




CAROTID STENTING- *WHO SHOULD GET IT?*

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Disclosures

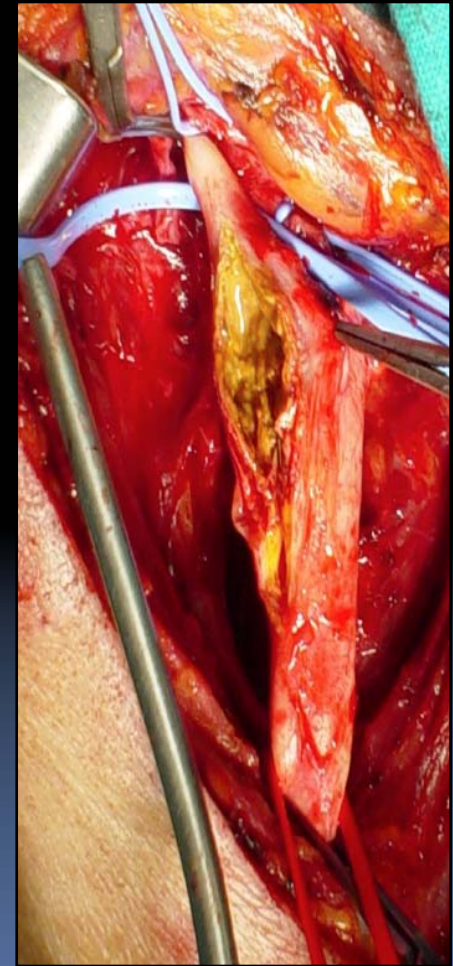
- Consultant/Research Support
 - Cordis
 - Abbott
 - Gore Medical
- 

My CAS Trials as PI

- CREST - *leading NE site*
- SAPPHIRE
- SAPPHIRE-WW
- CHOICE
- EXACT
- CARES
- CASES-PMS
- EMBOLDEN
- EPIC
- CREATE
- CREATE-PAS
- PROTECT
- ARCHER- Long Term
- SONOMA

Stroke- Scope of the Problem

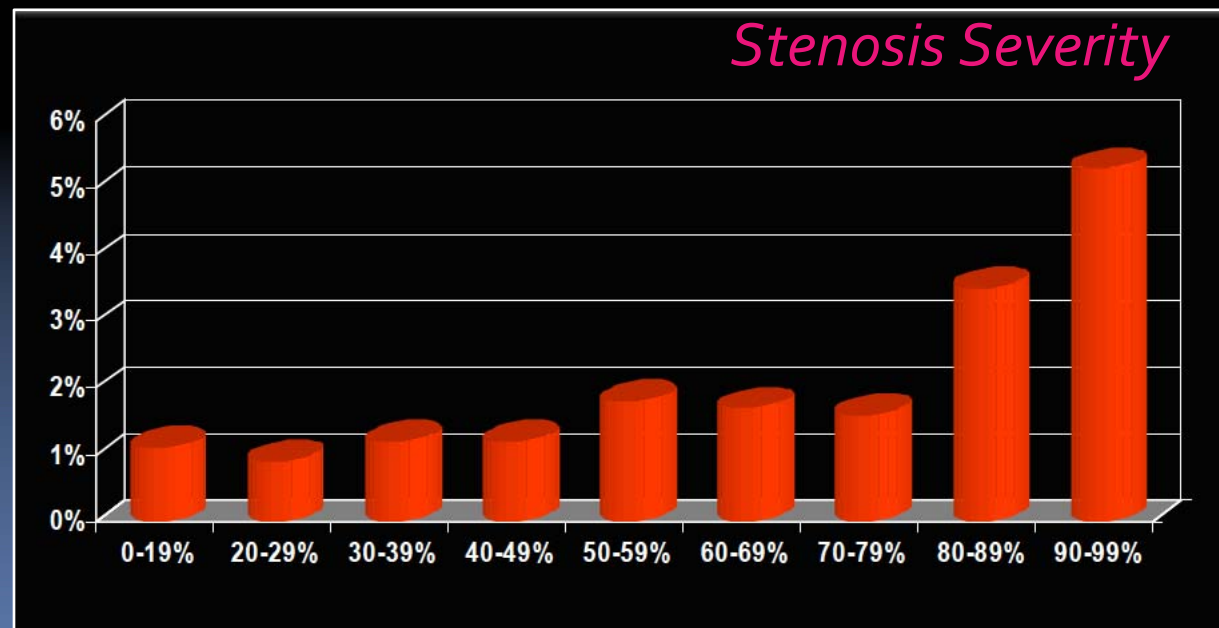
- ~ 700,000 strokes/yr: 1/min
- 3rd leading cause of death in the US- 150,000/yr.
- 4.4 million stroke survivors
 - 20% require institutional care
 - Up to 1/3 have permanent disability
- ~20% of stroke due to carotid disease
- Risk factors same as for CAD



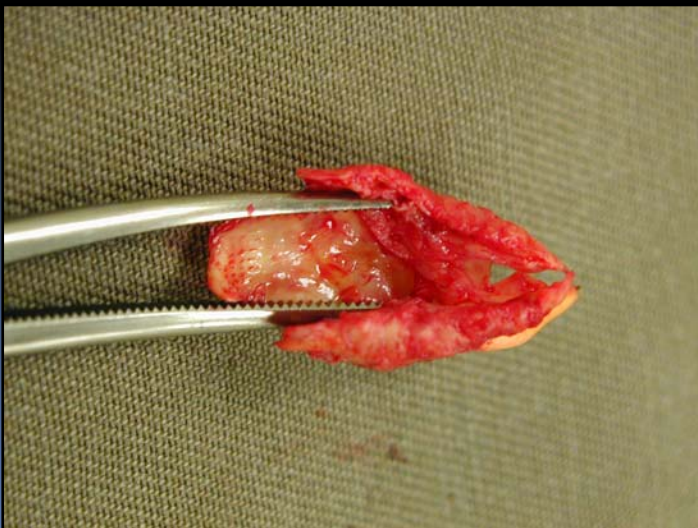
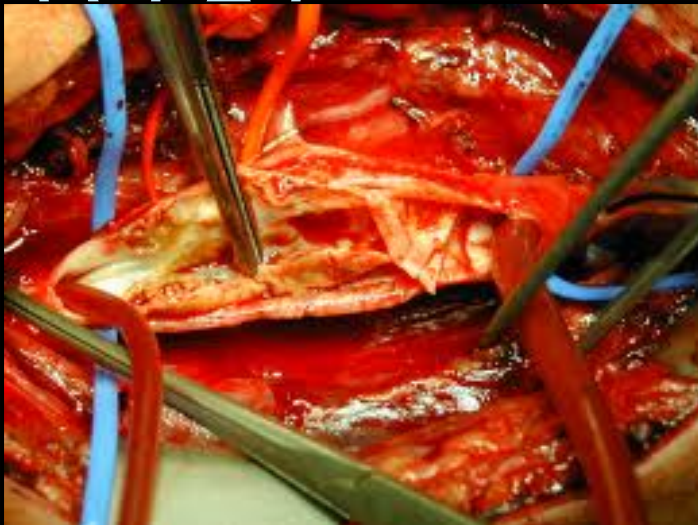
Stroke Risk of Extracranial Carotid Artery Disease- *Who's at risk?*

- Asymptomatic $\geq 80\%$
 - Annual risk of 1 - 4.3%
- TIA
 - 15% risk of stroke at 1 month
 - 30% risk of TIA/CVA/death within 3 months

Symptomatic Status



Carotid Endarterectomy (CEA)



First CEA performed in US
by Dr. Michael DeBakey

RCTs of CEA vs. BMT for Symptomatic Carotid Disease

| Primary End point | | | | | | | |
|-------------------|--------|--------------|-------------|--------------|----------------|----------------|----------------------------|
| Trial | # Pts. | Stenosis (%) | Medical (%) | Surgical (%) | <i>P</i> value | Annual ARR (%) | Peri-op Stroke & Death (%) |
| NASCET | 659 | ≥ 70 | 26 | 9 | <.001 | 11.3 | 5.8 |
| NASCET | 859 | 50-69 | 22.2 | 15.7 | .045 | 1.3 | |
| | 1368 | ≤ 50 | 18.7 | 14.9 | NS | NS | |
| ECST | 3008 | ≥ 70 | 13.6 | 9.5 | <.001 | 1.5 | 7.5 |
| | | 50-69 | | | NS | NS | |
| VASST | 189 | >50 | 19.4 | 7.7 | .01 | 17.2 | 6.5 |

