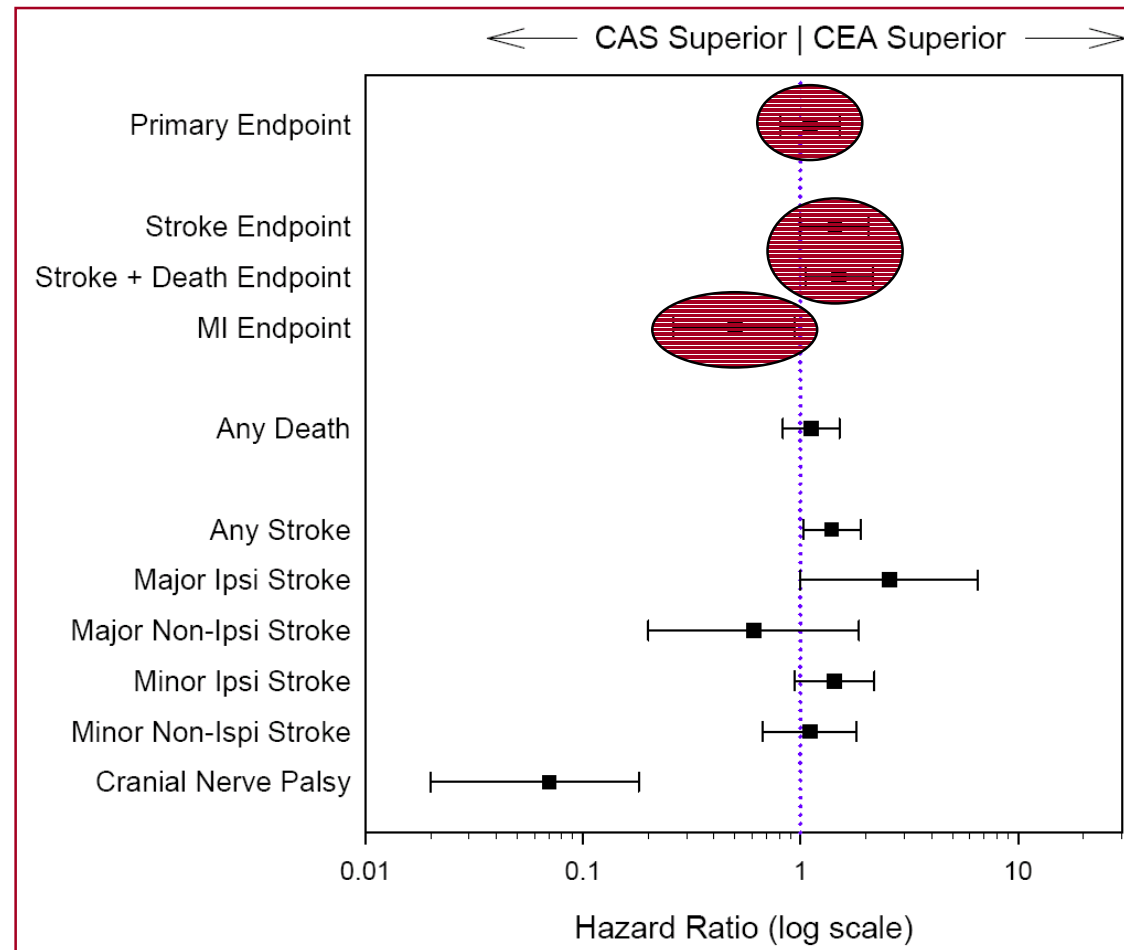
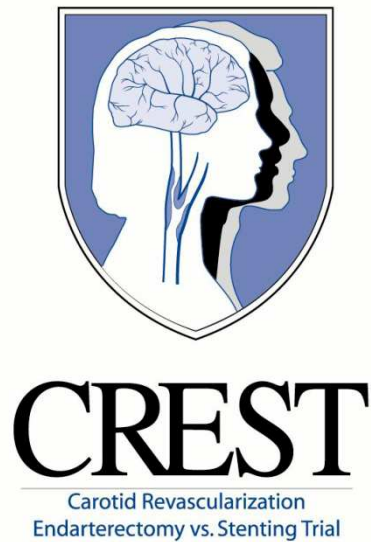
Per-protocol-analysis

Any stroke or death within 120 days of randomisation

CAS			CEA				
Subgroup	Risk	Pts (n)		Risk	Pts (n)	RR [95% CI]	P-value
Stroke before qualifying event							
No	8.0%	928		4.9%	939	1.62 [1.13-2.31]	
Yes	13.2%	190		5.0%	180	2.71 [1.30-5.66]	
Treatment within 14 days of qualifying event (PPA)							
No	7.3%	1062		4.0%	1089	1.82 [1.27-2.60]	
Yes	8.6%	372		3.2%	315	2.72 [1.36-5.45]	

