Proximal and Distal Protection for Carotid Intervention:

No Room for CEA?

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

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P: Proctor or Training Course Sponsorships
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Carotid Stenting Without Stroke: How to Achieve the Gold Safety Standard

- What is the “Gold Standard”
- What predicts stroke with carotid stenting
  - Arch and lesion characteristics
  - Patient characteristics
  - Symptomatic status
  - Operator experience
  - Devices and equipment

AHA Council on Stroke
1998 Endarterectomy Guidelines

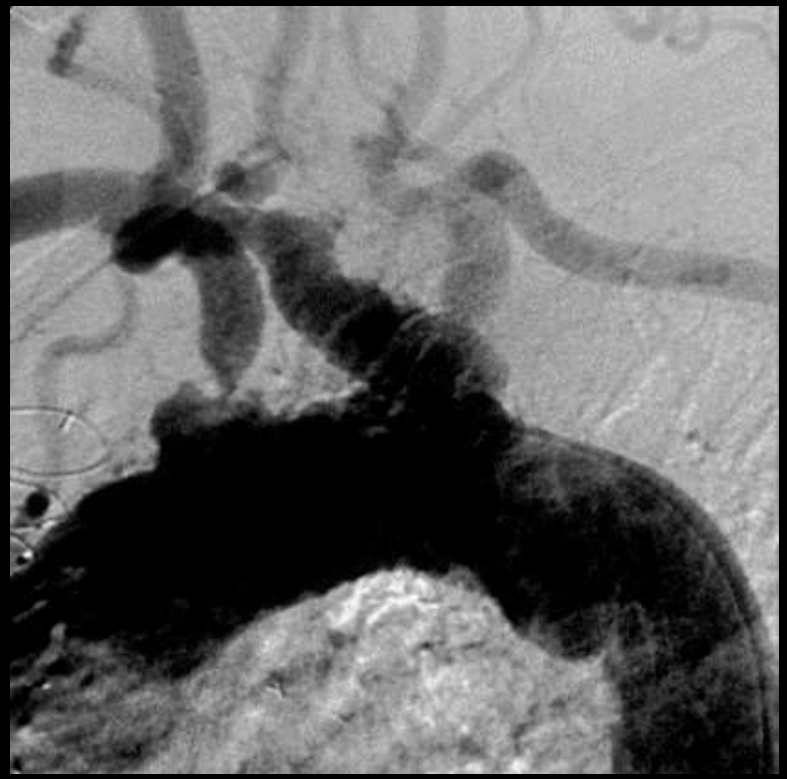
	% Stenosis	Maximum Acceptable Perioperative Death+CVA Rates, %
Asymptomatic	≥60	<3.0
Symptomatic	≥70	<6%
TIA		5.0
Prior CVA		7.0
Restenosis post-CEA		10.0
Contralateral ICA occlusion		14.0

But these are STANDARD risk patients…

Biller J et al *Circulation* 1998; 97; 501-509

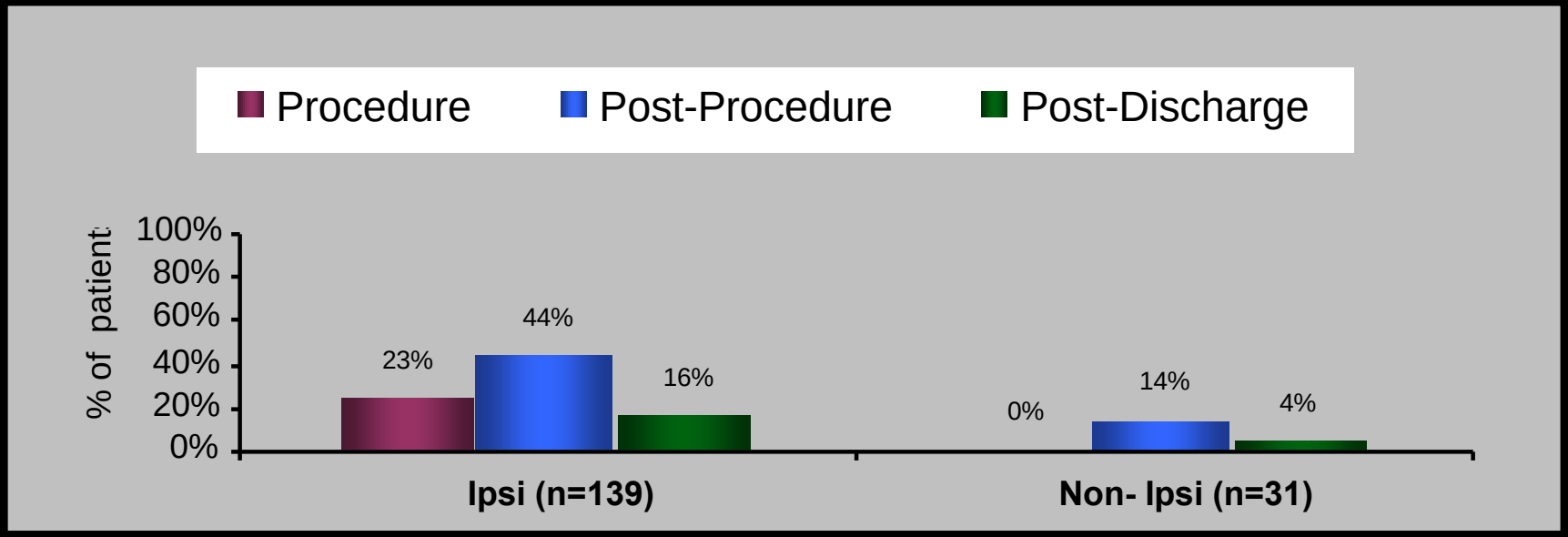
Challenging Arch Anatomy

Difficult Access Arches



CAPTURE Stroke Cohort: Location relative to procedure timing

All strokes (n=168*)