AHA Standard for Symptomatic Carotid Stenosis: < 6% CEA stroke/death rate

RCTs of CEA vs. BMT for Asymptomatic Carotid Disease

| Primary End Point | | | | | | |
|-------------------|--------|--------------|-------------|--------------|----------------|----------------|
| Trial | # Pts. | Stenosis (%) | Medical (%) | Surgical (%) | <i>P</i> Value | Annual ARR (%) |
| VA | 444 | ≥ 50 | 20.6 | 8 | <.001 | 3 |
| ACAS | 1662 | ≥ 60 | 11 | 5.1 | .004 | 1.2 |
| ACST | 3120 | ≥ 60 | 11.8 | 6.4 | <.001 | 1.1 |

AHA Standard for Asymptomatic Carotid Stenosis: < 3% stroke/death rate

RCTs **NOT** Reflective of “Real World” CEA Pts. & Outcomes

Medical Comorbidities

- Age > 79
- ACS
- MI in prior 6 months
- Cardiac valvular or rhythm abnormality likely to cause embolic stroke
- Uncontrolled HTN, DM
- Severe renal/lung disease
- Prior severe CVA

Anatomic Features

- Prior ipsilateral CEA
- Severe lesion cranial or caudal to surgical lesion
- Total occlusion
- Contralateral occlusion
- Prior radical neck surgery
- Prior neck radiation
- Tracheostoma

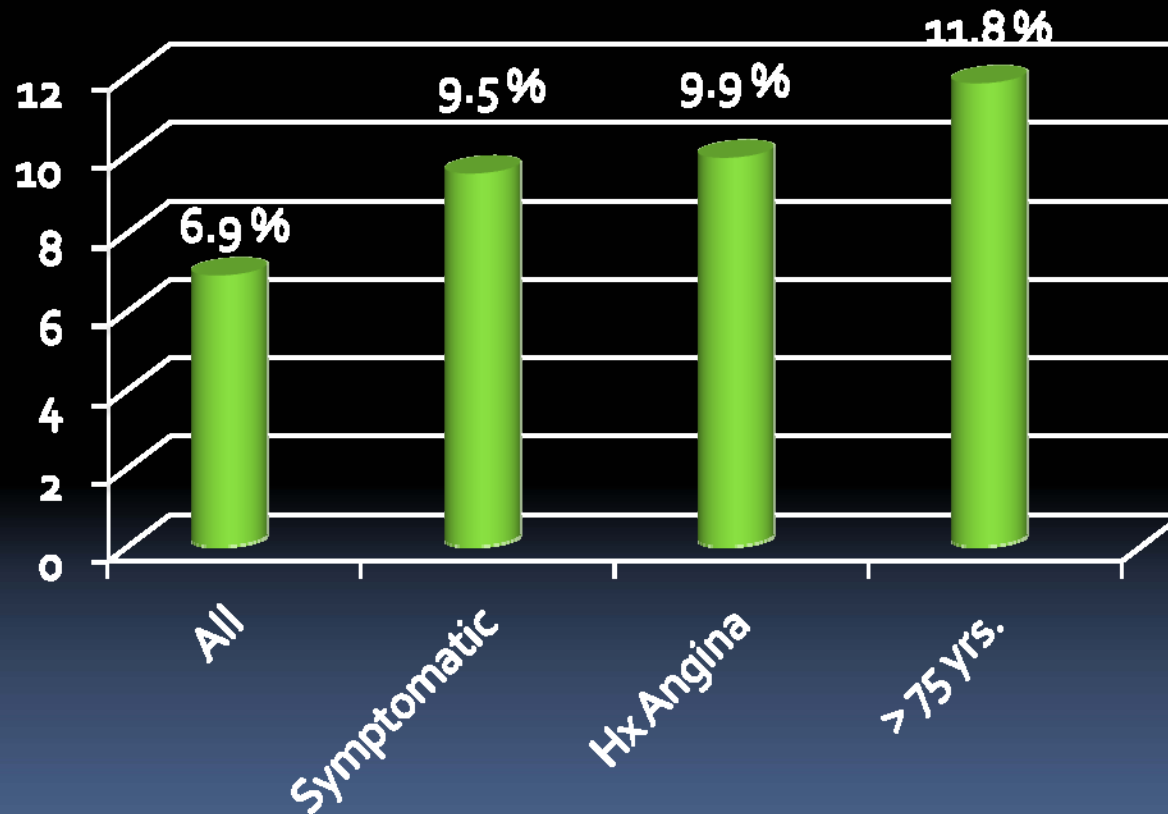
There are *NO* RCTs of CEA vs. BMT in high surgical risk patients

Risk of Stroke/Death in High Surgical Risk CEA

| | |
|--|--------|
| Age > 75 | 7-10 % |
| CHF | 8-9 % |
| Concomitant CAD requiring CABG | 8-10 % |
| Contralateral carotid occlusion (NASCET) | 14.3 % |
| Prior CEA and recurrent stenosis | 8-10 % |
| CRI, Cr > 1.5 mg/dl | 8.2 % |
| CRI, Cr > 2.9 mg/dl | 43 % |

CEA in US Academic Centers

12 hospital outcomes > 1100 pts for
Death/Stroke/MI



CEA Outcomes Assessment

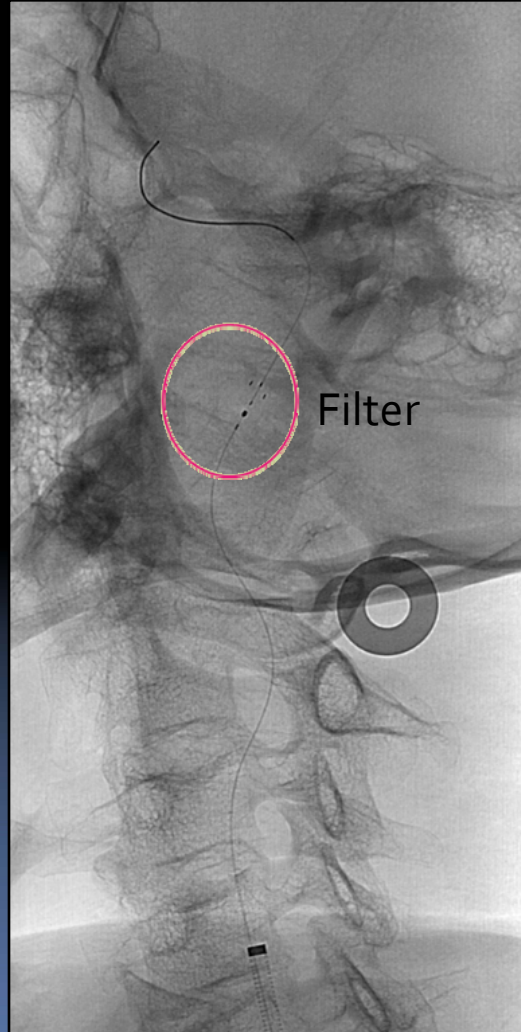
- Meta-analysis of published CEA outcomes in ~16,000 patients
 - 5.6% risk of stroke and death
 - 2.3% risk with single surgeon author
 - 7.7% risk with neurologist co-author
- Non-Endpoint Outcomes
 - 8.6% incidence of cranial nerve palsy (NASCET)
 - ~9% incidence of wound complication (NASCET)
 - Restenosis rate of 5-10% (ACAS)
 - 8.6% 30-day medical complication rate
 - pulmonary, cardiac etc.

