

**CEA is not superior to CAS: we
simply do not have the
answer yet**

Alison Halliday

Professor of Vascular Surgery
University of Oxford

**Session:Controversies
Saturday 19th January 2013**

Annual numbers of carotid procedures (CEA or CAS)

North America	>100,000 pa, 95% asymptomatic
Continental Europe + UK	>100,000 pa, 60% asymptomatic

Wide variation in current practice

North America	30% surgery, 70% stenting
Continental Europe	50% surgery, 50% stenting
United Kingdom	90% surgery, 10% stenting

What's the current evidence and opinion?

Starting with CAVATAS.....

**Carotid And Vertebral Artery Transluminal Angioplasty Study (CAVATAS):
long-term follow-up of a randomised trial
Lancet Neurol 2009; 8: 898–907**

504 patients, 90% symptomatic, randomised to CEA vs CAS

“More patients in the endovascular group had stroke during follow-up but.....

None of the differences in outcome was significant..... the study was underpowered and the confidence intervals were wide”

“More long-term data are needed from the on going stenting versus endarterectomy trials”

Carotid Stenting trialists' meta-analysis

	CAS (n=1679)	CEA (n=1645)	Risk ratio* (95% CI)	p value†	Risk difference* (95% CI)
Any stroke or death	130 (7.7%)	73 (4.4%)	1.74 (1.32 to 2.30)	0.0001	3.4 (1.8 to 5.0)
Disabling stroke or death	65 (3.9%)	43 (2.6%)	1.48 (1.01 to 2.15)	0.04	1.2 (0 to 2.4)
All-cause death	19 (1.1%)	10 (0.6%)	1.86 (0.87 to 4.00)	0.10	0.6 (-0.1 to 1.2)
Any stroke	125 (7.4%)	70 (4.3%)	1.74 (1.31 to 2.32)	0.0001	3.3 (1.7 to 4.9)
Stroke severity‡					
Fatal	12 (0.7%)	6 (0.4%)	1.97 (0.74 to 5.23)	0.16	0.4 (-0.1 to 0.8)
Disabling	47 (2.8%)	34 (2.1%)	1.35 (0.87 to 2.08)	0.18	0.6 (-0.4 to 1.6)
Non-disabling	66 (3.9%)	31 (1.9%)	2.09 (1.37 to 3.19)	0.0004	2.0 (0.8 to 3.2)
Stroke type§					
Ischaemic	118 (7.0%)	57 (3.5%)	2.02 (1.48 to 2.75)	<0.0001	3.7 (2.2 to 5.2)
Haemorrhagic	7 (0.4%)	12 (0.7%)	0.57 (0.23 to 1.45)	0.23	-0.3 (-0.8 to 0.1)
Unknown	0	1 (0.1%)
Stroke region§					
Ipsilateral carotid	113 (6.7%)	66 (4.0%)	1.67 (1.24 to 2.25)	0.0005	2.8 (1.3 to 4.3)
Contralateral carotid or vertebrobasilar	10 (0.6%)	4 (0.2%)	2.45 (0.77 to 7.81)	0.11	0.4 (-0.1 to 0.8)
Unknown	2 (0.1%)	0
Myocardial infarction	4 (0.2%)	7 (0.4%)
Non-fatal	1 (0.1%)	7 (0.4%)
Fatal	3 (0.2%)	0
Cranial nerve palsy¶	7 (0.4%)	99 (6.0%)	0.07 (0.03 to 0.15)	<0.0001	-5.6 (-6.7 to -4.4)
Severe haematoma	12 (0.7%)	32 (1.9%)	0.37 (0.19 to 0.71)	0.0016	..
Severe wound infection**	1 (0.1%)	4 (0.2%)

Data are number (%), unless otherwise indicated. Percentages are number of events divided by number of patients. CAS=carotid stenting. CEA=carotid endarterectomy. --=Adjusted risk ratio or risk difference and 95% CIs were not estimated because model did not converge. *Adjusted for source trial. †Derived by use of binomial regression likelihood ratio test, adjusted for source trial. ‡One patient in the endarterectomy group had two stroke events within 30 days after treatment. §Refers to first event. ¶In the stenting group, cranial nerve palsy was caused by carotid artery dissection in two patients; in three patients, cranial nerve palsy occurred after conversion to endarterectomy following unsuccessful initial attempts at stenting; and two patients had isolated dysphagia attributable to cranial nerve palsy after stent procedures. ||Defined as neck

Poor outcomes after endovascular treatment of symptomatic carotid stenosis: time for a moratorium

Peter Rothwell; Lancet Neurology 2009

....Most stenting for symptomatic stenosis (has) a greater procedural risk of stroke and a worse long-term outcome than ..endarterectomy

.....Routine use of stenting in (symptomatic) patients suitable for endarterectomy can no longer be justified...

...Vague and non-evidence-based categorisations, such as “high risk for surgery” which have been systematically misused to justify the uncontrolled roll-out of carotid stenting in many centres, must stop.....

There's a Perception that CEA is better after the symptomatic trials – but what has changed?

- **Experience, time and devices**
- **Symptomatic vs asymptomatic interventions**
- **Open vs closed cell stents (ICSS data)**
- **Filters vs no filters**
- **New devices – direct puncture, reverse flow, others arriving**

Carotid Artery Stenting: First Consensus Document of the ICCS-SPREAD Joint Committee

Stroke. 2006; 37: 2400-2409

CAS: Training and Expertise Recommendation:

Once the basic skill for catheter-based intervention has been achieved by the already-active interventionist, the minimum recommended training to achieve competence is as follows:

- 1. At least 150 procedures of supra-aortic vessel engagement(during diagnostic as well as interventional procedures)within 2 years, of which at least 100 as the primary operator;**
- 2. At least 75 carotid stenting procedures, of which at least 50 as the primary operator, within a 2-year fellowship.**

Carotid artery stenting versus surgery: adequate comparisons?

