XXII World Congress of Neurology
Santiago - Chile 2015
Changing Neurology Worldwide

UniversityHospital Heidelberg

Teaching Course Stroke TC 2

Update on extracranial carotid stenosis:

How best to diagnose, how best to treat?

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Disclosures

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- Member of the WSO, ESO, DGN, DSG, DGNI, DEGUM
- Secretary of the German Stroke Society
- National Coordinator of SITS
- **Clinical Coordinator of SPACE,**
  Member of the Steering-Committee of SPACE-2
- Member of the Steering-Committee of ECASS4
- Member of the Ethics Committee of the Medical Faculty of Heidelberg
- Lecture-fees and travel-expenses from Bayer, Boehringer Ingelheim, Covidien, Daiichi Sankyo, Ferrer, Glaxo Smith Kline, Lilly, Paion, Sanofi

Objective

Carotid artery stenosis (CS)

- Learn about validity of non-invasive diagnostic tools
- Discussion about the validity of older trials for treatment of asymptomatic CS
- Comparison of carotid artery stenting (CAS) and carotid endarterectomy (CEA) for treatment of patients with asymptomatic or symptomatic CS
- Learn about patient characteristic, which justify CAS in patients with symptomatic CS

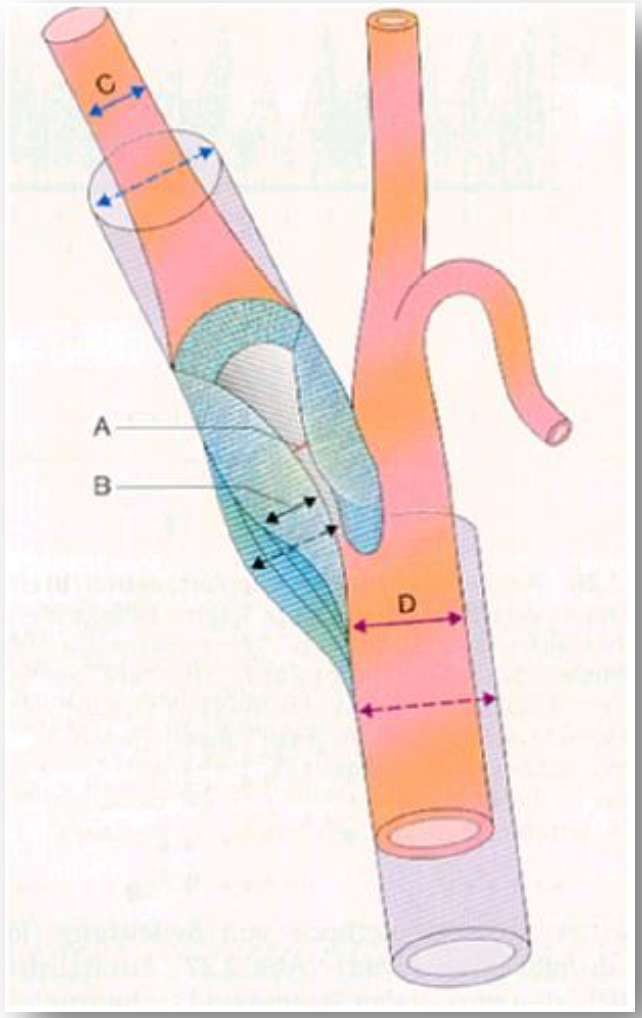
Agenda

Carotid artery stenosis

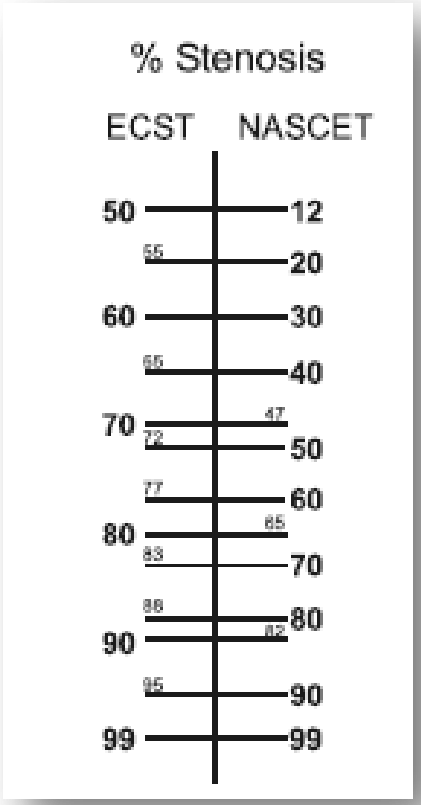
- Diagnosis
- Case-Discussion
- Trial-Summary
- Subgroup-Discussion
- Summary

Carotid artery stenosis

Quantification



- ECST (1 - A / B) x 100%
- NASCET (1 - A / C) x 100%



Nicolaides AN et al.: Eur J Vasc Endovasc Surg (2005) 30:275-284

Carotid artery stenosis

Comparison of non-invasive methods with DSA

	DUS	CTA	MRA	CEMRA
70–99% stenosis				
Sensitivity (95% CI)	0·89 (0·85–0·92	0·77 (0·68–0·84)	0·88 (0·82–0·92)	0·94 (0·88–0·97)
Specificity (95% CI)	0·84 (0·77–0·89)	0·95 (0·91–0·97)	0·84 (0·76–0·97)	0·93 (0·89–0·96)
50–69% stenosis				
Sensitivity (95% CI)	0·36 (0·25–0·49)	0·67 (0·30–0·90)	0·37 (0·26–0·49)	0·77 (0·59–0·89)
Specificity (95% CI)	0·91 (0·87–0·94)	0·79 (0·63–0·89)	0·91 (0·78–0·97)	0·97 (0·93–0·99)
0–49% stenosis or 100% occluded				
Sensitivity (95% CI)	0·83 (0·73–0·90)	0·81 (0·59–0·93)	0·81 (0·70–0·88)	0·96 (0·90–0·99)
Specificity (95% CI)	0·84 (0·62–0·95)	0·91 (0·74–0·98)	0·88 (0·76–0·95)	0·96 (0·90–0·99)