Carotid Artery Stenting

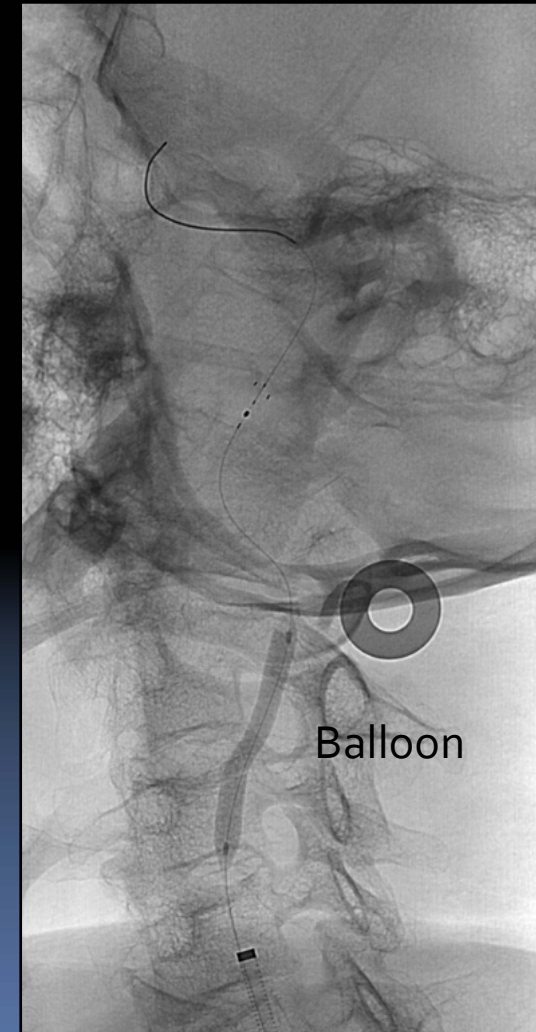
(CAS)
Baseline



EPD

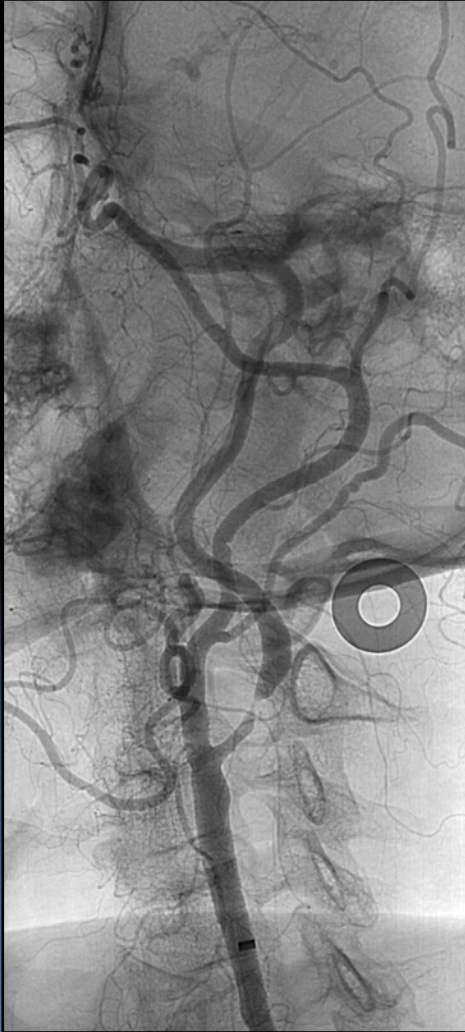


Pre-dilation

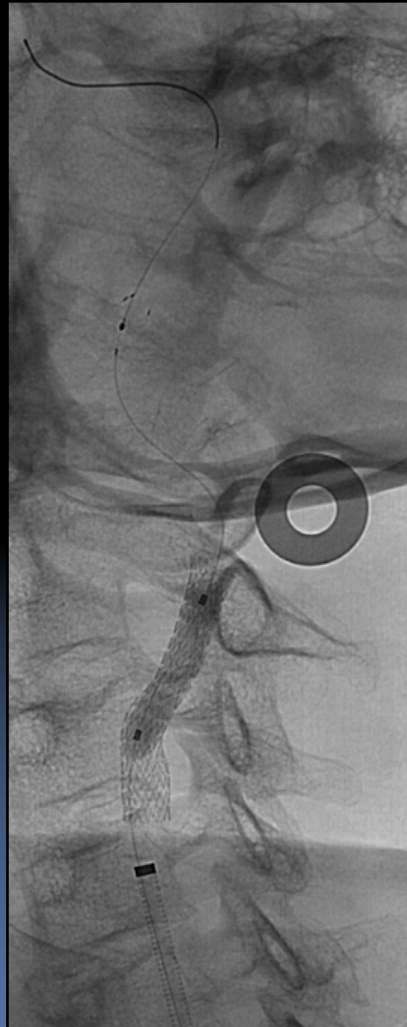


Carotid Artery Stenting (CAS)

Baseline



Post-dilation stent



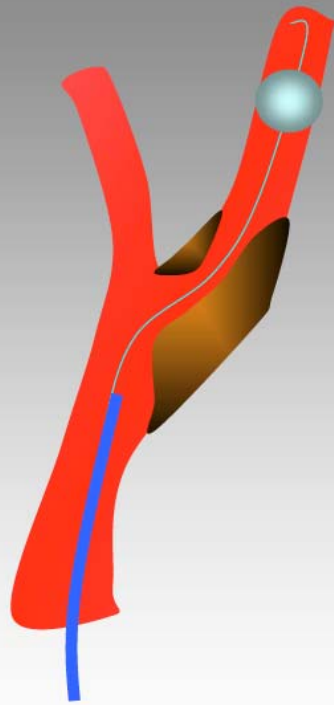
Final



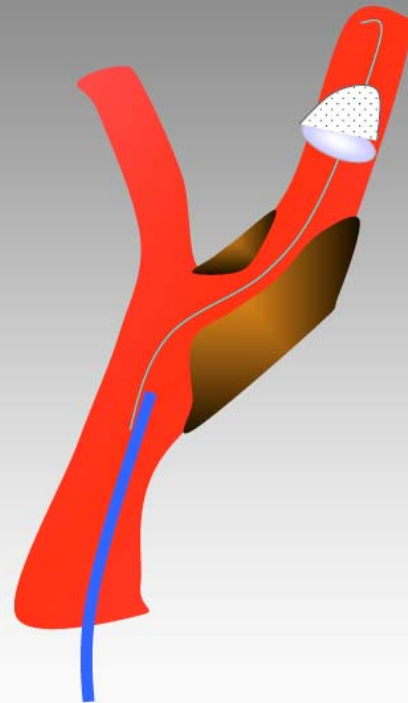
Gore
Embolden
EPD

Emboolic Protection for CAS

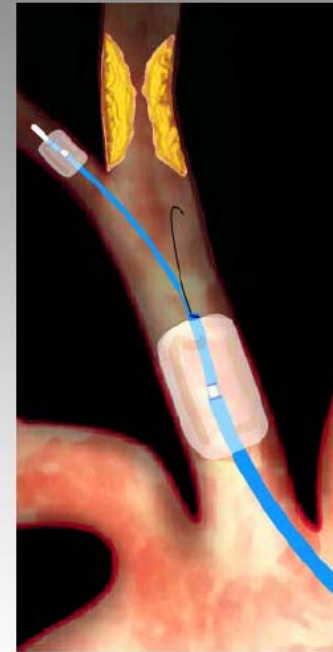
3 Different Systems of Cerebral Protection



Distal Balloon



Distal Filter



Proximal Balloon

Completed US Studies for CAS: Overview

- Multiple high surgical risk trials
 - Composite 1^o safety endpoint of death/stroke/MI
 - Efficacy endpoint of 30-day MAE plus ipsilateral stroke between 31 days-12 months
- Randomized CAS vs. CEA
 - High surgical risk: SAPPHIRE
 - Normal surgical risk: CREST
- Angiographic stenosis severity:
 - $\geq 50\%$ symptomatic
 - $\geq 80\%$ asymptomatic

What makes someone high risk for CEA? (*and eligible for CAS*)

Medical Co-morbidities

- EF < 30%, NYHA Class \geq III
- FEV₁ < 30%
- ESRD on dialysis
- Restenosis after prior CEA
- Need for CABG/valve surgery within 30 days
- 2 or more coronary vessels with \geq 70%
- Prior MI within 30 days
- Unstable angina

Unfavorable Anatomy

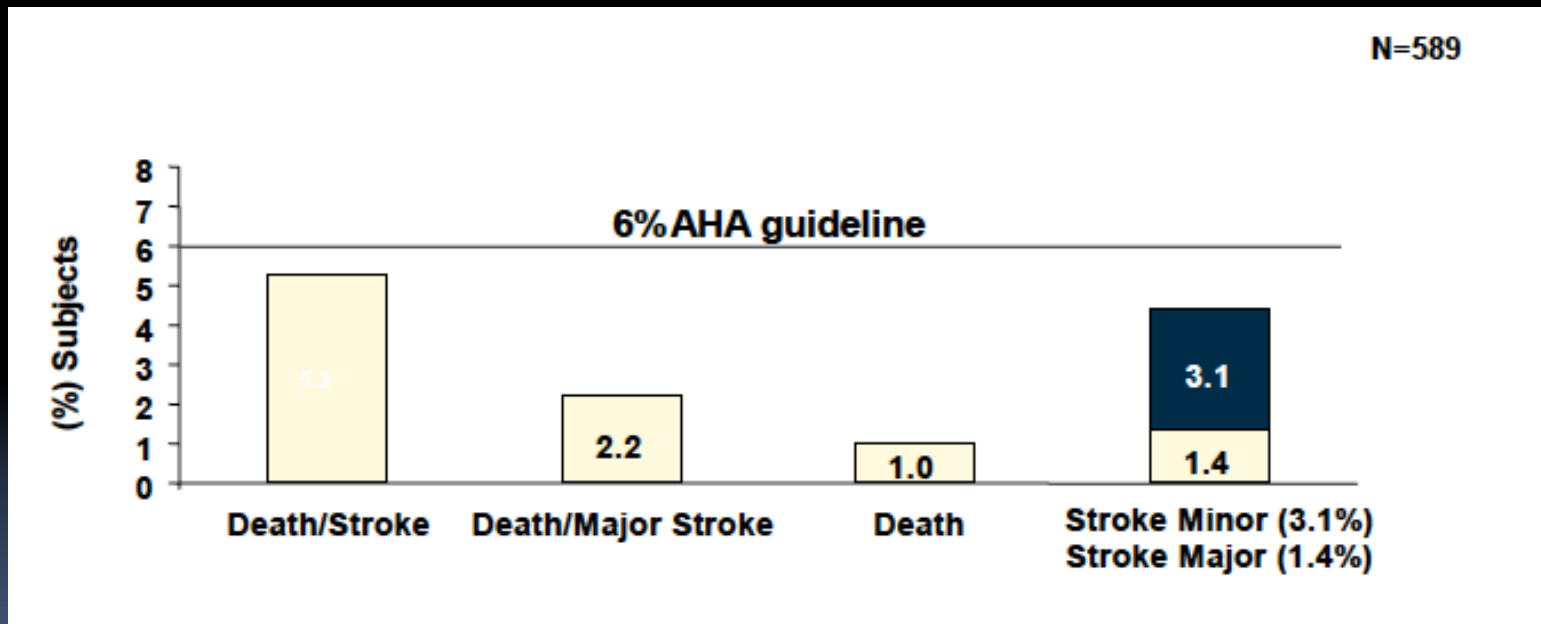
- S/P radical neck surgery
- S/P radiation therapy
- Surgically inaccessible lesions
- Spinal immobility
- Tracheostoma
- Contralateral ICA occlusion
- Contralateral laryngeal nerve paralysis