139/3500=4.0%

31/3500=0.9%

18% of all strokes in CAPTURE were non-ipsilateral

Gray W et al *Catheter Cardiovasc Interv* 2007; 69: 341–348

High Risk Type C Carotid Lesions

Lesion Predictors of Adverse Events Following CAS-SAPPHIRE WW

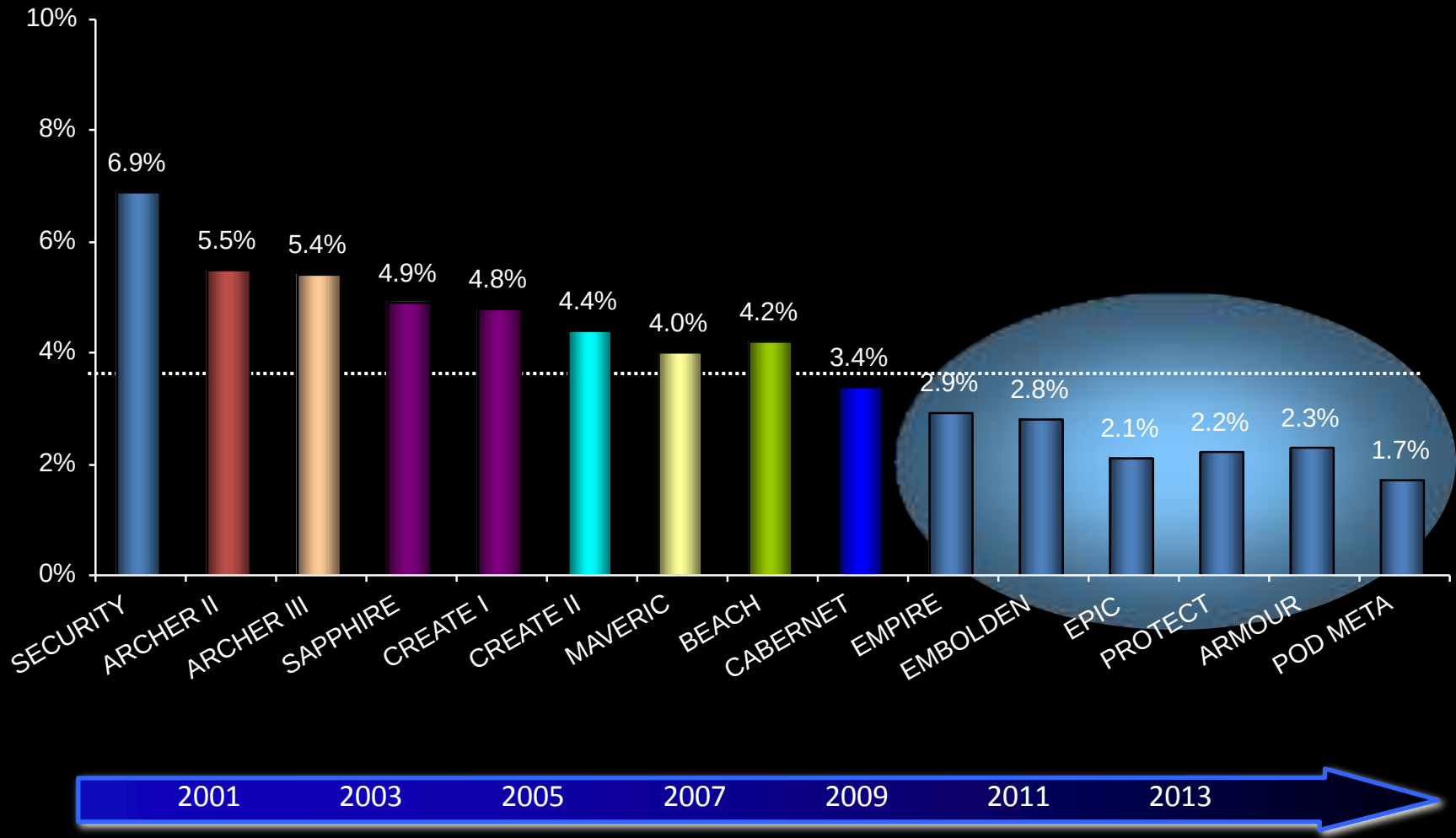
Multivariate Predictors of 30-Day MAE

(N=4001)

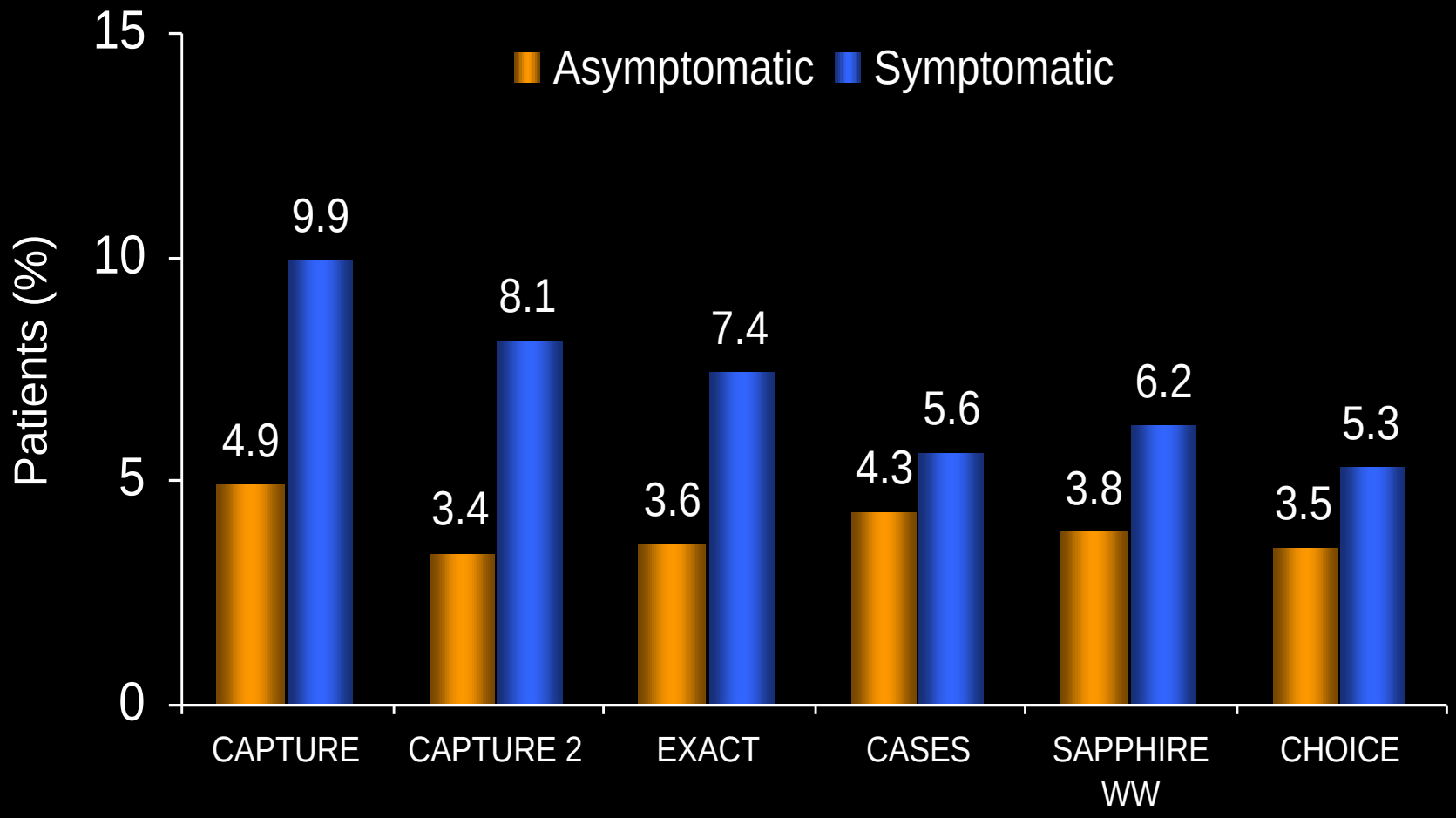
	Odds Ratio [95% CI]	P-value
Geometry of Target Lesion - Ulcerated	1.57 [1.10, 2.24]	0.012
Final Target Lesion % Diameter Stenosis	1.02 [1.00, 1.04]	0.045
Arch Type I	0.71 [0.49, 1.03]	0.068
Vessel Tortuosity - Moderate	1.37 [0.91, 2.06]	0.131
Lesion Calcification ≥ 3mm	1.33 [0.82,2.16]	0.241