Wardlaw JM, et al.: Lancet 2006; 367: 1503-1512

Carotid artery stenosis

Ultrasound grading

Degree of Stenosis as Defined by NASCET (%)	Grading of Internal Carotid Stenosis						
	10–40	50	60	70	80	90	Occlusion
Main criteria							
1. B-mode image, diameter	Applicable	Possibly applicable					Imaging of occluded artery
2. Color Doppler image	Plaque delineation	Flow	Flow	Flow	Flow	Flow	Absence of flow
3. PSV threshold (cm/s)		125		230		NA	NA
4a. PSV average (cm/s)	≤160	210	240	330	370	Variable	NA
4b. PSV poststenotic (cm/s)				≥50	<50	<30	NA
5. Collateral flow (periorbital arteries or circle of Willis)				Possible	Present	Present	Present
Additional criteria							
6. Prestenotic flow (diastole) (CCA)				Possibly reduced	Reduced	Reduced	Reduced
7. Poststenotic flow disturbances (severity and length)		Moderate	Pronounced	Pronounced	Pronounced	Variable	NA
8. End-diastolic flow velocity in the stenosis (cm/s)			<100	>100		Variable	NA
9. Carotid ratio ICA/CCA	<2	≥2	≥2	>4	>4	Variable	NA

von Reutern GM, et al.: Stroke 2012; 43: 916-921

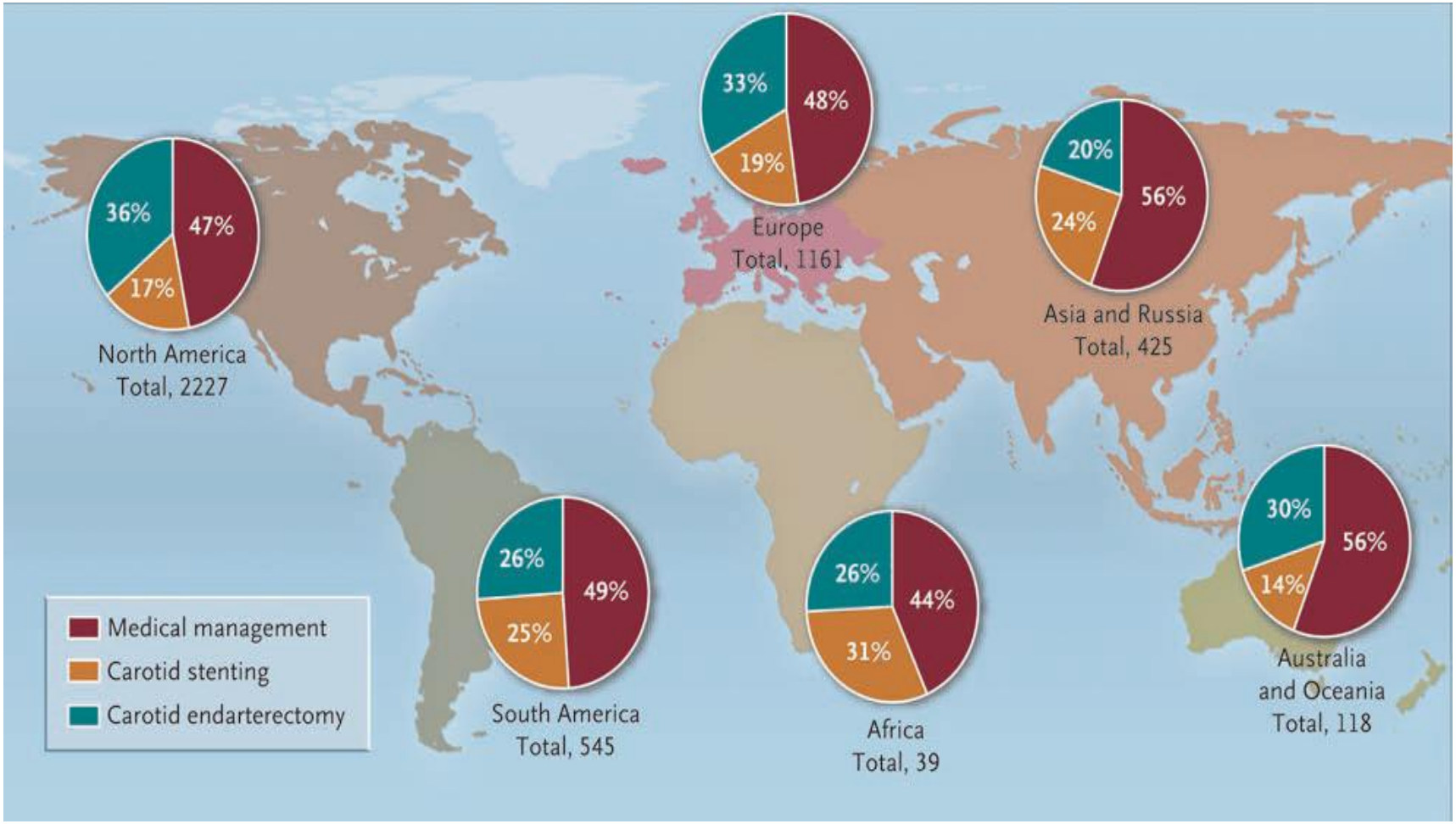
Mr. A.

67 years

- 05.09.2014:
  - Out patient visit, no history of focal neurological symptoms
- Risk factors:
  - Arterial hypertension, Hyperlipidemia
- Examinations:
  - neurological examination normal
  - MRT normal
  - Neurosonology: severe (~80%) stenosis of the left ICA