Stroke or Death							
< 7 days	3 (2.8%)	13 (9.4%)	3.79 [1.1-13.1]				0.03
8-14 days	7 (3.4%)	19 (8.1%)	2.42 [1.0-5.7]				0.04
> 14 days	44 (4.0%)	78 (7.3%)	1.82 [1.3-2.6]				0.001

„North American“ trial



Primary endpoint: Any clinical stroke or death & myocardial infarction

Primary endpoint in the periprocedural period

	CAS <i>no. of patients (% ±SE)</i>	CEA	Absolute Treatment Effect of CAS vs. CEA (95% CI) <i>percentage points</i>	Hazard Ratio for CAS vs. CEA (95% CI)	P Value
Myocardial infarction					
Asymptomatic patients	7 (1.2±0.4)	13 (2.2±0.6)	-1.0 (-2.5 to 0.4)	0.55 (0.22 to 1.38)	0.20
Symptomatic patients	7 (1.0±0.4)	15 (2.3±0.6)	-1.2 (-2.6 to 0.1)	0.45 (0.18 to 1.11)	0.08
Any periprocedural stroke or postprocedural ipsilateral stroke					
Asymptomatic patients	15 (2.5±0.6)	8 (1.4±0.5)	1.2 (-0.4 to 2.7)	1.88 (0.79 to 4.42)	0.15
Symptomatic patients	47 (6.3±0.9)	21 (3.2±0.7)	2.3 (0.1 to 4.3)	1.74 (1.02 to 2.98)	0.04
Any periprocedural stroke or death or postprocedural ipsilateral stroke					
Asymptomatic patients	15 (2.5±0.6)	8 (1.4±0.5)	1.2 (-0.4 to 2.7)	1.88 (0.79 to 4.42)	0.15
Symptomatic patients	40 (6.0±0.9)	21 (3.2±0.7)	2.8 (0.5 to 5.0)	1.89 (1.11 to 3.21)	0.02
Primary end point (any periprocedural stroke, myocardial infarction, or death or postprocedural ipsilateral stroke)					
Asymptomatic patients	21 (3.5±0.8)	21 (3.6±0.8)	0.0 (-2.2 to 2.1)	1.02 (0.55 to 1.86)	0.96
Symptomatic patients	45 (6.7±1.0)	35 (5.4±0.9)	1.4 (-1.2 to 3.9)	1.26 (0.81 to 1.96)	0.30

Outcome events CSTC vs CREST

	CAS	CEA	Risk ratio	P-value
CSTC	N=1725	N=1708		
CREST	N=668	N=653		
Any stroke or death	8.9%	5.8%	1.53	0.0006
	6.0%	3.2%	1.89	0.02
Any stroke	8.2%	4.9%	1.66	0.0001
	5.5%	3.2%	1.74	0.04

