

**Carotid Disease: Will ACT ONE Finally
Tell Us the Best Options for Our
Patients...Or are We on the CREST of a
New Wave?**

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Disclosures

- **Consultant/Advisory Board Member:**

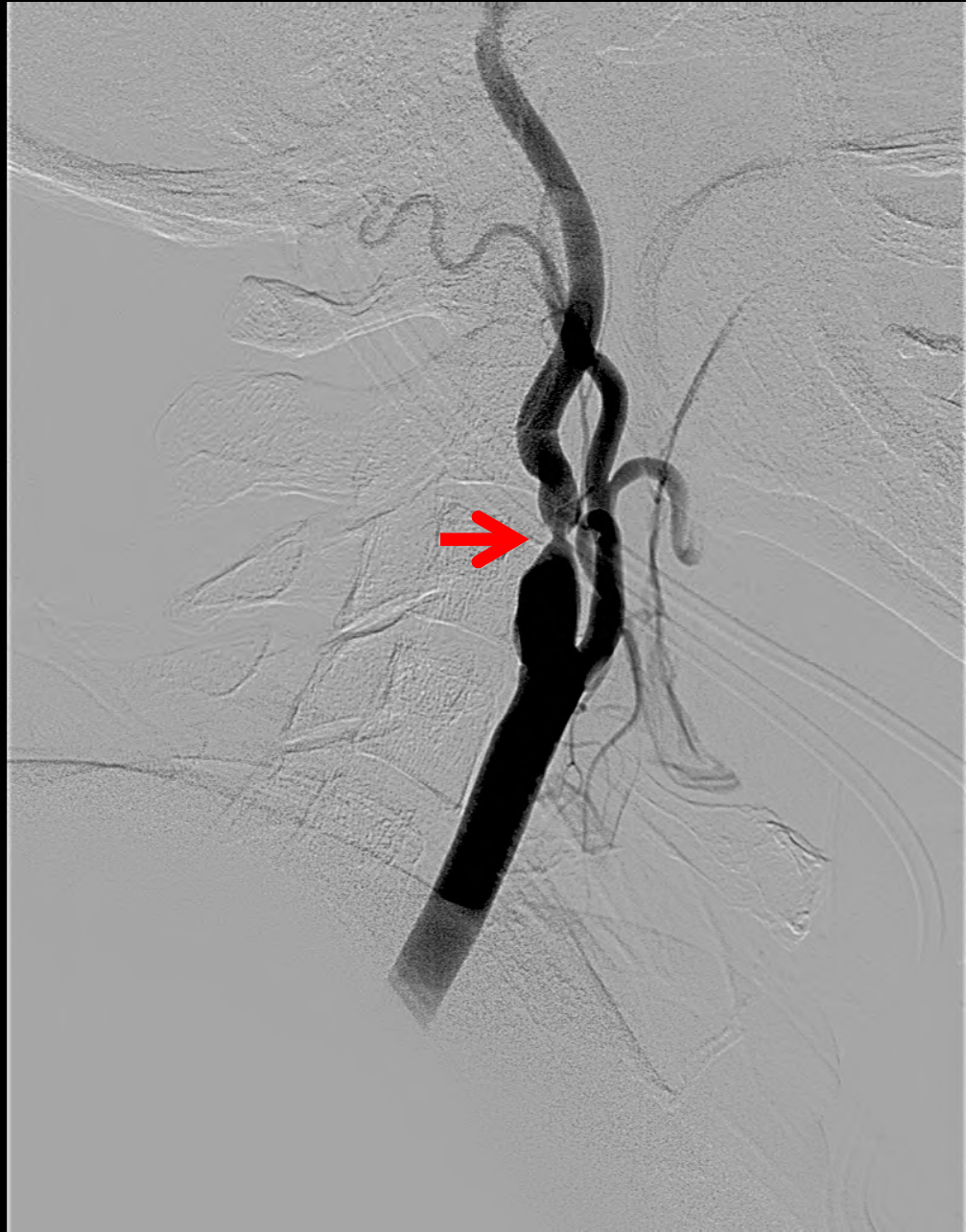
Abbott Vascular, Abiomed, Boston Scientific, Cardiovascular Systems, Medtronic, Merck, and Spectranetics

Outline

- **Rationale for Carotid Revascularization**
- **Treatment of Symptomatic Carotid Artery Disease**
- **Treatment of Asymptomatic Carotid Artery Disease**
- **Current Guidelines and Coverage For Carotid Stenting**

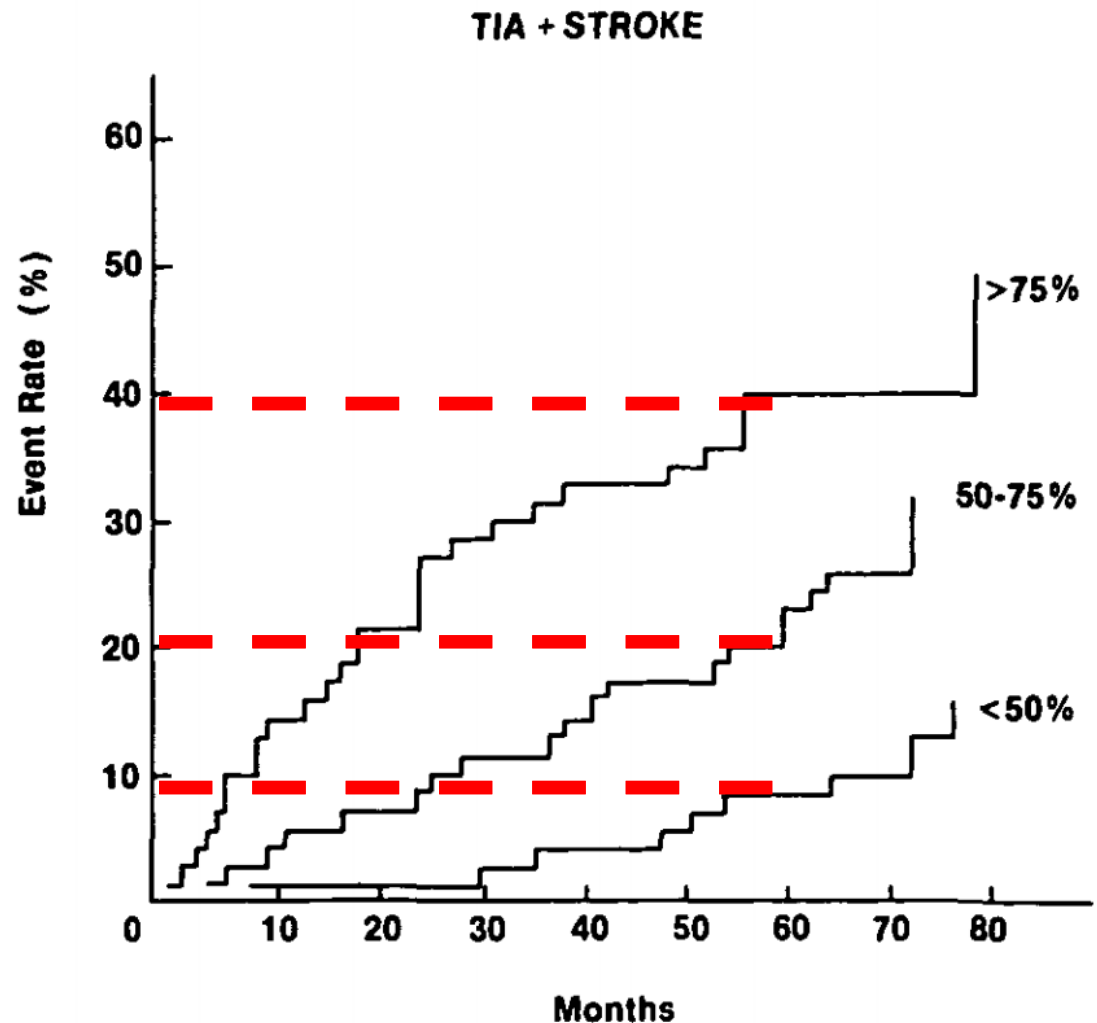
Pathophysiology of Symptoms from Carotid Artery Stenosis

- Symptoms occur from embolism or low flow.
- Present as ipsilateral ocular and/or cerebral hemisphere ischemia.
 - Amaurosis fugax.
- Carotid atherosclerosis generally occurs at bifurcation or within 2 cm.
 - “Hourglass” appearance

