PROTECT STUDY:
PROTECTed Carotid Artery Stenting in Subjects at High Risk for Carotid Endarterectomy

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Cardiovascular Research Foundation
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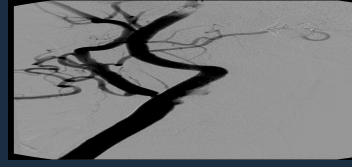
Disclosures

Consulting Agreement:
Abbott Vascular

Clinical Research Support:
Abbott Vascular

20 YEARS OF INNOVATION
TCT2008



SAPPHIRE WW CAS REGISTRY: Results of the First 2001 Patients

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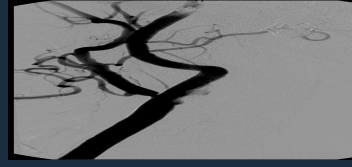

Disclosure Statement of Financial Interest

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

Speakers Bureau: **Boston Scientific, Abbott, St. Judes**

Proctor for Hands-on

***Carotid and PV Courses*: Cordis, ev3, Abbott, Boston Scientific**

***Scientific Advisory Board*: CoAxia, Kensey-Nash/Spectranetics**

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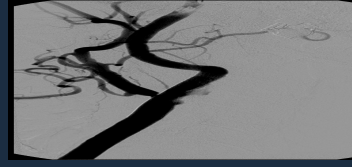
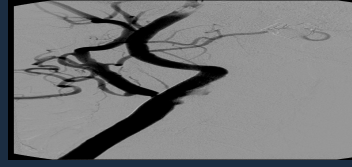


SAPPHIRE Worldwide

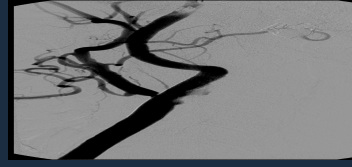
- The objective of the SAPPHIRE Worldwide registry is to evaluate outcomes after CAS performed by physicians with varied experience at multiple centers and utilizing a formal training program

- Data is available on the first 2,001 patients enrolled and followed to 30 days for the overall population and by high-risk inclusion criteria



SAPPHIRE WW: Study Design

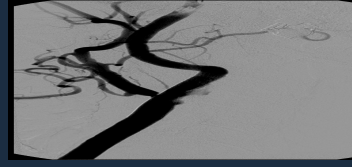
- Multicenter, prospective, post-approval registry to evaluate CAS using the Cordis PRECISE® Nitinol Stent and ANGIOGUARD® XP/RX Emboli Capture Guidewire System
- Patients were included if considered high-risk for adverse events from carotid endarterectomy and met the following criteria:
  - Symptomatic with ≥50% stenosis by ultrasound or angiogram
  - Asymptomatic with ≥80% stenosis by ultrasound or angiogram
  - Vessel diameter 4 - 9 mm at target lesion
  - Vessel distal to target lesion 3 - 7.5 mm for placement of ANGIOGUARD®



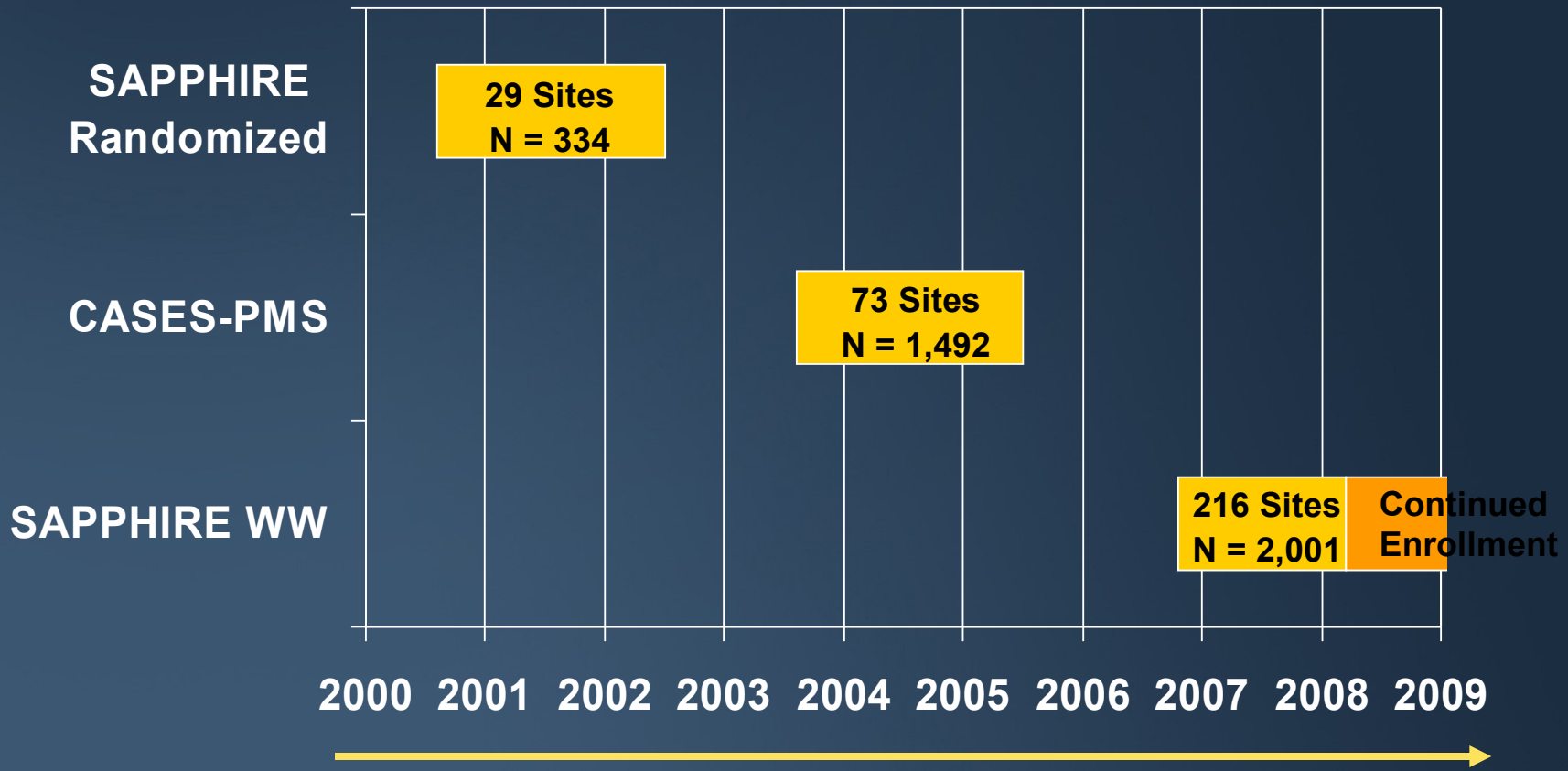
Study Endpoints

- Major adverse events (MAE) including any death, myocardial infarction or stroke to 30 days after the procedure