CAS for High Surgical Risk

Incidence of stroke and death in high risk carotid stent IDE trials: 2002-2008

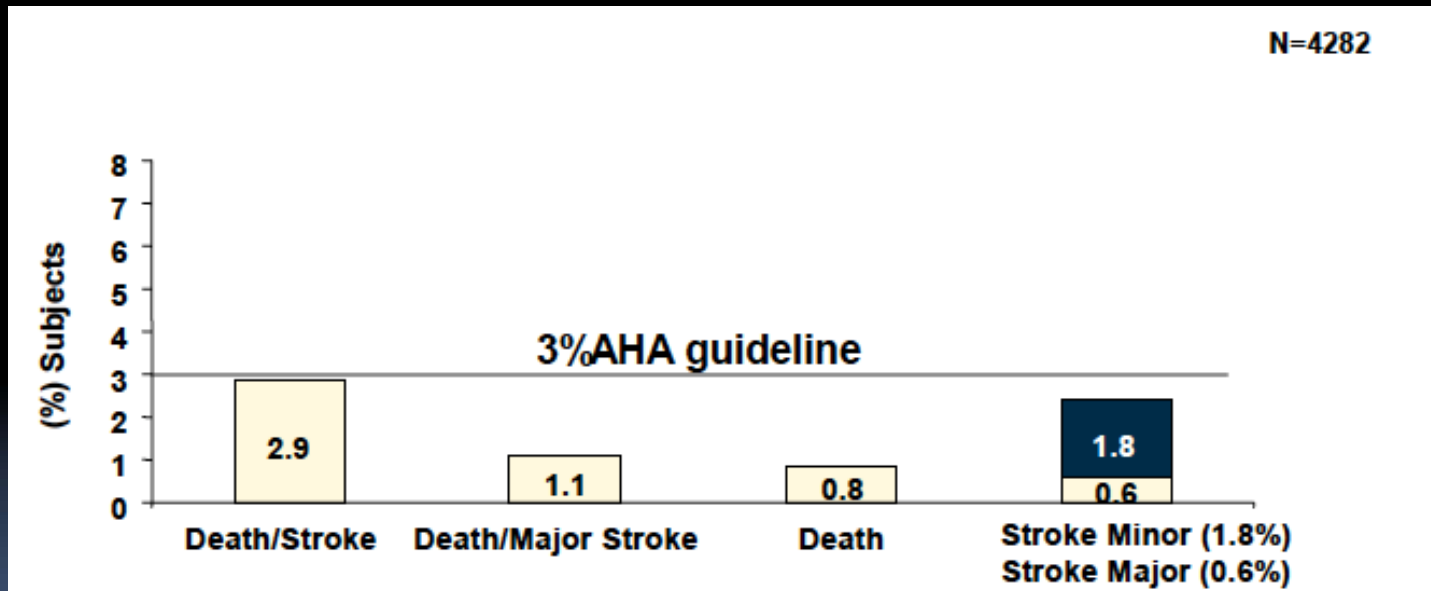


EXACT/CAPTURE Combined 30-day MAE: symptomatic < 80

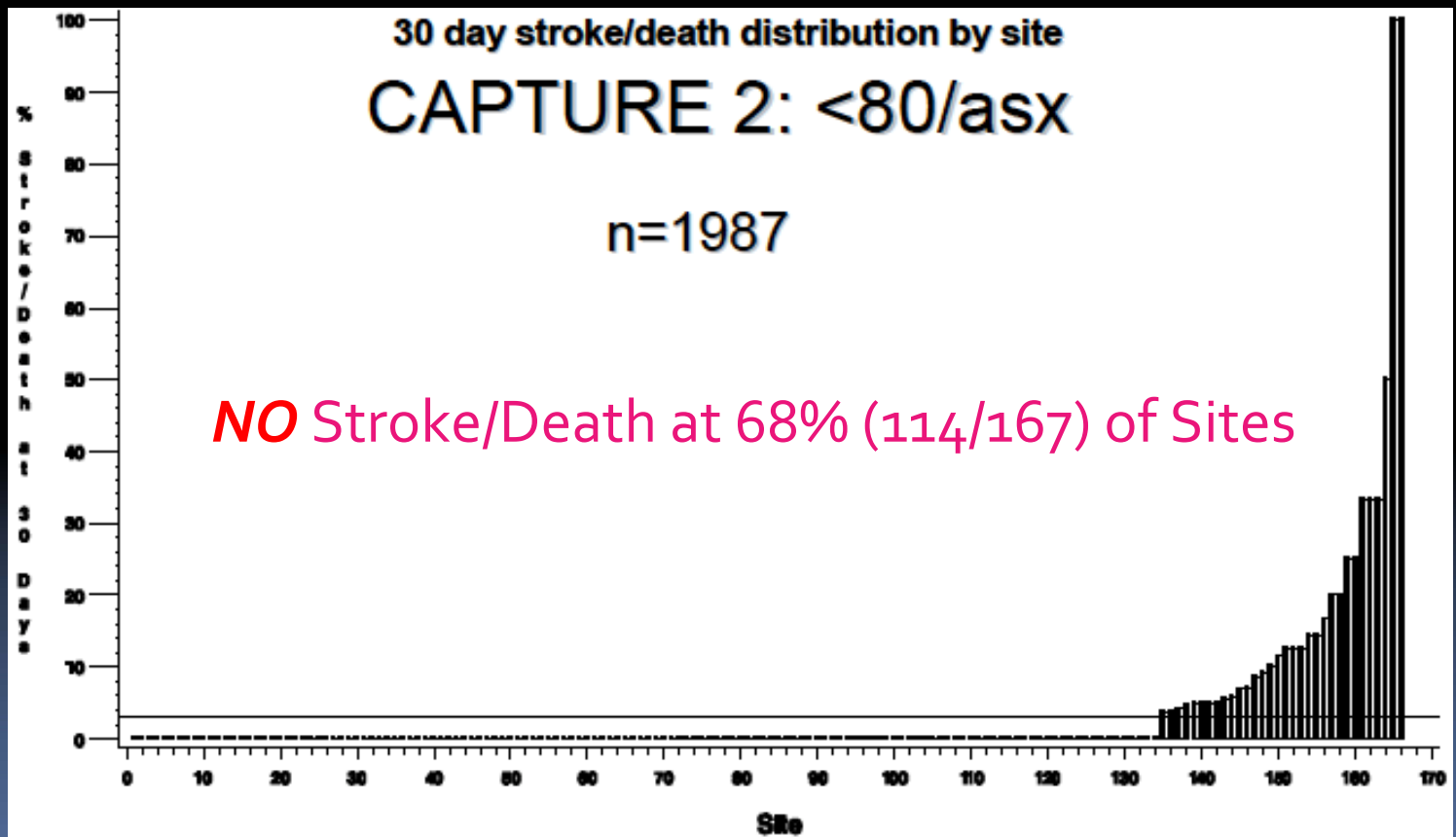


EXACT/CAPTURE 2 Combined

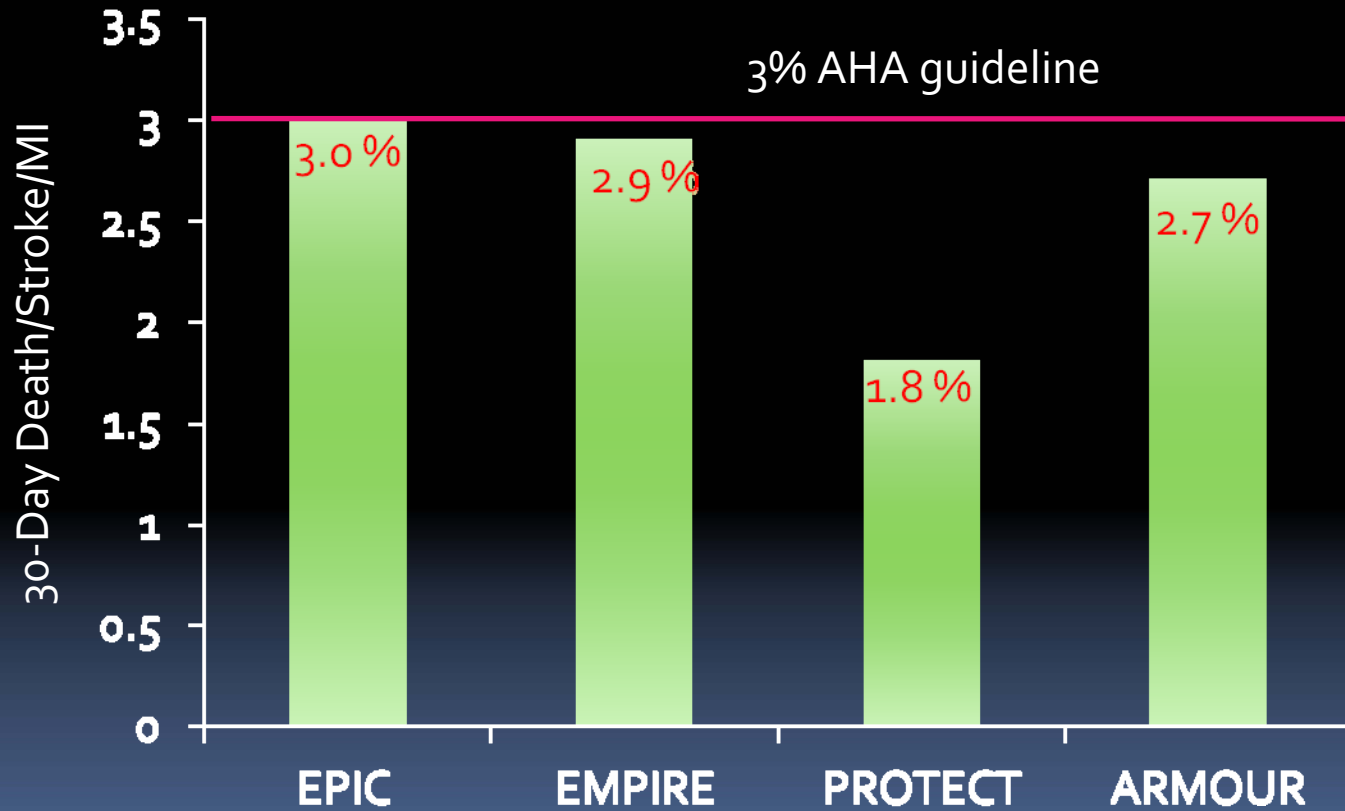
30-day MAE: asymptomatic < 80



Majority of CAS Sites Have Very Low Stroke/Death Rates



Remarkable Results for Latest High Surgical Risk Patients, N > 1000



SAPPHIRE: RCT of CEA vs. CAS in Surgical High-Risk Patients

- Hypothesis that CAS not inferior to CEA
- N=334; 29 centers; eligible for either Rx; *independent neuro evaluation*
- Symptomatic stenosis of $\geq 50\%$
- Asymptomatic stenosis of $\geq 80\%$
- Primary Endpoint: composite of death/stroke/MI within 30 days of intervention, or death or ipsilateral stroke between 31 days and 1 year

SAPPHIRE: Major Eligibility

Criteria

- **Inclusion Criteria**
- General criteria
 - Age \geq 18 yr
 - Unilateral or bilateral atherosclerotic or restenotic lesions in native carotid arteries
 - Symptomatic \geq 50% stenosis
 - Asymptomatic \geq 80% stenosis
- Criteria for high-risk (at least 1 required)
 - Significant cardiac disease (CHF, +ETT, need for CABG)
 - Severe pulmonary disease
 - Contralateral occlusion
 - Prior radical neck or radiation therapy to neck
 - Recurrent stenosis after CEA
 - Age $>$ 80 yr

SAPPHIRE: Exclusion

Criteria

- Ischemic stroke within previous 48 hr
- Presence of intraluminal thrombus
- Total occlusion of target vessel
- Vascular disease precluding catheter-based techniques
- Intracranial aneurysm > 9 mm in diameter
- Need for more than 2 stents
- History of bleeding disorder
- Percutaneous or surgical intervention planned within next 30 days
- Life expectancy of < 1 yr
- Ostial lesion of common carotid artery or brachiocephalic artery

