



UMC Utrecht

# Short-term safety of carotid revascularisation in patients with a history of coronary heart disease

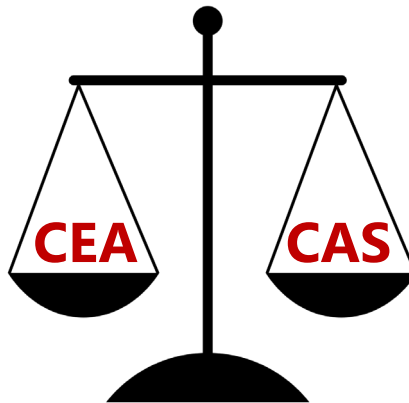
Carotid Stenosis Trialists' Collaboration

Munich Vascular Conference 2018



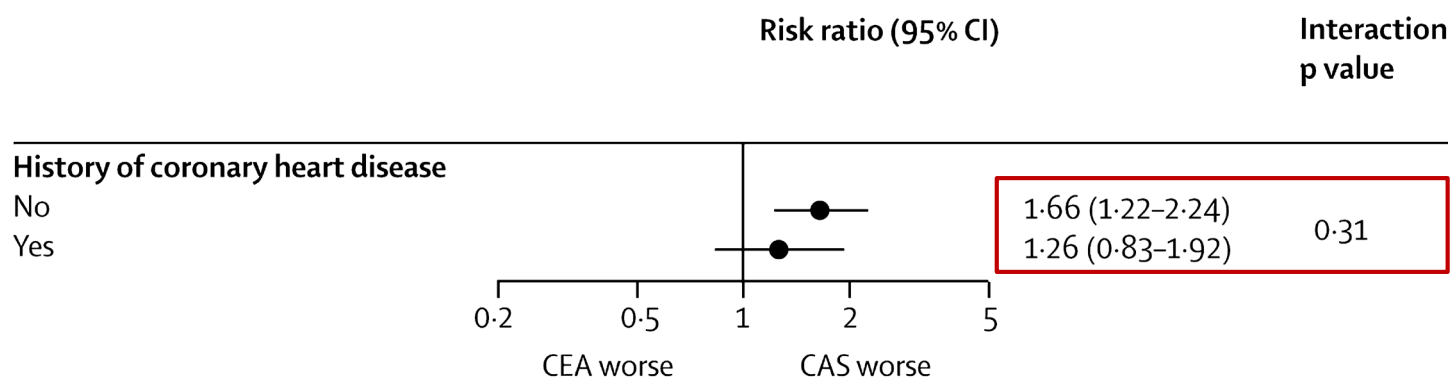
# Background

- Carotid revascularisation for symptomatic carotid artery stenosis
  - 30-day stroke or death risk higher after carotid artery stenting (CAS) than after carotid endarterectomy (CEA)
  - Long-term ipsilateral stroke risk similar
- What patient characteristics modify short-term complication risk?



# Background – History of coronary heart dis. (CHD)

- 120-day risk of stroke or death (sub-analysis 3 RCTs)

