

Restenosis and its impact on recurrent stroke risks after CAS and CEA for symptomatic carotid stenosis – results from the International Carotid Stenting Study

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For the ICSS Investigators

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Disclosures

- Bayer, Amgen, Claret Medical: travel, advisory boards, consultancy
- AstraZeneca: investigator-initiated research grant
- Member of the International Carotid Stenting Study (ICSS) Group
- Steering Committee Member of the 2nd European Carotid Surgery Trial (ECST-2)
- Co-Principal Investigator of the 2nd Asymptomatic Carotid Surgery Trial (ACST-2)
- Steering Committee Member of the Carotid Stenosis Trialists Collaboration (CSTC)

Background and aim

- Carotid artery stenting (CAS) is an alternative to carotid endarterectomy (CEA) for treatment of carotid stenosis.
- Recent trials in symptomatic carotid disease showed no difference in severe carotid restenosis, but a possible increase in moderate restenosis after CAS vs. CEA.
- It remained unclear if restenosis causes stroke.
- We compared rates of moderate and severe carotid restenosis and its impact on recurrent stroke up to 10 years after CAS or CEA in the International Carotid Stenting Study (ICSS).

International Carotid Stenting Study (ICSS)

- CAS versus CEA for symptomatic, at least moderate ($\geq 50\%$) atherosclerotic carotid stenosis.
- 50 centers, 1713 patients randomised 2000 – 2008, maximum follow-up 10 years.
- Carotid duplex ultrasound at clinical follow-up visits 1 month after treatment, 6 months and annually after randomisation.
- Duplex flow velocities recorded in common and internal carotid artery (CCA, ICA), and reported to study office.

Flow velocity criteria for degree of restenosis

Stenosis (%)	PSV ICA (m/s)	EDV ICA (m/s)	PSV ICA / CCA
<50	<1.3	<0.4	<3.2
50 – 59	>1.3 – 2.1	<0.4	<3.2
60 – 69	>1.3 – 2.1	0.4 – 1.1	3.2 – 4.0
70 – 79	>2.1	>1.1 – 1.4	>4.0
80 – 95	>2.1	>1.4	>4.0
96 – 99	String Flow		
100	Occlusion		

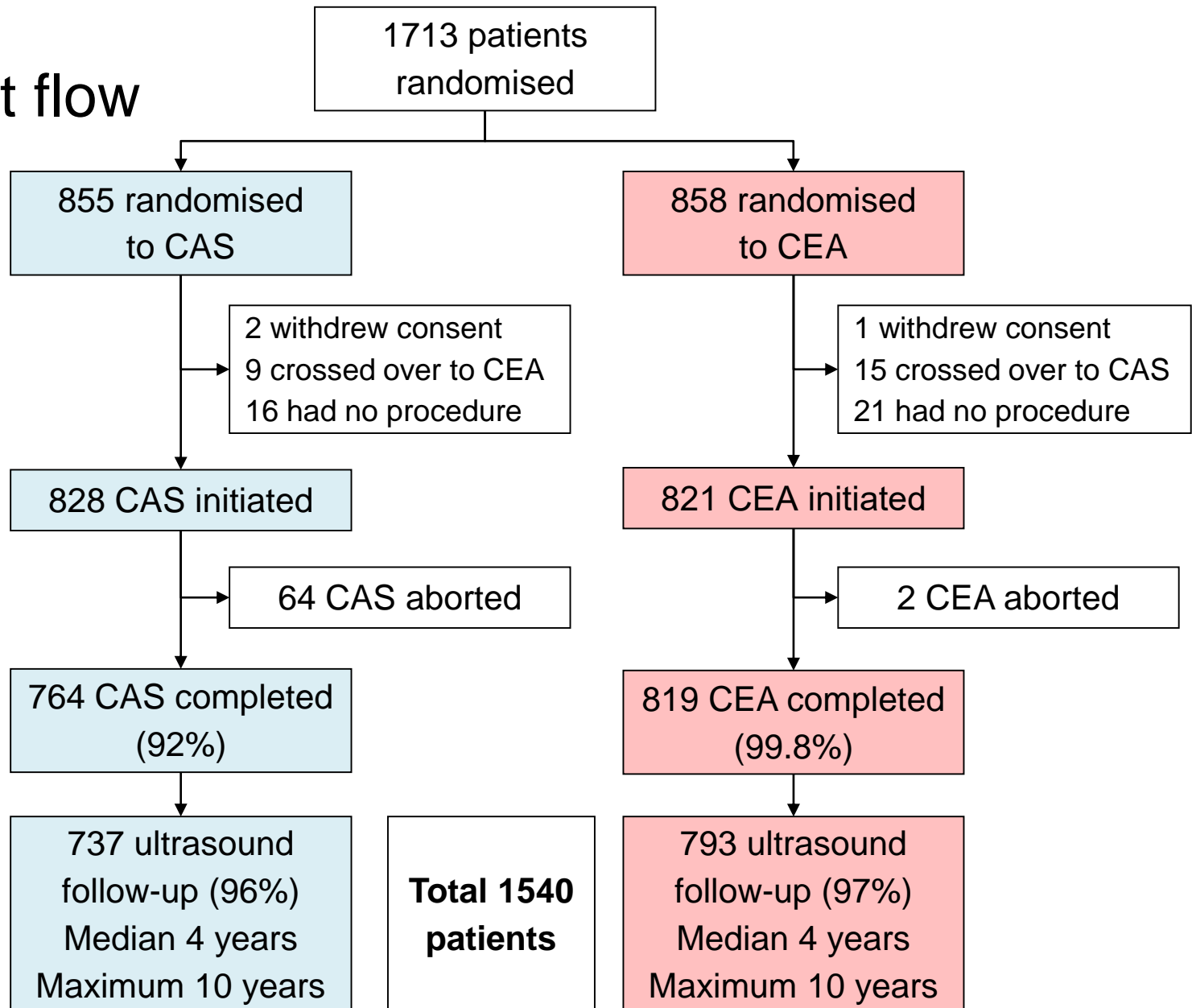
Comparison of restenosis between CAS and CEA