SAPPHIRE WW Registry data on file

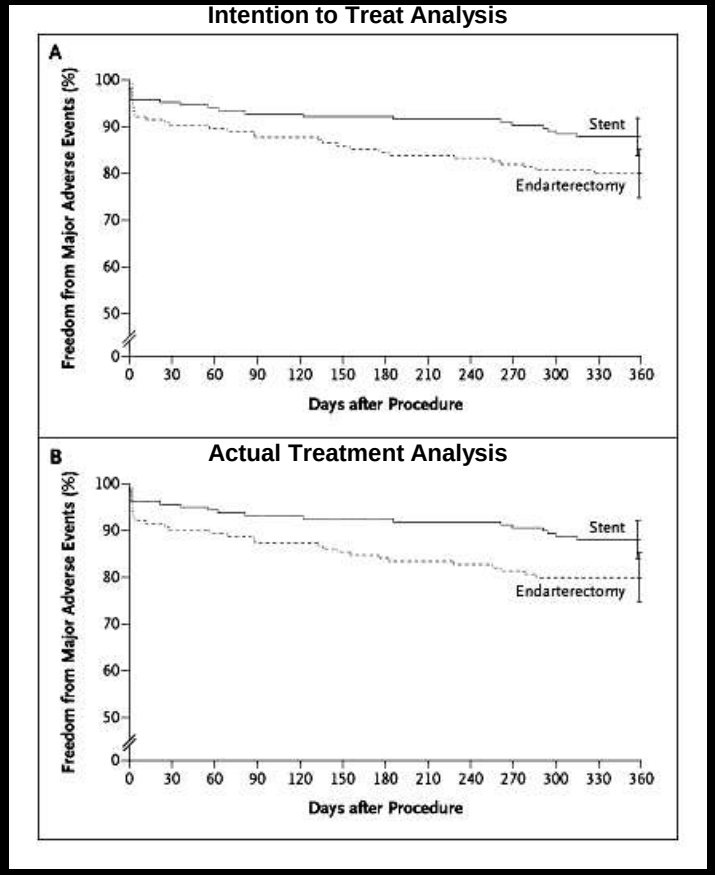
Total Stroke in High Risk Carotid Stent IDE Trials 2002-2011