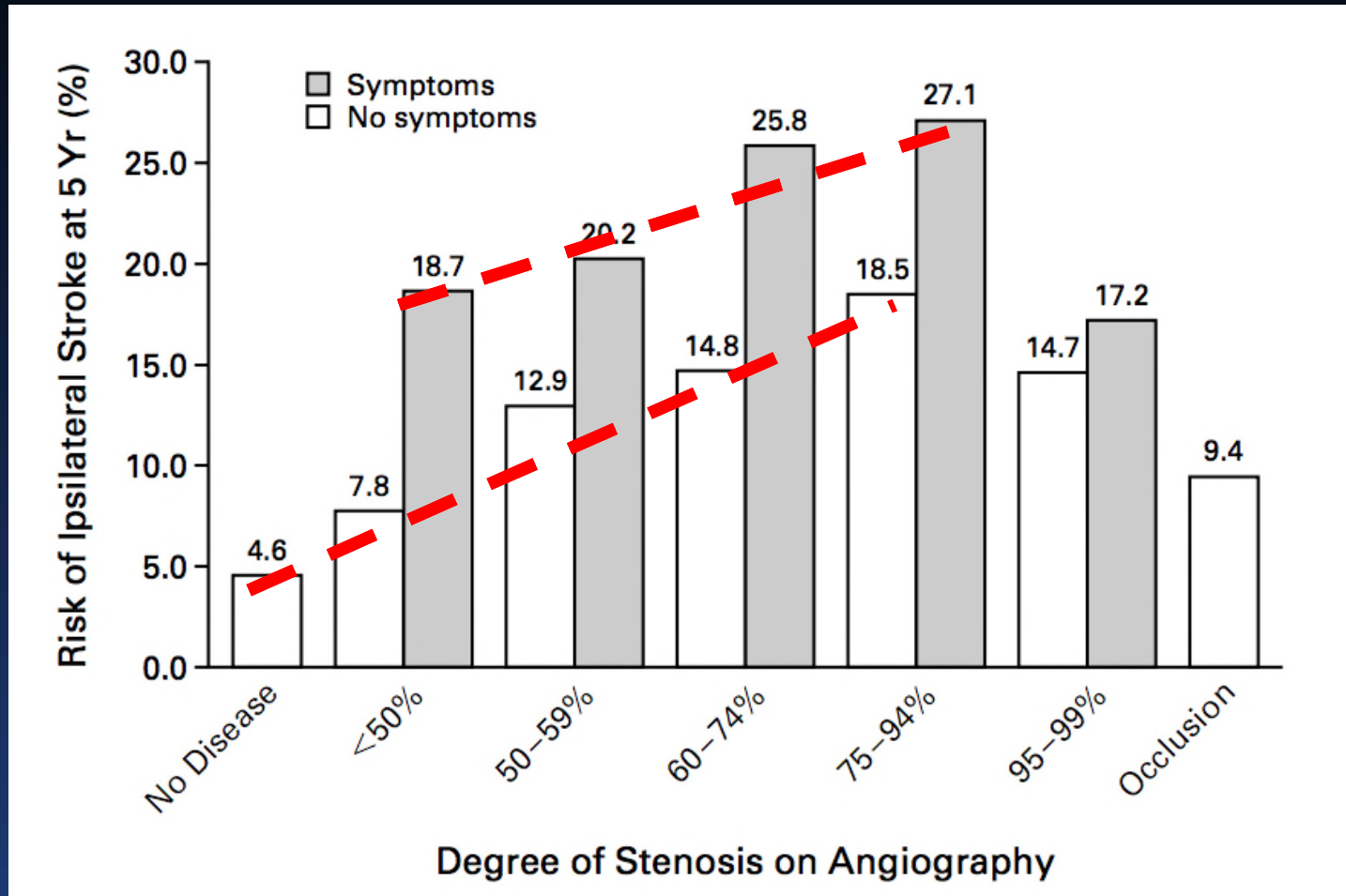


Association Between Carotid Artery Stenosis and Stroke

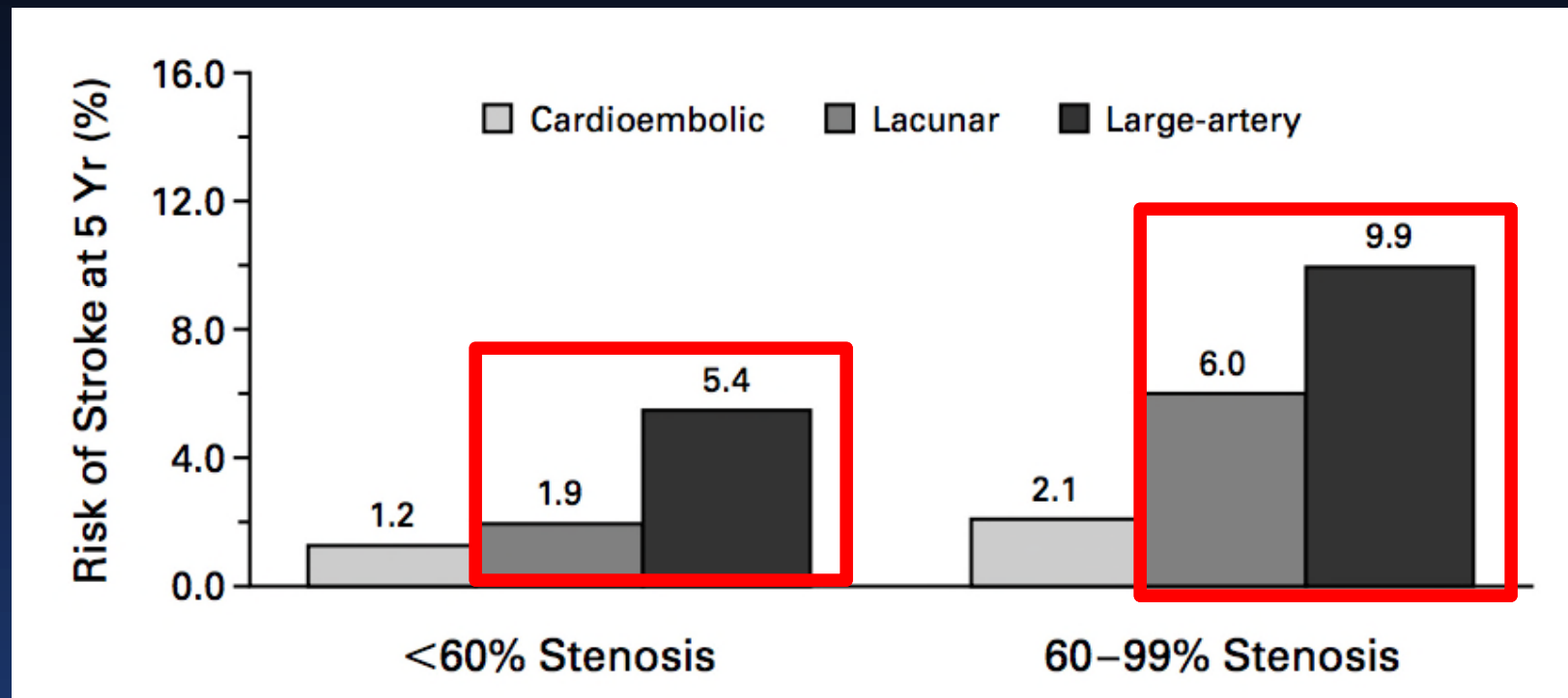
- 696 patients with asymptomatic carotid artery stenosis.
- Mean follow up 41 months
- 75% of events were ipsilateral to stenosis



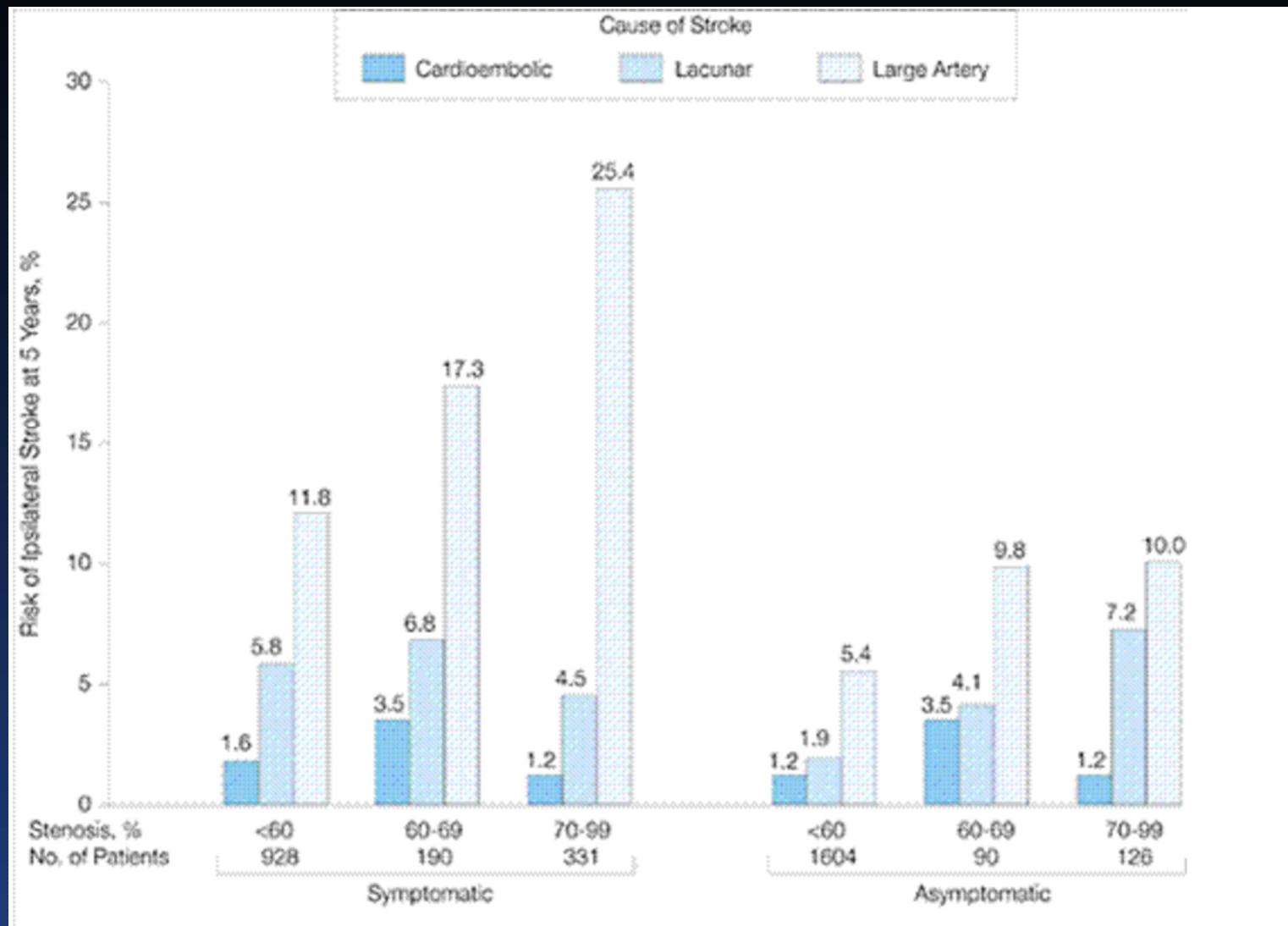
Carotid Artery Stenosis and Stroke Risk



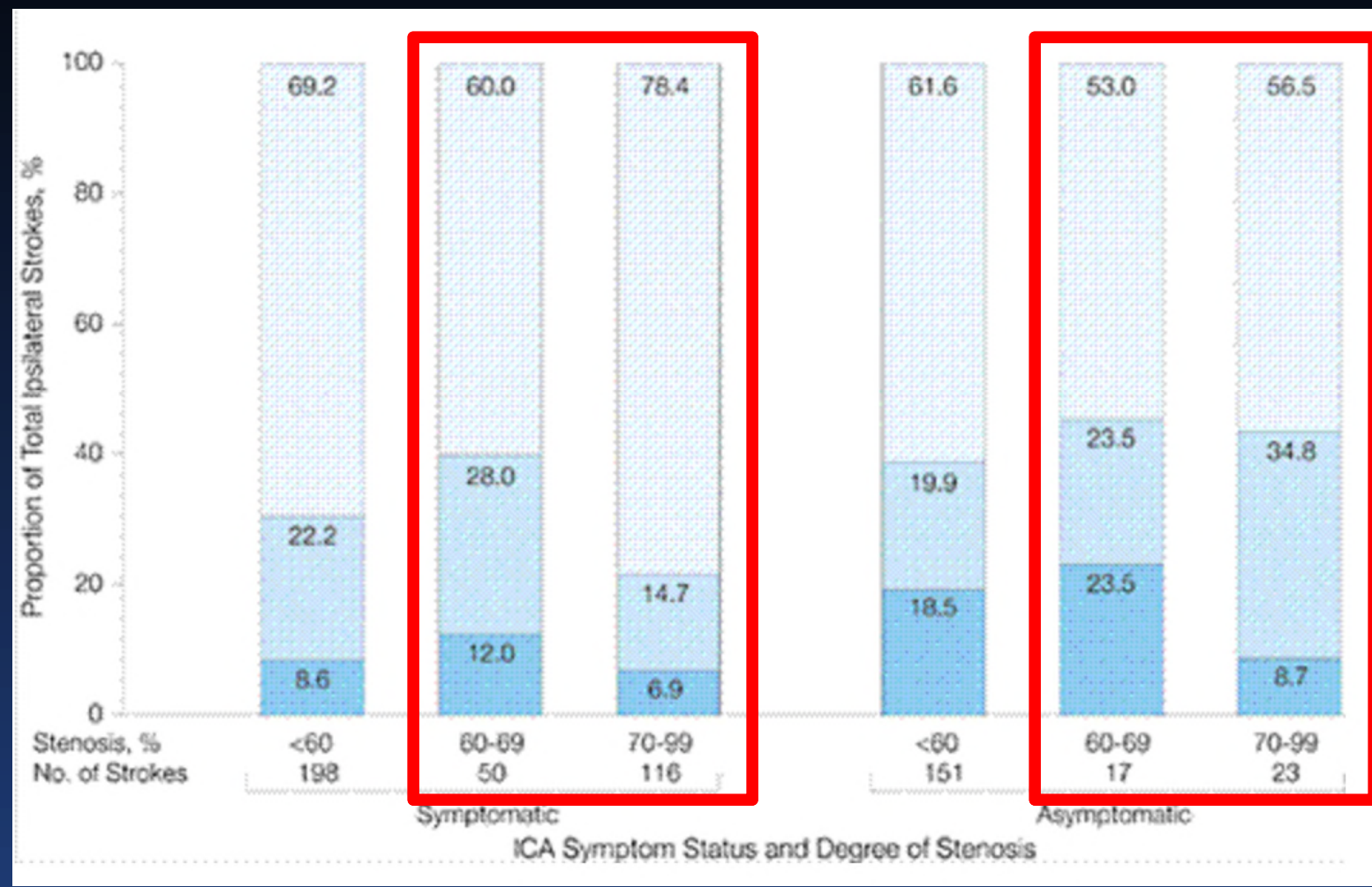
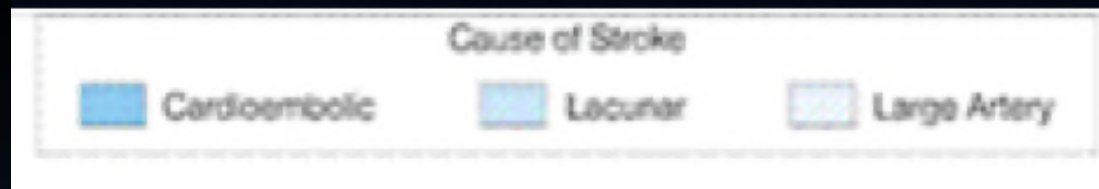
Carotid Artery Stenosis and Stroke Risk – Asymptomatic Disease