- Comparison of residual or recurrent carotid stenosis (**restenosis**) or occlusion after *completed* CAS versus CEA:
 - CAS: stent placed across stenosis
 - CEA: plaque removed and arteriotomy closed
- Generalised non-linear model, interval-censored
- Adjustment for patient baseline characteristics independently associated with restenosis
- Restenosis outcomes:
 - Moderate ($\geq 50\%$) or higher restenosis or occlusion
 - Severe ($\geq 70\%$) restenosis or occlusion

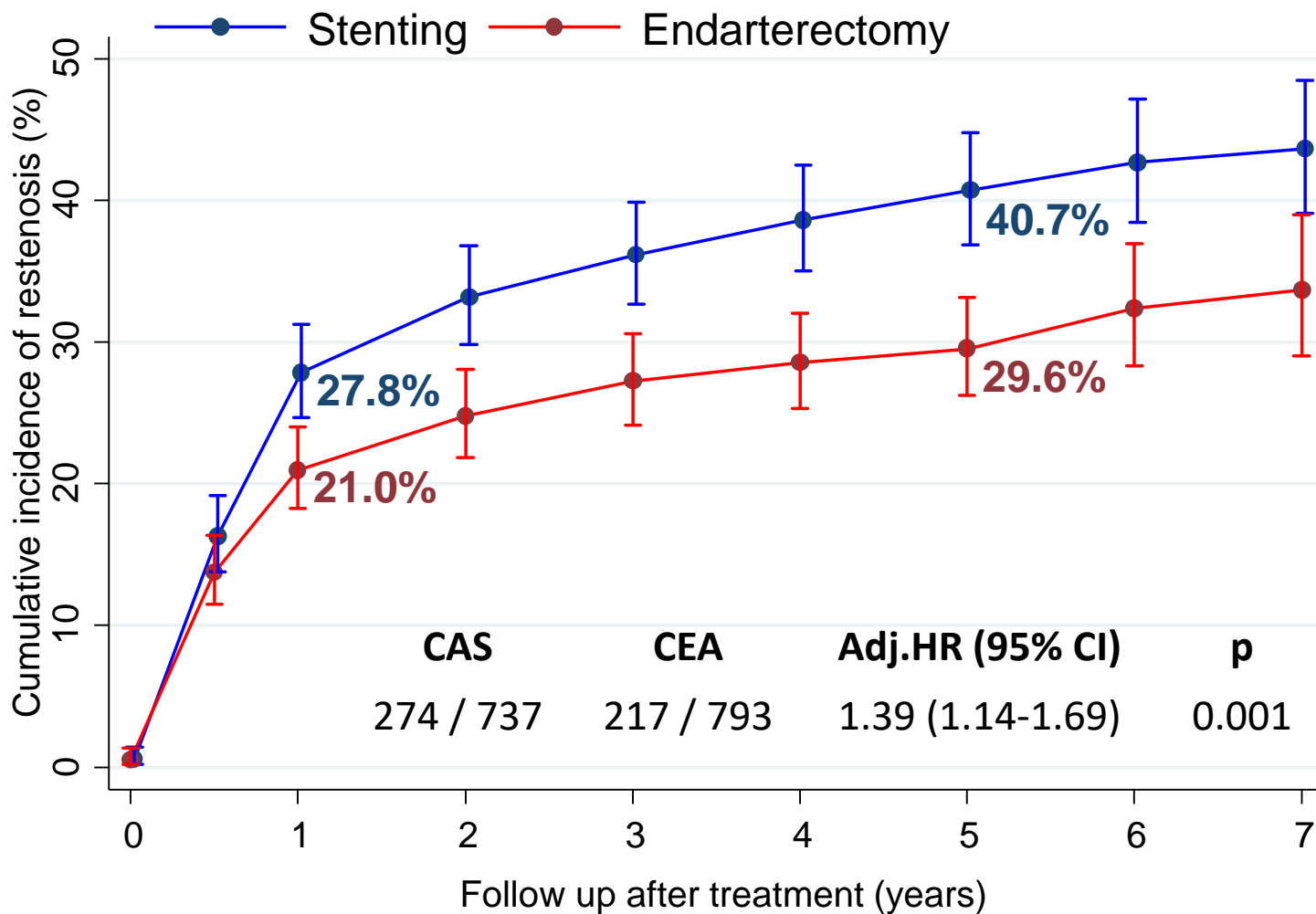
Restenosis and stroke risk

- Risk of **ipsilateral stroke** before and after diagnosis of restenosis
- Cox regression models, time-updated covariate
 - Planned for $\geq 50\%$ and $\geq 70\%$ restenosis
 - In both treatment groups combined
 - In the CAS and CEA group separately

Patient flow



Moderate ($\geq 50\%$) or higher restenosis or occlusion



CAS

274 / 737

CEA

217 / 793

Adj.HR (95% CI)

1.39 (1.14-1.69)