30-Day Stroke/Death Rates in U.S. High Risk CAS Post Market Studies



Sapphire Trial
Randomized Patients 1-Year Events

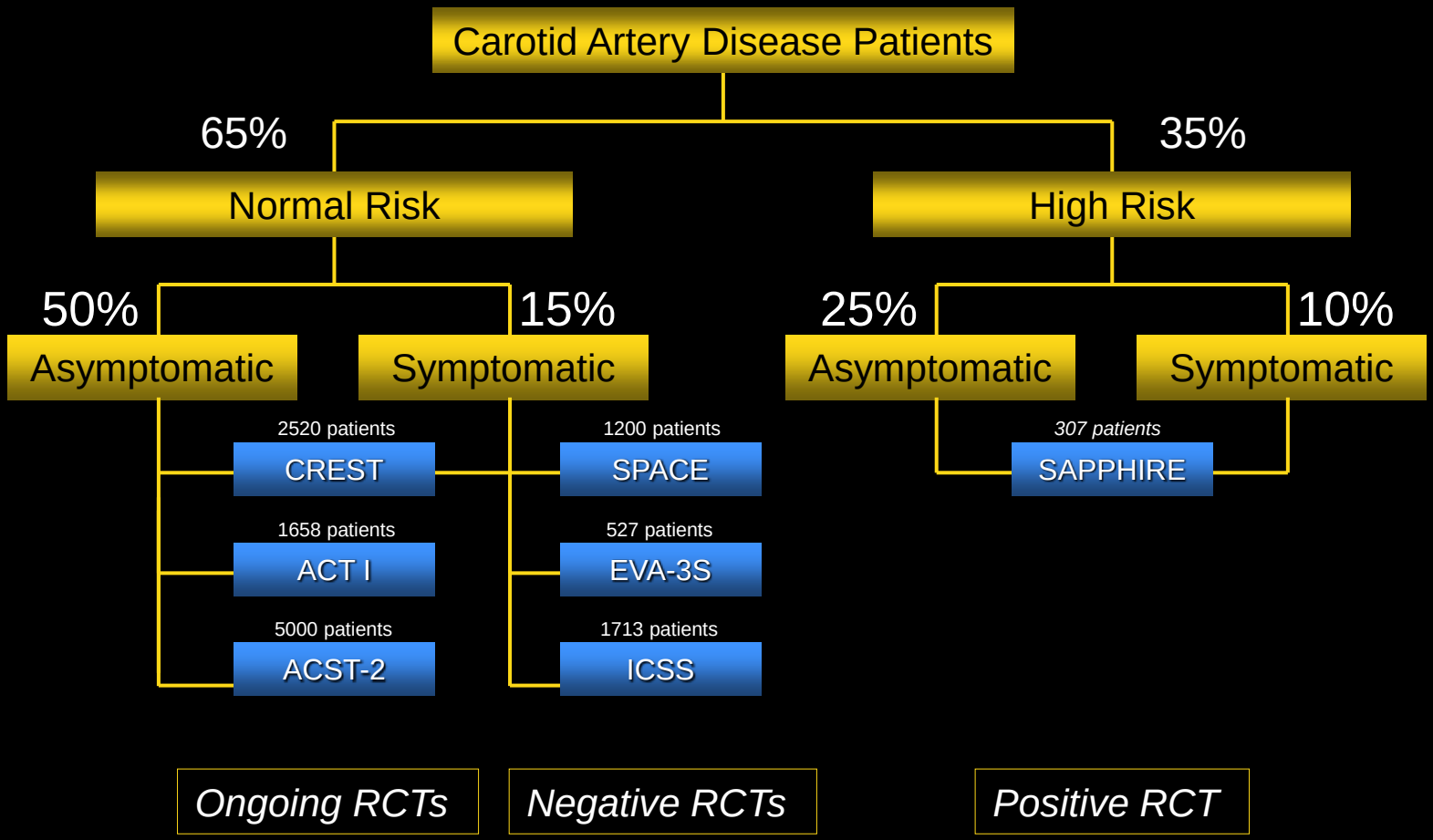


P=0.053

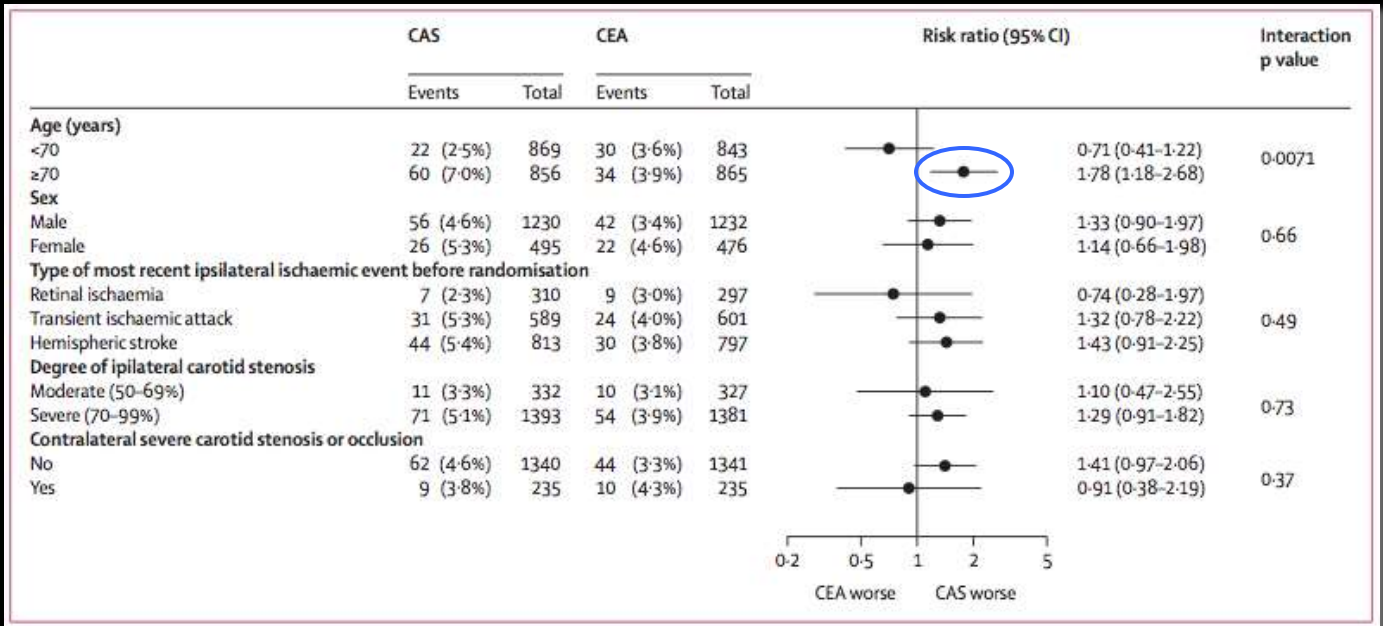
P=0.048

Yadav JS et al *N Eng J Med* 2004; 351: 1493-1501

Carotid Artery Stenting: Prospective Randomized Trials vs. CEA



Meta-analysis of 120-day Outcomes from SPACE, EVA-3S and ICSS



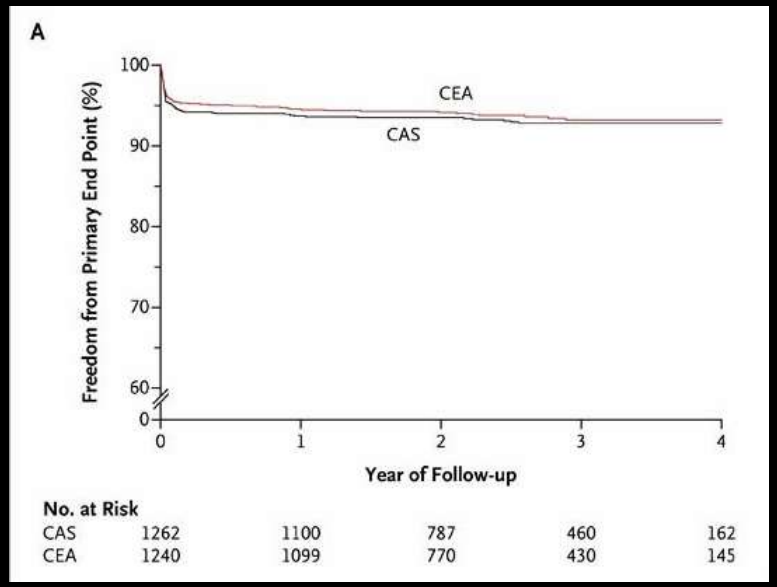
	CAS Events	CAS Total	CEA Events	CEA Total	Risk ratio (95% CI)	Interaction p value
Age (years)						
<70	22 (2·5%)	869	30 (3·6%)	843	0·71 (0·41–1·22)	0·0071
≥70	60 (7·0%)	856	34 (3·9%)	865	1·78 (1·18–2·68)	
Sex						
Male	56 (4·6%)	1230	42 (3·4%)	1232	1·33 (0·90–1·97)	0·66
Female	26 (5·3%)	495	22 (4·6%)	476	1·14 (0·66–1·98)	
Type of most recent ipsilateral ischaemic event before randomisation						
Retinal ischaemia	7 (2·3%)	310	9 (3·0%)	297	0·74 (0·28–1·97)	
Transient ischaemic attack	31 (5·3%)	589	24 (4·0%)	601	1·32 (0·78–2·22)	0·49
Hemispheric stroke	44 (5·4%)	813	30 (3·8%)	797	1·43 (0·91–2·25)	
Degree of ipilateral carotid stenosis						
Moderate (50–69%)	11 (3·3%)	332	10 (3·1%)	327	1·10 (0·47–2·55)	0·73
Severe (70–99%)	71 (5·1%)	1393	54 (3·9%)	1381	1·29 (0·91–1·82)	
Contralateral severe carotid stenosis or occlusion						
No	62 (4·6%)	1340	44 (3·3%)	1341	1·41 (0·97–2·06)	0·37
Yes	9 (3·8%)	235	10 (4·3%)	235	0·91 (0·38–2·19)	