- MAE including death, stroke, myocardial infarction, target vessel revascularization,and stent thrombosis will be assessed out to 12 months



Study Timelines



Number of participating sites and CAS patients studied continue to grow

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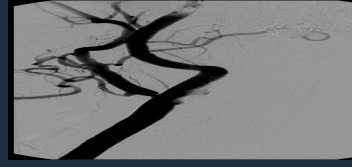

TOP ENROLLERS

- Chris Metzger, MD: Kingsport, TN
- Maurice Solis, MD: Macon, GA
- Majdi Aschi, MD: Jacksonville, FLA
- Rajesh Shah, MD: Norfolk, VA
- Tift Mann, MD: Raleigh, NC

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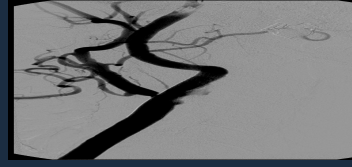
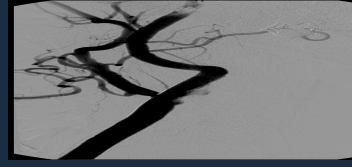
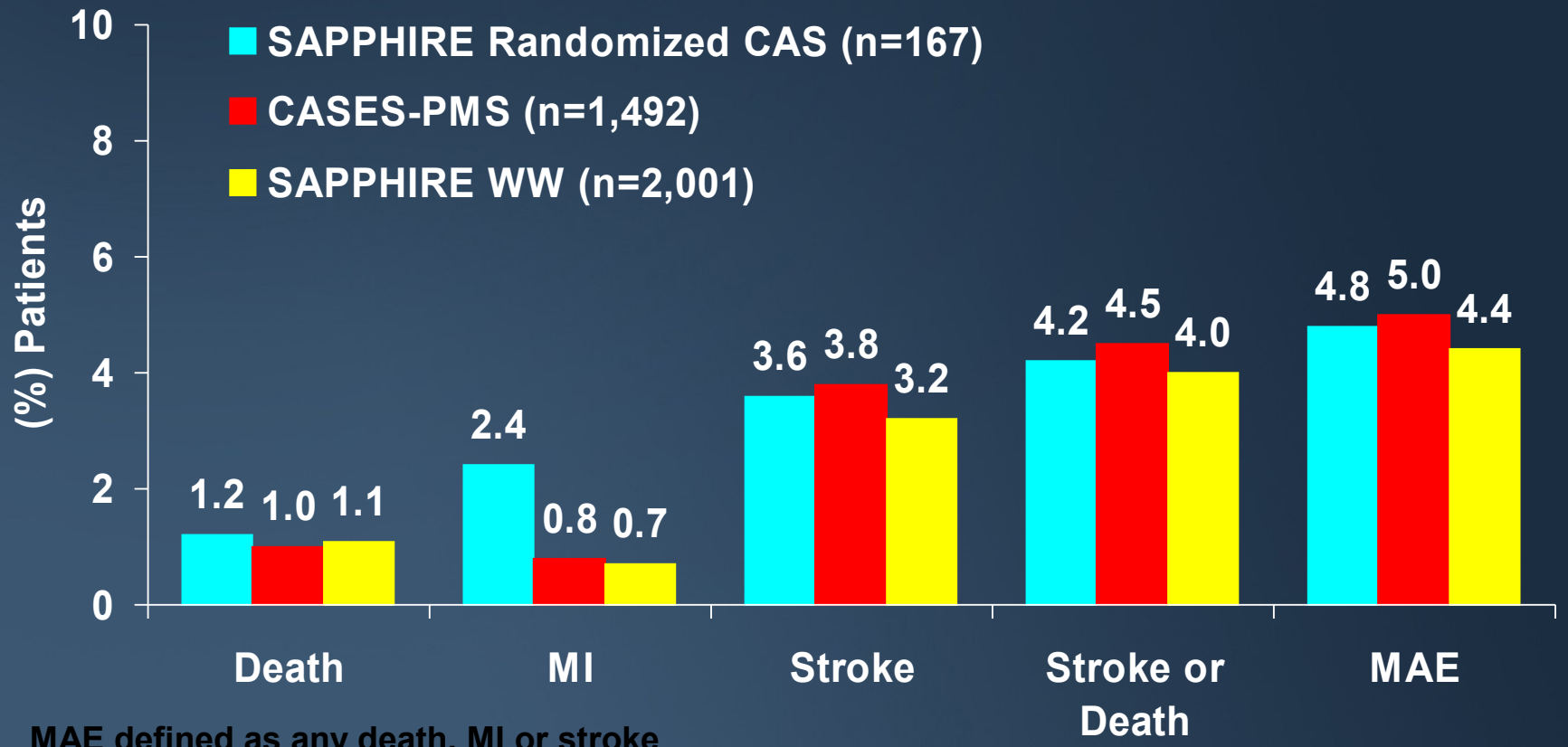


Baseline Demographics

	SAPPHIRE Randomized CAS N = 167	CASES-PMS N = 1,492	SAPPHIRE WW N = 2,001
Age (years)	72.5 ± 8.3	73.4 ± 9.5	72.2 ± 9.75
Age > 80 years	19.3%	25.9%	26.0%
Male	66.9%	62.7%	62.0%
Symptomatic	29.9%	21.8%	27.7%
Renal insufficiency (creatinine > 2.5mg/dl)	6.0%	6.5%	5.0%
History of Hypertension	85.5%	90.3%	81.9%
Diabetes Mellitus	25.3%	35.4%	33.3%
History of MI	29.7%	35.6%	20.8%
Prior PCI	34.8%	36.9%	19.3%
History of Cardiac Arrhythmia	15.9%	26.5%	15.5%
Previous PTA (carotid)	1.2%	3.5%	3.3%
Prior CEA	28.3%	29.9%	26.2%
History of TIA	31.1%	27.4%	21.6%
History of Stroke	27.1%	26.3%	21.0%