5 Year Risk of Stroke



Barnett et al, JAMA 2000;283:1429-1436



Barnett et al, JAMA 2000;283:1429-1436

Treatment of Symptomatic Carotid Artery Stenosis

- **Symptomatic carotid artery stenosis: defined as TIA or ipsilateral hemispheric stroke within the past six months.**
- **May present as amaurosis fugax.**
- **Benefit of early revascularization if significant stenosis present.**

Early Benefit of Revascularization if Symptomatic

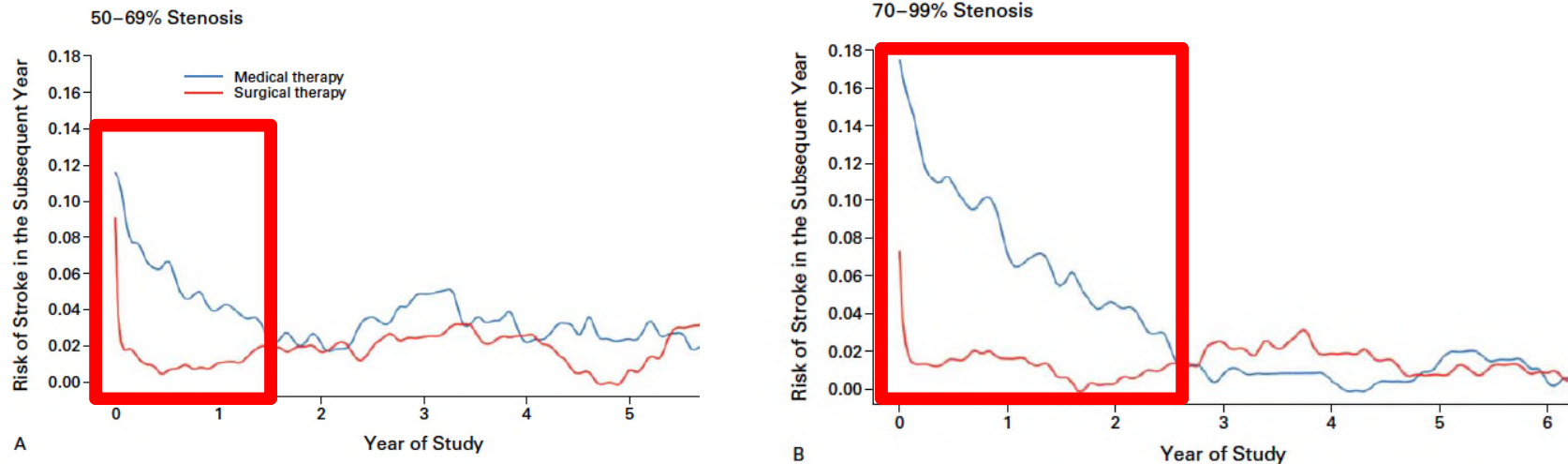


Figure 2. Change in the Risk of Ipsilateral Stroke over Time, According to Severity of Stenosis and Treatment Group. The curves show the risk of an ipsilateral stroke over the next year among patients who had not had an ipsilateral stroke since randomization. Separate calculations were made every 10 days from randomization to the sixth year of follow-up for patients with stenosis of 50 to 69 percent at base line (Panel A) and those with stenosis of 70 to 99 percent at base line (Panel B).

Symptomatic Stenosis – Carotid Endarterectomy

	Percent Stenosis	Patients	% Stroke Medical*	% Stroke Surgical*
ECST	70-99	778	17 (3 years)	10
NASCET	70-99	662	26 (2 years)	9
NASCET	50-69	858	22 (5 years)	16
VA	50-99	189	19 (1 year)	8

**Ipsilateral*

Pooled Analysis - Symptomatic

- Re-analysis of ECST angiograms to match NASCET method.
- CEA beneficial for $\geq 70\%$ stenosis
 - NNT 6.3 for one stroke over five years, ARR 16%.
- No benefit in “String Sign” or Occlusion
- CEA beneficial for 50-69% stenosis
 - NNT 22 for one stroke over five years, ARR 4.6%

Carotid Artery Stenting For Symptomatic Disease

- **Multiple trials of carotid artery stenting for patients with symptomatic carotid disease at average surgical risk**
 - **SPACE, EVA-3S, ICSS**
- **All three trials flawed**
 - **No consistent use of EPDs**
 - **Operator inexperience with stenting**

High Surgical Risk

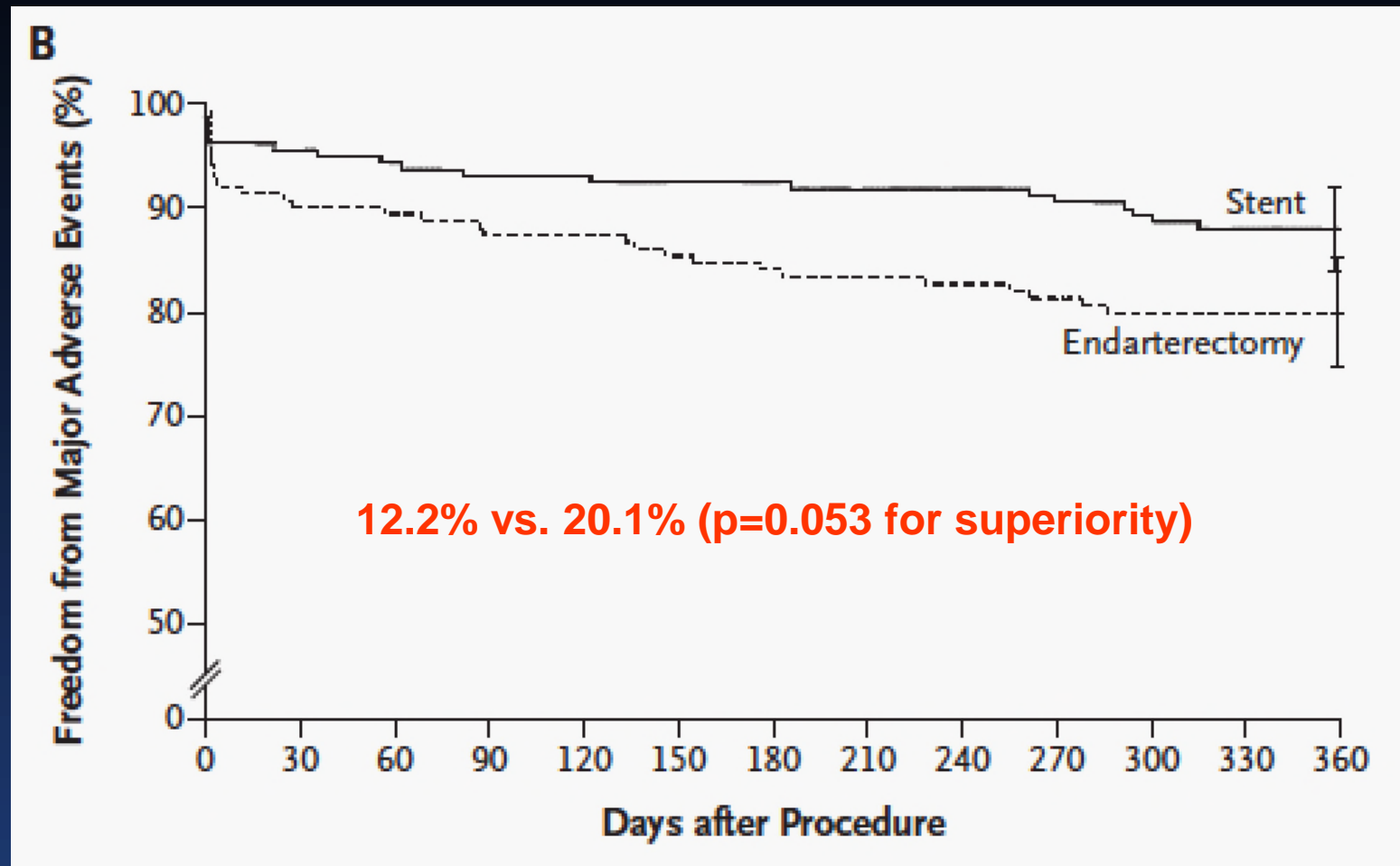
TABLE 1 Features Associated With High Risk of Carotid Endarterectomy

Medical Comorbidity	Anatomic Criteria
Elderly (>75/80 yrs)	Surgically inaccessible lesions
Congestive heart failure (NYHA functional class III/IV)	At or above C2
Unstable angina (CCS III/IV)	Below the clavicle
CAD with ≥ 2 vessels $\geq 70\%$ stenosis	Ipsilateral neck irradiation
Recent myocardial infarction (≤ 30 days)	Spinal immobility of the neck
Planned open heart surgery (≤ 30 days)	Contralateral carotid artery occlusion
Ejection fraction $\leq 30\%$	Laryngeal palsy
Severe pulmonary disease (COPD)	Tracheostoma
Severe renal disease	Previous ipsilateral CEA or neck surgery

SAPPHIRE Trial

- **334 patients with symptomatic or asymptomatic carotid artery disease at high surgical risk for CEA**
 - **>50% stenosis if symptomatic**
 - **>80% stenosis if asymptomatic**
- **Consistent use of embolic protection, more experienced operators**