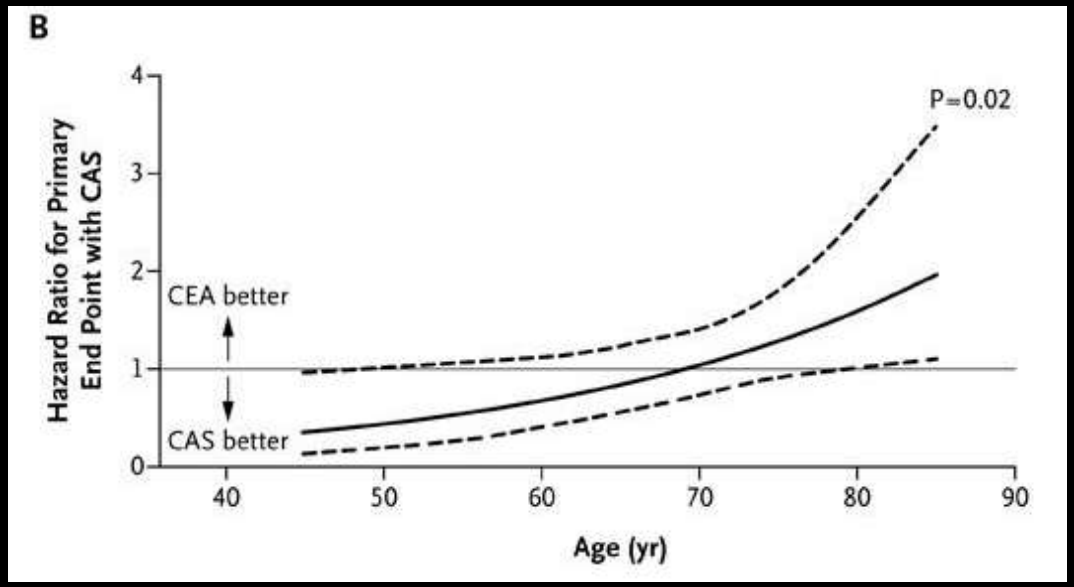
***Figure 5*: Treatment risk ratios of disabling stroke or death within 120 days of randomisation in selected patient subgroups**
Data are number or number (%), unless otherwise indicated. Percentages are number of events divided by number of patients. Analysis was by intention to treat. Dots and horizontal bars represent treatment risk ratios and 95% CIs, respectively, within subgroups, with carotid endarterectomy (CEA) as the reference group, on a log scale. Risk ratios and interaction p values (categorical interaction) were adjusted for source trial. Patients with missing subgroup data were excluded from subgroup analysis (for details of missing data see webappendix pp 2–4). CAS=carotid stenting.

Carotid Stenting Trialists' Collaboration *Lancet* 2010; 376: 1062–1073

CREST: CAS vs. CEA
Outcomes as a Function of Age

Primary composite 4-year outcomes as a function of age





Brott TG et al *N Engl J Med* 2010; 363(1): 11-23

CANOPY vs CREST

DS at 30 days by Symptomatic Status

	CANOPY (N=1200)		CREST (N=1262)	
	Symptomatic (N=335)	Asymptomatic (N=865)	Symptomatic (N=668)	Asymptomatic (N=594)
Death and All Stroke	**5.8%**	**2.5%**	**6.0%**	**2.5%**
All Stroke	**5.2%**	**2.3%**	**5.5%**	**2.5%**

CANOPY DS definition: death and *all stroke*

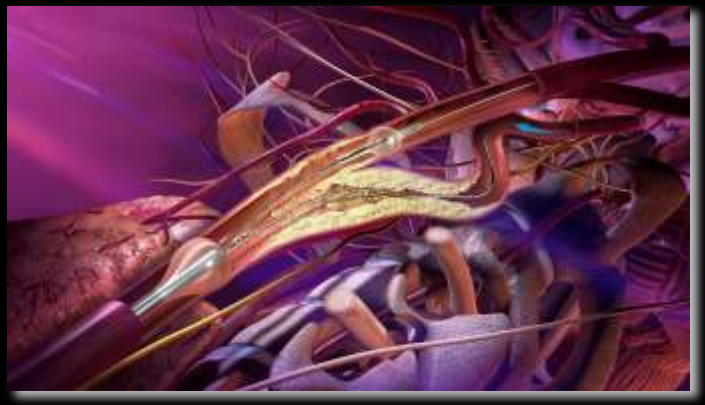
CREST DS definition: any periprocedural stroke or death or post-procedural *ipsilateral stroke*

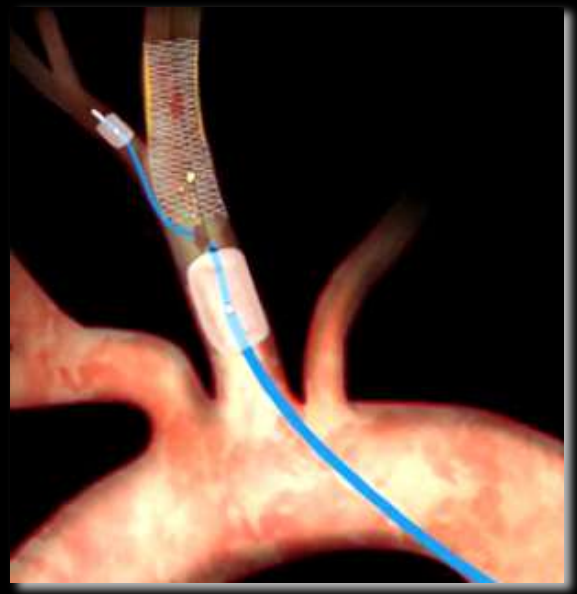
Multivariable Cox Regression Analysis

Variable	**Coefficient**	**Hazard Ratio** [95% CI]	**P-value**
Symptomatic (Yes vs. No)	0.92	2.51 [1.35, 4.68]	0.0038
Multiple stent used	1.17	3.22 [1.26, 8.23]	0.0149