Asymptomatic carotid artery stenosis

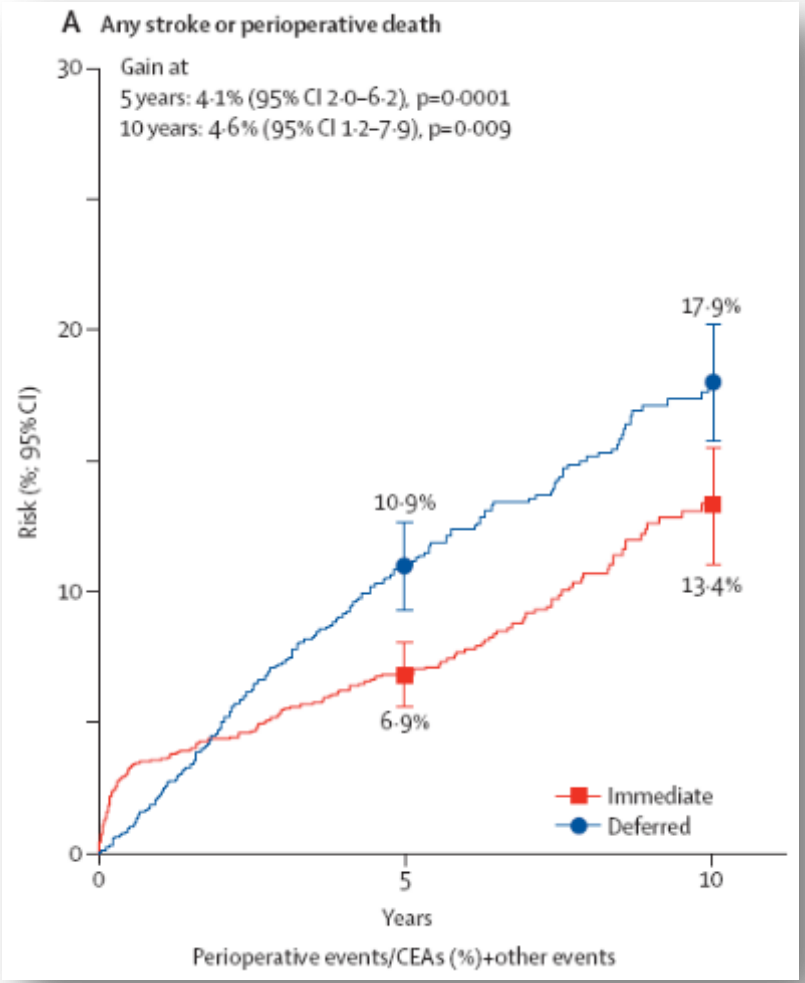
Matter of confusion

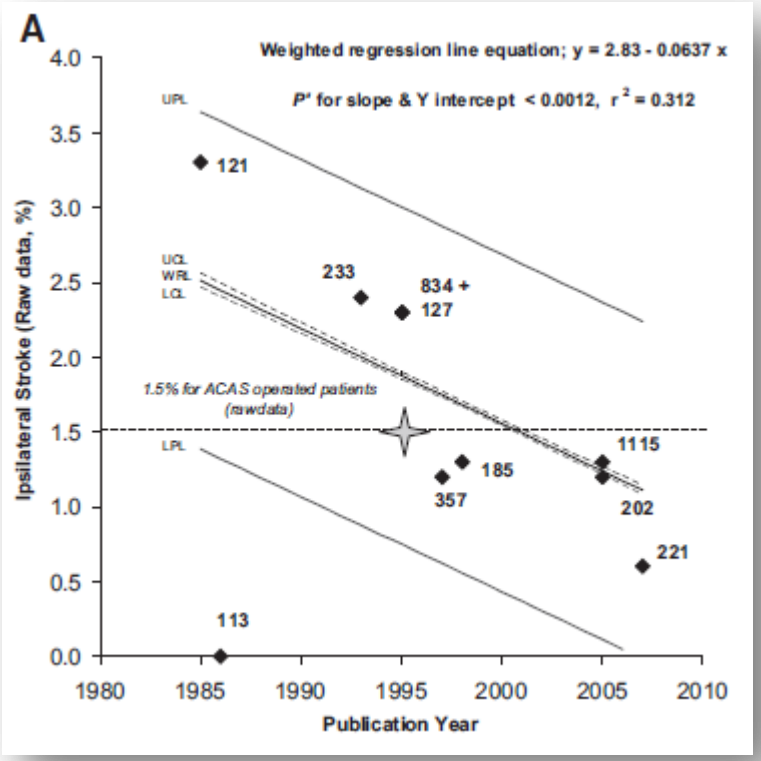


N Engl J Med 2008;358:1617-21

Asymptomatic Carotid Artery Stenosis

Primary prevention

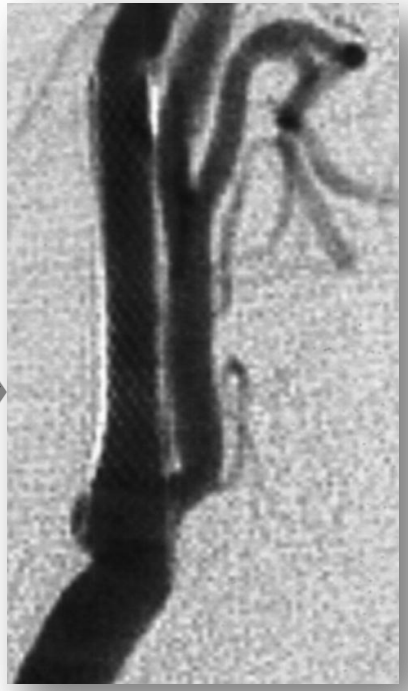




Halliday A et al.: Lancet (2010) 376:1074-1084 / Abbott A Stroke (2009) 40;e573-e583

Asymptomatic Carotid Artery Stenosis

Primary prevention methods



SPACE-2

Stent-Protected Angioplasty in Asymptomatic Carotid Artery Stenosis vs. Endarterectomy

- Are **CAS** or **CEA** superior to a modern medical therapy (**OMT**) in the primary prevention of ischemic stroke in patients with a severe asymptomatic carotid stenosis?
- Is **CAS** at least non-inferior to **CEA** in terms of safety and efficacy?