Major Adverse Events at 30 Days: SAPPHIRE vs. CASES vs. SAPPHIRE WW



MAE defined as any death, MI or stroke

Note: Collection of cardiac enzymes differed among all three studies

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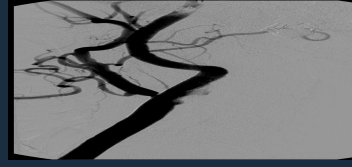
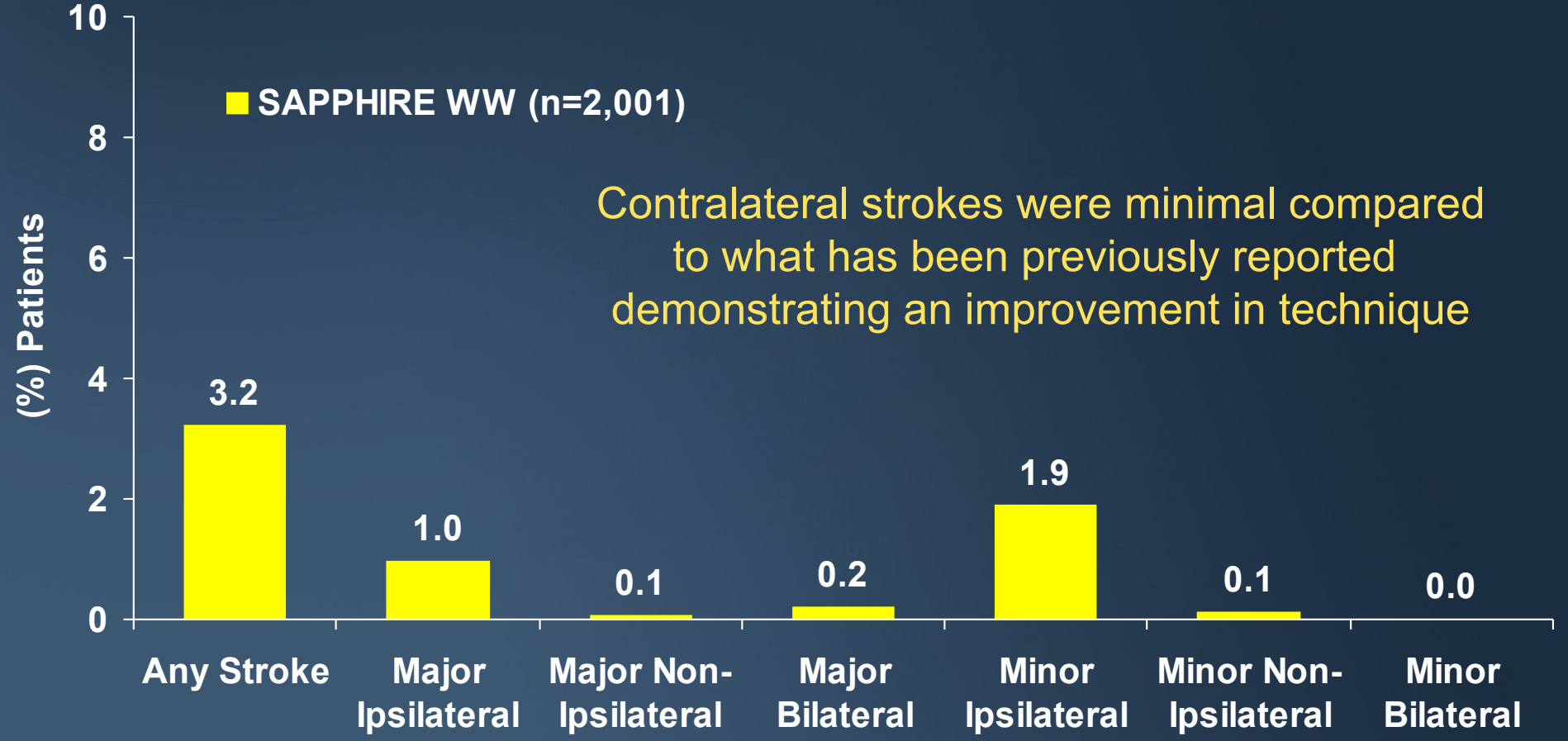


Stroke at 30 Days: SAPPHIRE WW – All Patients



Contralateral strokes were minimal compared to what has been previously reported demonstrating an improvement in technique

