

The procedural risk of carotid revascularisation declined over time

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Data from the Carotid Stenosis Trialists' Collaboration

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Disclosure

Speaker name:

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I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

- I do not have any potential conflict of interest**

Background

- Risk of stroke associated with carotid disease decreased over the past decades
- So far, it has been unclear whether the procedural risk of revascularisation (carotid endarterectomy and carotid artery stenting) also decreased over time

NASCET Collaborators, *N Engl J Med.* 1991;325:445–453; Ederle et al. *Lancet.* 2010;375:985–997; Alberts et al. *Stroke.* 2001;32:325; Brott et al. *N Engl J Med.* 2010;363:11–23.

Aim

To analyse changes in procedural risk of stroke or death over time in patients with symptomatic carotid stenosis treated with carotid endarterectomy (CEA) or carotid artery stenting (CAS)

Methods

- Individual patient data (IPD) meta-analysis with data from 4 trials (EVA 3-S, SPACE, ICSS and CREST)
- Randomised clinical trials with blinded outcome adjudication
- Patients were randomised 1:1 to endarterectomy or carotid stenting
- We included patients with
 - Symptomatic carotid stenosis
 - Moderate or severe degree of carotid stenosis
 - Normal surgical risk

Methods (continued)

- Per protocol analysis: all patients in whom randomly allocated treatment was initiated
- Change in baseline characteristics over years of recruitment
- Primary outcome measure: any procedural **stroke or death** (occurring within 30 days after treatment)
- Generalised linear mixed-effects (GLM) model with a random intercept for each source trial
 - Change in procedural CAS risk over time
 - Change in procedural CEA risk over time
 - Change in CAS vs CEA treatment effect over time
- Adjustment for age and other baseline characteristics predicting treatment risk (e.g. hypertension, diabetes mellitus etc.)

Results

- 4775 patients with symptomatic carotid stenosis were enrolled in 4 trials
- 4597 patients were included in the per protocol analysis
 - **ICSS** (International Carotid Stenting Study): **1649** patients
 - **CREST** (Carotid Revascularization Endarterectomy versus Stenting Trial): **1273** patients
 - **SPACE** (Stent-Protected Angioplasty versus Carotid Endarterectomy): **1158** patients
 - **EVA-3S** (Endarterectomy vs. Angioplasty in Patients with Symptomatic Severe Carotid Stenosis): **517** patients

Baseline characteristics by year of treatment

| | 2000-04 (n = 2044) | 2005-08 (n = 2553) | p-value |
|---|-----------------------|-----------------------|---------|
| Male | 69.8% | 69.8% | ns |
| Age, <i>years</i> (mean, SD) | 69.2 ± 9.4 | 69.3 ± 9.1 | ns |
| Systolic blood pressure at baseline, <i>mmHg</i> (mean, SD) | 143.7 ± 20 | 143.1 ± 22 | ns |
| Hypertension | 73.8% | 77% | 0.015 |
| Diabetes | 25.8% | 24.4% | ns |
| Hyperlipidaemia or LLT* | 57.4% | 68.9% | <0.001 |
| Smoking (current or past) | 62.0% | 67.3% | <0.001 |
| Coronary artery disease | 26.2% | 29.3% | 0.025 |
| mRS* at baseline (mean, SD) | 0.76 ± 0.9 | 0.85 ± 1.03 | 0.002 |

LLT – lipid lowering therapy; mRS – modified Rankin Scale; ns – not significant

Baseline characteristics by year of treatment (continued)

| | 2000-04 (n = 2044) | 2005-08 (n = 2553) | p-value |
|--|-----------------------|-----------------------|---------|
| Degree of ipsilateral carotid stenosis | | | <0.001 |
| Moderate (50-69%) | 22.4% | 16.7% | |
| Severe (70-99%) | 77.6% | 83.3% | |
| Contralateral stenosis or occlusion | 14.5% | 15.0% | ns |
| Qualifying event type | | | ns |
| Retinal ischaemia | 15.7% | 18.3% | |
| Transient ischaemic attack | 37.9% | 36.0% | |
| Hemispheric stroke | 46.4% | 45.8% | |

ns – not significant

Procedural risk for stroke or death: crude risks over time

| Year of treatment | All patients (n = 4597) | Endarterectomy (n = 2271) | Stenting (n = 2326) |
|-------------------|----------------------------|------------------------------|------------------------|
| 2000-2002 | 7.7% | 7.1% | 8.2% |
| 2003 | 6.5% | 5.5% | 7.6% |
| 2004 | 4.5% | 3.2% | 5.8% |
| 2005 | 6.3% | 3.2% | 9.2% |
| 2006 | 5.9% | 4.2% | 7.5% |
| 2007-2008 | 3.9% | 2.0% | 5.8% |