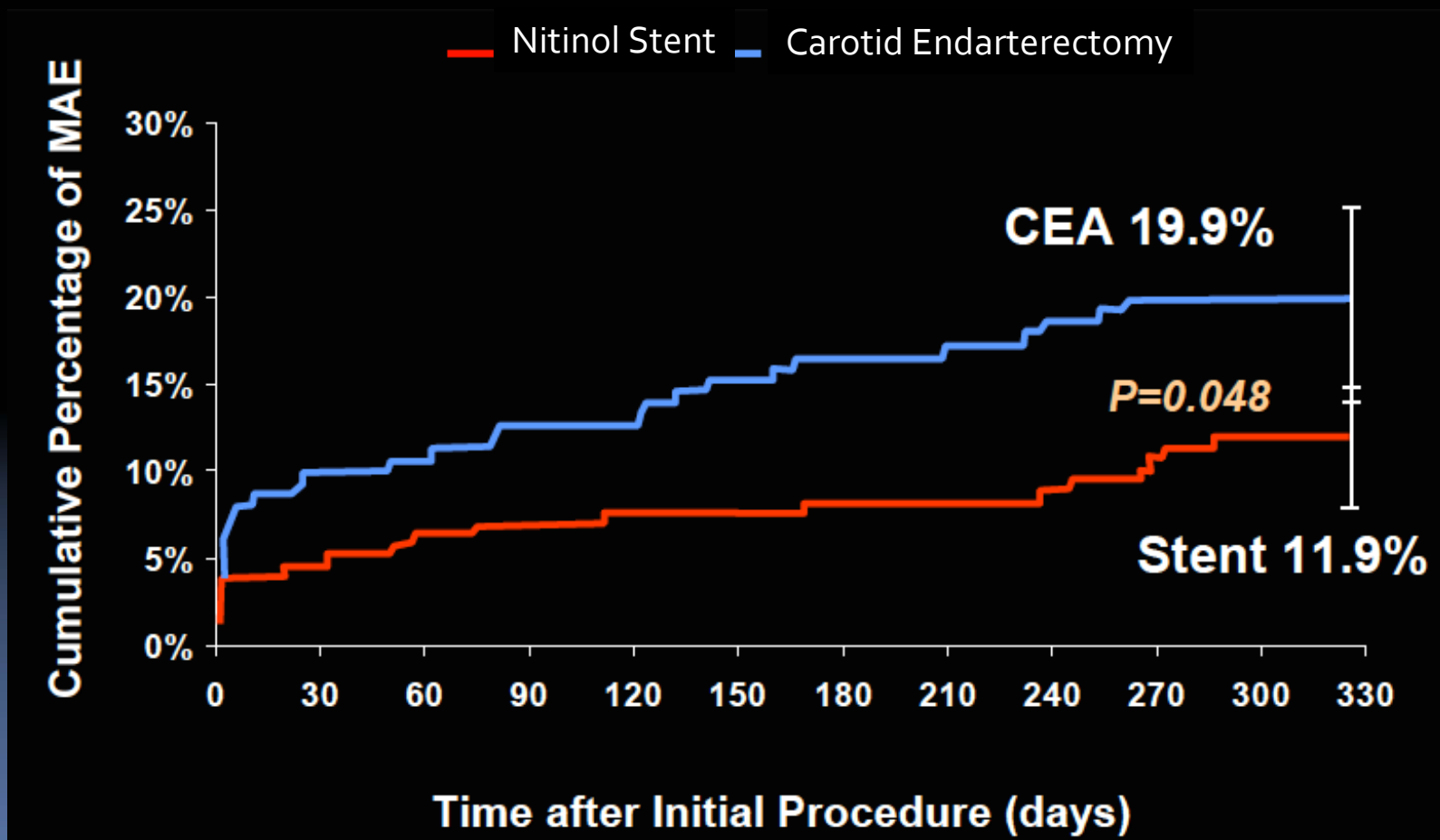
SAPPHIRE: RESULTS AT 1 YEAR

Table 3. Cumulative Incidence of Adverse Events within One Year.*

| Event | Intention-to-Treat Analysis | | | Actual-Treatment Analysis | | |
|---|--------------------------------|--------------------------------------|---------|--------------------------------|--------------------------------------|---------|
| | Stenting (N=167) no. (%) | Endarterectomy (N=167) no. (%) | P Value | Stenting (N=159) no. (%) | Endarterectomy (N=151) no. (%) | P Value |
| Death | 12 (7.4) | 21 (13.5) | 0.08 | 11 (7.0) | 19 (12.9) | 0.08 |
| Stroke | 10 (6.2) | 12 (7.9) | 0.60 | 9 (5.8) | 11 (7.7) | 0.52 |
| Major ipsilateral | 1 (0.6) | 5 (3.3) | 0.09 | 0 | 5 (3.5) | 0.02 |
| Major nonipsilateral | 1 (0.6) | 2 (1.4) | 0.53 | 1 (0.6) | 1 (0.7) | 0.97 |
| Minor ipsilateral | 6 (3.7) | 3 (2.0) | 0.34 | 6 (3.8) | 3 (2.2) | 0.37 |
| Minor nonipsilateral | 3 (1.9) | 4 (2.7) | 0.64 | 3 (2.0) | 3 (2.1) | 0.89 |
| Myocardial infarction | 5 (3.0) | 12 (7.5) | 0.07 | 4 (2.5) | 12 (8.1) | 0.03 |
| Q-wave | 0 | 2 (1.2) | 0.15 | 0 | 2 (1.3) | 0.15 |
| Non-Q-wave | 5 (3.0) | 10 (6.2) | 0.17 | 4 (2.5) | 10 (6.7) | 0.08 |
| Cranial-nerve palsy | 0 | 8 (4.9) | 0.004 | 0 | 8 (5.3) | 0.003 |
| Target-vessel revascularization | 1 (0.6) | 6 (4.3) | 0.04 | 1 (0.7) | 6 (4.6) | 0.04 |
| Conventional end point (stroke or death at 30 days plus ipsilateral stroke or death from neurologic causes within 31 days to 1 yr) | 9 (5.5) | 13 (8.4) | 0.36 | 8 (5.1) | 11 (7.5) | 0.40 |
| Primary end point (death, stroke, or myocardial infarction at 30 days plus ipsilateral stroke or death from neurologic causes within 31 days to 1 yr) | 20 (12.2) | 32 (20.1) | 0.05 | 19 (12.0) | 30 (20.1) | 0.05 |

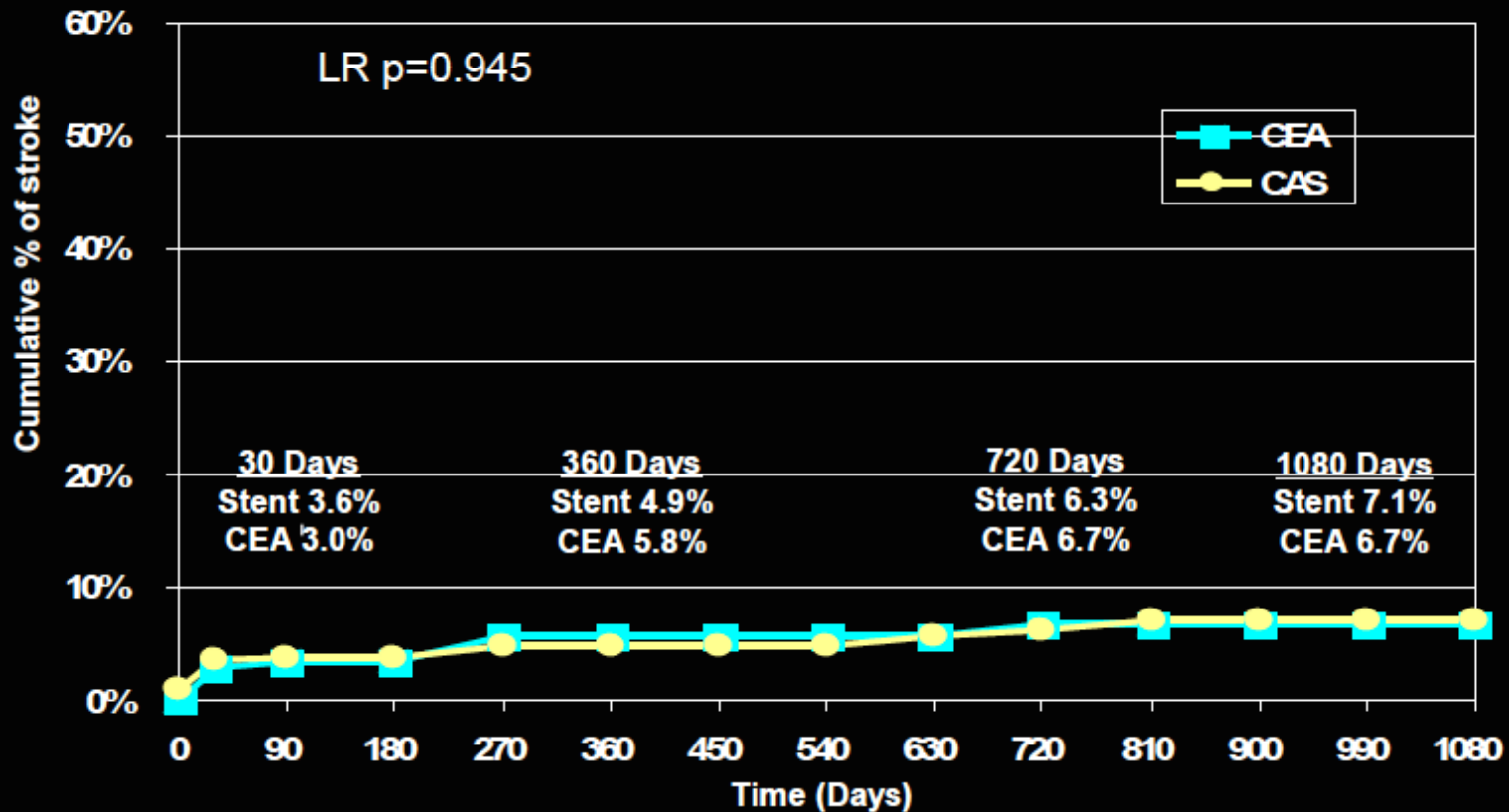
* Patients may have had more than one event. P values were determined by the log-rank test. Rates of adverse events were estimated with the use of the Kaplan–Meier method.

SAPPHIRE: RCT of CEA vs. CAS in Surgical High-Risk Patients

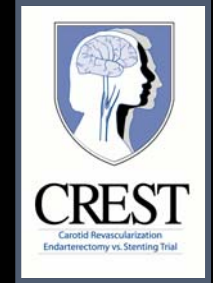


SAPPHIRE: RCT of CEA vs, CAS in Surgical High-Risk Patients

No advantage of CEA over CAS in efficacy

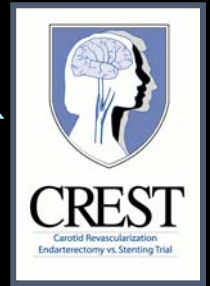


CREST: Carotid Revascularization Endarterectomy vs. Stenting Trial



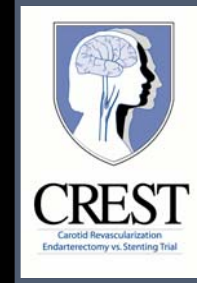
- NINDS/NIH sponsored, prospective, MC, RCT of CEA vs. CAS, with blinded endpoint adjudication
- Independent angio, EKG, MI, U/S core labs
- Included ***normal surgical risk*** symptomatic (53%), asymptomatic (47%) patients
- 108 US, 9 Canadian sites
- 52% of eligible CAS operators were certified
- Surgeons had to have stroke/death rate of < 3% for asymptomatics, < 6% for symptomatic
- Began in 2000, completed in 2008
- Team included CAS operator, surgeon, neurologist