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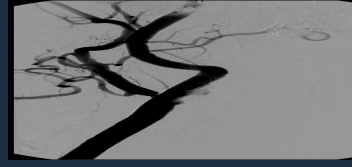
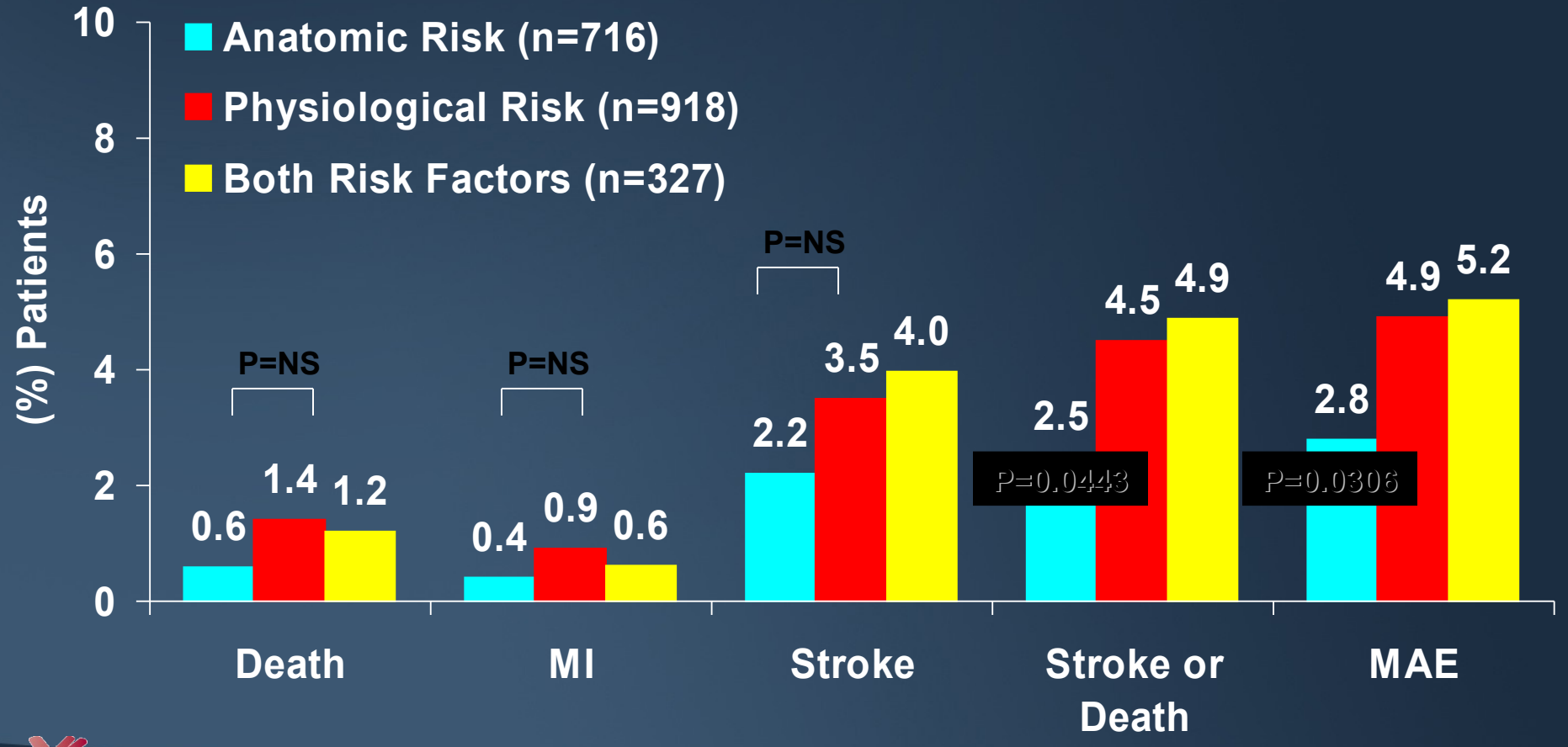


Major Adverse Events at 30 Days: Anatomic Risk vs. Physiologic Risk



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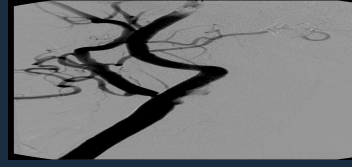
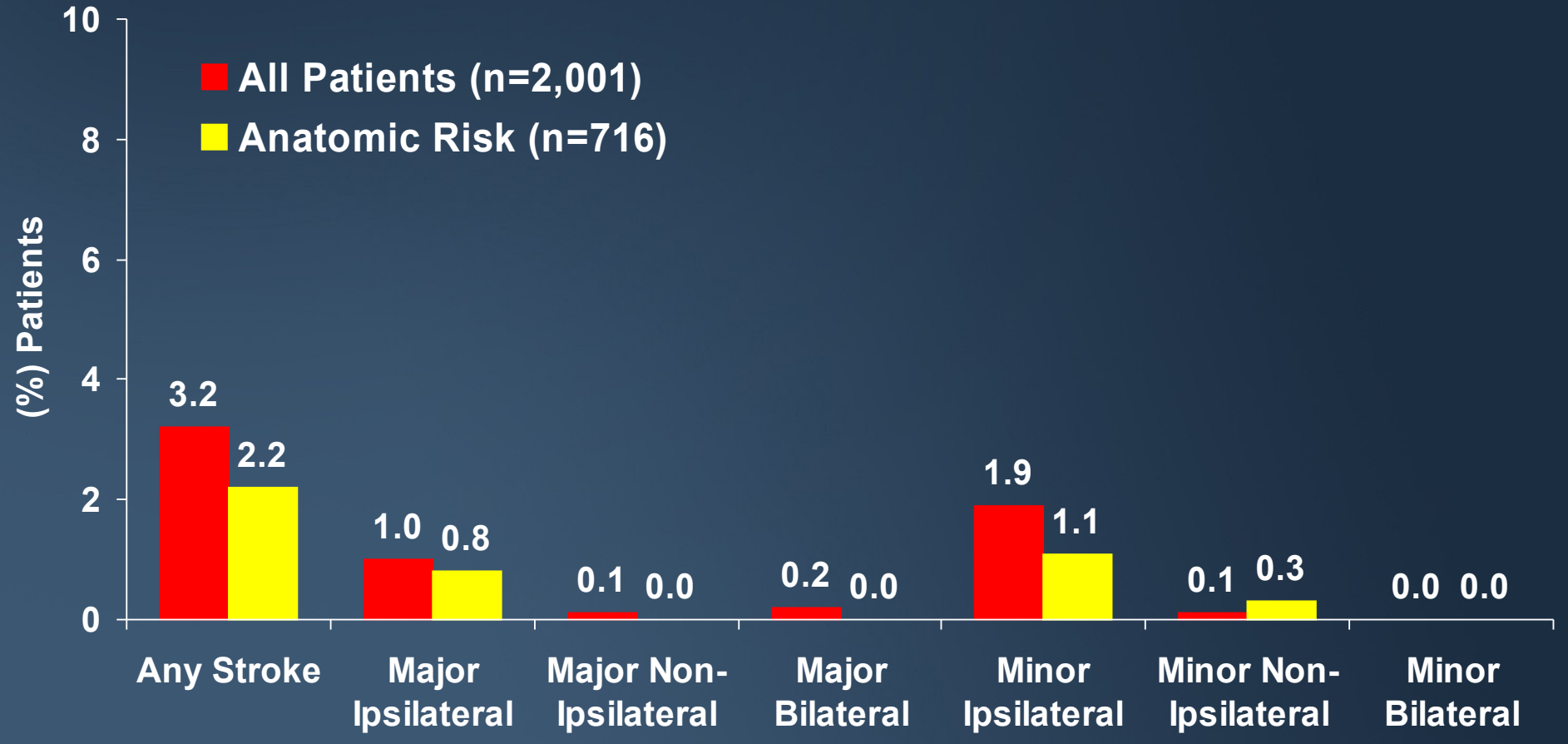