SAPPHIRE Trial – Overall Results

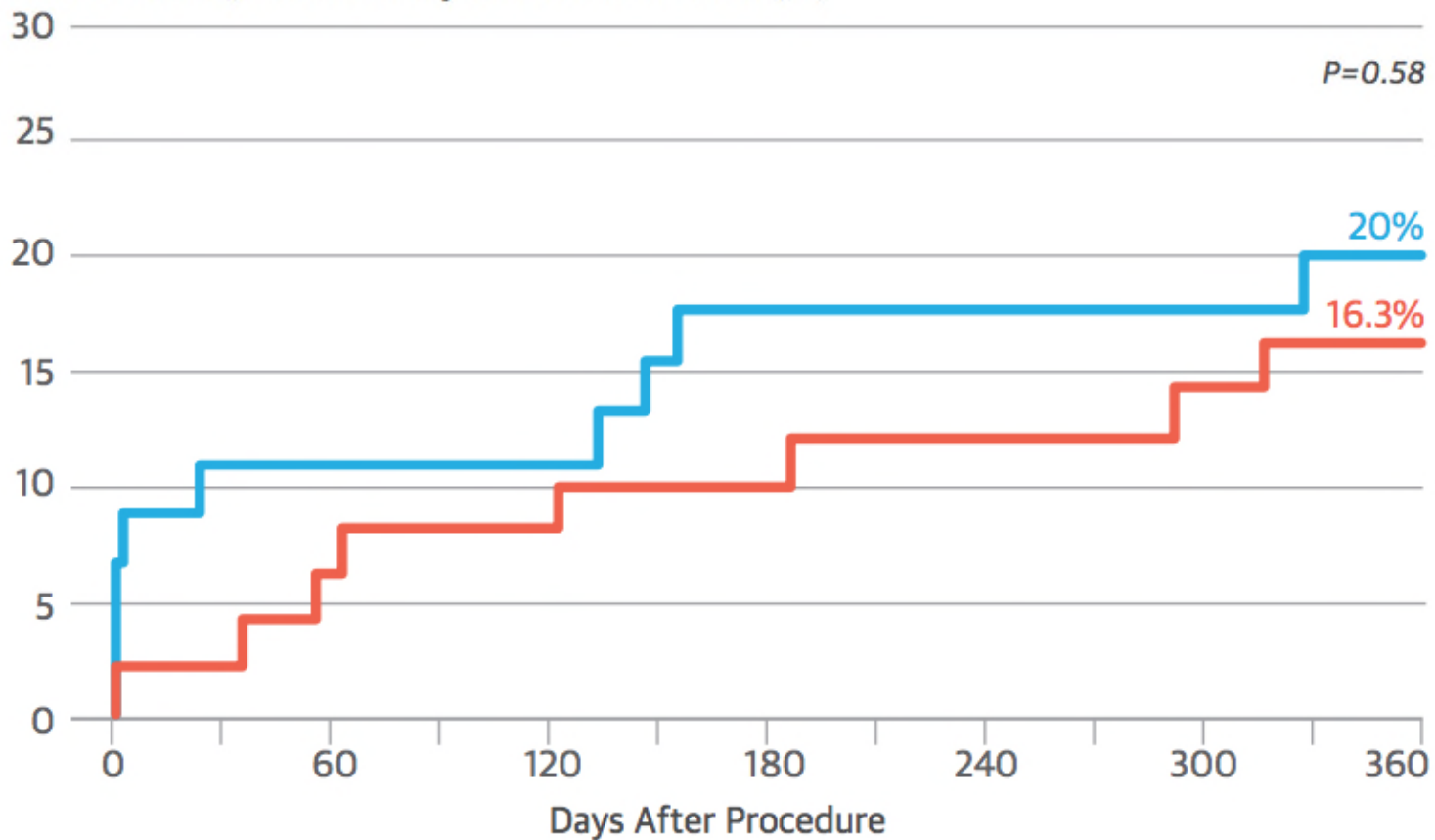


SAPPHIRE Trial – Symptomatic Patients

Comparing CAS and CAE Results In High Surgical Risk Symptomatic Patients²⁴

■ Treated with Carotid Artery Stenting ■ Treated with Carotid Endarterectomy

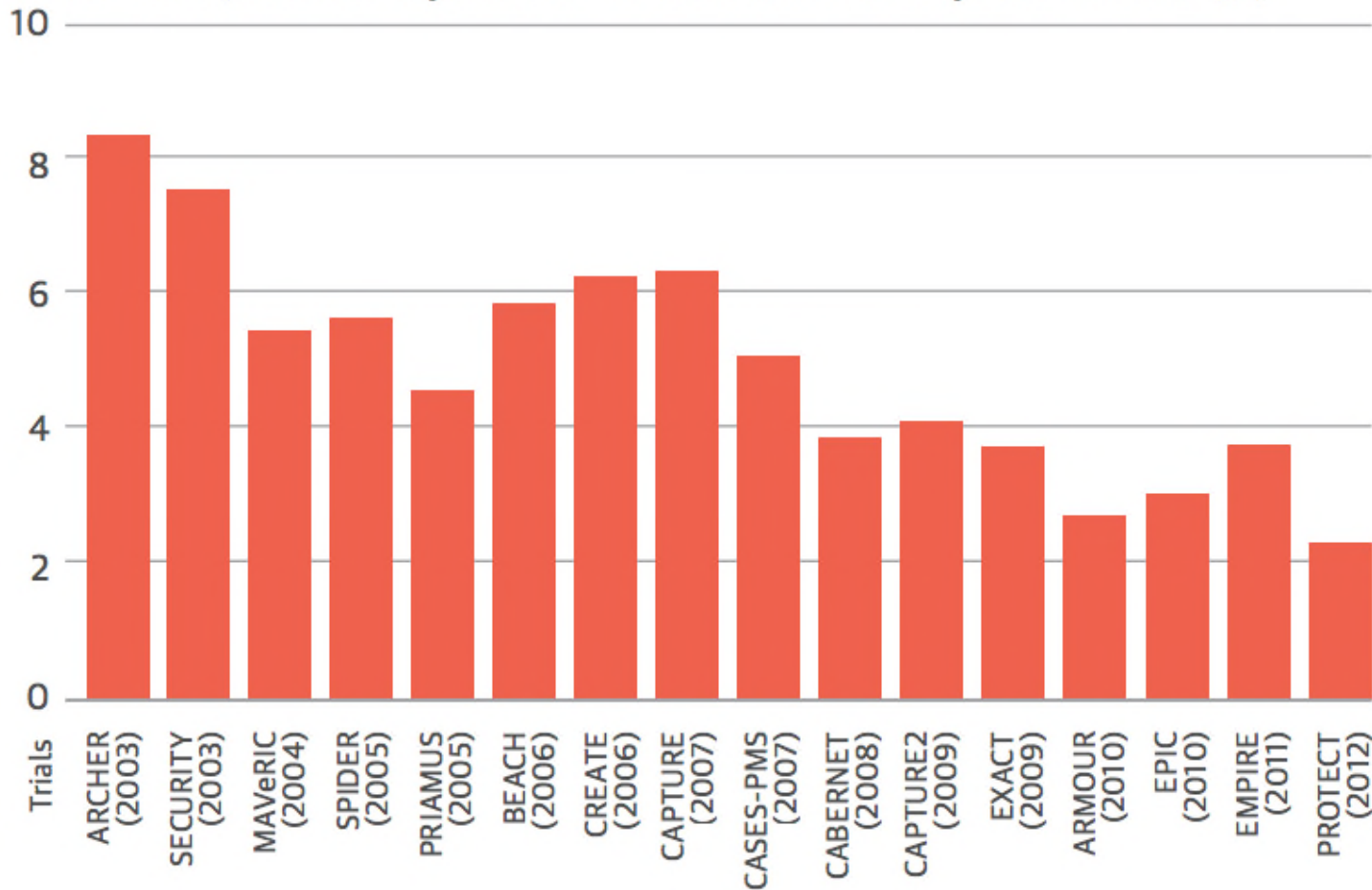
Risk of Death, Stroke or Myocardial Infarction (%)



Decreasing Stroke Risk With Improved Techniques

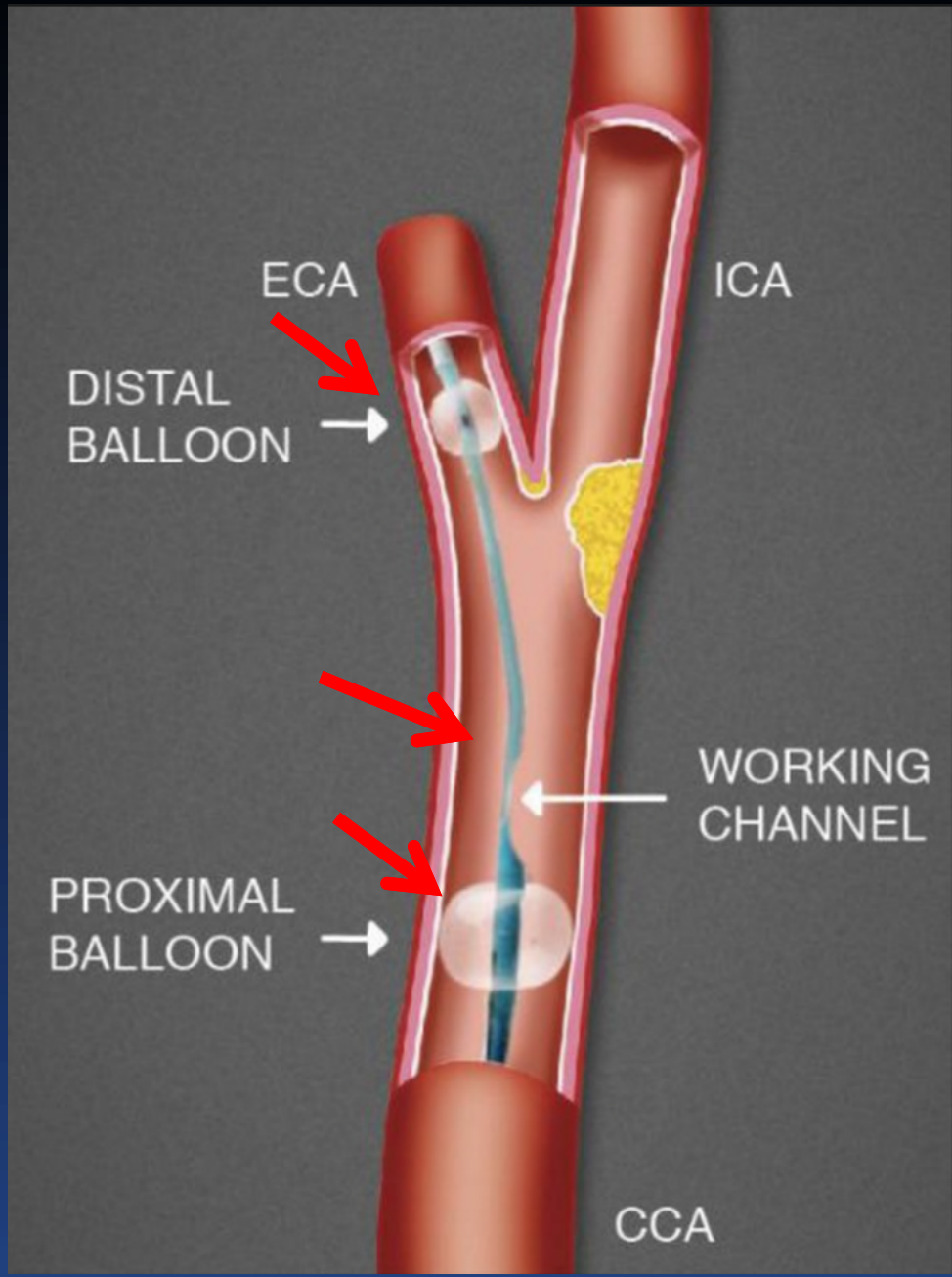
CAS Results Show an Improving Trend In High Surgical Risk Patients (2003–2012)

Risk of Death, Stroke or Myocardial Infarction Within 30 Days of Procedure (%)



Proximal Embolic Protection for Symptomatic Carotid Artery Disease

- **Initial crossing of carotid lesion is performed “unprotected”**
- **Possible benefit of proximal embolic protection**
- **Fewer carotid Doppler signals with proximal protection**



Carotid Angiogram

Image size: 1024 x 1024
View size: 703 x 703
WL: 570 WW: 683

1512685 (88 y , 88 y)
Thorax - Cerebral 3 fps
3701341
6

Zoom: 69% Angle: 0
Inn: 1/15
Uncompressed

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Made In OsiriX



Carotid Angiogram

Image size: 1024 x 1024

View size: 703 x 703

WL: 570 WW: 683

1512685 (88 y , 88 y)