CREST: Primary Endpoint & Eligibility Criteria

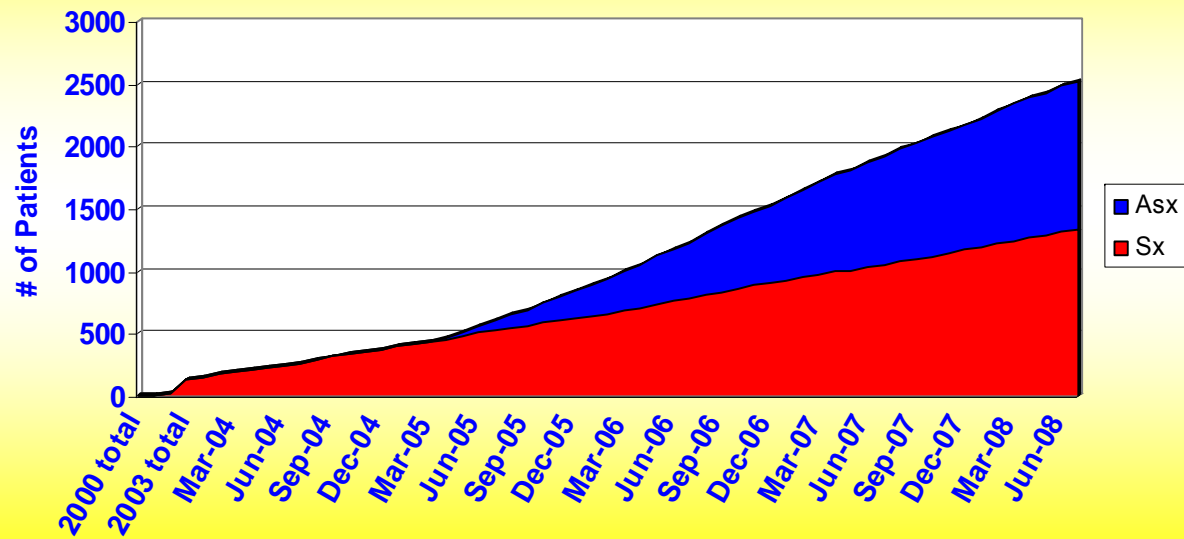


- Composite of Death/Stroke/MI peri-procedurally and ipsilateral stroke to 4 years
- Symptomatic: $\geq 50\%$ by angio, $\geq 70\%$ by US; $> 70\%$ by CTA/MRA if US 50-69%
- Asymptomatic: $\geq 60\%$ by angio; $\geq 70\%$ by US, or $> 80\%$ by CTA/MRA if US 50-69%
- **Excluded** if evolving or major stroke, chronic Afib, MI w/in previous 30 days, USA

CREST Timeline



CREST Cumulative Randomizations 2000 through July 2008



CREST: *Primary Endpoint:*
(any peri-procedural
death/stroke/MI)

| CAS vs. CEA | Hazard Ratio, 95% CI | P value |
|---------------|----------------------|---------|
| 5.2 vs. 4.5 % | 1.18; 0.82-1.68 | 0.38 |

CREST: 30-day Endpoints

| | CAS | CEA | HR | 95% CI | P value |
|--|-------|-------|------|-----------|---------|
| Peri-procedural CVA | 4.1 % | 2.3 % | 1.79 | 1.14-2.82 | 0.01 |
| Peri-procedural MI | 1.1 % | 2.3 % | 0.59 | 0.26-0.94 | 0.03 |
| Peri-procedural Major CVA | 0.9 % | 0.7 % | 1.35 | 0.54-3.36 | 0.52 |
| Peri-procedural CN palsies | 0.3 % | 4.8 % | 0.07 | 0.02-0.18 | <.0001 |
| Ipsilateral CVA | 2.0 % | 2.4 % | 0.94 | 0.50-1.76 | 0.85 |
| Combined peri-procedural CN palsies and CVA | 4.4 % | 7.1% | | | |

Clinical Impact of Peri- Procedural Minor Strokes

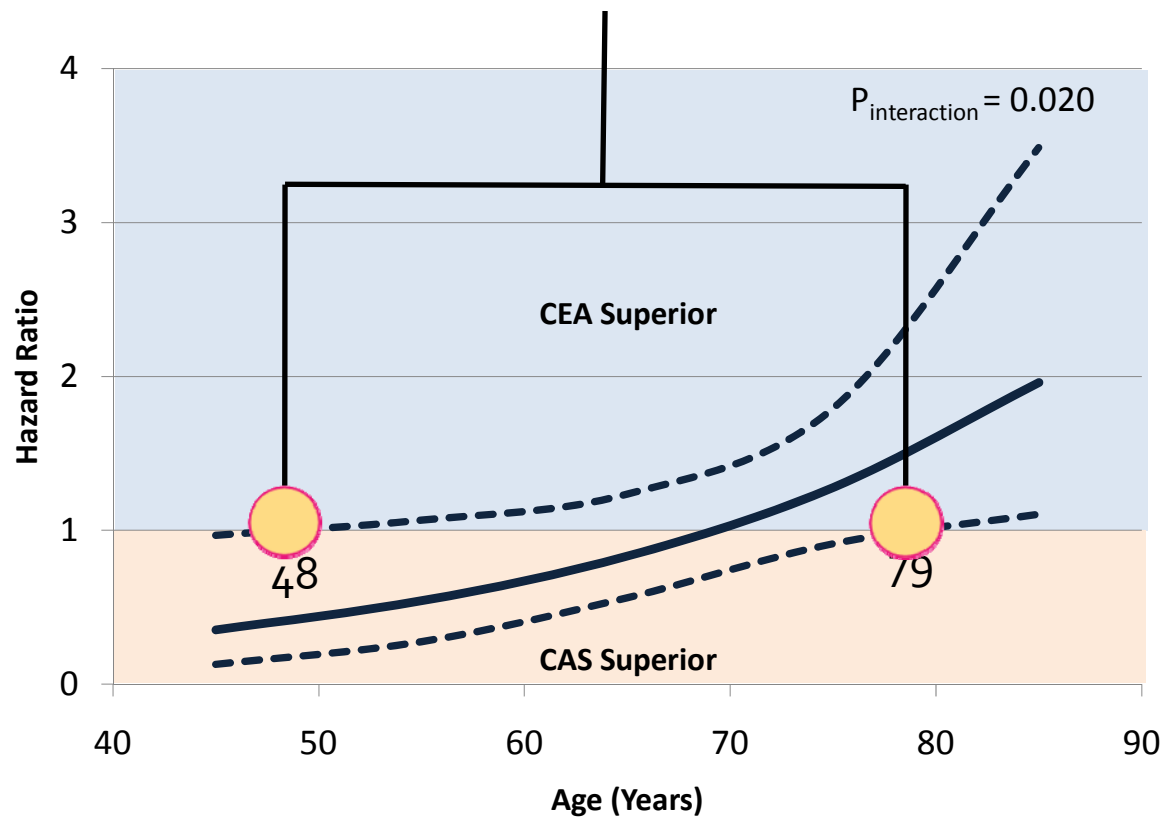
1 year neurological status in patients with minor stroke

| | NIHSS= 0 or 1 | NIHSS > 1 |
|----------------|---------------|-----------|
| ARCHER 1 and 2 | 100 % | 0 % |