ITT

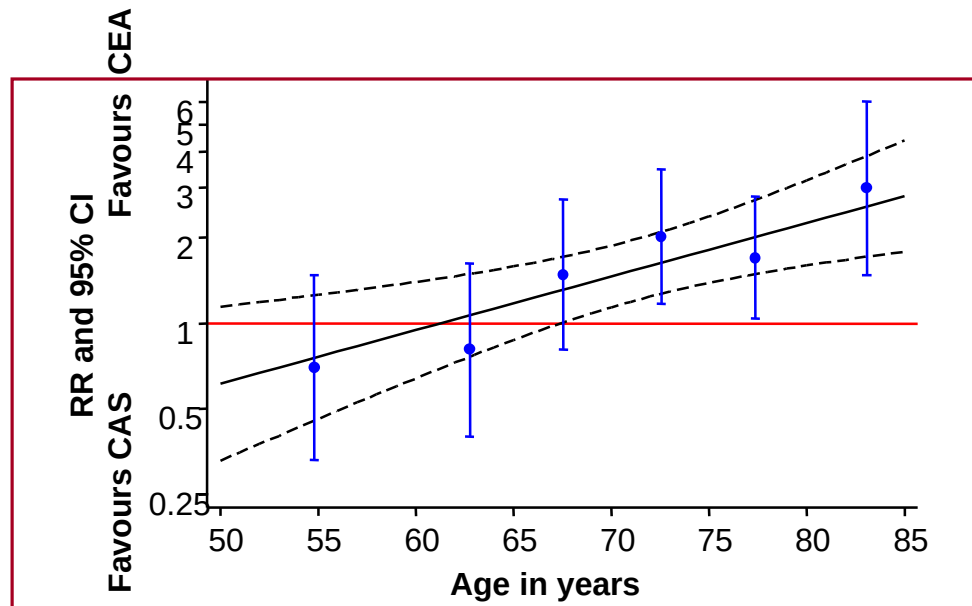
CEA vs CAS for asymptomatic patients

	CAS <i>no. of patients (% ±SE)</i>	CEA <i>no. of patients (% ±SE)</i>	Absolute Treatment Effect of CAS vs. CEA (95% CI) <i>percentage points</i>	Hazard Ratio for CAS vs. CEA (95% CI)	P Value
Myocardial infarction					
Asymptomatic patients	7 (1.2±0.4)	13 (2.2±0.6)	-1.0 (-2.5 to 0.4)	0.55 (0.22 to 1.38)	0.20
Symptomatic patients	7 (1.0±0.4)	15 (2.3±0.6)	-1.2 (-2.6 to 0.1)	0.45 (0.18 to 1.11)	0.08
Any periprocedural stroke or postprocedural ipsilateral stroke					
Asymptomatic patients	15 (2.5±0.6)	8 (1.4±0.5)	1.2 (-0.4 to 2.7)	1.88 (0.79 to 4.42)	0.15
Symptomatic patients	37 (5.5±0.9)	21 (3.2±0.7)	2.3 (0.1 to 4.5)	1.74 (1.02 to 2.98)	0.04
Any periprocedural stroke or death or postprocedural ipsilateral stroke					
Asymptomatic patients	15 (2.5±0.6)	8 (1.4±0.5)	1.2 (-0.4 to 2.7)	1.88 (0.79 to 4.42)	0.15
Symptomatic patients	40 (6.0±0.9)	21 (3.2±0.7)	2.8 (0.5 to 5.0)	1.89 (1.11 to 3.21)	0.02
Primary end point (any periprocedural stroke, myocardial infarction, or death or postprocedural ipsilateral stroke)					
Asymptomatic patients	21 (3.5±0.8)	21 (3.6±0.8)	0.0 (-2.2 to 2.1)	1.02 (0.55 to 1.86)	0.96
Symptomatic patients	45 (6.7±1.0)	35 (5.4±0.9)	1.4 (-1.2 to 3.9)	1.26 (0.81 to 1.96)	0.30

CEA vs CAS for asymptomatic patients

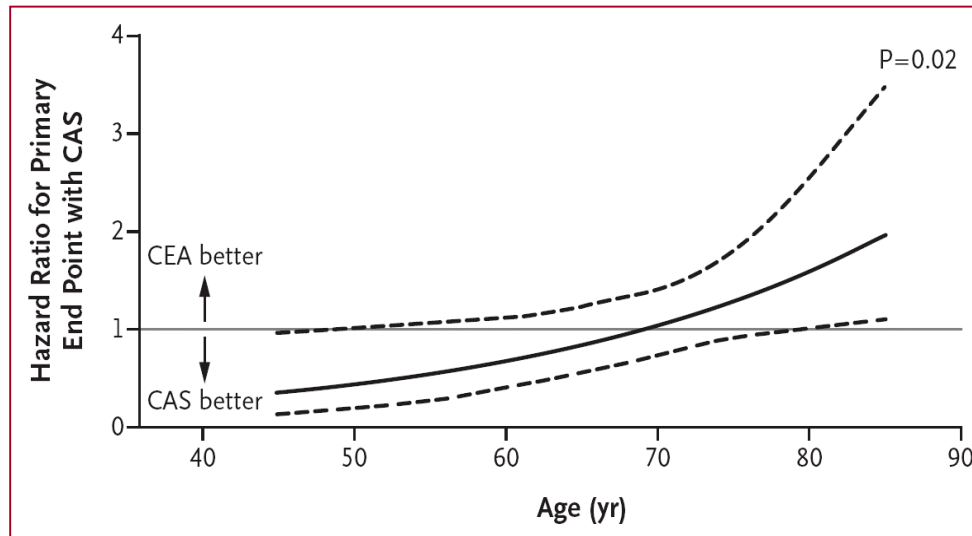
		CAS	CEA	Risk ratio	P-value
		N=594	N=587		
Any stroke	30d	2.5%	1.4%	1.88	0.15
	4a	4.5%	2.7%	1.86	0.07
Any stroke or death	30d	2.5%	1.4%	1.88	0.15
	4a	4.5%	2.7%	1.86	0.07
Any stroke or death or MI	30d	3.5%	3.6%	1.02	0.96
	4a	5.6%	4.9%	1.17	0.56

Relative risk of any stroke or death with age



CSTC ($n = 3.433$)

Risk ratio
pts > 70 yrs
2.04



CREST ($n = 2.502$)