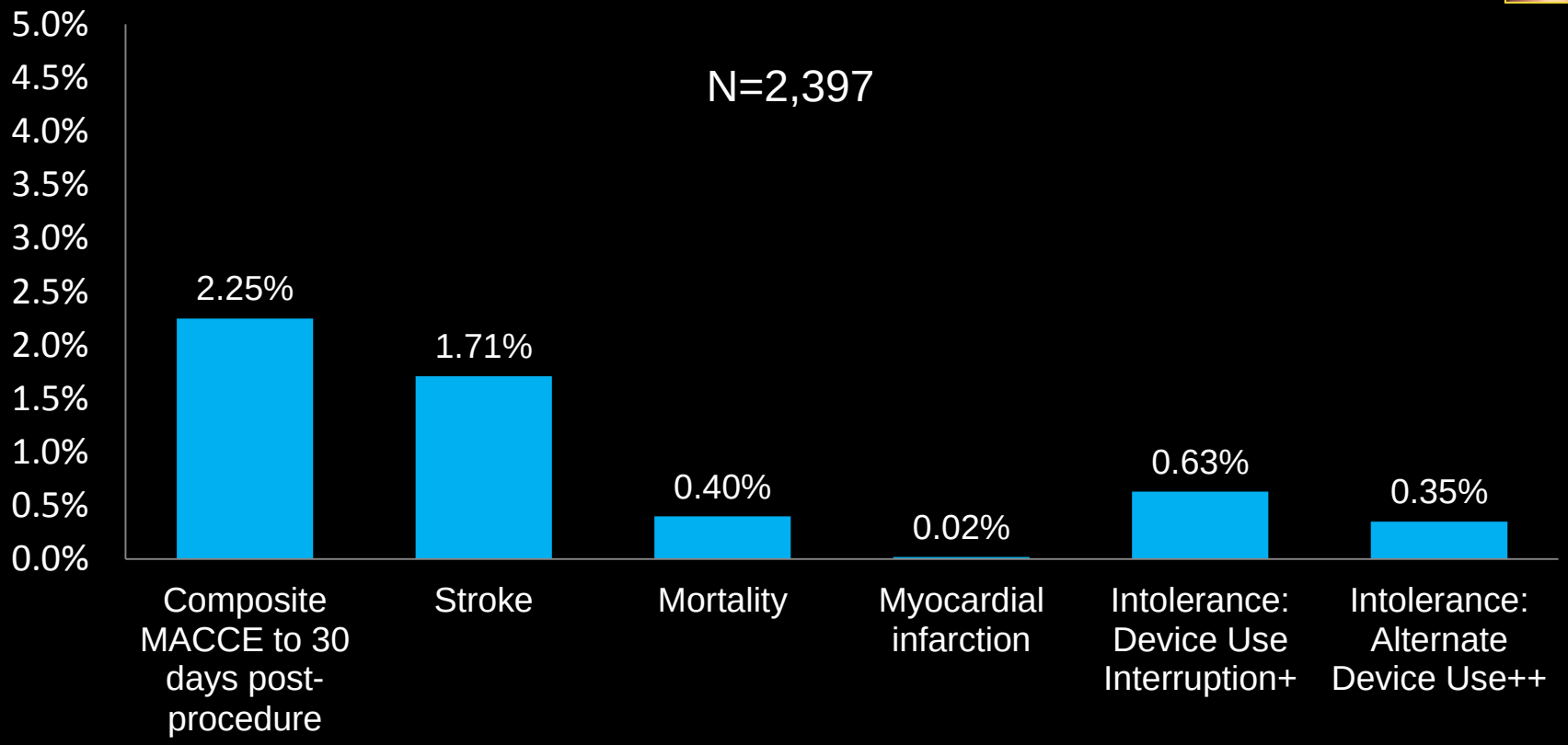
Neither age > 80, or age as a linear variable, were predictors of DS at 30 days.

Carotid Stenting
Emboli Protection Systems





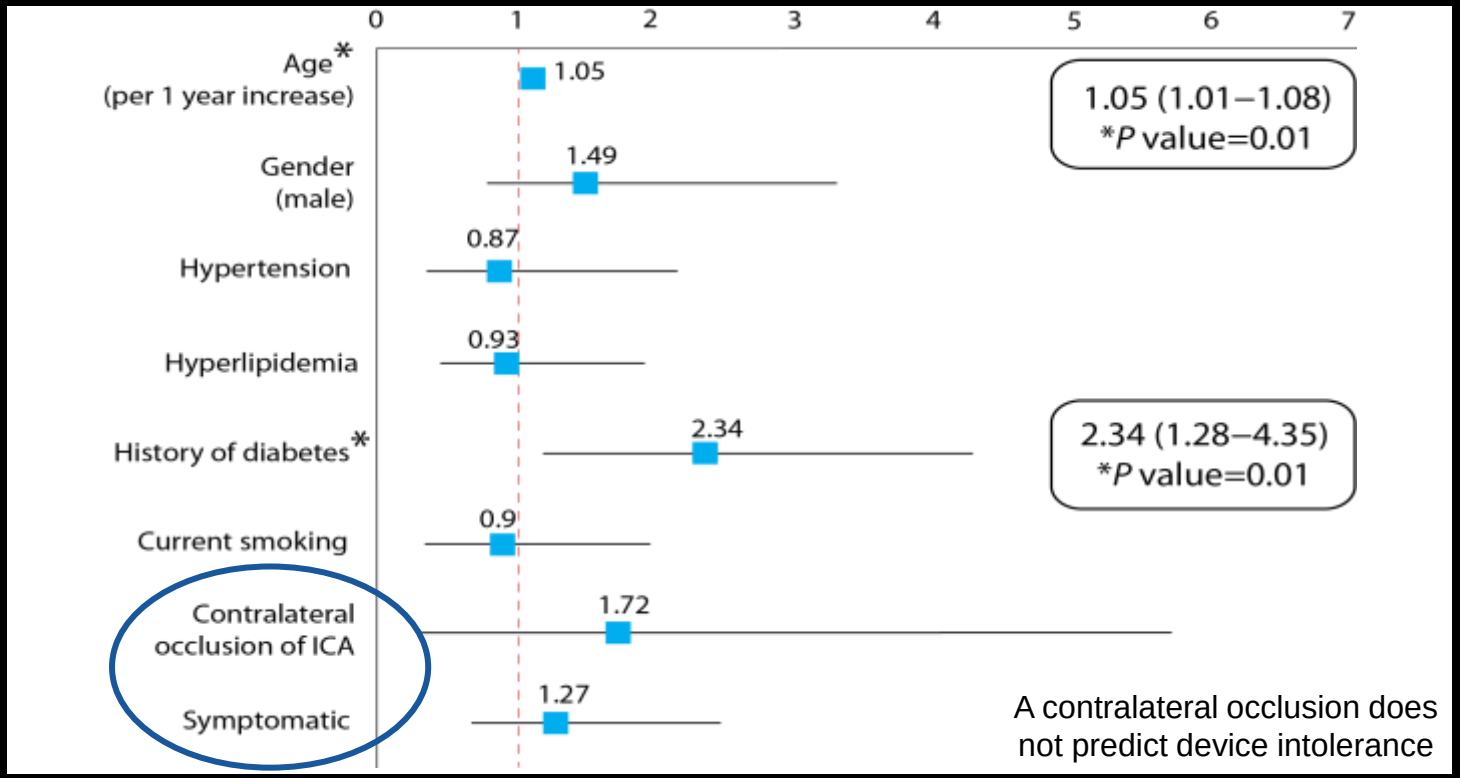
POD Meta-analysis
Overall 30-day Event Rates