Stroke at 30 Days: All Patients vs. Patients with Anatomic Risk



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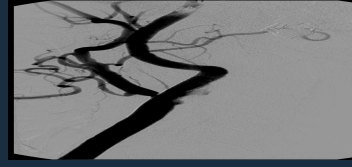
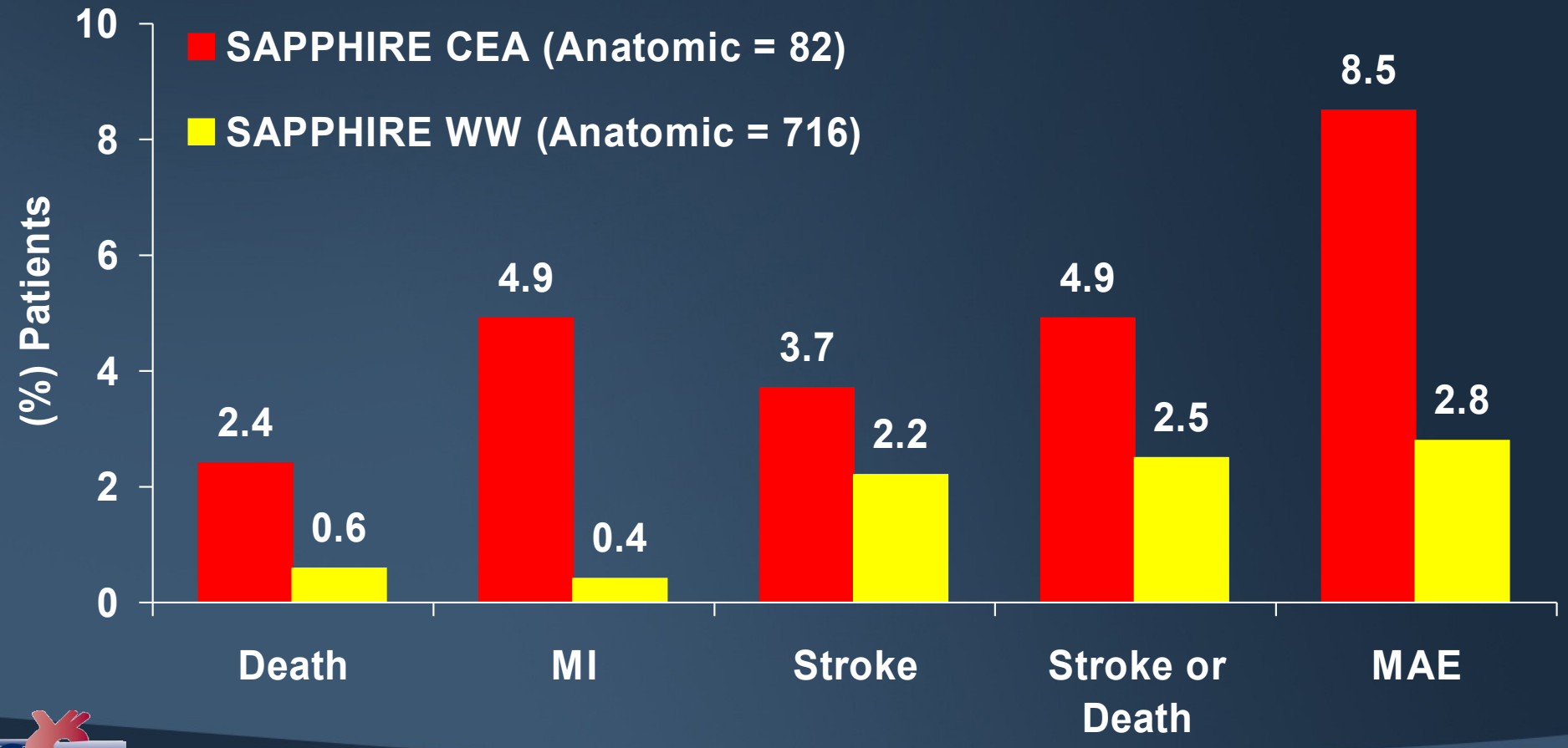
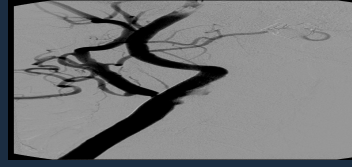
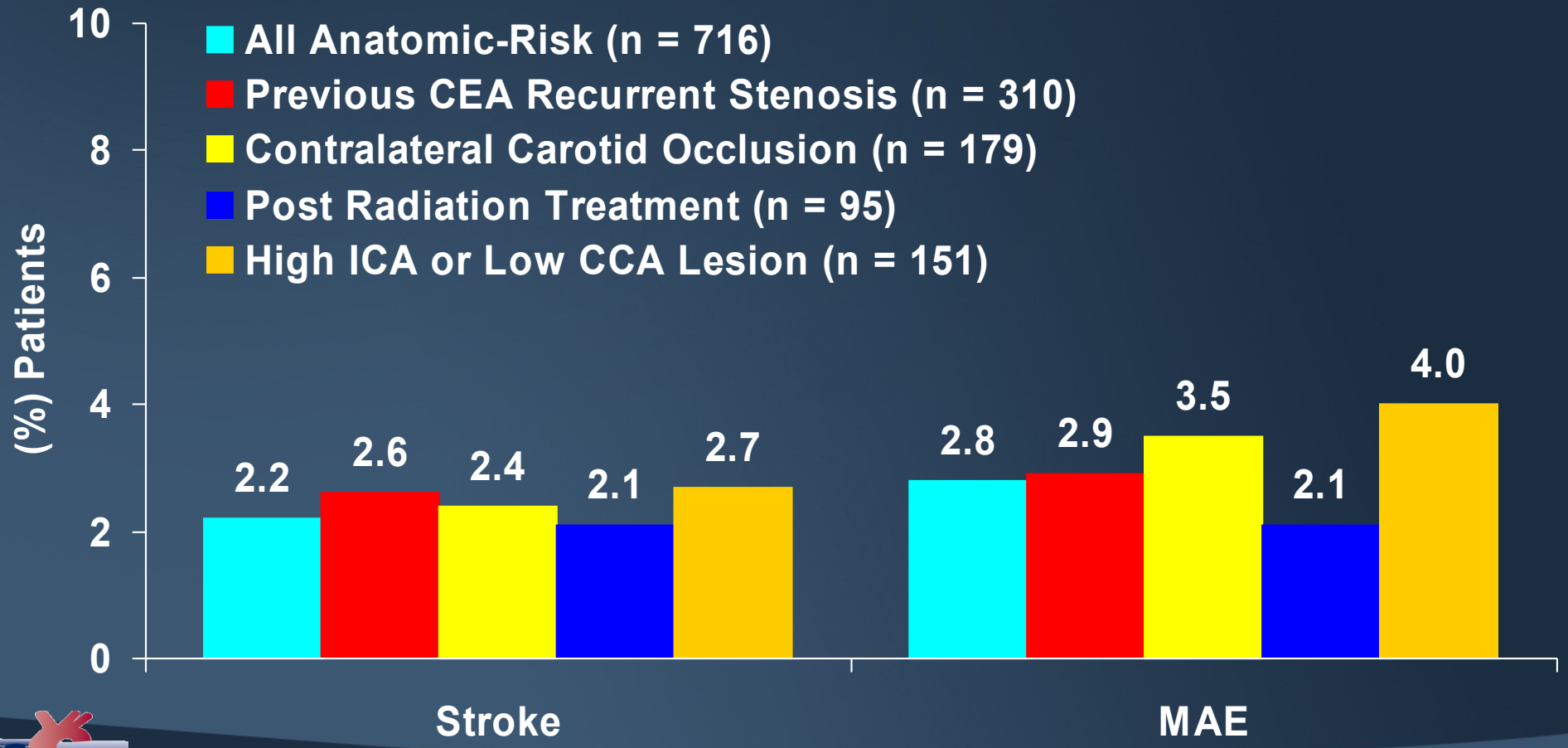