Thorax — Cerebral 3 fps

3701341

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Zoom: 69% Angle: 0

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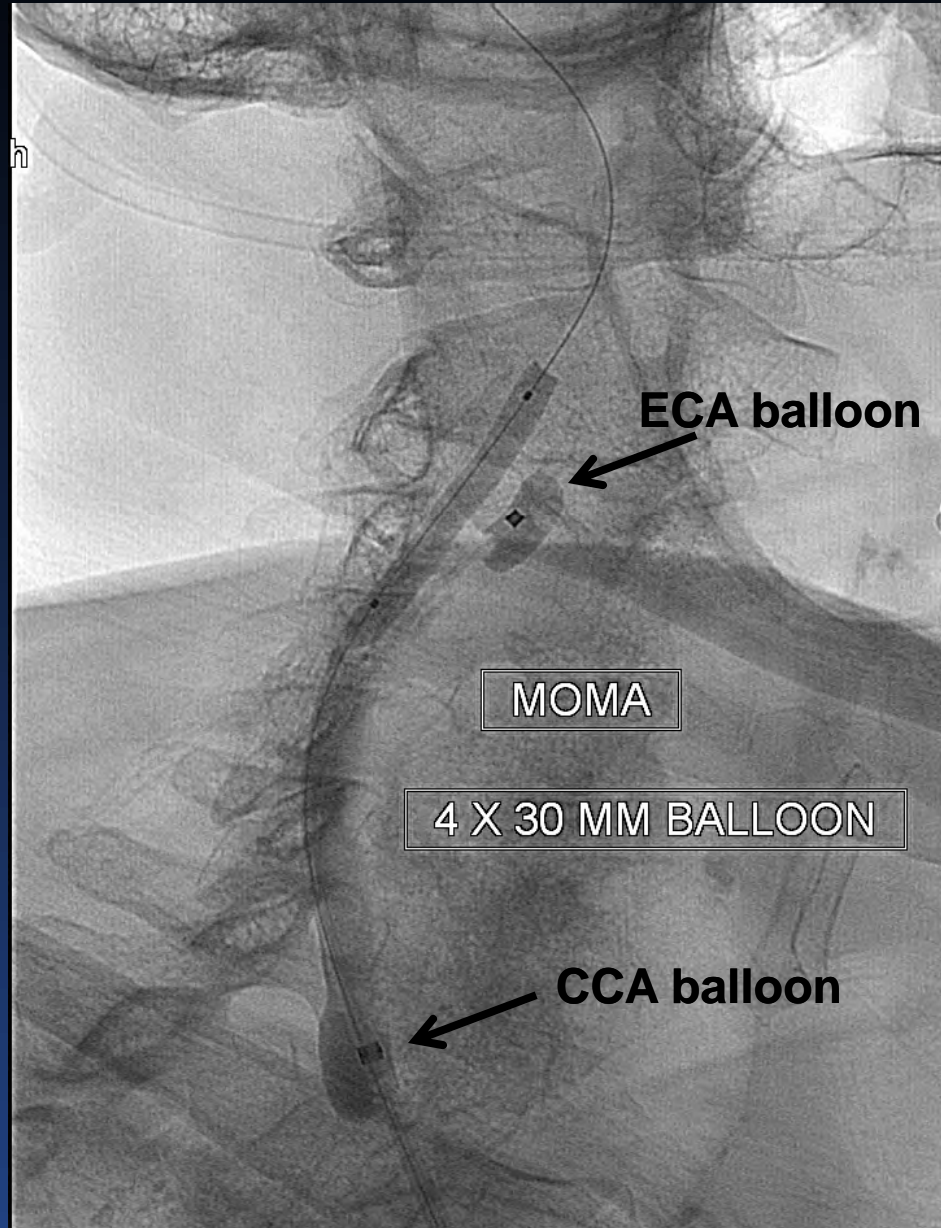
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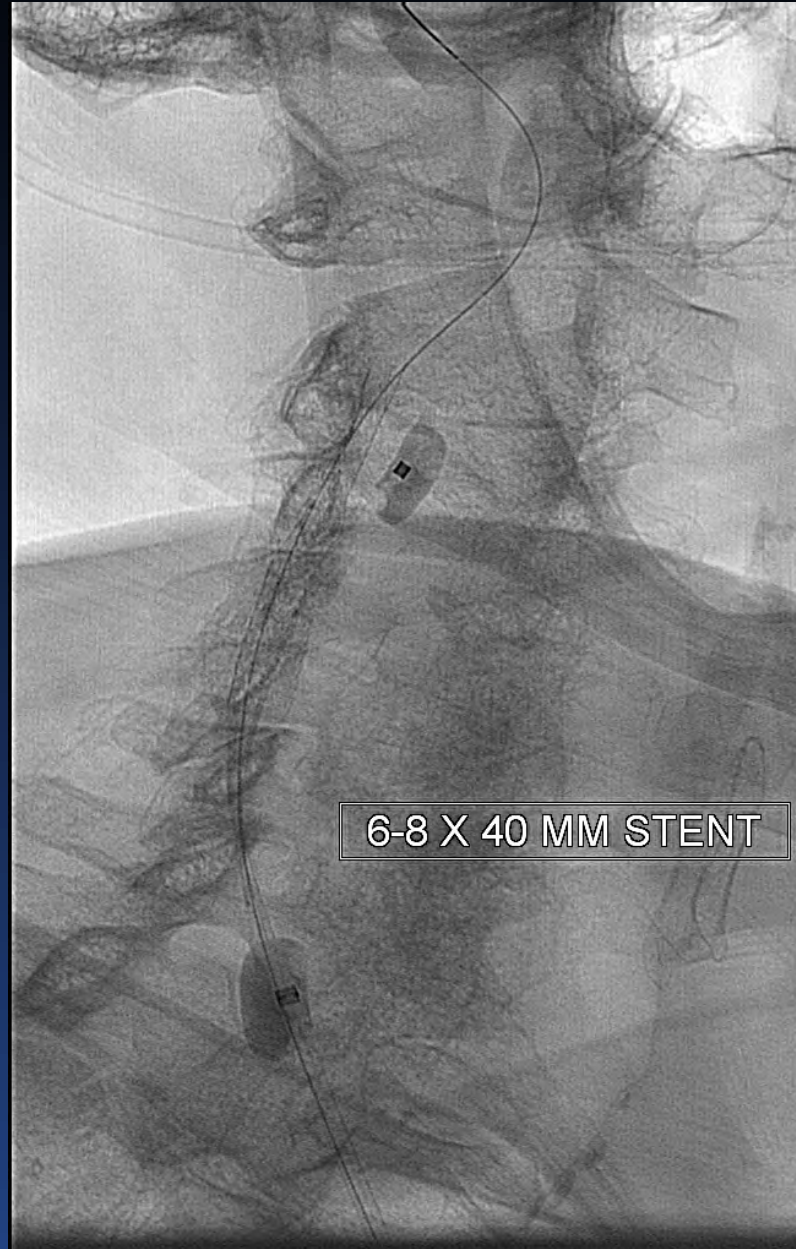
Carotid Angiography



MOMA Deployed



Stent Deployed



Post Dilatation



Post Stent – MOMA Still In

Image size: 1024 x 1024
View size: 703 x 703
WL: 570 WW: 683

1512685 (88 y , 88 y)
Thorax – Cerebral 3 fps
3701341
19



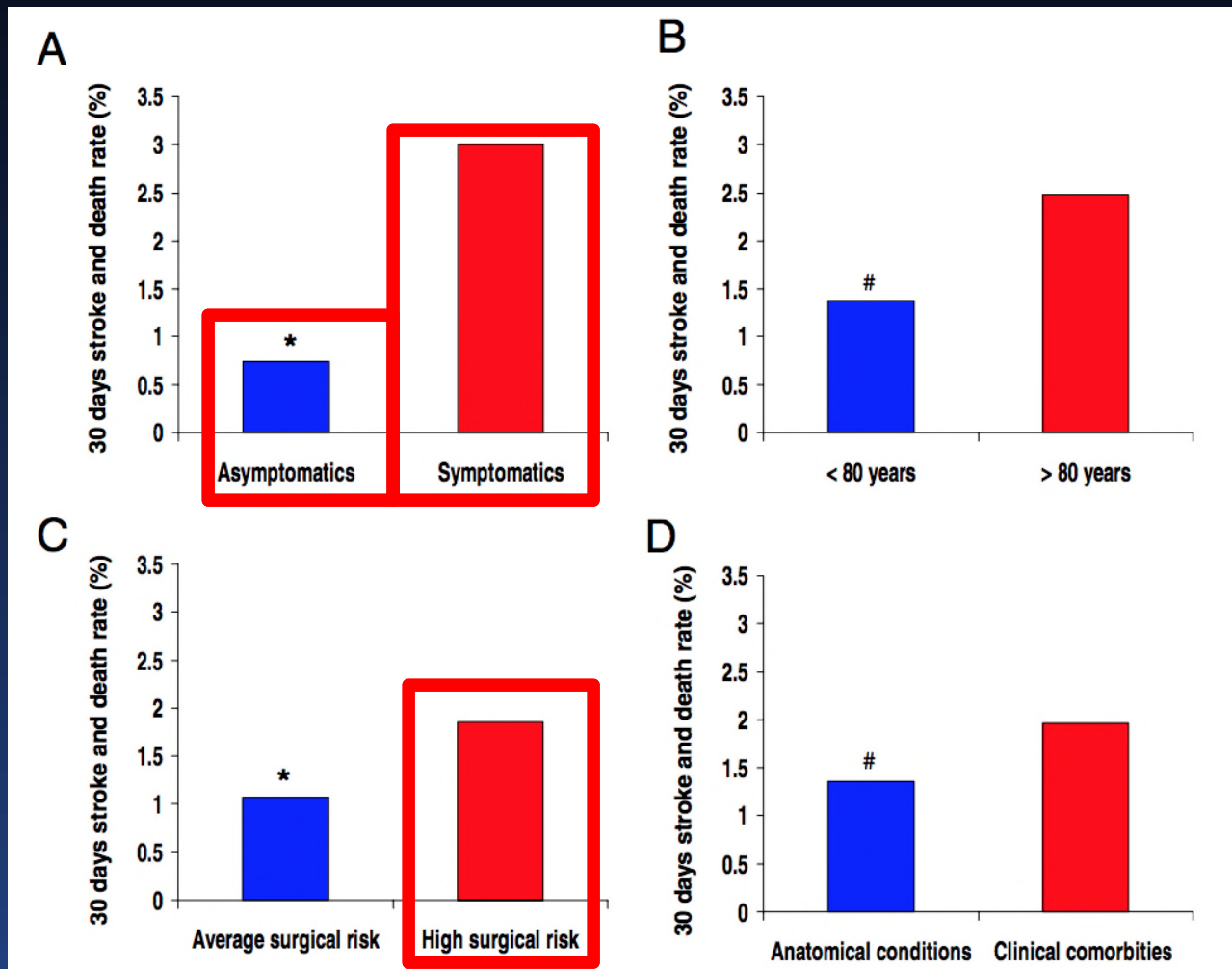
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Final Angiography