Minor strokes with negligible clinical impact at 1 year

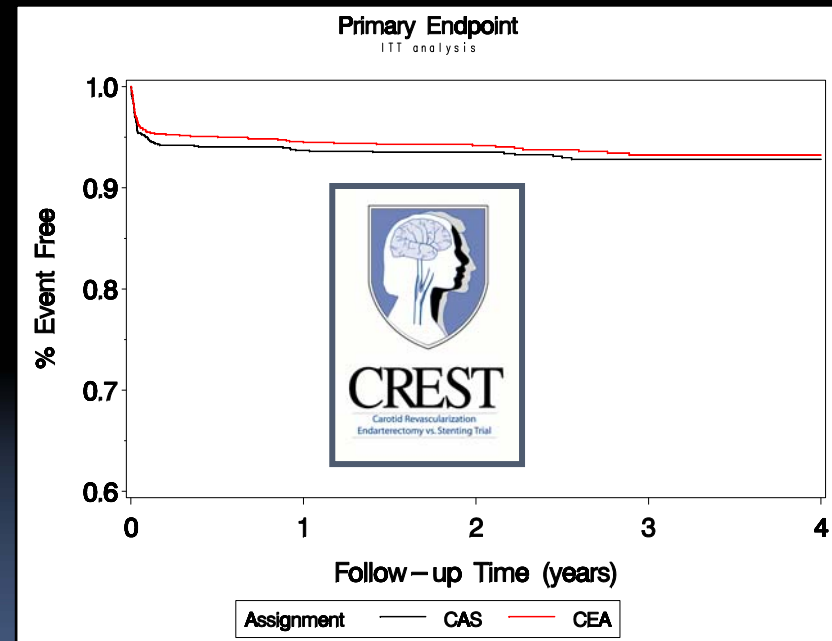
CREST: Primary Outcome- 4 yr

90% of subjects: no difference between therapies

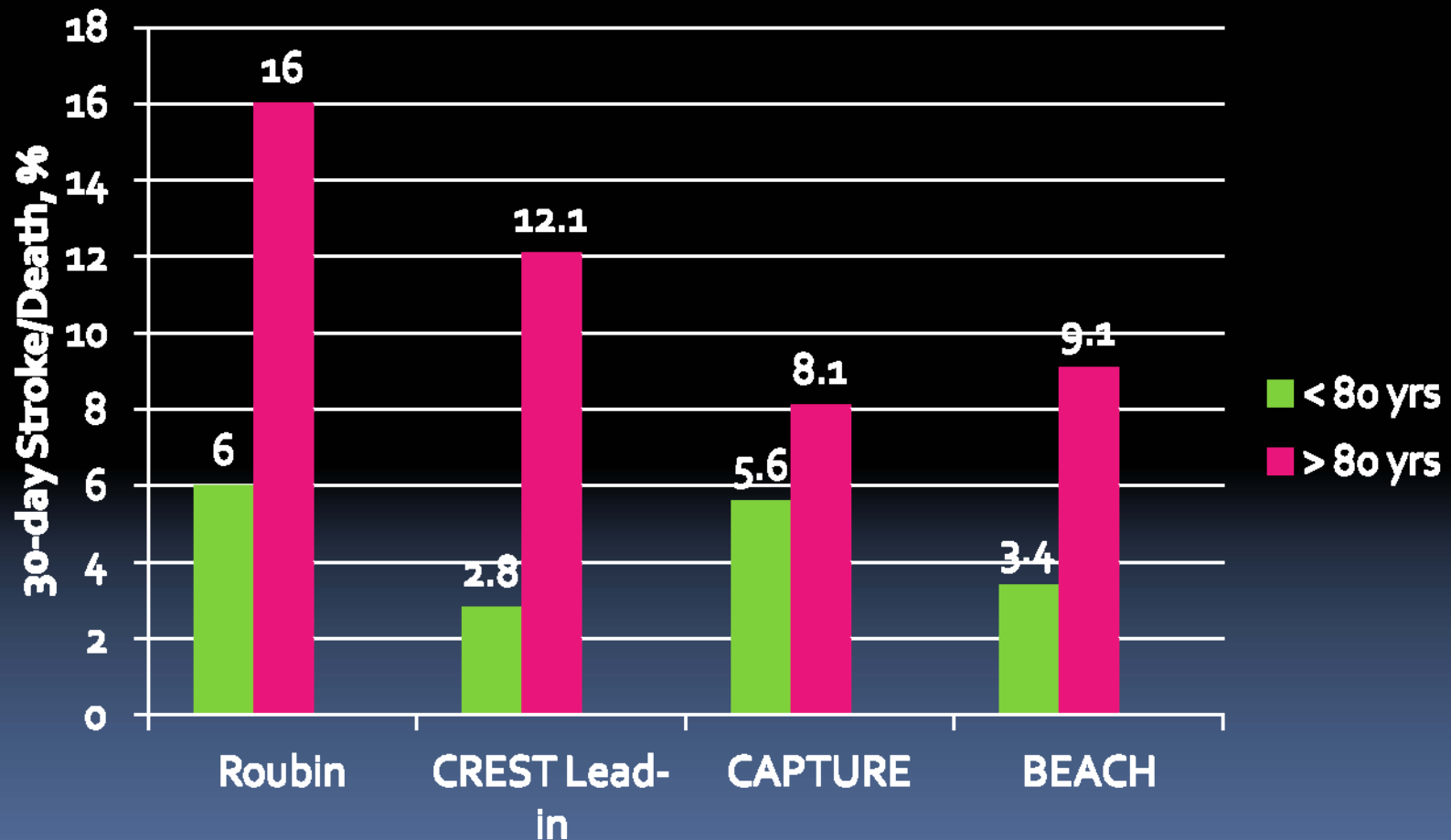


CREST: Summary

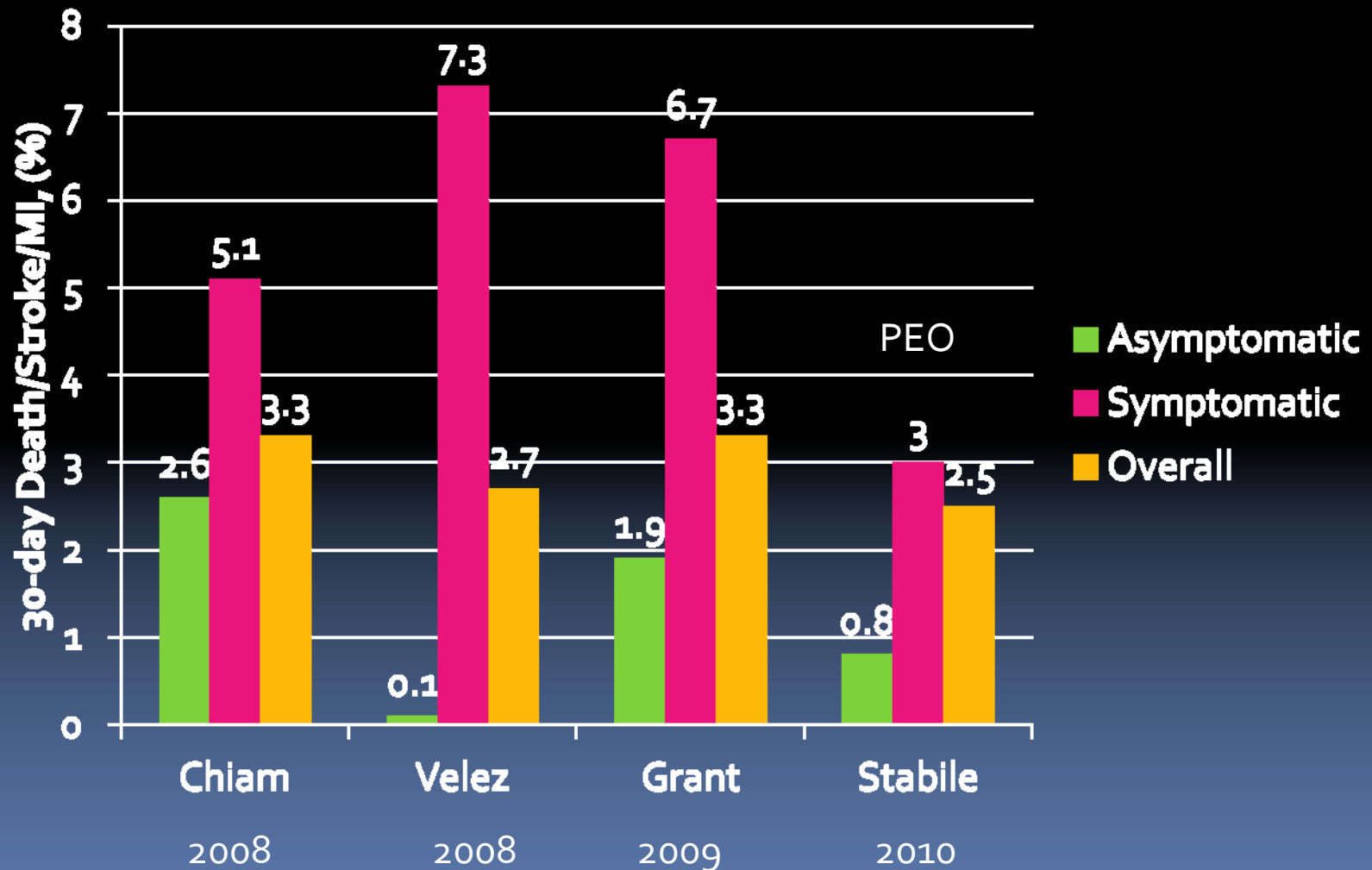
- Similar 1° endpoint driven by differences in peri-operative stroke and MI
 - More MI after CEA
 - More minor strokes after CAS
- No interaction for symptom status or gender
- Interaction suggested for age
- Younger patients may have improved efficacy with CAS; older patients may have improved efficacy with CEA
- Both CAS and CEA have low peri-operative complications, excellent long-term results



CAS in Octogenarians: Is it Safe?



CAS in Octogenarians- Recent Data



So, Who Should **NOT** get CAS?

- Symptomatic, ≥ 80 yrs.
- Decreased cerebral reserve
- Severe renal disease
- Complex aortic arch
- Tortuous anatomy
- Calcification
- Echolucent plaque
- Thrombus at lesion site
- Operator inexperience

So Who *Should* Get CAS?

Everybody Else!