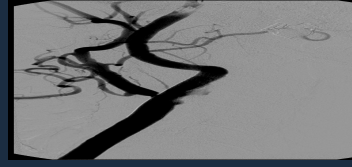
MAE at 30 Days:
Anatomic Risk SAPPHIRE CEA vs. SAPPHIRE WW





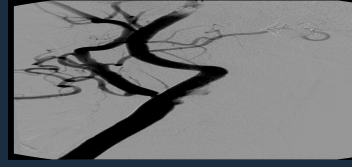
Major Adverse Events at 30 Days: Anatomic Risk Variables



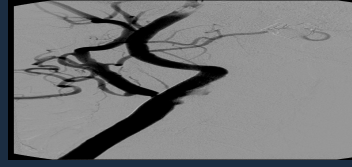


Conclusions

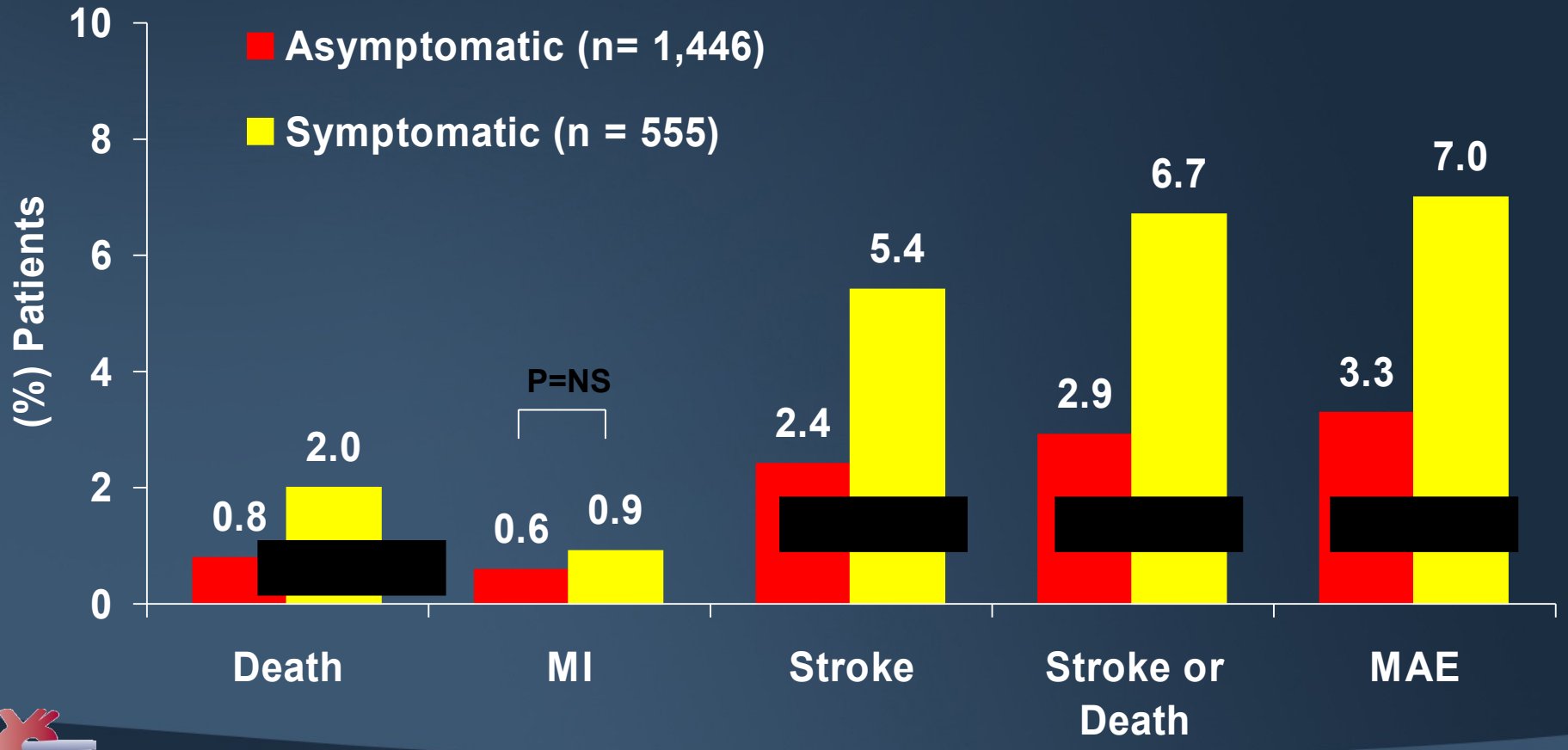
- While the number of physicians performing CAS continues to increase, major adverse event rates seen in this registry (4.4%) are well within an acceptable range, as was first seen in the SAPPHIRE randomized trial (4.8%)
- A significant decrease in MAE was seen in patients with anatomical risk factors compared with patients with physiological risk factors (2.8% vs. 4.9%, p=0.0306), respectively
- The SAPPHIRE WW registry supports the use of CAS as an alternative to carotid endarterectomy, especially in patients who are at high-risk for surgery due to anatomical risk factors