Reiff T et al., Int J Stroke (2014); 9: E12-3

SPACE-2

Key in- and exclusion criteria

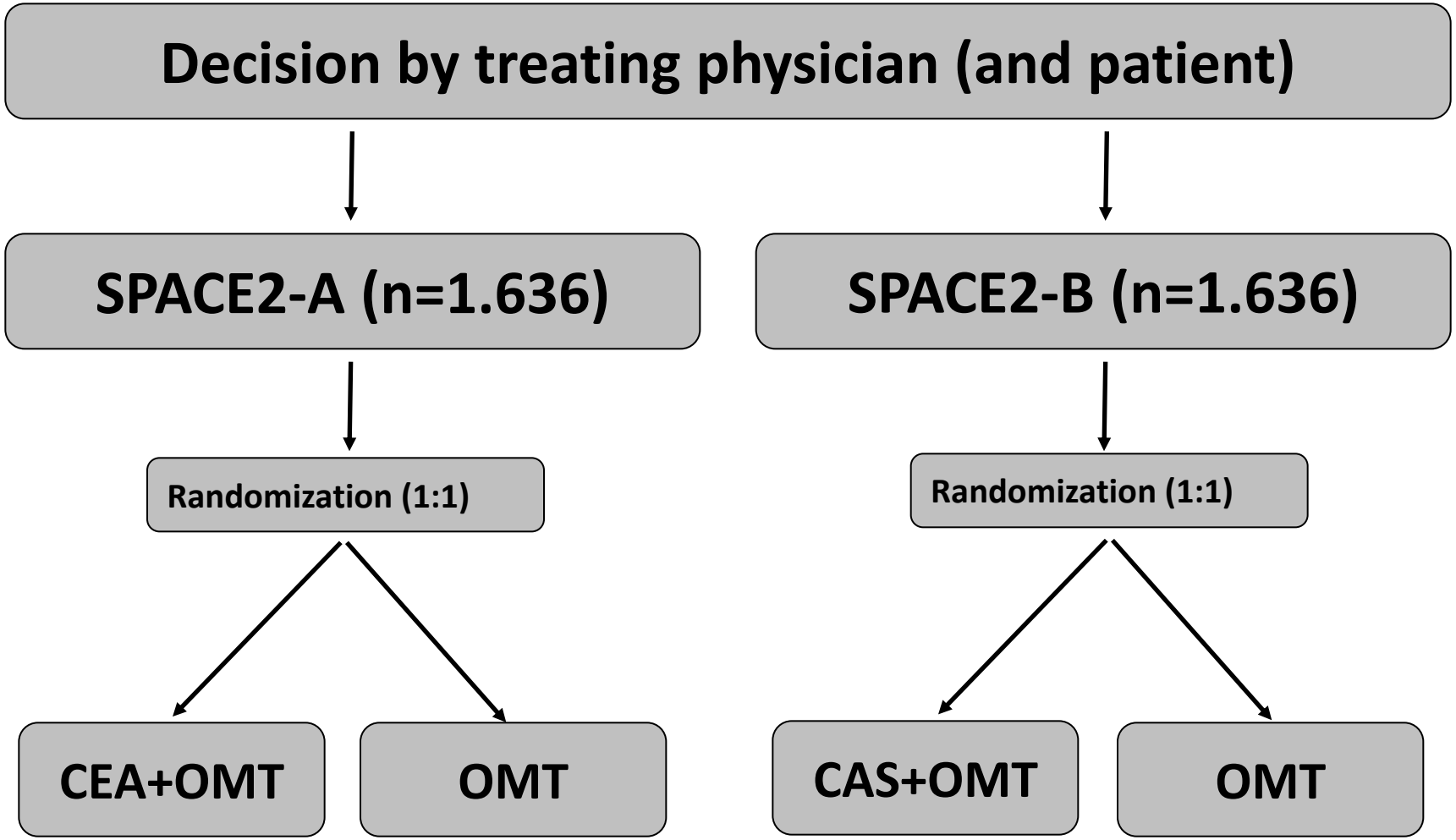
- Atherosclerotic carotid stenosis ≥70% (ECST)
- Age from 50 to 85 yrs.
- No stroke or stroke-like symptoms within 180 days
- Stenosis treatable with CEA and CAS

- Preexisting disability (modified RS ≥ 2)
- Radiation induced stenosis, recurrent stenosis
- High grade tandem stenosis
- Cardiac embolism source (atrial fibrillation, prosthetic heart valve)
- Life expectancy < 5yrs.