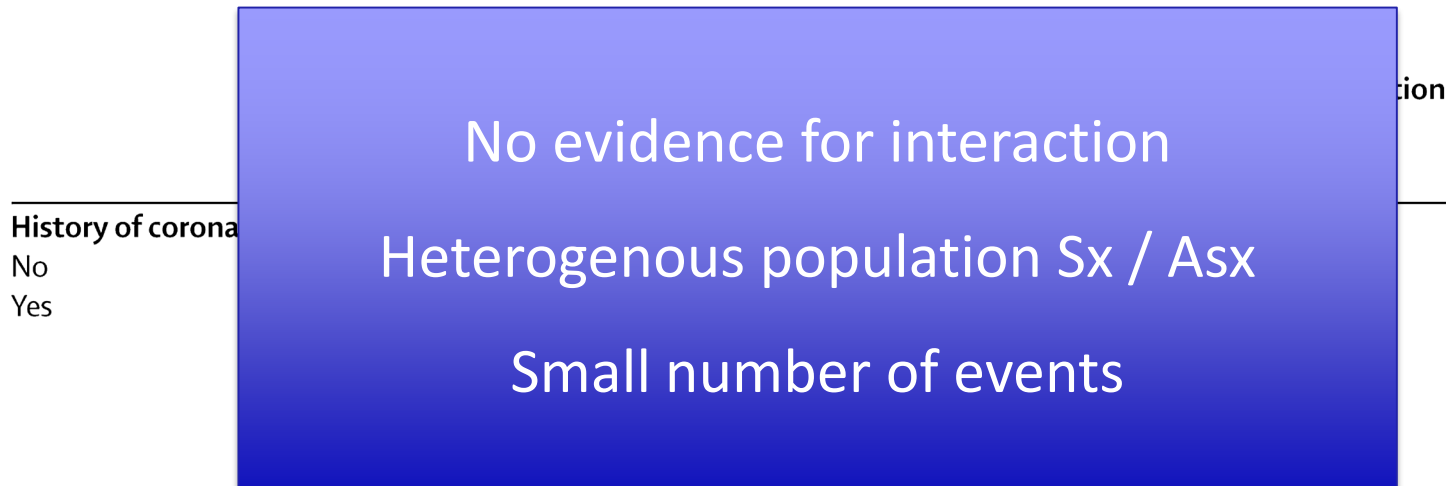


- 30-day risk of myocardial infarction (history of CHD yes vs. no)
  - CEA: RR 2.90 (95% CI 1.54-5.47)
  - CAS: RR 1.00 (95% CI 0.18-5.62)



# Background – History of coronary heart dis. (CHD)

- 120-day risk of stroke or death

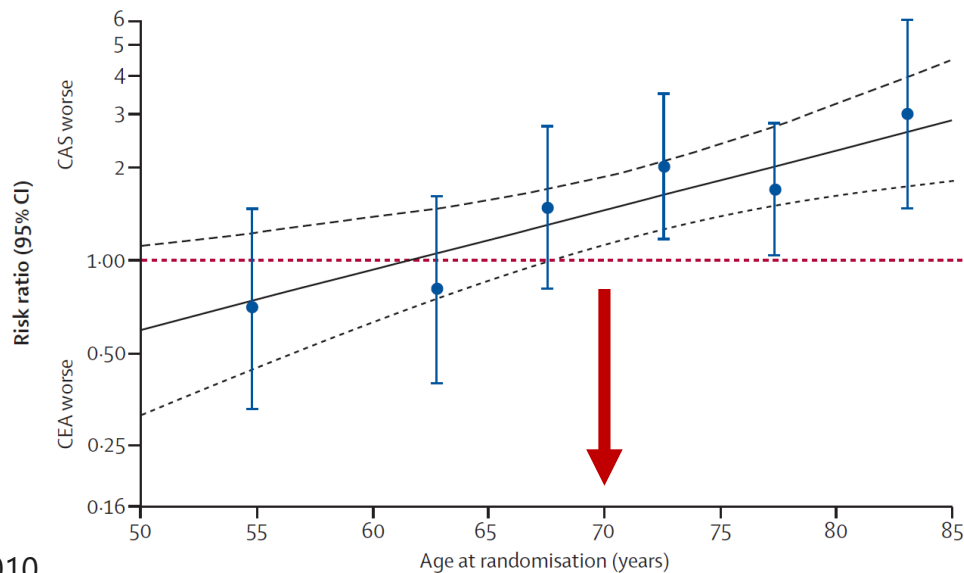


- 30-day risk of myocardial infarction (history of CHD yes vs. no)
  - CEA: RR 2.90 (95% CI 1.54-5.47)
  - CAS: RR 1.00 (95% CI 0.18-5.62)



# Aims

- To investigate whether safety of CAS vs. CEA differs between patients with and without history of CHD
- To investigate whether the impact of age on short-term safety of CAS vs. CEA differs between patients with and without history of CHD



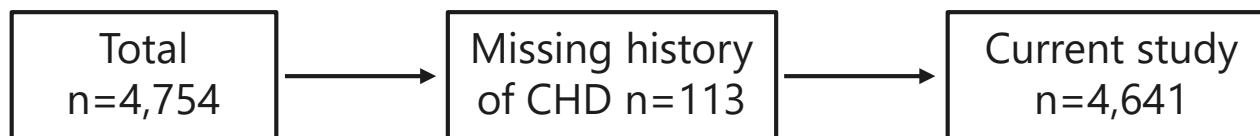
History of CHD?