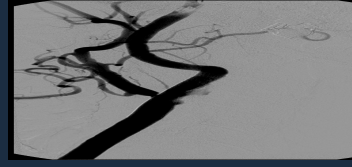


30-Day Outcomes by Other Subgroups

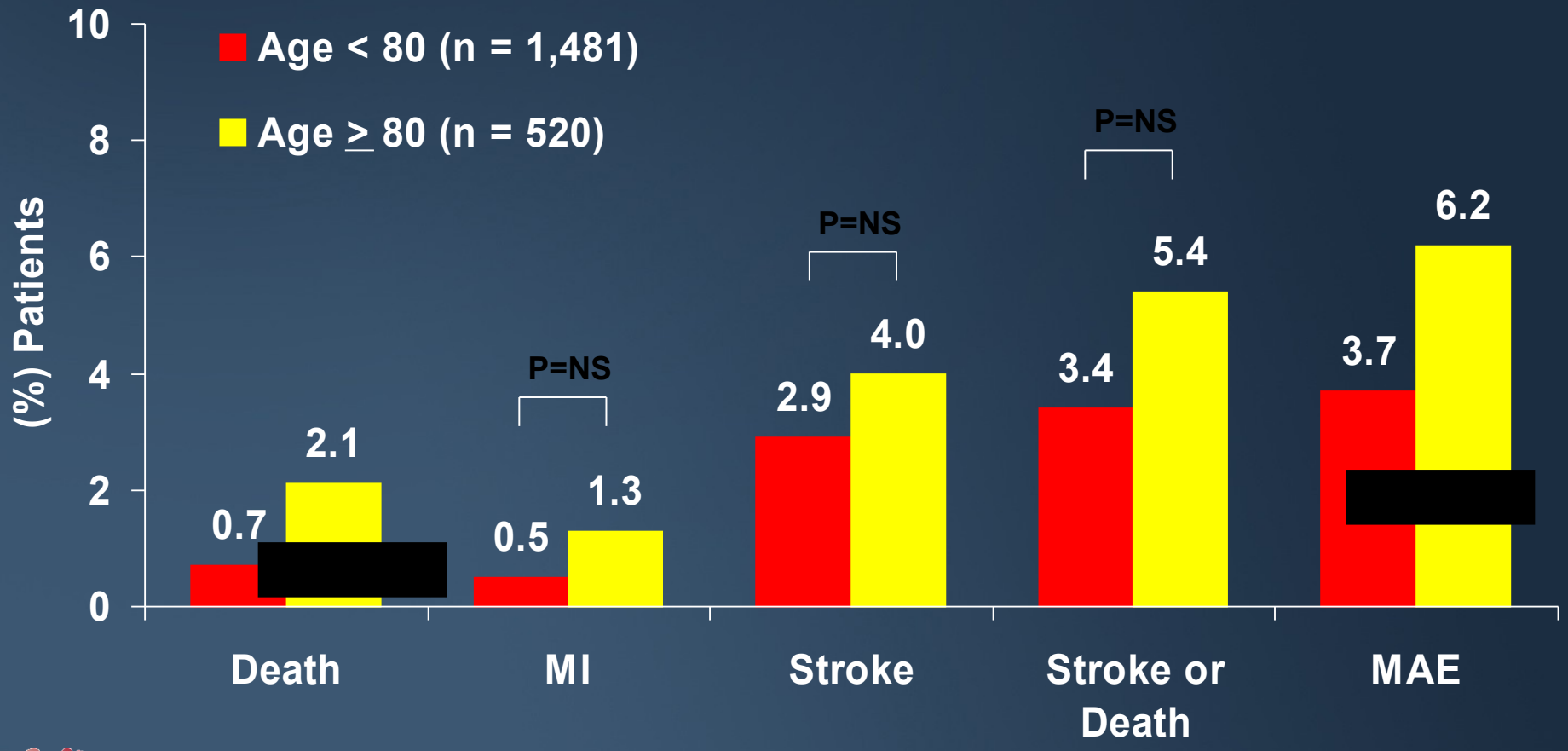


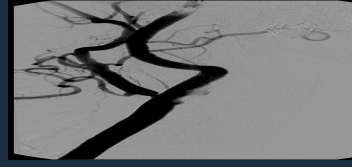
Major Adverse Events at 30 Days: Asymptomatic vs. Symptomatic





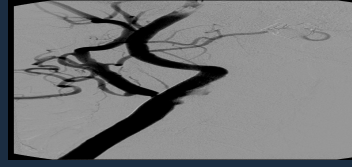
Major Adverse Events at 30 Days: Age < 80 vs. ≥ 80 Years





Conclusions (1)

- MAE rates were significantly lower in asymptomatic patients compared with symptomatic patients (3.3% vs. 7.0%, p=0.0005), however, perioperative stroke or death in both groups are comparable to the historical carotid endarterectomy trials
- As expected, patients ≥ 80 years had a significantly higher rate of MAE than younger patients (6.2% vs. 3.7%, p=0.0240), increased by the significant number of deaths in the ≥ 80 population



Conclusions (2)

- Multivariate predictors of both MAE and stroke at 30 days included symptomatic status, as well as several other physiological risk factors
- Further enrollment and follow-up will continue to provide evidence in support of optimal patient selection, lesion criteria, and operator experience in performing CAS in this high-risk population

PROTECT: Purpose of the trial

- Sponsor: Abbott Vascular
- Purpose:
  - Pivotal IDE trial assessment of the Generation 5 Emboshield Pro Rapid Exchange Embolic Protection
  - Fulfill the long-term follow-up requirement of the Xact stent PMA conditions of approval: 3-year follow-up on at least 305 subjects
- Analysis Cohort:
  - Enrollment completed in 20 months (Nov 2006-June 2008); 274 patient cohort with 30 day follow-up analysis of embolic protection presented here.
  - 3 year Xact stent follow-up ongoing (n=322)