Bersin RM et al Cath Cardiovasc Interv 2012; 80: 1072-1078

POD Meta-analysis
Independent Risk Predictors

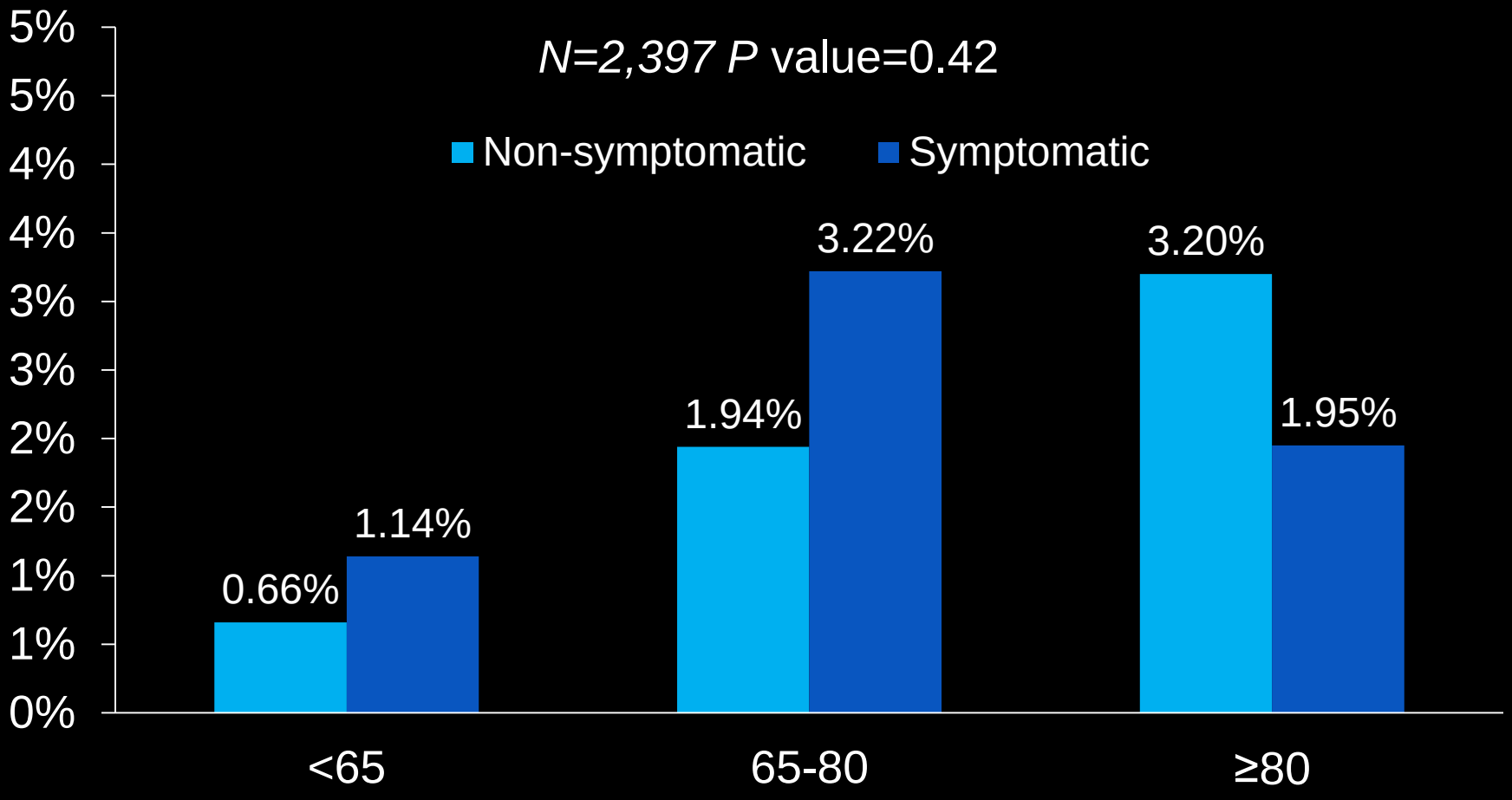
Odds of Baseline Characteristics to Predict Composite MACCE



Bersin RM et al Cath Cardiovasc Interv 2012; 80: 1072-1078

POD Meta-analysis
Overall 30-day Event Rates

Composite MACCE by Age Group and Symptomatic Status

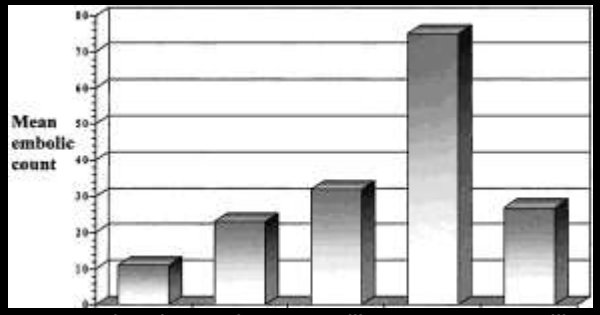


Bersin RM et al *Cath Cardiovasc Interv* 2012; 80: 1072-1078

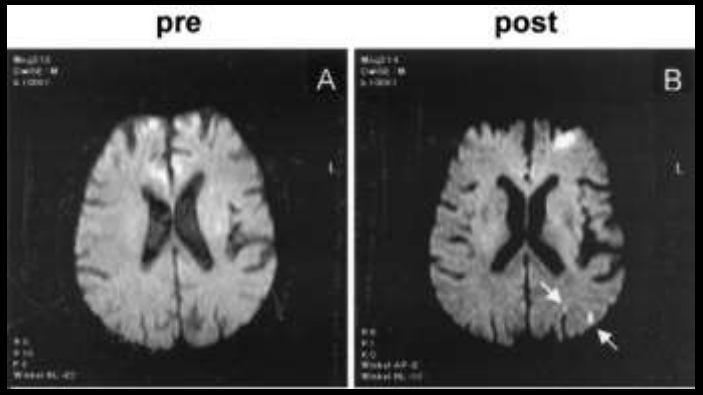
Studies of PODs vs. EPDs

MES by TCD and new embolic lesions by DW-MRI are surrogate markers of embolic events with adequate sensitivity to detect differences between MO.MA and Filters

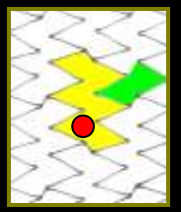
Author	Schmidt	El Koussy	Montorsi	Bijuklic
Enrollment year	2002 - 2003	2003	2009 – 2010	2010 - 2011
Design	Non Rand. MO.MA vs Filter	Non Rand. MO.MA vs Filter	RANDOM MO.MA vs. Filter	RANDOM MO.MA vs. Filter
# patients	42 (21 + 21)	44 (25 + 19)	53 (26 vs 27)	62 (31 vs 31)
% symptom.	33% vs 29%	60% vs 52.6%	15% vs 7%	41.9% vs 38.7%
Risk profile	normal	normal	high-risk, lipid-rich plaque	normal
Primary EP	TCD MES count 57 vs 196	New DW-MRI lesions 18 vs 43	TCD MES count 16 vs 93	New DW-MRI lesions 45 vs 87