Reiff T et al., Int J Stroke (2014); 9: E12-3

SPACE-2

Protocol Modification

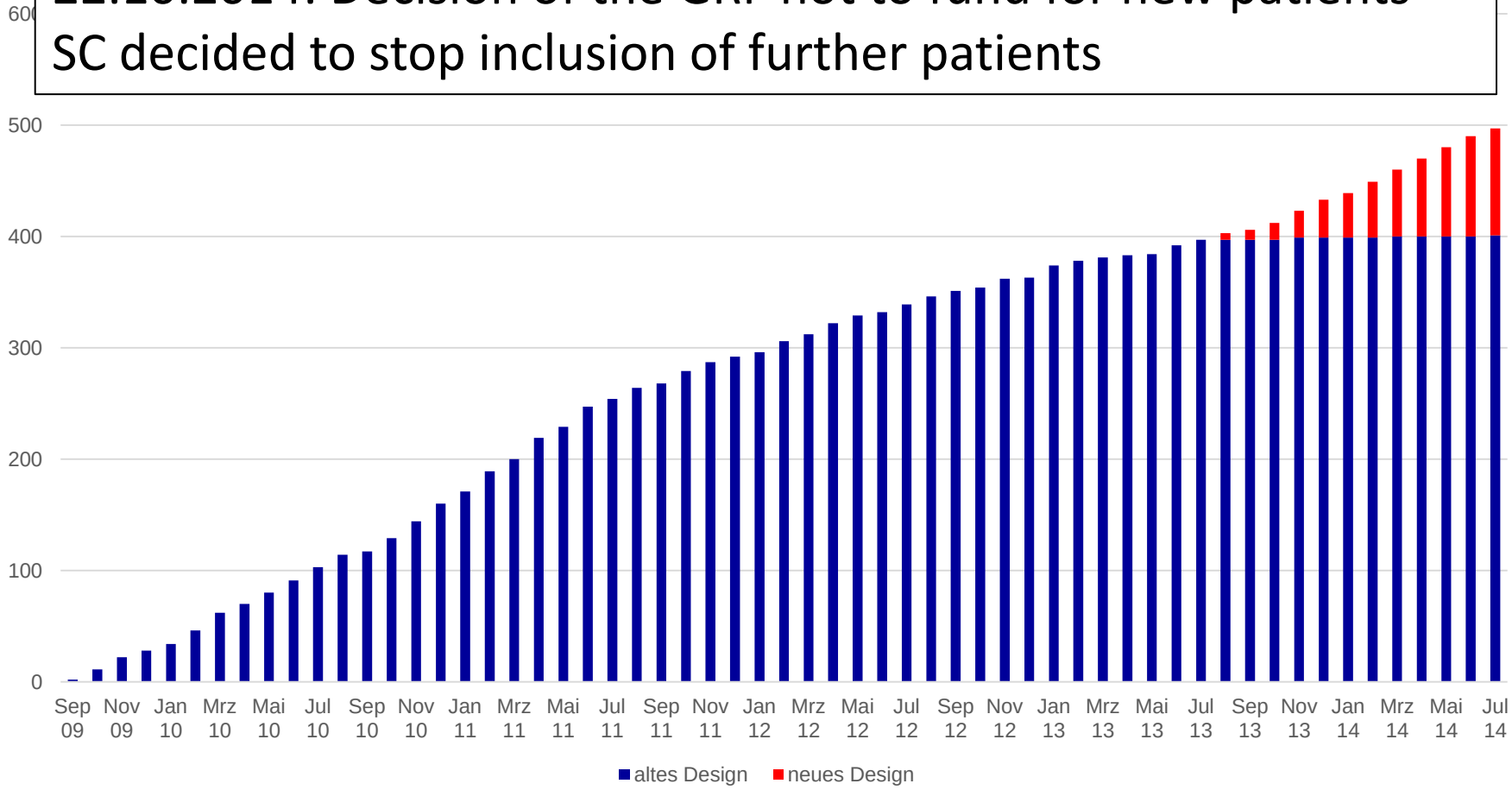


Reiff T et al., Int J Stroke (2014); 9: E12-3

SPACE-2

Study Status as of July 2014

22.10.2014: Decision of the GRF not to fund for new patients
SC decided to stop inclusion of further patients



SPACE-2

Study Status as of August 2015

- 513 patients randomized
- Close out monitoring not finished
- Database clearing in process
- Endpoint events adjudication finalized in about 99%

- Therefore, preliminary results will be demonstrated

Symptomatic carotid artery stenosis

Background

- Extracranial carotid artery stenoses causes approximately 10% of all ischemic strokes[1]
- Symptomatic carotid artery stenosis have a high recurrence risk[2]
- Carotid endarterectomy (CEA) is highly effective in symptomatic (TIA/non disabling stroke) severe carotid artery stenosis[3]

1: Grau et al., Stroke. 2001;32 (11):2559-2566
2: Rothwell et al., 1996;27 (2):260-265
3: Rothwell PM et al., Lancet (2004); 363: 915-24

Mrs. B.

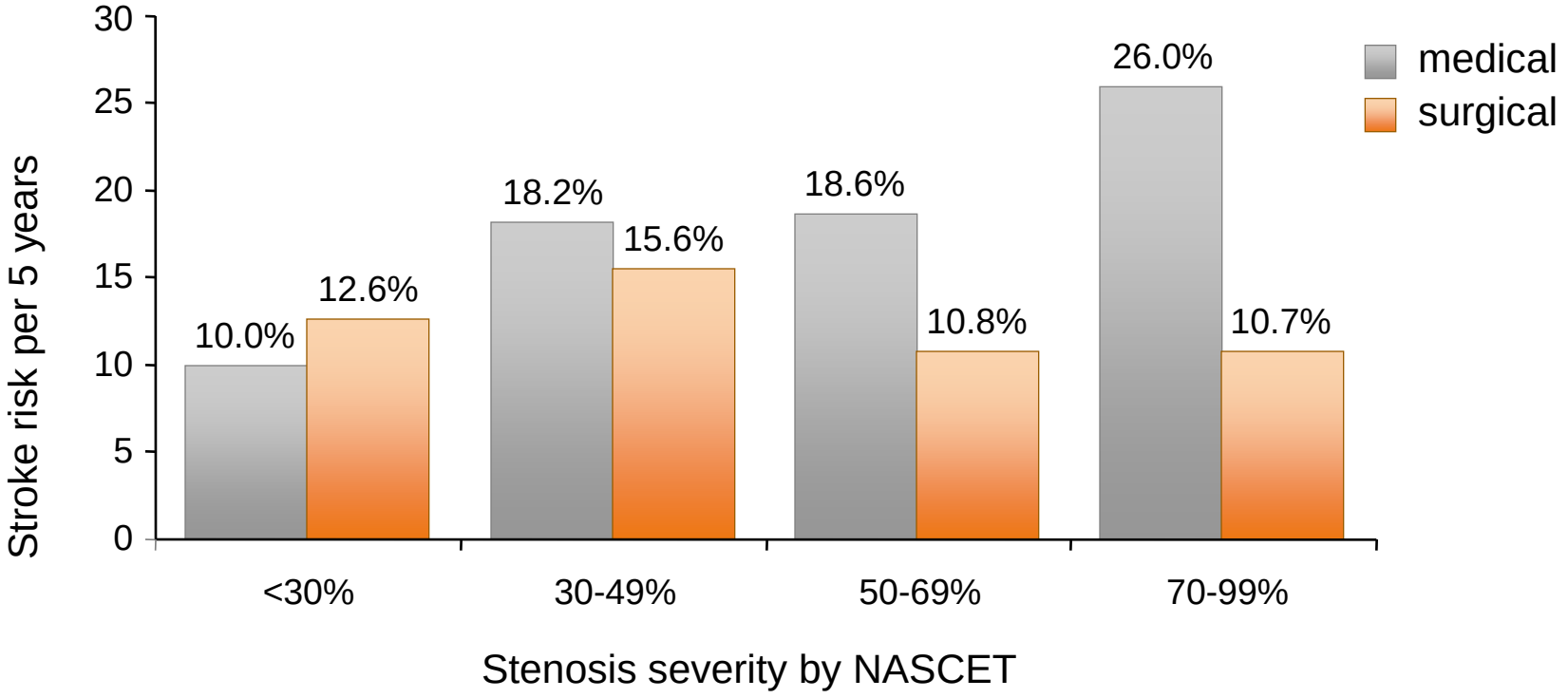
63 years

- 28.10.2015:
  - Mild weakness of the right arm and speech disturbance
- Risk factors:
  - CHD, Hypertension, Smoking stopped 4 years ago
- Examinations:
  - Neurological exam: normal
  - MRT: small left-hemispheric cortical stroke
  - Ultrasound: Severe (around 80%) stenosis at the origin of the left ICA due to an echolucent plaque