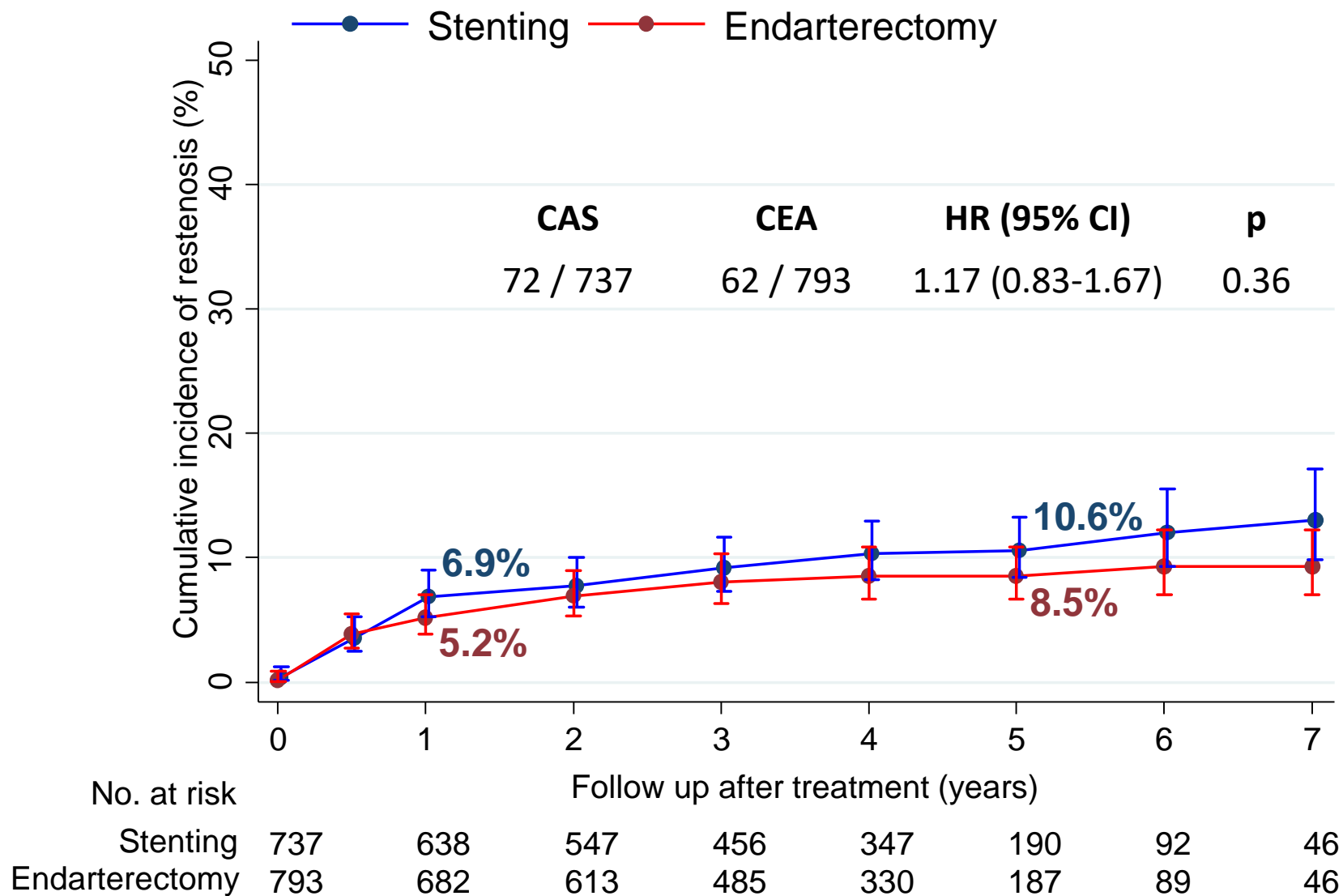
p

0.001

No. at risk

Stenting	737	496	407	333	245	137	63	33
Endarterectomy	793	568	502	399	269	149	70	36

Severe ($\geq 70\%$) restenosis or occlusion



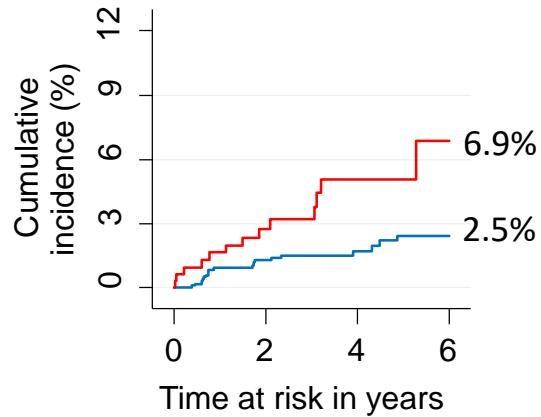
≥50% Restenosis and risk of ipsilateral stroke

— Before restenosis — After restenosis

Both trial arms

HR 2.98 (1.39 - 6.40)

P=0.005



N at risk

1136	773	455	132	Before restenosis
322	227	105	34	After restenosis

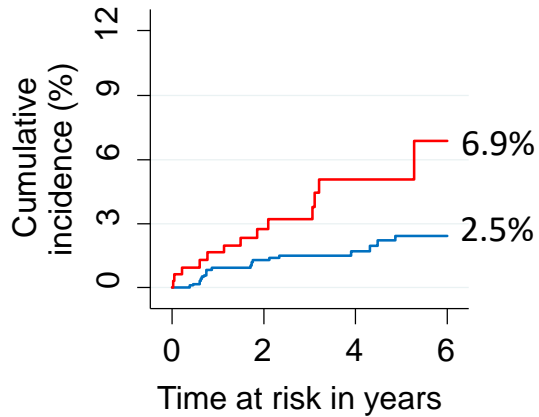
≥50% Restenosis and risk of ipsilateral stroke

— Before restenosis — After restenosis

Both trial arms

HR 2.98 (1.39 - 6.40)