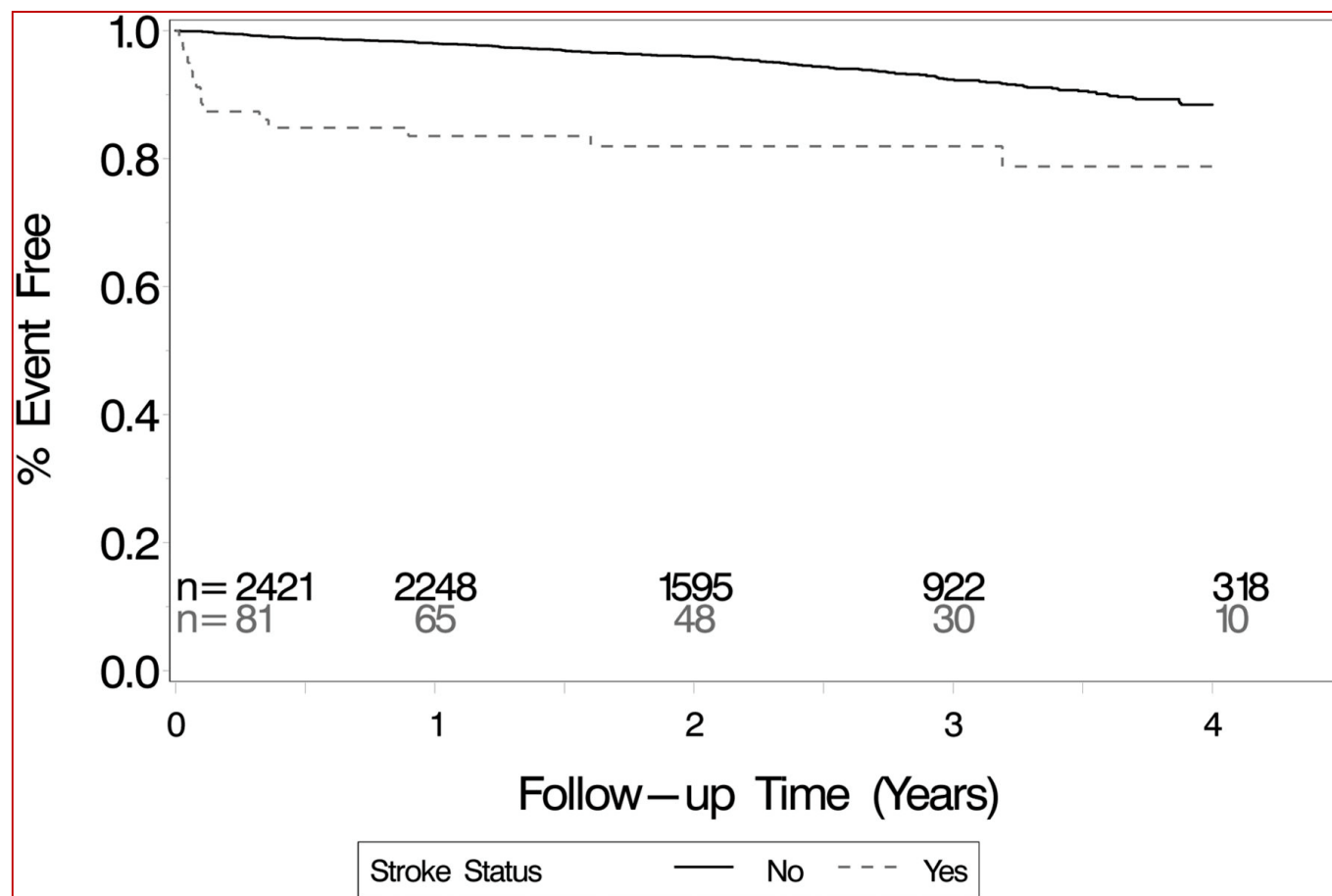
Myocardial infarction & cranial nerve palsy

	CAS	CEA	Risk ratio	P-value
EVA-3S & ICSS	N=1116	N=1114		
CREST	N=668	N=653		
Myocardial ischemia	0.4%	0.6%	0.66	n.s.
	1.0%	2.3%	0.45	0.08
Cranial nerve palsy	0.3%	5.7%*	0.02	0.001
	0.3%	4.7%	0.02	0.001