Lancet Neurology 2010, 339–341 Correspondence

[Marco Roffi^a](#), [Horst Sievert^b](#), [William A Gray^c](#), [Christopher J White^d](#), [Giovanni Torsello^e](#), [Piergiorgio Cao^f](#), [Bernhard Reimers^g](#), [Klaus Mathias^h](#), [Carlo Setacciⁱ](#), [Claudio Schönholz^j](#), [Daniel G Clair^k](#), [Martin Schillinger^l](#), [Iris Grunwald^m](#), [Marc Bosiersⁿ](#), [Alex Abou-Chebl^o](#), [Issam D Moussa^p](#), [Harald Mudra^q](#), [Sriram S Iyer^r](#), [Dierk Scheinert^s](#), [Jay S Yadav^t](#), [Marc R van Sambeek^u](#), [David R Holmes^v](#), [Alberto Cremonesi^w](#)

As randomised clinical trials are the gold standard of clinical investigation, it seems unwise to challenge them. However, for the comparison of CAS versus CEA, most of the randomised trials should be considered not only scientifically but also ethically questionable because the endovascular experience required for interventionalists to be eligible for the studies was minimal

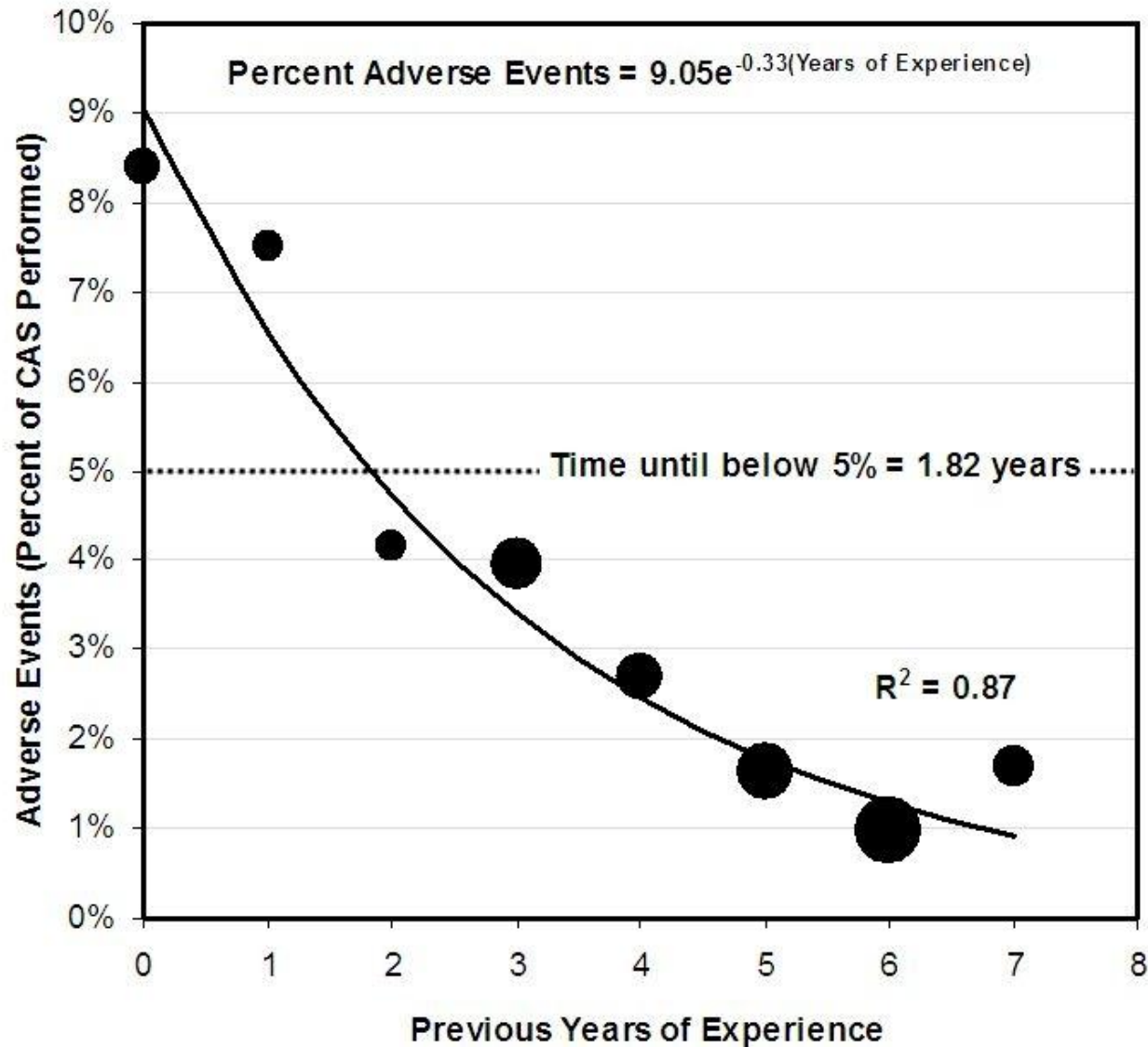
Carotid artery stenting versus surgery: adequate comparisons? – Triallists' reply