# Methods

- Data from Carotid Stenosis Trialists' Collaboration

Trial	Recruitment period	Number of patients	Definition of history of CHD
EVA-3S	2000-2005	527	History of myocardial infarction, or Any type of previous coronary revascularisation
SPACE	2001-2006	1,196	History of CHD (not further specified)
ICSS	2001-2008	1,710	History of angina, or History of myocardial infarction, or Previous coronary artery bypass grafting
CREST	2000-2008	1,321	History of angina, or History of myocardial infarction, or Previous coronary artery bypass grafting



# Methods

- Outcome measures:
  - Primary: stroke or death  $\leq 30$  days after procedure
    - ↳ Per-protocol analysis in all 4 trials
  - Secondary: stroke, MI or death  $\leq 30$  days after procedure
    - ↳ Per-protocol analysis in EVA-3S, SPACE, and ICSS
- Cox regression analysis adjusted for trial
- Age classified into three groups:  $<70$ ,  $70-74$ ,  $\geq 75$  years



# Results

- 1,293/4,641 (28%) with history of CHD
  - Range 18-38%

Baseline characteristics	History of CHD	
	Yes (n=1,293)	No (n=3,348)
Age at randomisation in years, mean (SD)	70.6 ( $\pm$ 8.7)	68.8 ( $\pm$ 9.4)
Male sex, n (%)	995 (77%)	2,243 (67%)
History of, n (%)		
Hypertension	1,083 (84%)	2,414 (72%)
Hyperlipidaemia	1,003 (78%)	1,951 (58%)
Diabetes	415 (32%)	754 (23%)
Current smoking	241 (19%)	950 (28%)
Stroke or TIA	192 (34%)	565 (34%)
Peripheral artery disease	126 (23%)	219 (13%)



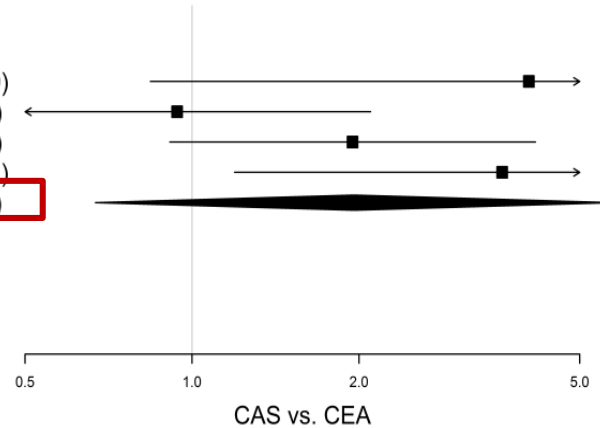


# Results – primary outcome

- Stroke or death  $\leq 30$  days: n=251/4,486 (5.6%)

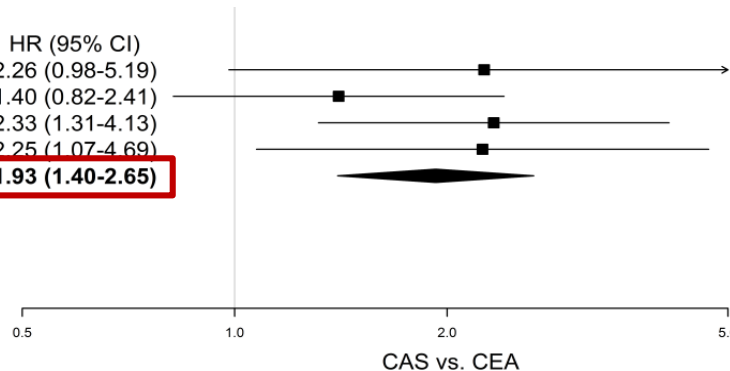
CHD	CAS		CEA		HR (95% CI)
Study	Events	Total	Events	Total	
EVA-3S	7 (15.9%)	44	2 (4.2%)	48	4.05 (0.84-19.49)
SPACE	11 (8.9%)	124	13 (9.5%)	137	0.94 (0.42-2.10)
ICSS	20 (8.6%)	232	10 (4.6%)	219	1.95 (0.91-4.16)
CREST	14 (6.2%)	225	4 (1.8%)	226	3.62 (1.19-11.01)
<b>Pooled</b>	<b>52 (8.3%)</b>	<b>625</b>	<b>29 (4.6%)</b>	<b>630</b>	<b>1.96 (0.67-5.73)</b>