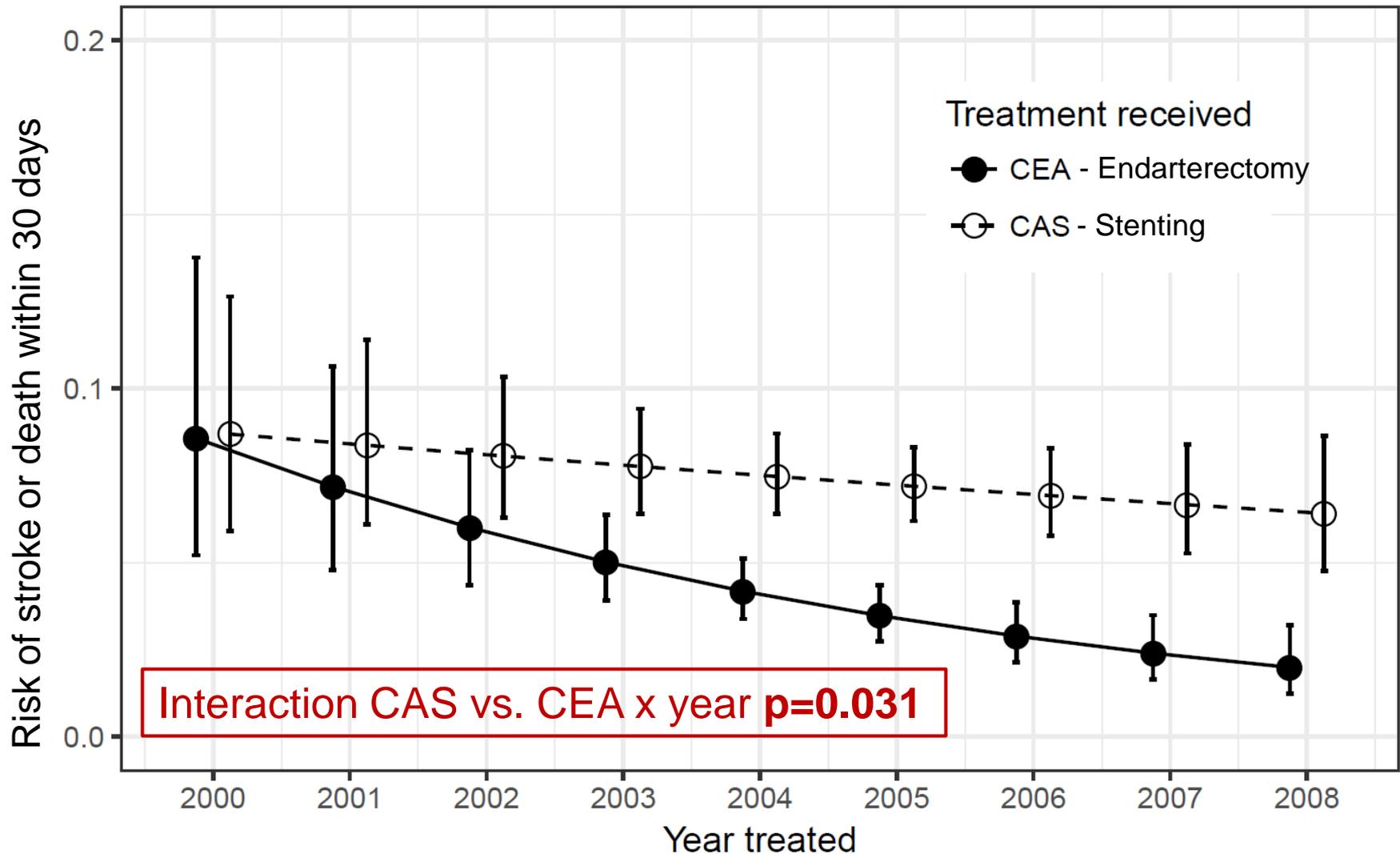
Effect of treatment year on procedural risk (GLM model)

| | All patients | Endarterectomy | Stenting |
|--------------------------|-------------------|-------------------|-------------------|
| Unadjusted effect | n = 4597 | n = 2271 | n = 2326 |
| OR (95% CI) | 0.910 (0.85-0.97) | 0.822 (0.73-0.92) | 0.959 (0.88-1.04) |
| p-value | 0.0057 | 0.0032 | 0.33 |