Symptomatic Carotid artery stenosis

Secondary prevention with CEA

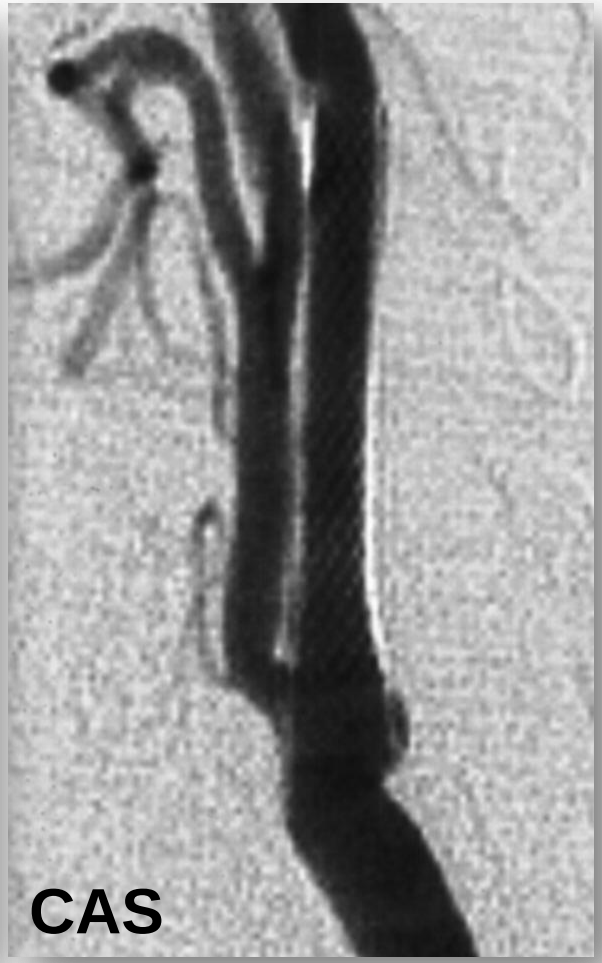
- Efficacy of surgery increases with stenosis severity
- Above 50%^{NASCET} surgery is superior to medical treatment