* 1/45 pts suffered a disabling nerve palsy

ITT

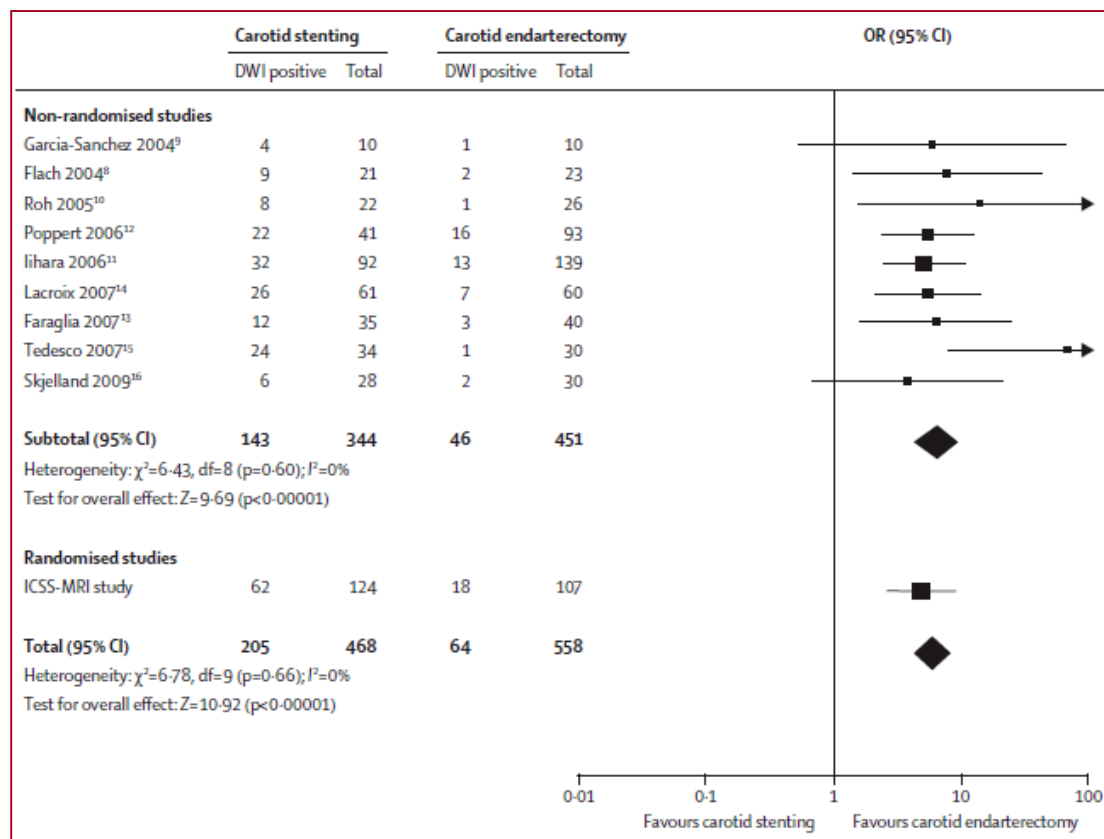
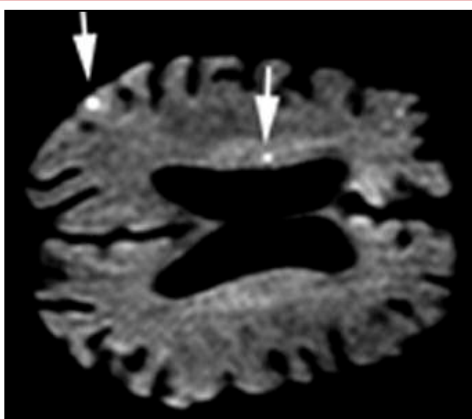
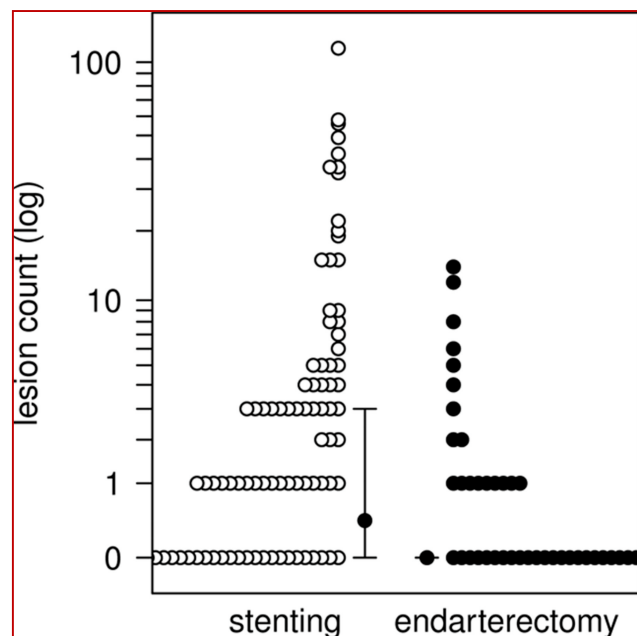
Long-term survival CREST



Late mortality (4 yrs)

CAS 94 (7.50 %) 6 MI (0.48 %)
CEA 83 (6.71 %) 7 MI (0.56 %)

Open issues: Ischemic lesions on DWI MRI



SVS registry 2005 -2010

Table IV. Thirty-day outcomes for symptomatic and asymptomatic patients ≥ 65 years by treatment arm^a