Lancet Neurology, April 2010, Pages 341–342

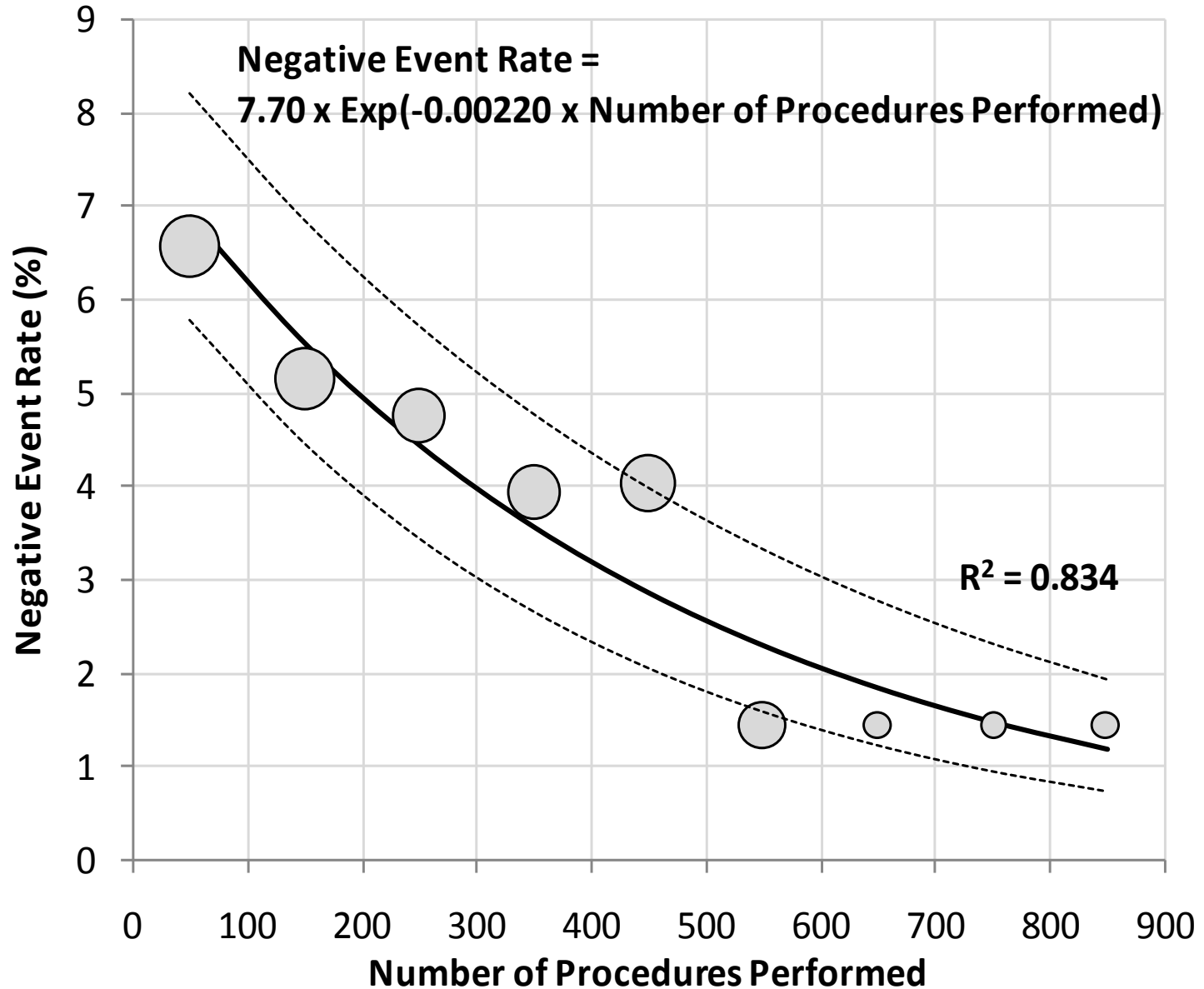
[Martin M Brown](#), [Jean-Louis Mas](#), [Peter A Ringleb](#), [Werner Hacke](#)

	Year	Number	Lifetime endovascular requirements
CAVATAS	2001	504	Training in neuroradiology and angioplasty (but not necessarily in the carotid artery); tutor-assisted procedures allowed
SAPPHIRE	2004	334	Procedures submitted to an executive review committee; CAS periprocedural death or stroke rate had to be <6%; no tutor-assisted procedures allowed
SPACE	2006	1200	At least 25 successful CAS or assistance of a tutor for interventionalists who have done at least 10 CAS
EVA-3S	2006	527	≥12 CAS cases or ≥5 CAS and ≥30 cases of endovascular treatment of supra-aortic trunks; tutor-assisted CAS allowed for centres not fulfilling minimum requirements
ICSS	2010	1710	A minimum of 50 total stenting procedures, of which at least ten should be in the carotid artery; tutor-assisted procedures allowed for interventionalists with insufficient experience