Rothwell PM: Cerebrovasc Disease (2004) 17 Suppl 1:89-104

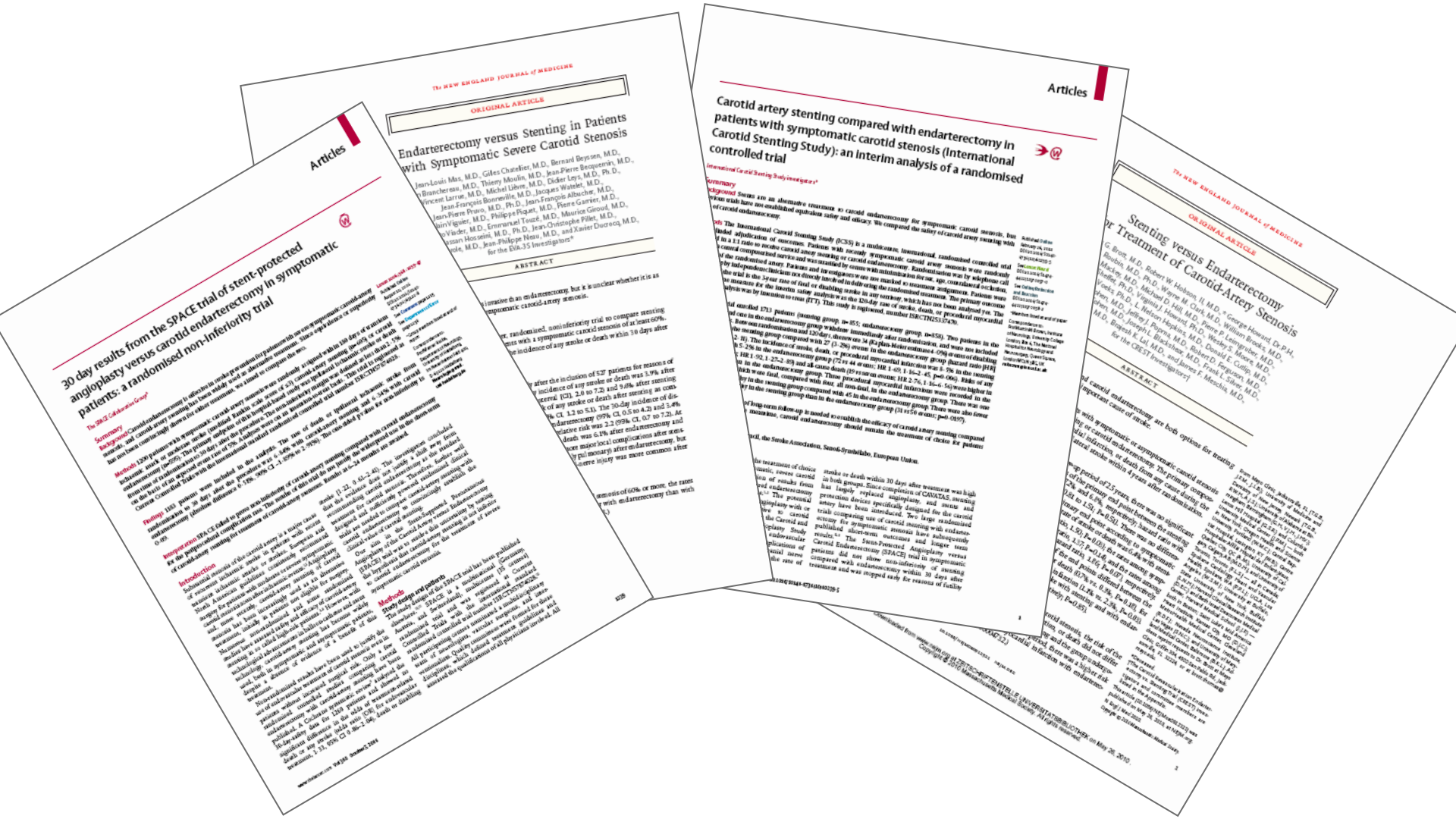
Carotid Artery Stenosis

Treatment options



Randomized clinical trials

CAS vs. CEA



Randomized clinical trials

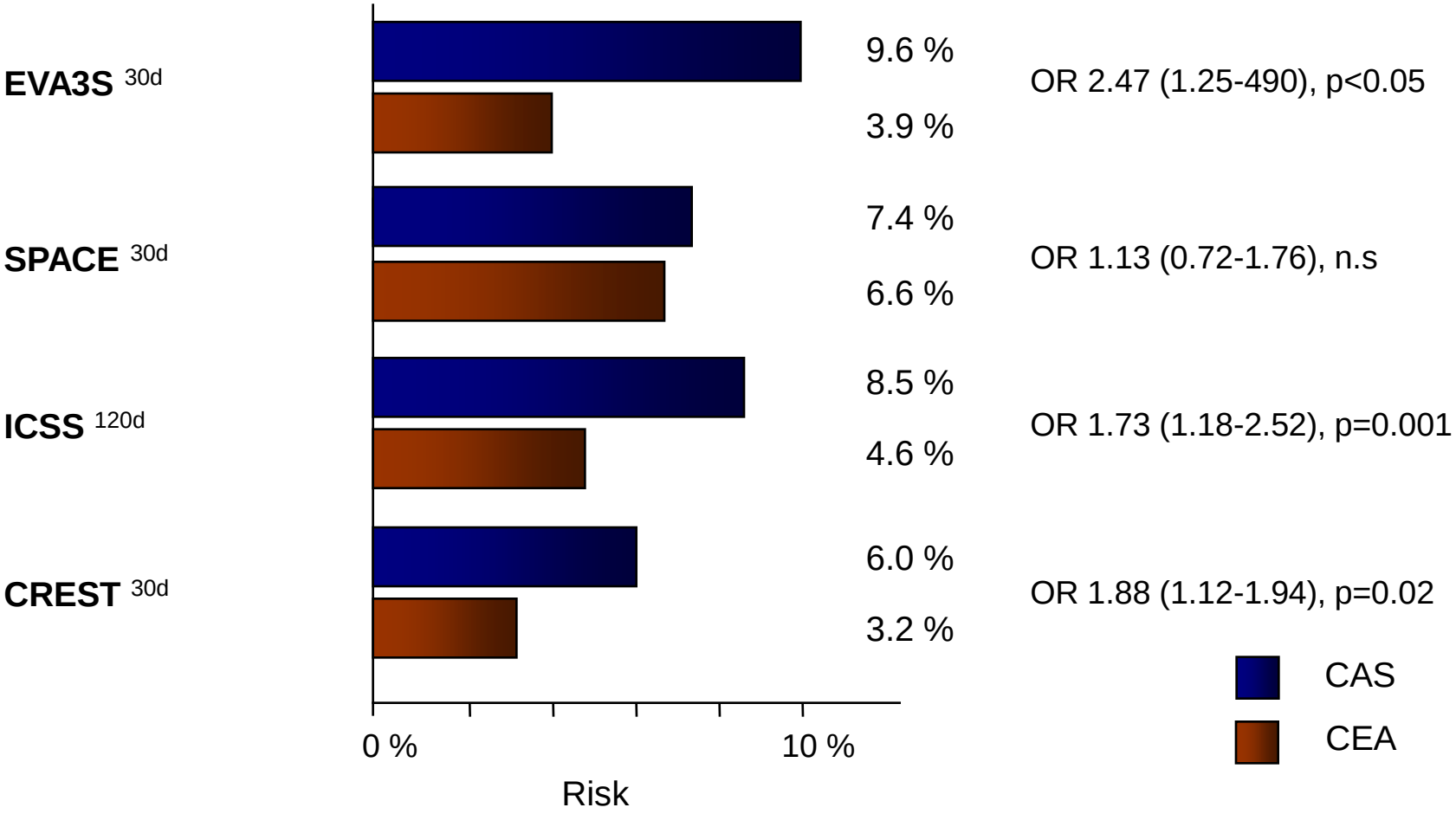
CAS vs. CEA

Characteristics	SPACE (N=1196)		EVA3S (N=527)		ICSS (N=1713)		CREST (N=2502)	
	CAS	CEA	CAS	CEA	CAS	CEA	CAS	CEA
Randomized	607	589	261	259	855	858	1262	1240
Symptomatic	100%		100%		100%		53%	53%
Age (mean)	68y	68y	69y	70y	70y	70y	69y	69y
Men	72%	72%	72%	78%	70%	71%	64%	66%
History of Stroke	44%	43%	13%	20%	46%	44%	unk	unk
History of TIA	30%	31%	25%	23%	32%	35%	unk	unk
Hypertension	75%	76%	74%	73%	69%	69%	86%	86%
Diabetes mellitus	26%	28%	22%	26%	22%	22%	31%	30%
Hyperlipidemia	unk	unk	58%	56%	61%	66%	83%	86%
Stenosis <70%	37%	40%	6%	8%	11%	9%	13%	15%
Stenosis >/= 70%	63%	60%	94%	92%	89%	91%	87%	85%
Contralat. Occlusion	3%	3%	5%	1%	6%	4%	3%	3%

CAS or CEA

Peri-procedural risk in randomized trials (ITT-data)