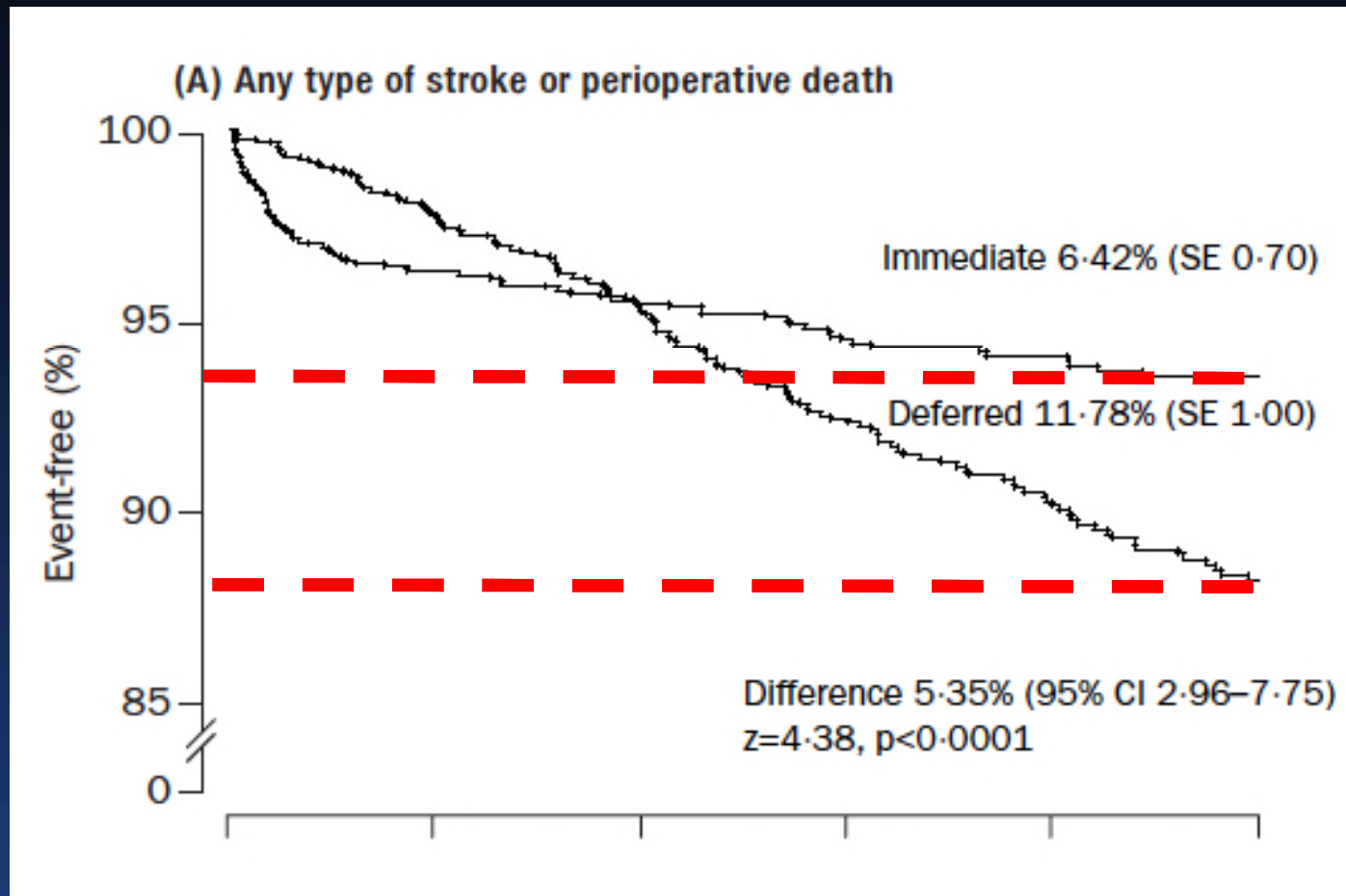
Prospective Registry of 1,300 Patients Treated with Proximal Embolic Protection



Treatment of Asymptomatic Carotid Artery Stenosis

- Data for benefit of asymptomatic carotid artery stenosis revascularization is based primarily on CEA vs. medical therapy data from the 1990's.
- Early risk associated with revascularization, long-term benefit over five years.
- No definite benefit in women (under-representation?)

Short-Term Risk, Long-Term Benefit



Asymptomatic Stenosis: Carotid Endarterectomy

	Percent Stenosis	Patients	% 5 year stroke, medical	% 5 year stroke, surgical
VA	>50	444	9.4*	4.7*
ACAS	>60	1662	11.0*	5.1*
ACST	>60	3120	11.8**	6.4**

**Ipsilateral only **Any stroke*

CREST Trial

- **2,502 patients with symptomatic or asymptomatic carotid artery stenosis, enrolled from 2000-2008.**
- **Randomized to CEA or CAS.**
- **Primary composite endpoint of stroke, myocardial infarction, or death.**
- **Median follow up of 7.4 years.**

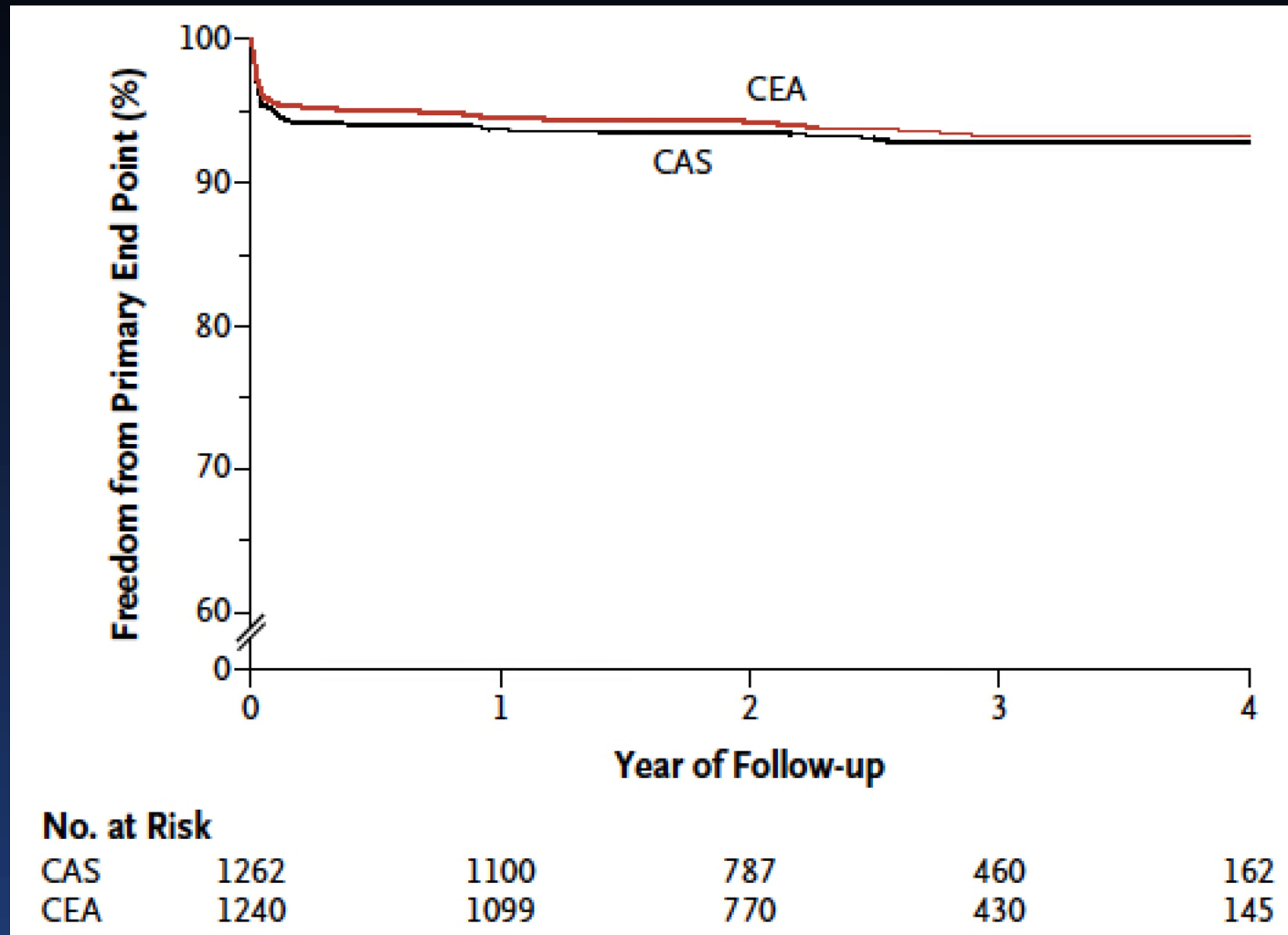
Brott et al, NEJM 2016; 374: 1021-1031.

CREST Peri-Procedural Outcomes

- **Death: 0.7% stenting vs. 0.3% CEA (P=0.18)**
- **Stroke: 4.1% vs. 2.3% (P= 0.01)**
- **Myocardial Infarction: 1.1% vs. 2.3% (P=0.03)**
- **Age interaction: Stenting better for patients <70 years of age, CEA better for >70 years of age**

Brott et al, NEJM 2010; 363: 11-23.

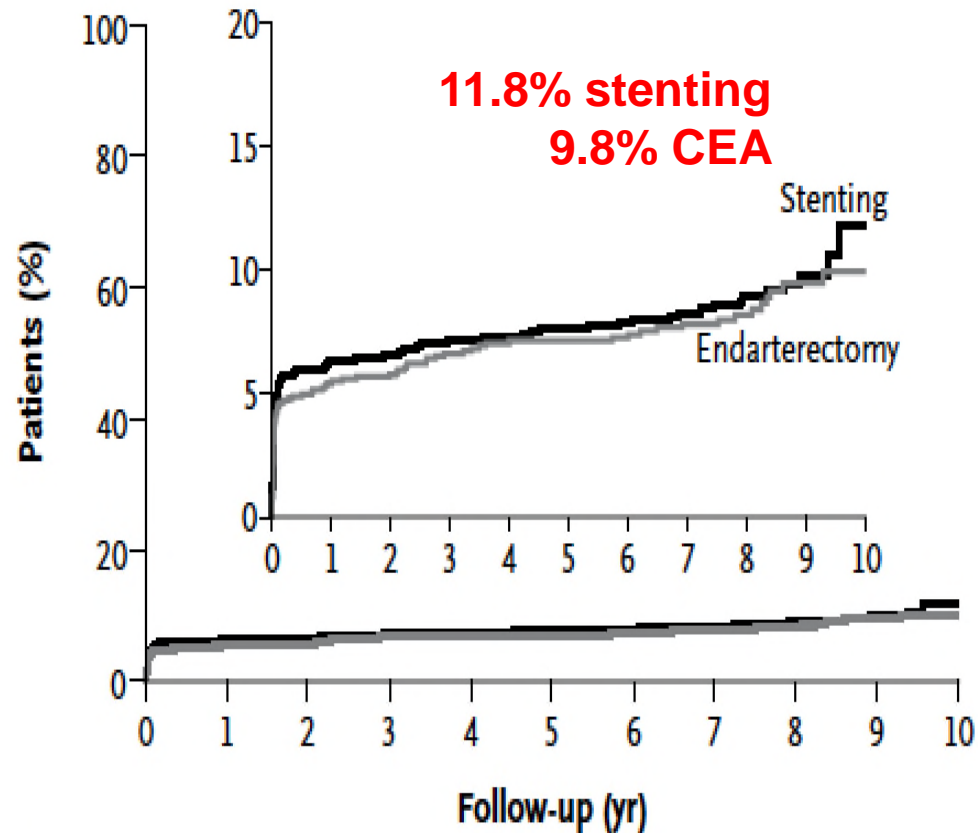
CREST Primary Endpoint



Brott et al, NEJM 2010; 363: 11-23.