30-day events	Symptomatic, % (n)			Asymptomatic, % (n)		
	CEA (n = 585)	CAS (n = 443)	P ^b	CEA (n = 762)	CAS (n = 428)	P ^b
Death	0.68 (4)	0.92 (4)	.7290	0.79 (6)	1.40 (6)	.3679
Stroke	4.79 (28)	4.62 (20)	>.9999	1.31 (10)	2.34 (10)	.2394
MI	0.17 (1)	0.69 (3)	.3177	0.39 (3)	1.17 (5)	.1447
Death/Stroke/MI	5.47 (32)	6.00 (26)	.7848	2.49 (19)	4.91 (19)	.0306

Table IX. Thirty-day outcomes for symptomatic and asymptomatic patients < 65 years by treatment arm^a

30-day events	Symptomatic, % (n)			Asymptomatic, % (n)		
	CEA (n = 1513)	CAS (n = 1114)	P ^b	CEA (n = 2656)	CAS (n = 1422)	P ^b
Death	1.26 (19)	2.42 (27)	.0340	0.72 (19)	1.62 (23)	.0087
Stroke	3.77 (57)	6.73 (75)	.0008	1.81 (48)	3.45 (49)	.0016
MI	1.72 (26)	1.62 (18)	.8789	1.20 (32)	1.05 (15)	.7591
Death/Stroke/MI	5.05 (80)	6.53 (80)	.0007	3.31 (88)	5.52 (75)	.0037

ESC guidelines 2011

Symptomatic stenosis

In patients with symptomatic 70-99% stenosis of the internal carotid artery, CAS is recommended for the prevention of recurrent stroke.	I	A
In symptomatic patients at high surgical risk requiring revascularization, CAS should be considered as an alternative to CEA.	IIa	B
In symptomatic patients requiring carotid revascularization, CAS may be considered as an alternative to CEA in high-volume centres with documented death or stroke rate <6%.	IIb	B

Asymptomatic stenosis

In asymptomatic patients with carotid artery stenosis $\geq 60\%$, CAS should be considered as long as the perioperative stroke and death rate for procedures performed by the surgical team is <3% and the patient's life expectancy exceeds 5 years.	IIa	A
In asymptomatic patients with an indication for carotid revascularization, CAS may be considered as an alternative to CEA in high-volume centres with documented death or stroke rate <3%.	IIb	B

Conclusions

The periprocedural risk of stroke and death is higher after CAS than after CEA particularly in patients older than 70 years.

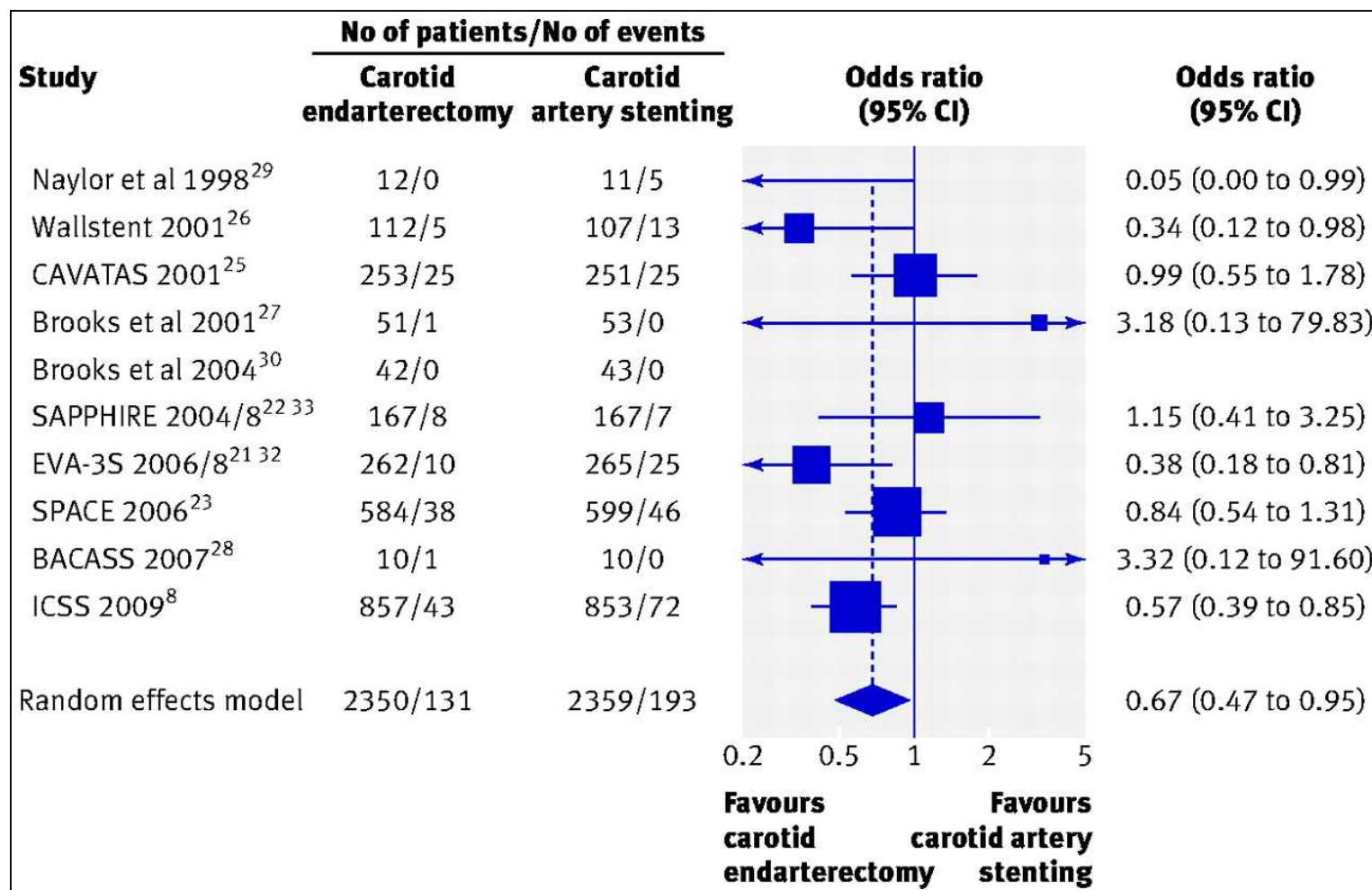
The risk of CAS compared with CEA appears greatest in patients treated within 7 days of symptoms.