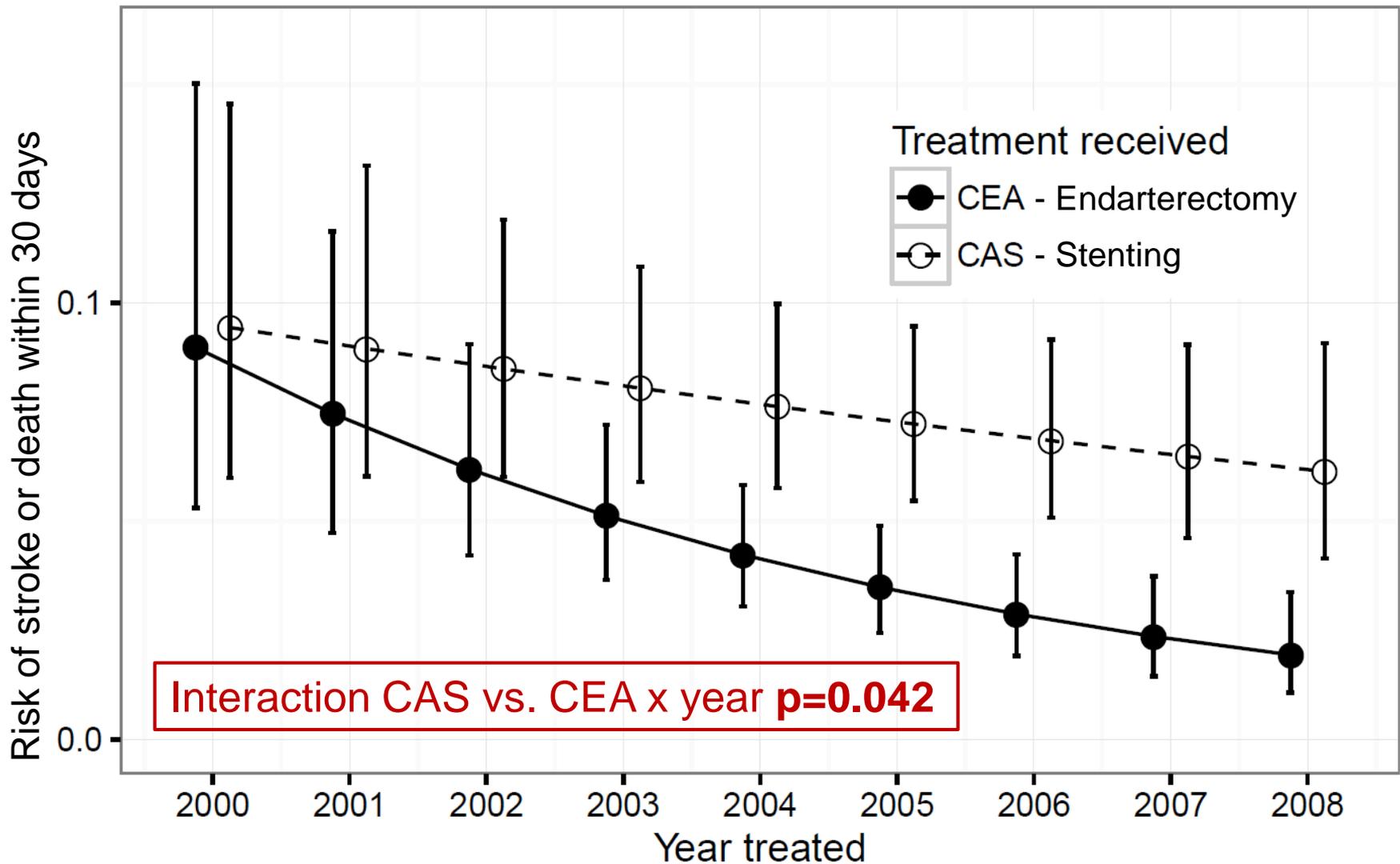
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| p-value | 0.0057 | 0.0032 | 0.33 |
| Adjusted effect* | n = 4461 | n = 2005 | n = 2311 |
| OR (95% CI) | 0.813 (0.72-0.91) | 0.816 (0.72-0.93) | 0.963 (0.89-1.05) |
| p-value | <0.001 | 0.002 | 0.299 |
| *Adjusted for: | mRS Hypertension Age Diabetes Hyperlipidaemia /LLT Coronary heart disease Ipsilateral severe carotid stenosis | mRS Hypertension Diabetes Coronary heart disease Ipsilateral severe carotid stenosis Contralateral stenosis/occlusion | Age Diabetes Hyperlipidaemia /LLT Ipsilateral severe carotid stenosis Qualifying event type |

Development in risk of stroke or death: modelled risks over time – unadjusted



Development in risk of stroke or death: modelled risks over time – adjusted



Summary

- Increase in some vascular risk factors over the years of recruitment in the source trials
- Risk of procedural stroke or death associated with carotid revascularisation decreased over time - independent of clinical risk factors
- The decrease in procedural risk over time was greater in the endarterectomy group than in the stenting group

Conclusion

- Treatment of symptomatic carotid stenosis within the examined trials became safer over time.
- The risk reduction was especially driven by a decrease of procedural risk in patients treated with endarterectomy.
- Mechanisms underlying this decrease remain to be investigated.

Thank you for your attention!