CREST 10 Year Outcomes

A Primary Composite End Point



No. at Risk

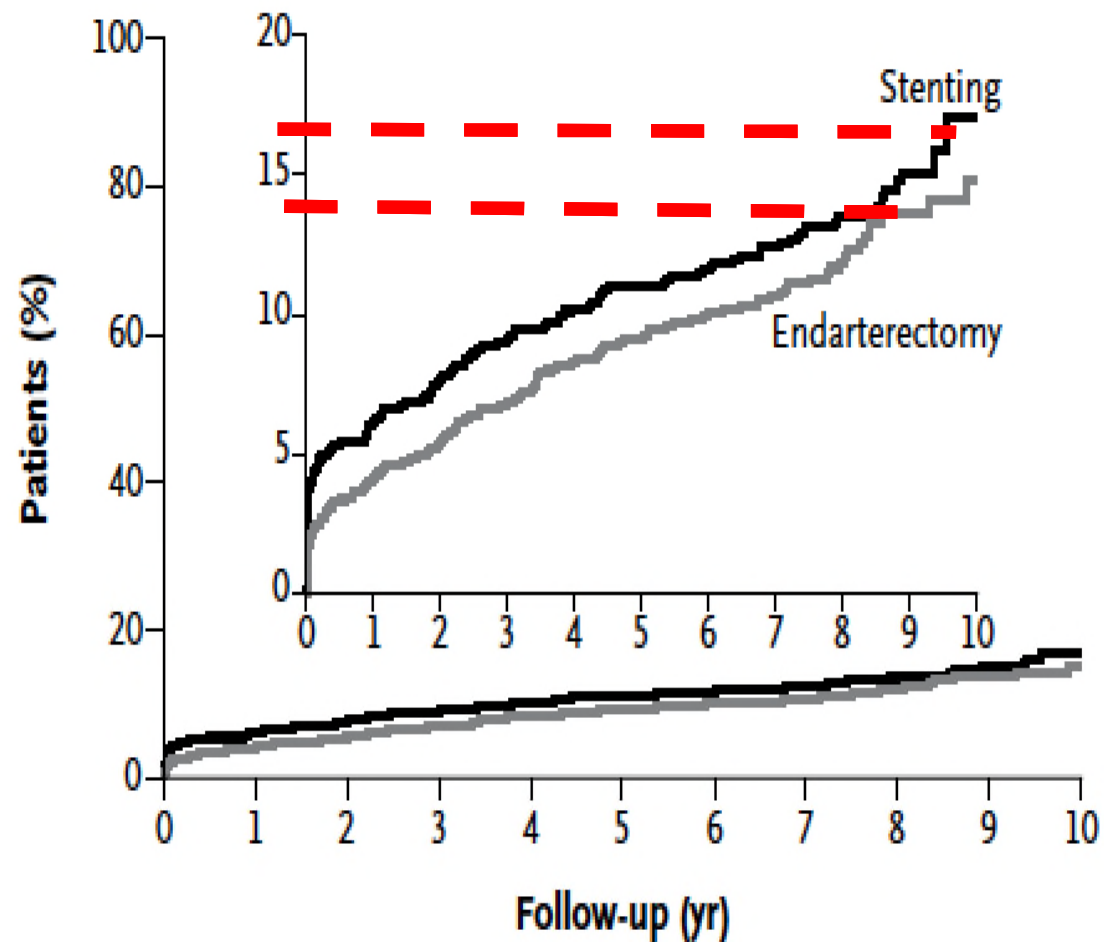
Endarterectomy	1240	1104	1036	949	833	736	695	620	438	243	66
Stenting	1262	1103	1041	972	884	774	738	676	477	264	68

Brott et al, NEJM 2016; 374: 1021-1031.

CREST 10 Year Outcomes

- **Post-procedural ipsilateral stroke: 6.9% vs. 5.6%**
- **5 year rates of post-procedural stroke by symptoms:**
 - **Asymptomatic: 2.5% stenting, 2.5% CEA**
 - **Symptomatic: 2.7% stenting, 2.7% CEA**

C Any Stroke



No. at Risk

Endarterectomy	1240	1118	1037	945	825	721	676	603	420	234	63
Stenting	1262	1103	1030	957	861	750	714	654	461	257	65

Brott et al, NEJM 2016; 374: 1021-1031.

Asymptomatic Carotid (ACT)-1 Trial

- Randomized trial of asymptomatic patients ≤ 79 years of age who were not high surgical risk.
- CEA or carotid stenting with embolic protection (Nav6) using closed cell stent (Xact).
- Enrolled 2005-2013.

ACT-1 Trial Characteristics

Lesion characteristics

Stenosis — % of vessel diameter¶¶

Mean	73.7±8.8	73.9±10.2
Range	33.8–98.6	34.7–96.0

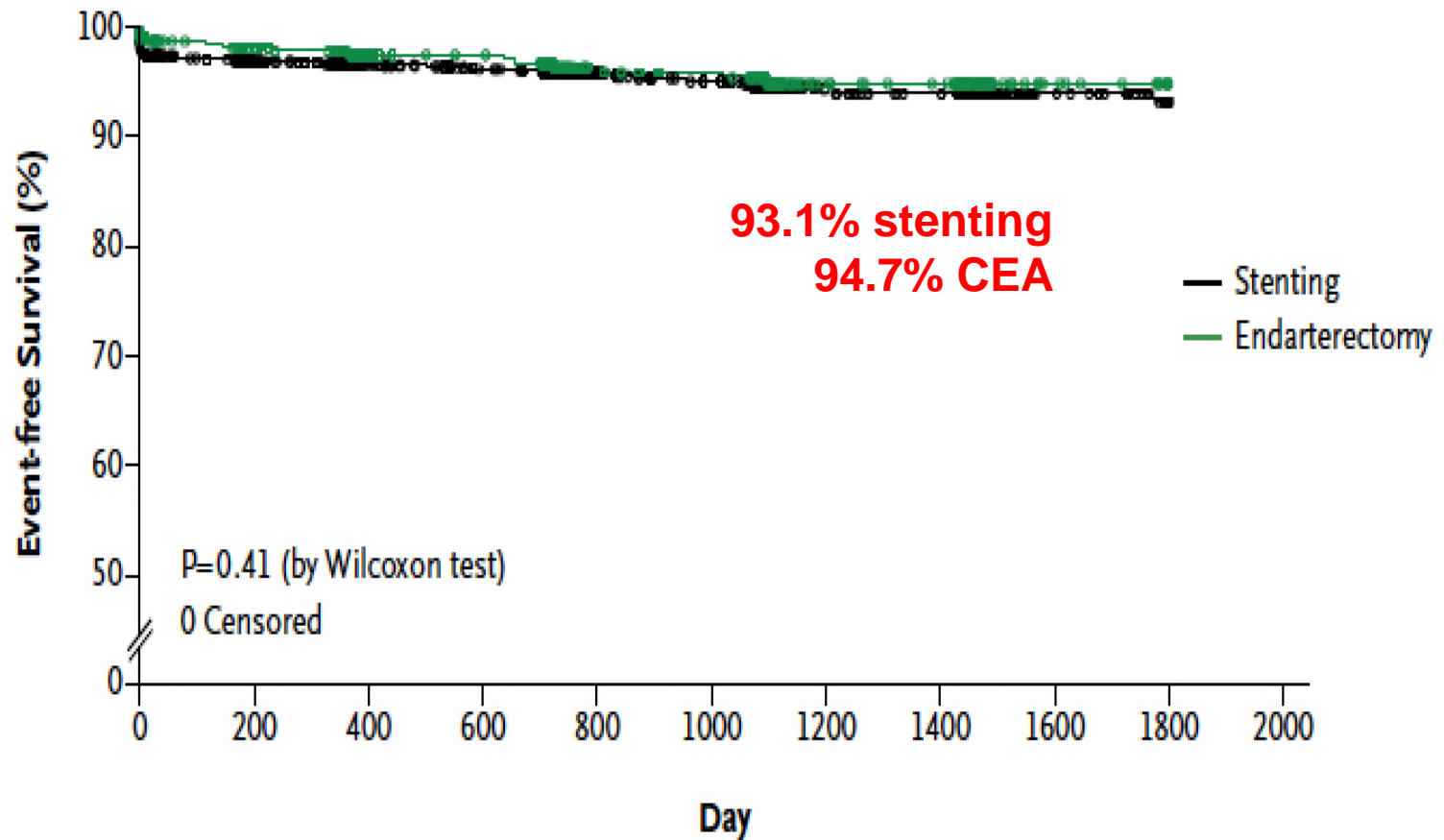
Lesion length — mm¶

Mean	19.0±5.8	18.0±6.2
Range	2.5–40.0	4.9–41.1

Ulcerated — no./total no. (%) 172/1062 (16.2) 37/255 (14.5)

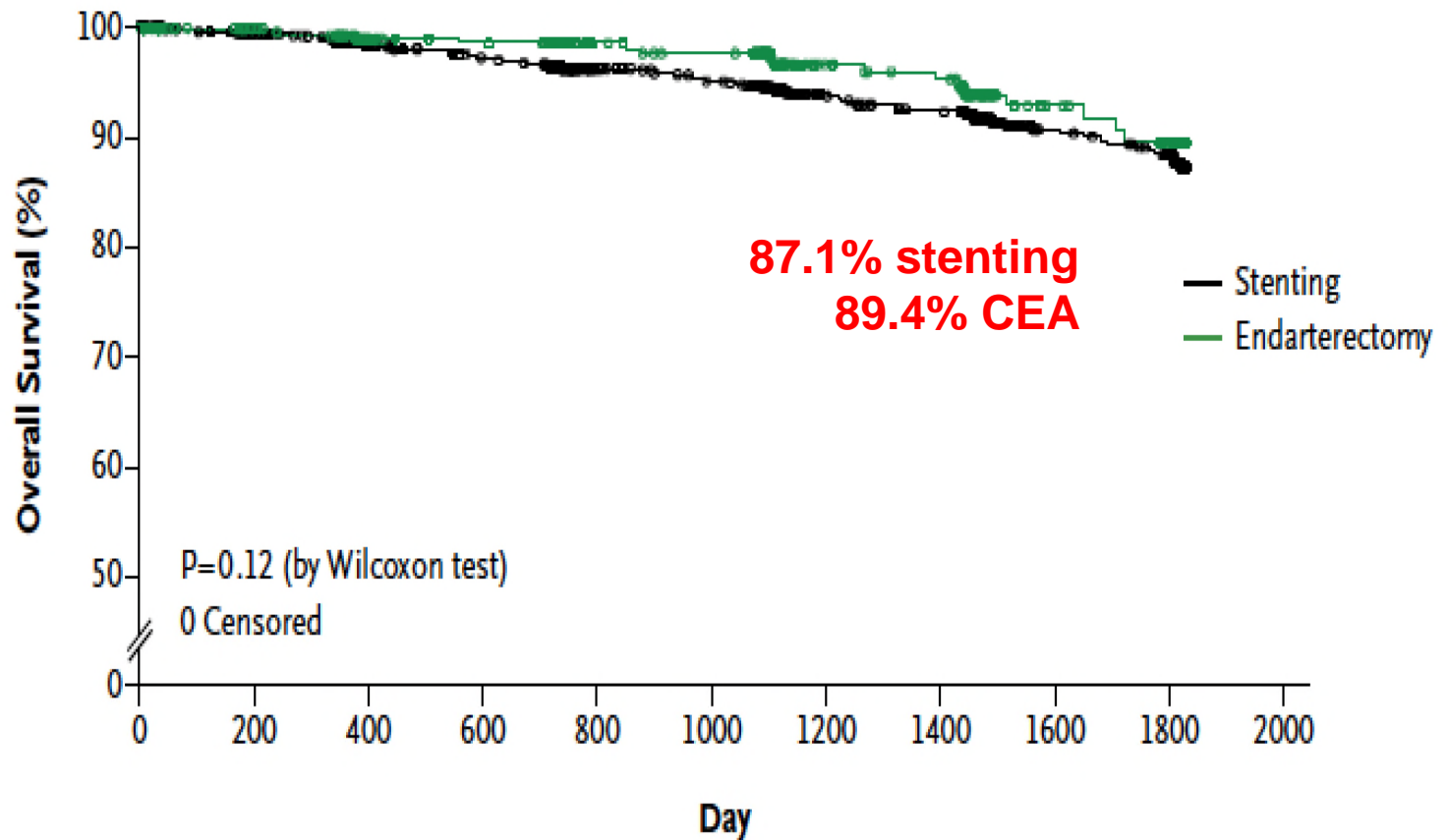
Thrombus — no./total no. (%) 10/1061 (0.9) 7/254 (2.8)

C Freedom from All Stroke through 5 Yr



Days	0	1-365	366-730	731-1095	1096-1460	1461-1825
Stenting (no. at risk)	1089	1068	865	730	541	363
Endarterectomy (no. at risk)	364	355	287	244	180	112

B Overall Survival through 5 Yr



Days	0	1-365	366-730	731-1095	1096-1460	1461-1825
Stenting (no. at risk)	1089	1082	892	756	567	381
Endarterectomy (no. at risk)	364	357	294	254	189	116