Meta-regression analysis: Years of experience



Numbers of Procedures



Comparison of Carotid Stents: An In-Vitro Experiment Focusing on Stent Design

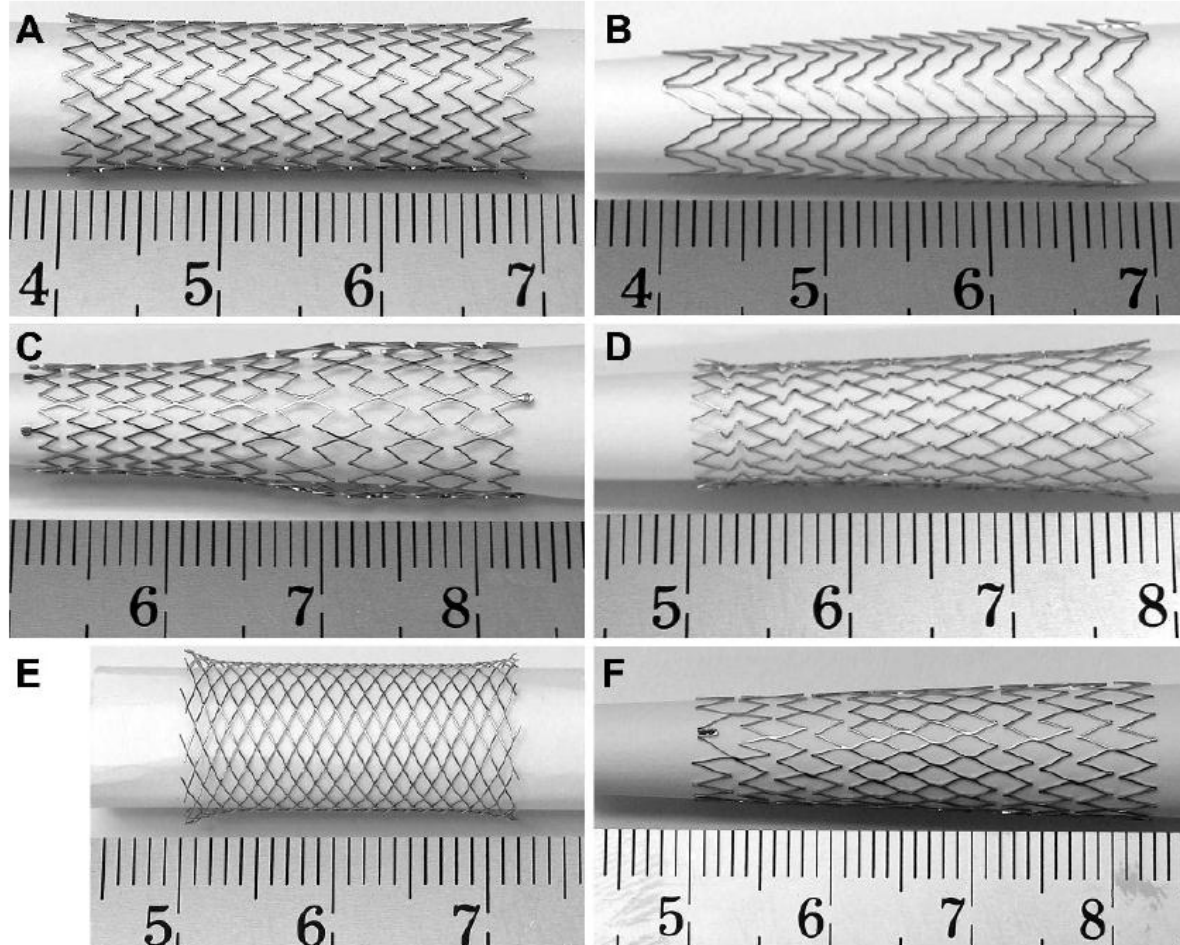
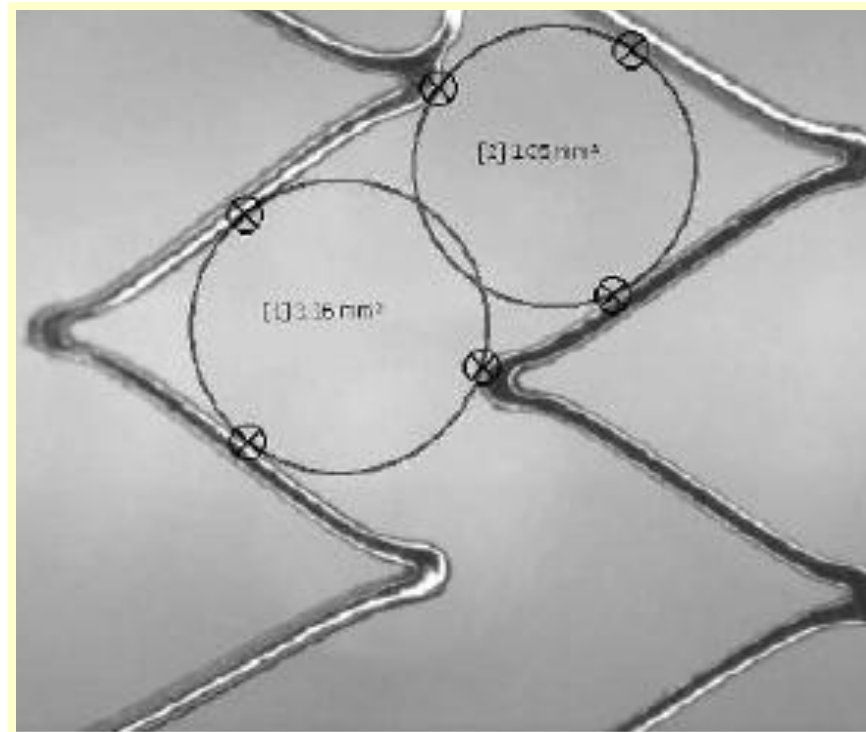


Figure 1 ♦ (A) Precise, (B) Acculink, (C) Protégé, (D) Xact, (E) Wallstent, and (F) Cristallo Ideale.