The relevance of an increased incidence of myocardial ischemia after CEA seems overestimated, the relevance of increased silent cerebral ischemic lesions after CAS has to be validated.

Thus, carotid endarterectomy is safer than carotid stenting for the majority of patients with symptomatic stenosis.

There are not sufficient data currently to adapt these results for patients with asymptomatic carotid stenoses.

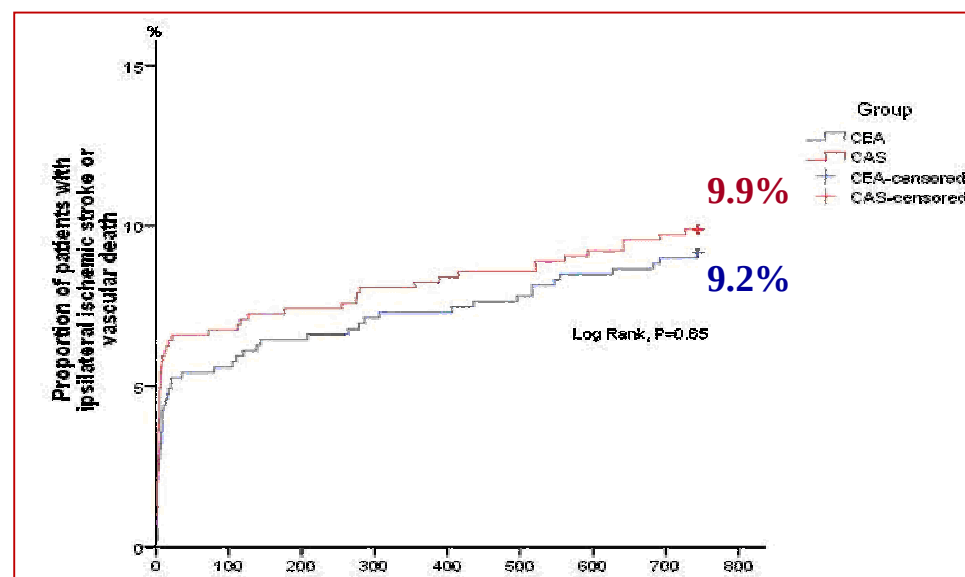
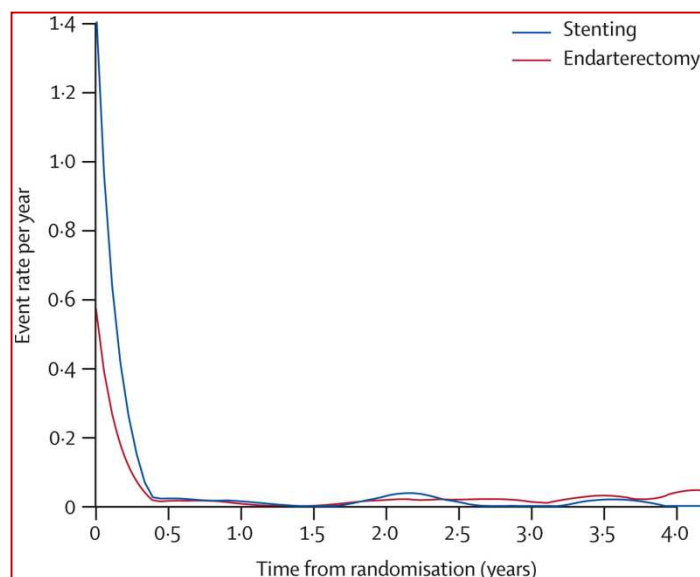
CEA vs CAS - RCTs 2009