**2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/
SAIP/SCAI/SIR/SNIS/SVM/SVS Guideline on the
Management of Patients With Extracranial
Carotid and Vertebral Artery Disease**

- **80 pages**
- **748 references**
- **Comprehensive review of the body of knowledge regarding extracranial carotid and vertebral artery disease**
- **Unprecedented collaboration between multiple societies**

7.1. Recommendations for Selection of Patients for Carotid Revascularization*

CLASS I

1. Patients at average or low surgical risk who experience nondisabling ischemic stroke[†] or transient cerebral ischemic symptoms, including hemispheric events or amaurosis fugax, within 6 months (symptomatic patients) should undergo CEA if the diameter of the

2. CAS is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery is reduced by more than 70% as documented by noninvasive imaging or more than 50% as documented by catheter angiography and the anticipated rate of periprocedural stroke or mortality is less than 6% (360). (*Level of Evidence: B*)

mortality is less than 6% (360). (*Level of Evidence: B*)

3. Selection of asymptomatic patients for carotid revascularization should be guided by an assessment of comorbid conditions, life expectancy, and other individual factors and should include a thorough discussion of the risks and benefits of the procedure with an understanding of patient preferences. (*Level of Evidence: C*)

CLASS IIa

1. It is reasonable to perform CEA in asymptomatic patients who have more than 70% stenosis of the internal carotid artery if the risk of perioperative stroke, MI, and death is low (74,76,359,361–363).
(*Level of Evidence: A*)

2. It is reasonable to choose CEA over CAS when revascularization is indicated in older patients, particularly when arterial pathoanatomy

3. It is reasonable to choose CAS over CEA when revascularization is indicated in patients with neck anatomy unfavorable for arterial surgery (369–373).[§] (*Level of Evidence: B*)

indicated in patients with neck anatomy unfavorable for arterial surgery (369–373).[§] (*Level of Evidence: B*)

4. When revascularization is indicated for patients with TIA or stroke and there are no contraindications to early revascularization, intervention within 2 weeks of the index event is reasonable rather than delaying surgery (374). (*Level of Evidence: B*)

CLASS IIb

1. Prophylactic CAS might be considered in highly selected patients with asymptomatic carotid stenosis (minimum 60% by angiography, 70% by validated Doppler ultrasound), but its effectiveness compared with medical therapy alone in this situation is not well established (360). (*Level of Evidence: B*)
2. In symptomatic or asymptomatic patients at high risk of complications for carotid revascularization by either CEA or CAS because of comorbidities,^{||} the effectiveness of revascularization versus medical therapy alone is not well established (35,361,362,366, 369–372,375,376). (*Level of Evidence: B*)

Current Coverage for Carotid Artery Stenting

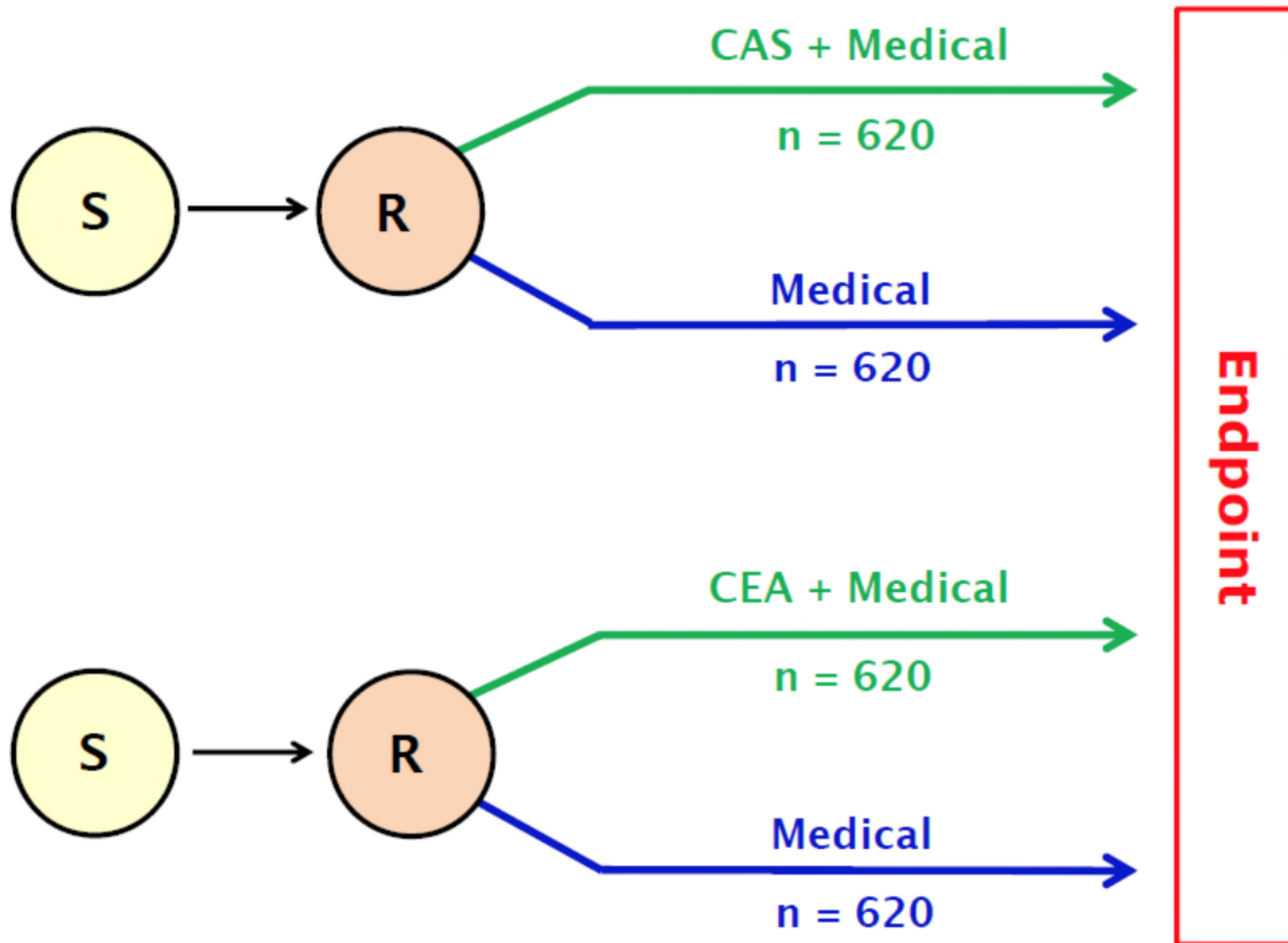
- **CMS covers:**
 - **Symptomatic 70% stenosis**
 - **High risk for CEA**
 - **FDA-approved CAS system**
 - **Emboolic protection device**
 - **CMS-approved institution**

 - **IDE trials or post-approval registries**

CREST-2 Trial

- **Asymptomatic patients with $\geq 70\%$ asymptomatic stenosis.**
- **Two parallel arms**
 - **Medical management vs. CEA**
 - **Medical management vs. CAS**

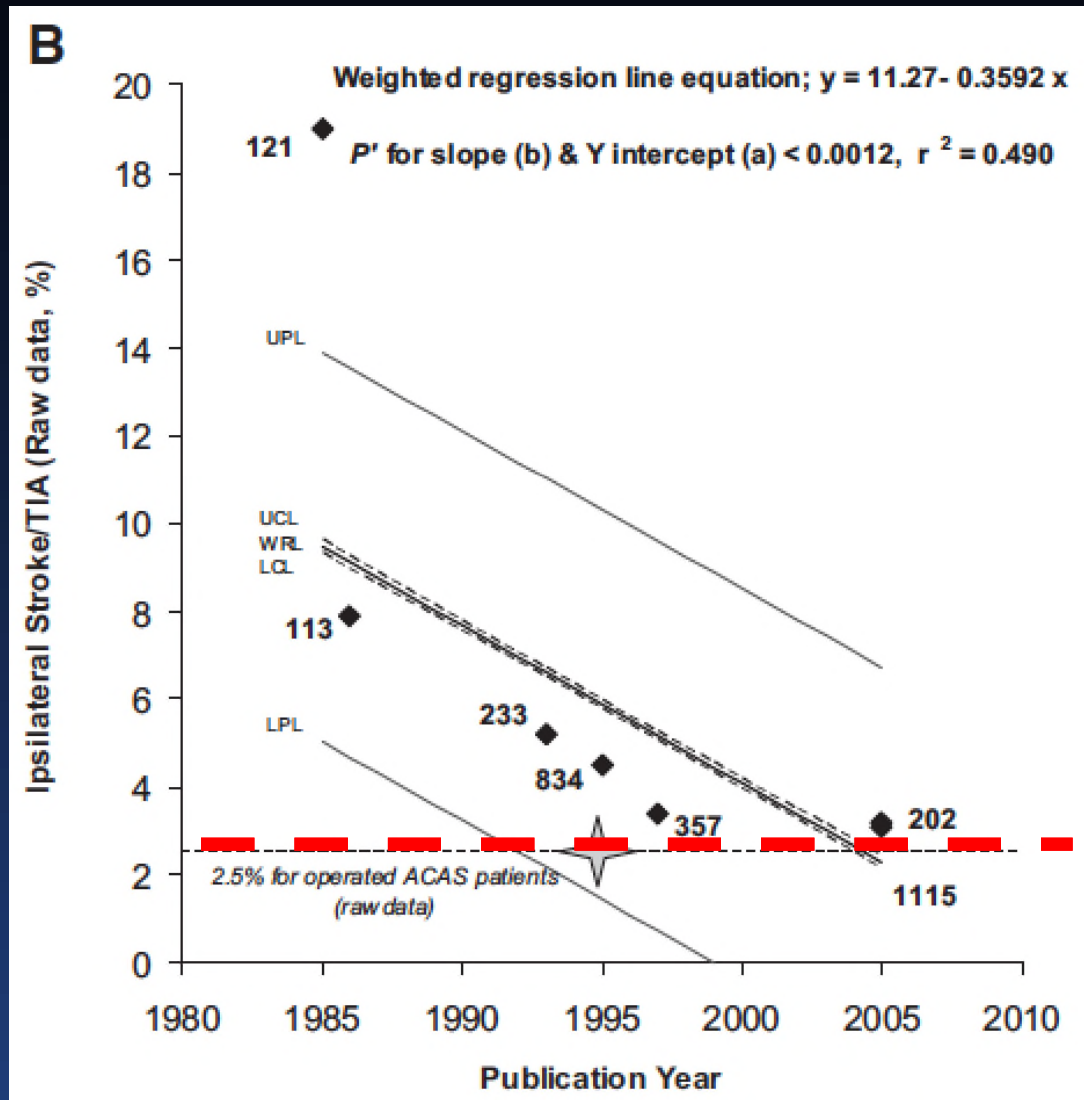
Trial Protocol



Medical Management in CREST-2

- ASA 325 mg daily.
 - Clopidogrel after CAS
- Primary risk factor management
 - Directed by neurologist
 - Target SBP <140 mm Hg
 - Target LDL < 70 mg/dl
- Secondary risk factor management
 - HbA1C <7%, smoking cessation, weight management, moderate exercise

Decreasing Stroke Rates in Patients Managed Medically



Abbott, Stroke 2009;40:e573-e583

How Will CREST-2 Add to Our Knowledge of CEA?

- **First trial to compare CEA + medical therapy to modern medical therapy in asymptomatic patients.**
- **Goal enrollment 2,480 patients (620 in each arm).**
 - **328 currently enrolled (October 2016)**
- **Includes patients with >70% stenosis.**

Conclusions

- **Robust data to support carotid artery revascularization for symptomatic stenosis.**
- **Most data on asymptomatic stenosis revascularization derived prior to modern medical therapy.**
- **Recent data demonstrate excellent long-term results of carotid artery stenting.**

Thank You

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