Comparison of Carotid Stents: An In-Vitro Experiment Focusing on Stent Design

Maximum number of fitted-in circles at the proximal, middle & distal parts of the stents



“ Free Cell Area ” & Outcome

N =3179

Stent name

X-act

Nexstent

Wallstent

Precise

Protégé

Acculink

Exponent

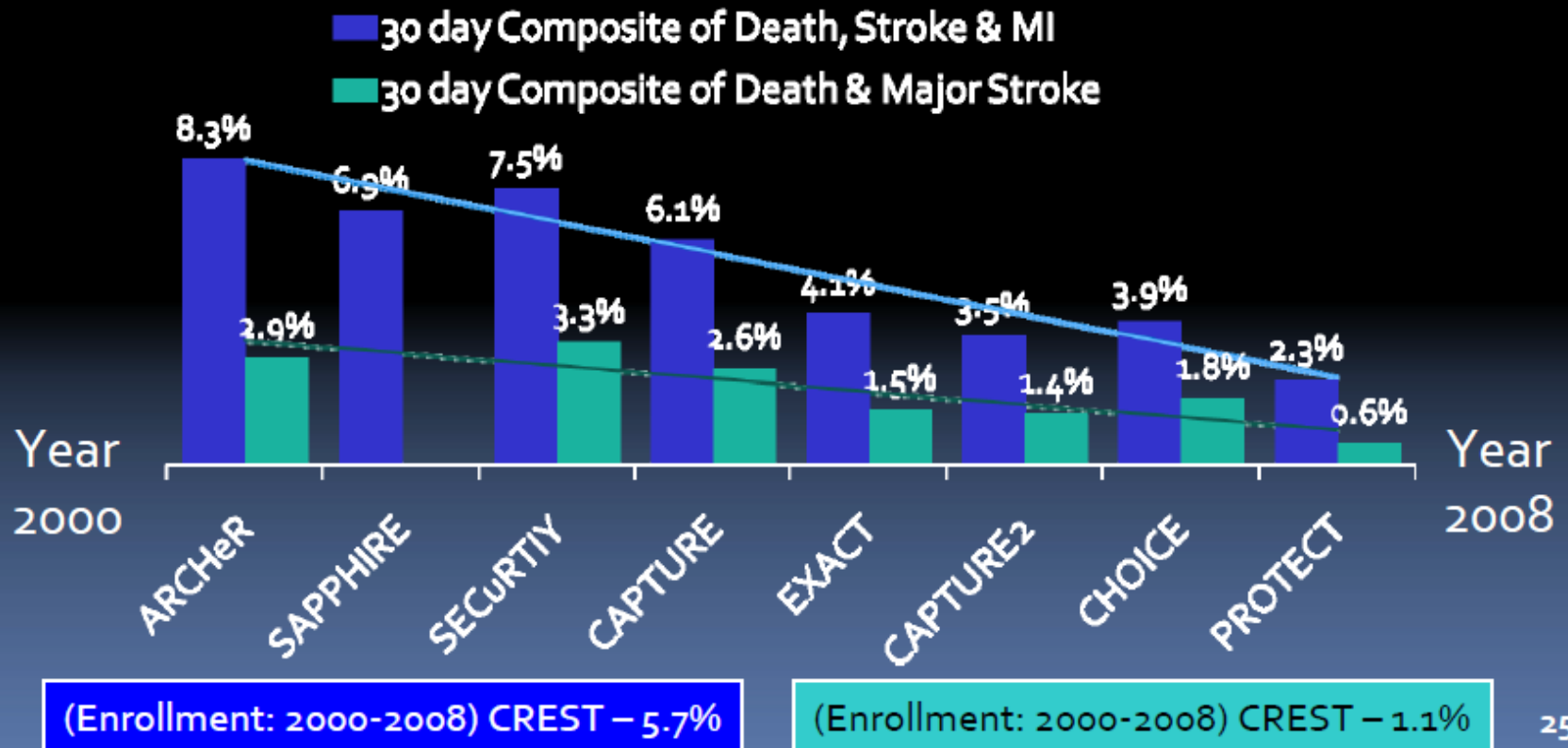
P-values for the test that event rates differ between stents

Population	Outcome	<i>p</i> -value
<i>Total</i>	All events	0.018
	Post-procedural events	0.002
<i>Symptomatic</i>	All events	0.006
	Post-procedural events	<0.0001
<i>Asymptomatic</i>	All events	0.248
	Post-procedural events	0.790