Heterogeneity:  
 Q=5.1004 (df=3),  
 p-value=0.1646,  
 I-square=41.2%



No CHD	CAS		CEA		HR (95% CI)
Study	Events	Total	Events	Total	
EVA-3S	18 (8.4%)	215	8 (3.8%)	209	2.26 (0.98-5.19)
SPACE	33 (7.1%)	466	22 (5.1%)	429	1.40 (0.82-2.41)
ICSS	38 (6.5%)	584	17 (2.9%)	595	2.33 (1.31-4.13)
CREST	24 (6.3%)	382	10 (2.8%)	351	2.25 (1.07-4.69)
<b>Pooled</b>	<b>113 (6.9%)</b>	<b>1,647</b>	<b>57 (3.6%)</b>	<b>1,584</b>	<b>1.93 (1.40-2.65)</b>

Heterogeneity:  
 Q=2.0475 (df=3),  
 p-value=0.5626,  
 I-square=1.0%



- Interaction p-value (treatment \* history of CHD): 0.89



## Results – secondary outcome

- Stroke, myocardial infarction or death  $\leq 30$  days:  
n=206/3,302 (6.2%) in EVA-3S, SPACE, and ICSS
  - Only n=8 non-fatal myocardial infarction
- Results essentially the same
  - History of CHD: CAS vs. CEA HR 1.44 (95% CI 0.87-2.38)
  - No history of CHD: CAS vs. CEA HR 1.74 (95% CI 1.23-2.46)
- Interaction p-value (treatment \* history of CHD): 0.57



# Results

- Stroke or death  $\leq 30$  days

Age	CAS		CEA		All CAS-CEA HR (95% CI)	Total, n	Interaction Treatment * history of CHD
	Events, n (%)	Total, n	Events, n (%)	Total, n			
<b>CHD</b>							
<70	18 (6.2%)	288	10 (3.6%)	276	1.71 (0.79-3.71)	564	0.26
70-74	11 (8.1%)	135	9 (7.3%)	124	1.09 (0.45-2.65)	259	
$\geq 75$	23 (11.4%)	202	10 (4.3%)	230	2.78 (1.32-5.85)	432	
Total	52 (8.3%)	625	29 (4.6%)	630		1,255	
<b>No CHD</b>							
<70	32 (3.6%)	880	29 (3.5%)	833	1.05 (0.63-1.73)	1,713	0.008
70-74	38 (11.9%)	318	10 (3.6%)	279	3.62 (1.80-7.29)	597	
$\geq 75$	43 (9.6%)	449	18 (3.8%)	472	2.64 (1.52-4.59)	921	
Total	113 (6.9%)	1,647	57 (3.6%)	1,584		3,231	



# Results

- Stroke or death  $\leq 30$  days

Age	CAS		CEA		All	Interaction Treatment * history of CHD
	Events, n (%)	Total, n	Events, n (%)	Total, n	CAS-CEA HR (95% CI)	
CHD						
<70	18 (6.2%)	288	10 (3.6%)	276	1.71 (0.79-3.71)	0.26
70-74	11 (8.1%)	135	9 (7.3%)	124	1.09 (0.45-2.65)	
$\geq 75$	23 (11.4%)	202	10 (4.3%)	230	2.78 (1.32-5.85)	
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$\geq 75$	43 (9.6%)	449	18 (3.8%)	472	2.64 (1.52-4.59)	
Total	113 (6.9%)	1,647	57 (3.6%)	1,584		

- Three-way interaction p-value: 0.09 (age/treatment/CHD)



## + Strengths

- Pooled analysis of individual patient data
- Small number of patients with missing data

## — Limitations

- Inconsistent definitions of history of coronary heart disease
- Endpoint myocardial infarction unavailable for CREST
- Not enough data to classify age into smaller age groups



# Discussion

- History of CHD did not modify short-term safety of CAS compared with CEA
- CAS might be as safe as CEA until the age of 75 years in patients with history of CHD
- Caution: not consistent findings for modification of treatment effect in both the PP and ITT analyses and for primary and secondary outcome measures.



# Acknowledgements

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