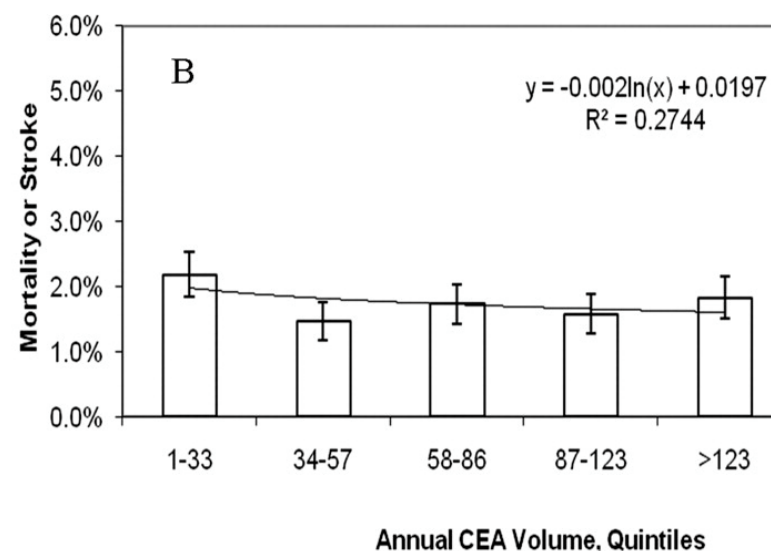
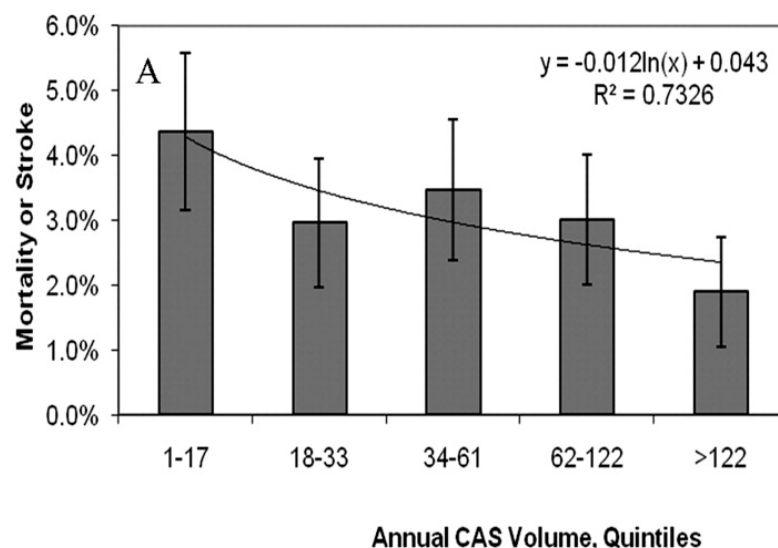
Long-term events CAS vs CEA

Table 3. Intermediate to Long-Term Events Comparing Carotid Artery Stenting vs Carotid Endarterectomy and Excluding Periprocedural Events

Outcome	OR (95% CI)			I^2	$P_{\text{Interaction}}$
	Overall	Symptomatic	Asymptomatic		
Death or any stroke	0.98 (0.79-1.22)	1.03 (0.82-1.29)	0.69 (0.37-1.28)	0.0	.23
Death or ipsilateral stroke	0.99 (0.81-1.23)	1.04 (0.83-1.30)	0.67 (0.35-1.28)	0.0	.21
Any stroke	1.20 (0.86-1.67)	1.25 (0.88-1.78)	0.76 (0.26-2.23)	4.5	.39
Ipsilateral stroke	1.19 (0.78-1.82)	1.27 (0.82-1.98)	0.61 (0.15-2.50)	0.0	.33



Medicare/Medicaid 2005 - 2007 (NY & CA 47.752 pts.)



Periop. stroke & death:	asymptomatic	2.4 vs 1.9%	p=0.15
	symptomatic	8.3 vs 4.6%	p=0.01

CAS is equivalent to CEA in asymptomatic and inferior in symptomatic patients

Death and stroke within 30 days of randomisation