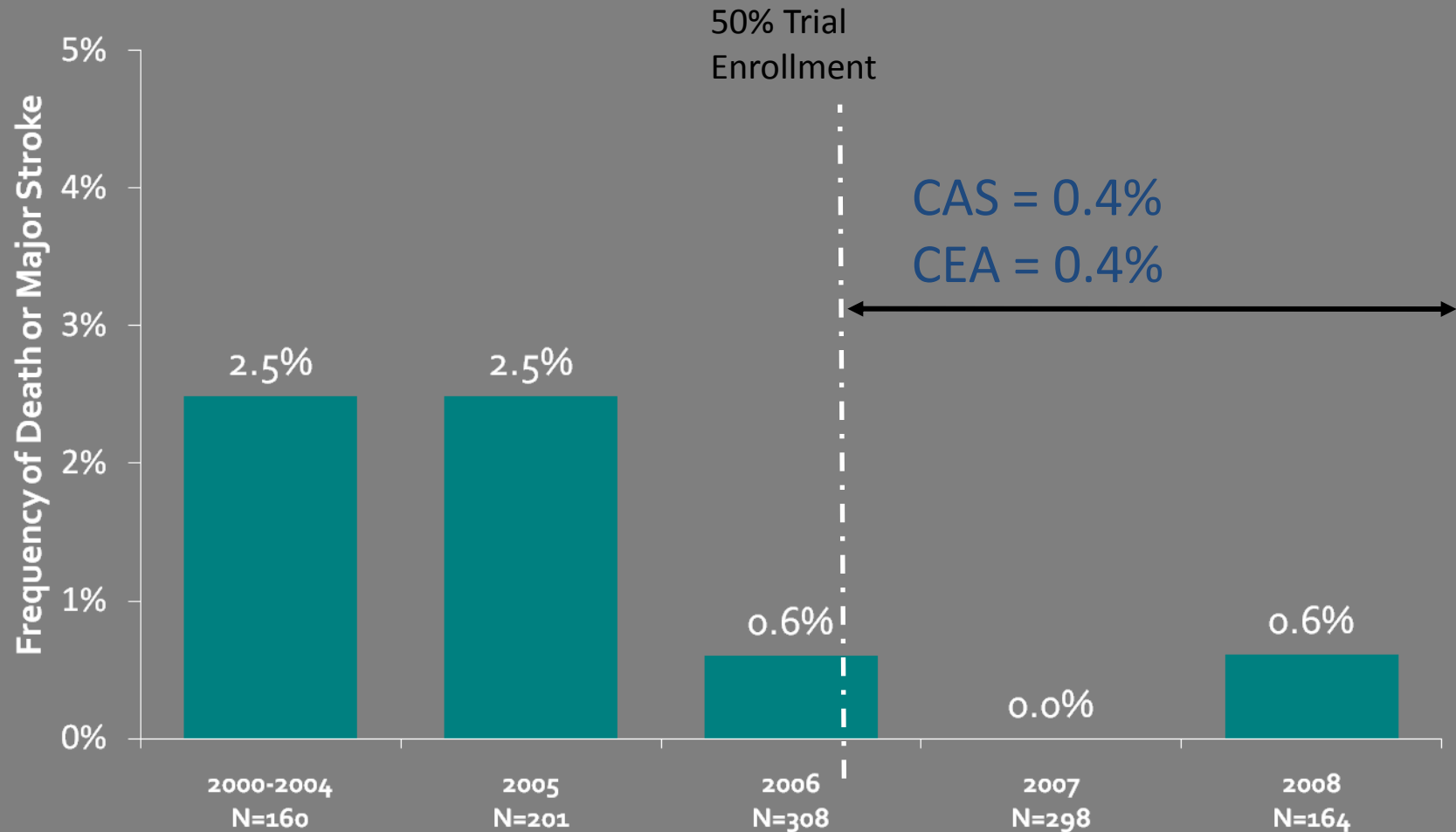
Bosiers M e al. Does Free Cell Area Influence the Outcome in Carotid Artery Stenting ? EJVES 2007;33:135 - 141

Outcomes of CAS Trials Over Time

- CAS results have vastly improved over time due to: (1) more experienced operators; (2) better patient selection and; (3) a wider spectrum of technology
- CAS outcomes have evolved over time similarly to CEA



CREST: Major Stroke/Death (CAS) during Enrollment



Editorial

Asymptomatic Carotid Stenosis Identifying Patients at High Enough Risk to Warrant Endarterectomy or Stenting

J. David Spence, MD, FRCPC; David Pelz, MD, FRCPC; Frank J. Veith, MD, FACS

is at best misguided and at worst unjustified. We are concerned that too many of these procedures are being done because of the remuneration for them.¹³