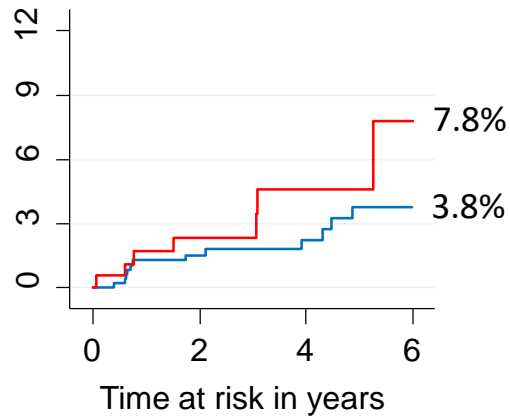
P=0.005



Stenting

HR 2.06 (0.75 - 5.63)

P=0.161



N at risk

1136	773	455	132	Before restenosis	550	348	207	67
322	227	105	34	After restenosis	185	131	57	19

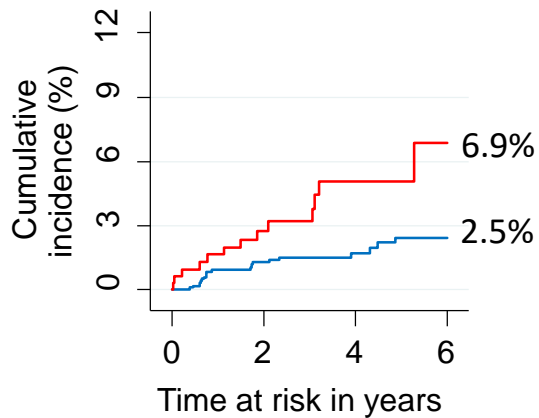
≥50% Restenosis and risk of ipsilateral stroke

— Before restenosis — After restenosis

Both trial arms

HR 2.98 (1.39 - 6.40)

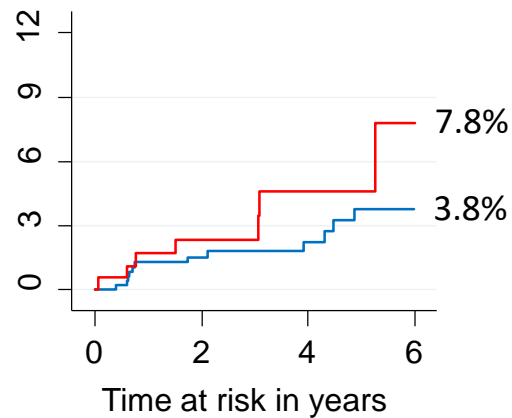
P=0.005



Stenting

HR 2.06 (0.75 - 5.63)

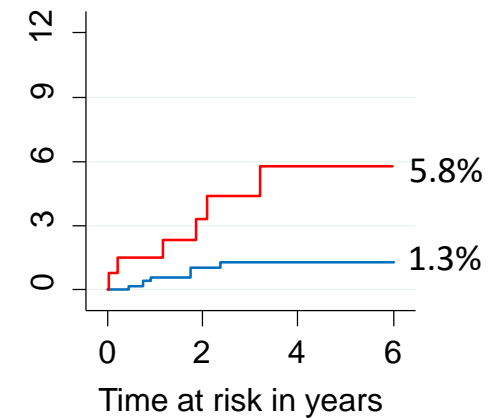
P=0.161



Endarterectomy

HR 5.83 (1.76 - 19.33)

P=0.004



N at risk

1136	773	455	132	Before restenosis	550	348	207	67
322	227	105	34	After restenosis	185	131	57	19

586	425	248	65
137	96	48	15

Interaction restenosis x treatment: P=0.1

≥70% Restenosis and risk of ipsilateral stroke

- No significant increase in all patients, CAS only, or CEA only
- Possibly due to lack of power

Summary and conclusion

- Greater incidence of moderate ($\geq 50\%$) or higher restenosis or occlusion after CAS versus CEA.
- Treatments similarly effective at preventing severe ($\geq 70\%$) restenosis or occlusion.
- Ipsilateral stroke risk is increased in patients with $\geq 50\%$ restenosis, particularly in the CEA group.
- Between-treatment differences might indicate differences in pathogenesis of restenosis.
- Pooled analyses of trial data are warranted to corroborate these findings and to determine restenosis cut-off identifying patients at risk.