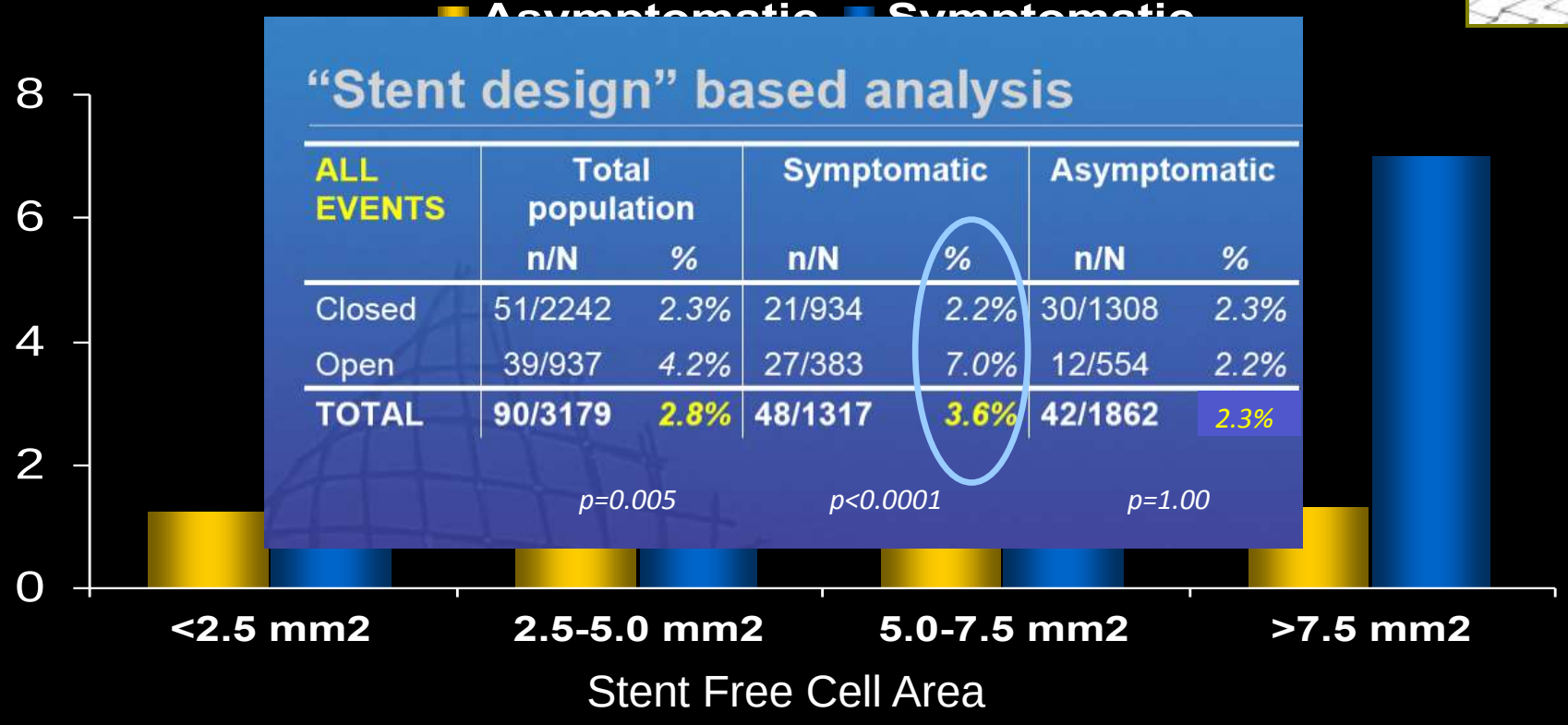
Al – Mubarak et al. Circulation 2001



Carotid Stent Post-Procedural Events By Free Cell Area



Post-procedure to 30-days

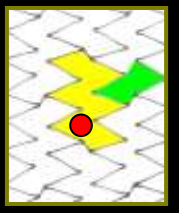


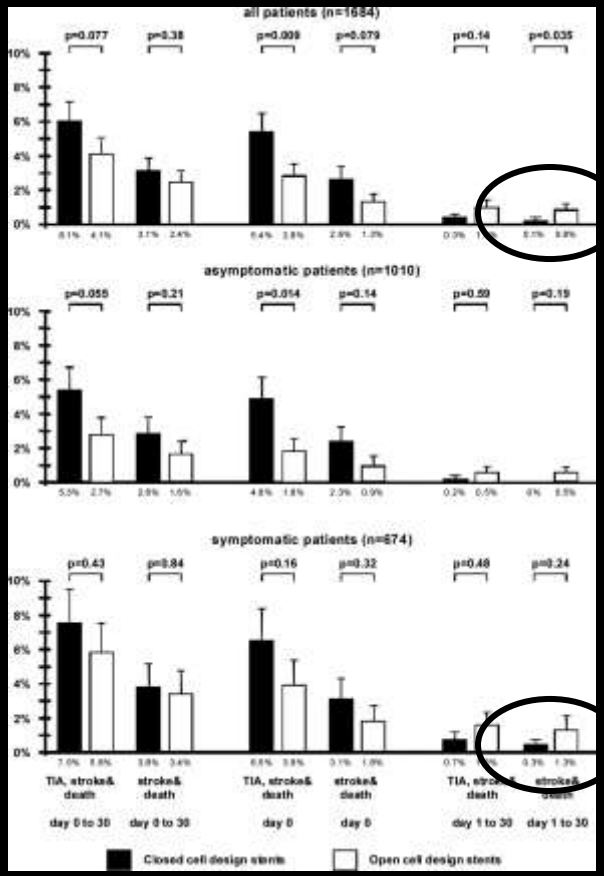
"Stent design" based analysis

ALL EVENTS	Total population		Symptomatic		Asymptomatic	
	n/N	%	n/N	%	n/N	%
Closed	51/2242	2.3%	21/934	2.2%	30/1308	2.3%
Open	39/937	4.2%	27/383	7.0%	12/554	2.2%
TOTAL	90/3179	2.8%	48/1317	3.6%	42/1862	2.3%
			p=0.005	p<0.0001	p=1.00	

Bosiers M et al *Eur J Vasc Endovasc Surg 2007;* 33:135-141

Carotid Stent Design
Closed Cell vs. Open Cell





Day 1-30 Events in Symptomatic Patients:
0.3% closed cell
1.3% open cell (N=1864)

Schillinger, M et al *Stroke* 2008; 39: 905-909

Conclusions

- The “Gold Standards” for CEA outcomes were established by ACAS and NASCET in standard surgical risk patients.
- Clinical factors that increase stroke risk with CAS include: Adverse arch anatomy, lesion ulceration, symptomatic status and patient age.
- Technical factors that increase stroke risk with CAS include: Lack of use of a protection device, pre-dilation prior to protection, and use of multiple stents.
- Symptomatic patients have a 2-fold greater risk of stroke with CEA and CAS using filter EPDs. The use of proximal protection reduces the risk of stroke in symptomatic patients to that of asymptomatic patients.
- The use of closed cell stents may further reduce the overall stroke rates by reducing peri-procedural events in symptomatic patients.