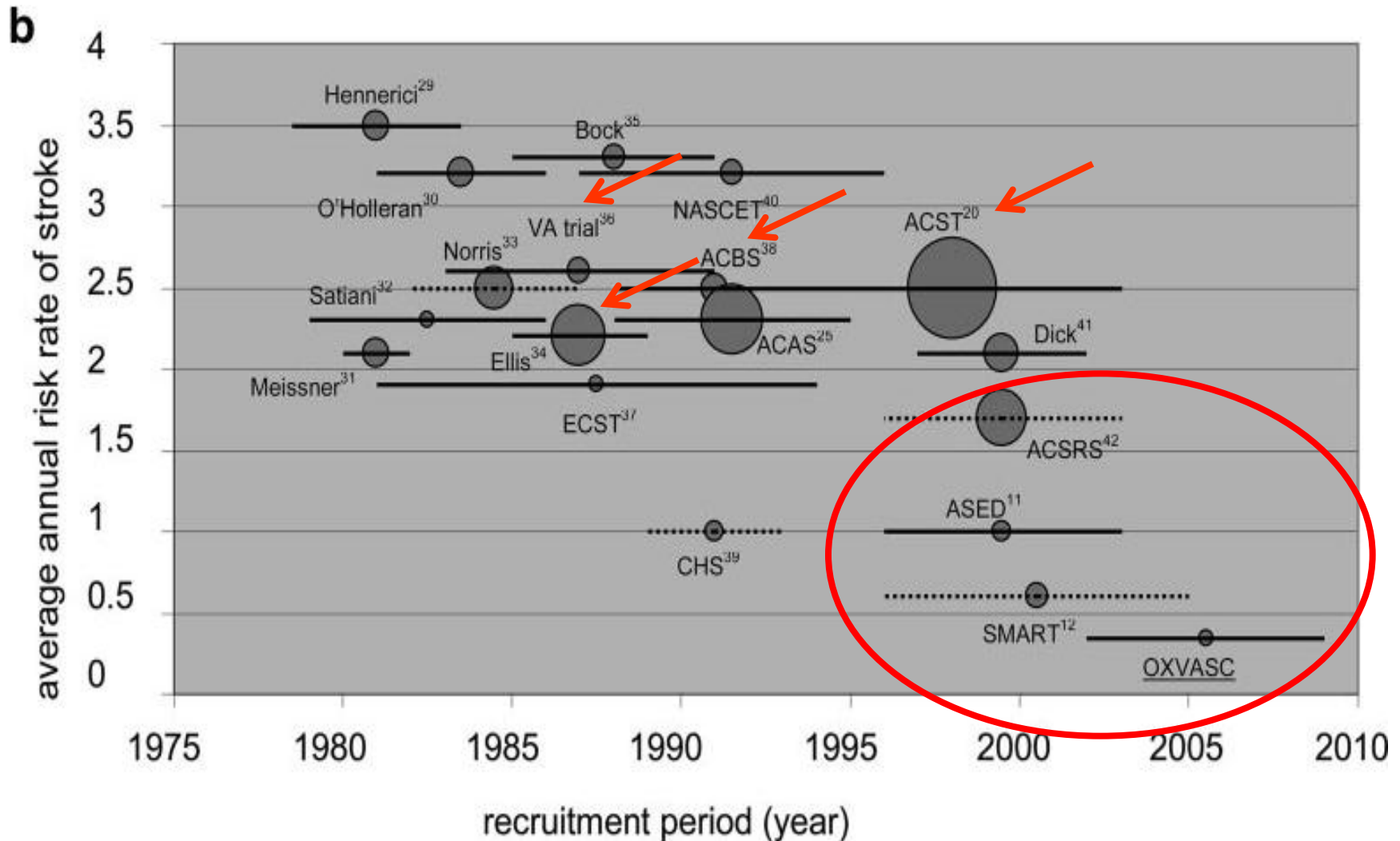
Future of carotid surgery trials

- Reducing procedural hazards
(stent design, *insertion, drug elution*)
- Changing spectrum of patients
(*older, chronically ill, screen-detected*)

And..

- Improving medical treatments

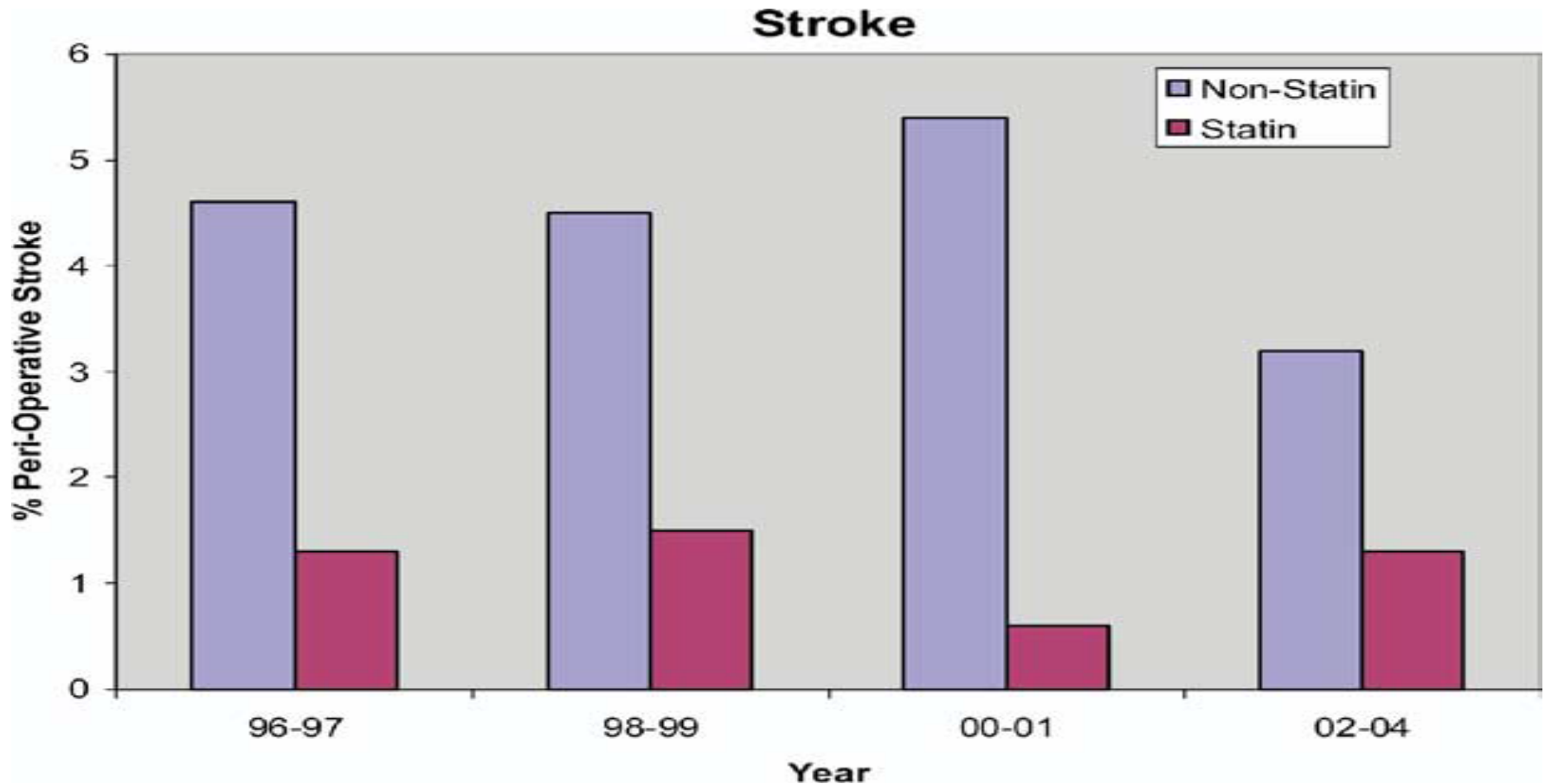
Medical treatment for asymptomatics



Medical Treatment for Asymptomatic Carotid Stenosis

Study	Reference	Patients	PSV	Details
SMART (>3000)	Goessens Stroke 2007	96 with $\geq 70\%$ stenosis	150cm/s	Only 96 pts had PSV ≥ 210 , 7% had carotid repair
OxVasc (>90,000)	Marquardt Stroke 2010	32 with $\geq 70\%$ stenosis	150cm/s	Vascular death in 7.7%
ASED	Abbott Stroke 2005	202 with $\geq 50\%$ stenosis	150cm/s	TCD

Statins lower stroke risk in CEA



(J Vasc Surg 2005;42:829-836)

70-99% carotid stenosis & no recent symptoms

Should any carotid procedure be done?