Endpoint: Any Stroke or death



Symptomatic Carotid artery stenosis

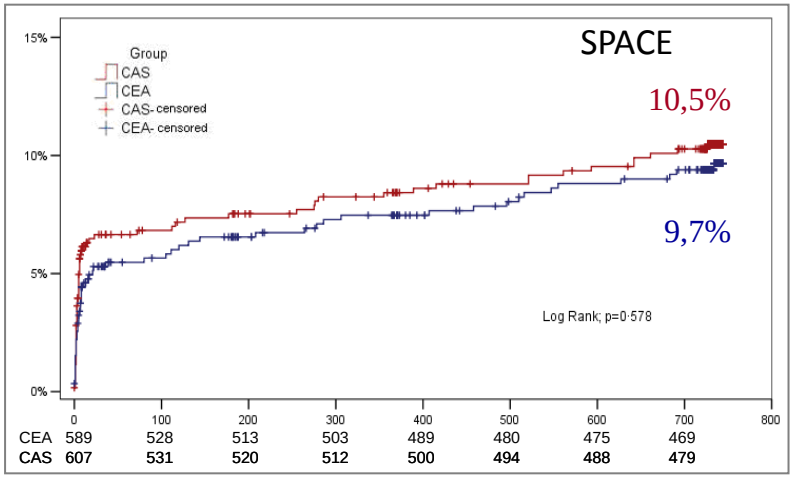
Guideline recommendations

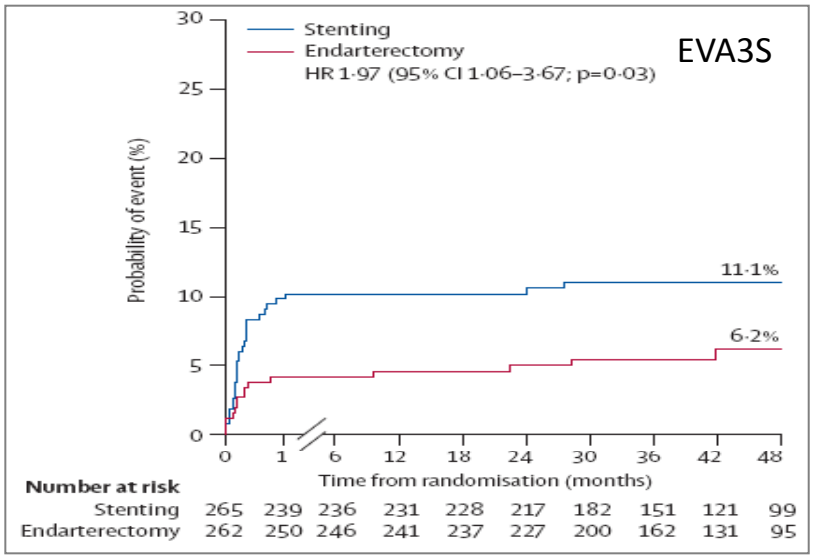
- CEA:
  - Recommended almost in any guideline, if periprocedural risk (Stroke/death) <6% (Class I, LoE A)[1-4]
- CAS
  - AHA (2011[1]): indicated as an alternative to CEA … (I,B)
  - ESC (2011[2]), DGN (2012[4]): may be considered as an alternative .. if death or stroke risk <6%(IIb, B)
  - RACP (2011[3]): may be considered as treatment option for patients who are .. unsuitable for CEA

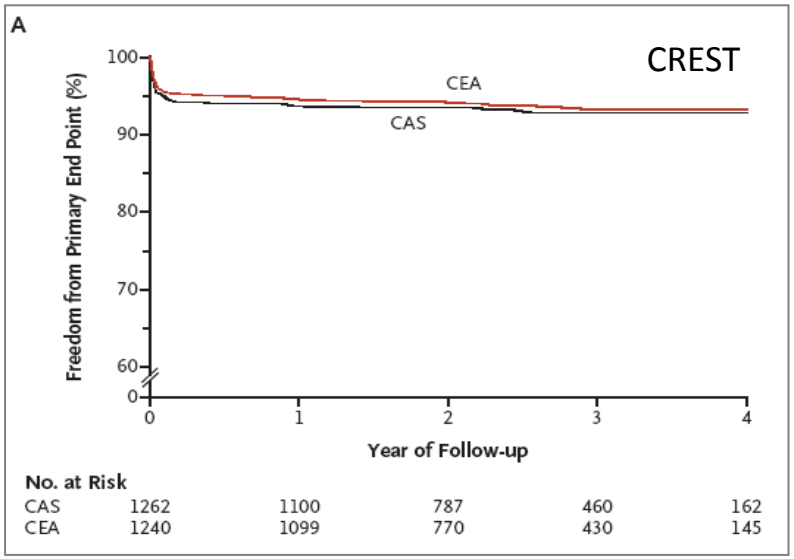
1: Brott Th et al., Circulation (2011) 123:
2: European Heart Journal (2011) 32: 2851–2906
3: Internal Medicine Journal (2011) 41: 344-347
4: www.awmf.org: Reg-Nr. 004-028 (2012)

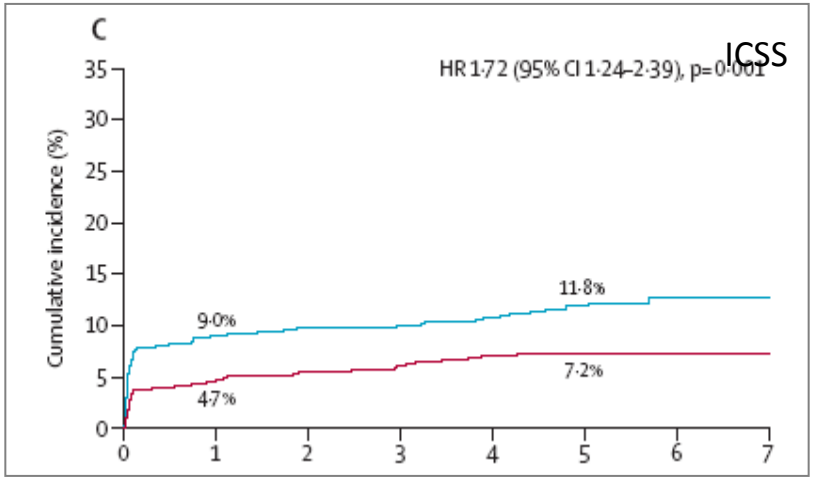
CEA or CAS

Long term efficacy









Eckstein HH, et al.: The Lancet. Neurology 2008; 7: 893-902 / Mas JL, et al.: Stroke 2014; 45: 2750-2756
Brott TG, et al.: The New England journal of medicine 2010; 363: 11-23/ Bonati LH, et al.: Lancet 2015; 385: 529-538

CEA or CAS

Factors for individual decision

- Patient‘s characteristics
  - age, type of symptoms, time since event
- Anatomical factors
  - Aortic arch configuration (esp. angulation)
  - Lesion length and -configuration
  - contra-lateral lesion (?)
- Center factors
  - Experience of center and physician
- Patient‘s preference

CEA or CAS for symptomatic Carotid Artery Stenosis

Summary and conclusions

- Strong evidence from randomized trials and meta-analyses that CEA is safer than CAS
- Almost twice as many strokes after CAS than after CEA
- Difference largely driven by non-disabling stroke
- Carotid endarterectomy is the treatment of choice for suitable patients with recently symptomatic carotid stenosis
- Individual factors allow to select patients also suitable for stenting