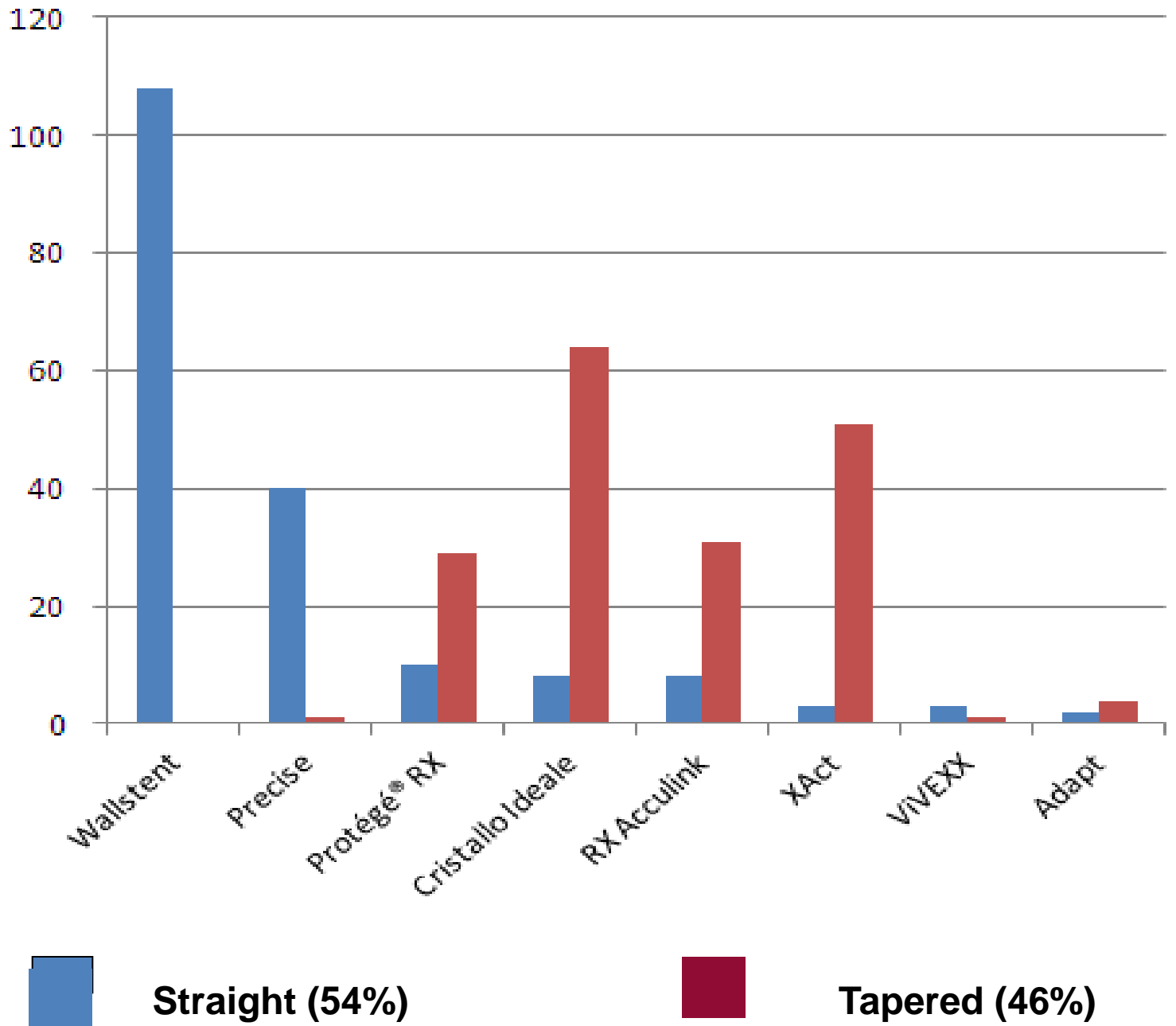
If **uncertain**: Consider a trial with a
no-procedure control
(SPACE-2, ECST-2)

If **Yes**: Consider ACST-2
(CAS vs CEA)

less severe stenosis but recent symptoms

Consider ESCT-2

ACST-2: STENTS USED IN FIRST 800 PATIENTS



ACST-2 – current status

1100 patients recruited January 2013

Soon will have more asymptomatic patients
randomised 1:1 than CREST or any other trial

Many more needed – so do join us!

**Trials need VERY large numbers of patients,
because they study MODERATE effects**

Current trials, mostly asymptomatic

ACST-2 recruiting (now >1000): CEA vs CAS

CREST 1 ended (1183 asymptom.): CEA vs CAS

CREST 2 not yet funded: 2-way comparisons

SPACE 2 : CEA vs CAS vs neither (3-way)

SPACE 2 redesigned: 2-way comparisons

ECST-2 starting: 2-way comparisons

So...CEA is not superior to CAS: we simply do not have the answer yet.....