PROTECT: Design, conduct, and endpoints

- Design:
  - Prospective, single-arm registry for patients with carotid stenosis anatomic or physiologic high surgical risk features
  - Stenosis: Symptomatic >50% or asymptomatic >80%
- Study requirements:
  - Neurologic exam pre-enrollment, 24 hour, 30 day and annually (3 years) performed by an independent neurologist
  - Independent adjudication of neurological events by a CEC
  - Independent outcome monitoring by the DSMB
- 1^{o} Endpoints: OPC based on 30-day MAE rates of SECuRITY, SAPPHIRE, ARCHeR, BEACH and MAVErIC
  - For Emboshield® Pro Rapid Exchange Embolic Protection System: 30-day composite rate of DSMI for first 220 consecutively enrolled subjects.
  - For Xact stent: Composite 30-day DSMI, plus ipsilateral strokes from 31-365 days and annually (3) years.

Anatomic high surgical risk features

- Previous radiation treatment to the neck or radical neck dissection
- Target lesion is at or above the second vertebral body C2 (level of jaw)
- Inability to extend the head due to cervical arthritis or other cervical disorders
- Tracheostomy or tracheal stoma
- Laryngectomy
- Contralateral laryngeal nerve palsy
- Severe tandem lesions

Physiologic high surgical risk features

- Previous CEA with significant restenosis
- Total occlusion of the contralateral carotid artery
- Dialysis dependent renal failure
- CCSA Class III or higher or unstable angina. Requires coronary artery bypass surgery, cardiac valve surgery, peripheral vascular surgery, or abdominal aortic aneurysm repair within 60 days
- ∀ ≥ 80 years of age
- Myocardial infarction within previous 6 weeks
- Severe pulmonary disease, including at least one:
  - requires chronic O2 therapy
  - resting PO2 ≤ 60 mm Hg
  - Hematocrit ≥ 50%,
  - FEV1 or DLCO ≤ 50% of normal

36 investigative sites in US

- Pinnacle Health Hospital, Harrisburg, PA
- Lenox Hill Hospital, New York, NY
- Washington Hospital, Fremont, CA
- Our Lady of Lourdes Medical Center, Camden, NJ
- Austin Heart P.A., Austin, TX
- Memorial Hospital Jacksonville, Jacksonville, FL
- St. Joseph's Medical Center, Wyomissing, PA
- Millard Fillmore Hospital-Kaleida Health Systems, Buffalo, NY
- El Camino Hospital, Mountain View, CA
- Stanford University Medical Center, Stanford, CA
- Chesapeake General Hospital, Norfolk, VA
- Hoag Memorial Hospital Presbyterian, Newport Beach, CA
- Massachusetts General Hospital, Boston, MA Parkview Hospital, Fort Wayne, IN
- St. John's Hospital, Springfield, IL Memorial Medical Center, Springfield, IL
- Baptist Hospital of East Tennessee, Knoxville, TN
- Washington Adventist Hospital, Takoma Park, MD
- Hawaii Permanente Medical Group-Kaiser Foundation Hospital, Honolulu, HI
- Greenville Memorial Medical Center, Greenville, SC
- St. Luke's Episcopal Hospital, Houston, TX
- Terrebonne General Medical Center, Houma, LA
- St. Luke's Medical Center, Milwaukee, WI
- Lakeland Regional Medical Center, Lakeland, FL
- Genesys Regional Medical Center, Grand Blanc, MI
- Oregon Health & Science University, Portland, OR
- St. Joseph's Mercy Hospital, Ann Arbor, MI
- University of Connecticut Health Center, Farmington, CT
- Northwestern University Memorial Hospital, Chicago, IL
- Bon Secours St. Mary's Hospital, Richmond, VA
- McLaren Regional Medical Center, Flint, MI
- St. Vincent Hospital and Health Care Center, Indianapolis, IN
- William Beaumont Hospital, Royal Oak, MI
- Presbyterian Hospital of Dallas, Dallas, TX
- Wake Medical Hospital, Raleigh, NC
- Holston Valley Medical Center, Kingsport, TN
- St. Michael's Medical Center, Newark, NJ
- Lehigh Valley Hospital, Allentown, PA

PROTECT: Patient Demographics

Characteristic	PROTECT N=274	SECuRITY N=305	ARCHeR N=581
Mean Age	72.3	74.5	72.6
Age ≥ 80	28.8	34	15.5%
% Symptomatic	12.1%	21%	23.8%
% Male	67.6%	64%	67.1%
Diabetes Mellitus	29.9%	31%	37.9%
Hypertension	87.2%	87%	83.8%
Hypercholesterolemia	86.5%	74%	72.6%
CHF	19.3%	6%	33.6%
Anatomic §	16.0%	NA	19.3%
Current Smoker	16.8%	NA	19.3%
PVD	38.0%	NA	36.6%
Renal Failure	3.3%	NA	2.9%

§ Excluding co-morbidities

PROTECT: Patient Demographics

Characteristic	CAPTURE N=4225	EXACT N=2232	CAPTURE 2 N=4356
Mean Age	72.7	72.5	72.5
Age ≥ 80	23.4%	23.9%	22.5%
% Symptomatic	13.8%	10.3%	13.2%
% Male	60.8%	63.2%	61.7%
Diabetes Mellitus	34.9%	34.7%	36.2%
Hypertension	88.4%	89.5%	89.7%
Hypercholesterolemia	78.0%	74.4%	88.6%
CHF	16.3%	18.3%	17.9%
Anatomic §	11.4%	10.6%	20.5%
Current Smoker	21.0%	19.6%	23.3%
PVD	37.4%	44.8%	46.2%
Renal Failure	8.2%	7.2%	3.0%

§ Excluding co-morbidities

PROTECT
Primary endpoint: 30-day major adverse events

EVENT	PROTECT (N=274)
Death, Stroke and MI*	1.8% (12% OPC)
Death#	0.4%
All Stroke#	1.5%
Major Stroke#	0.4%
Minor Stroke#	1.1%
MI#	0.4%
All Stroke and Death*	1.5%
Major Stroke and Death*	0.4%

*Hierarchical- Includes only the most serious event for each patient and includes only each patient first occurrence of each event.

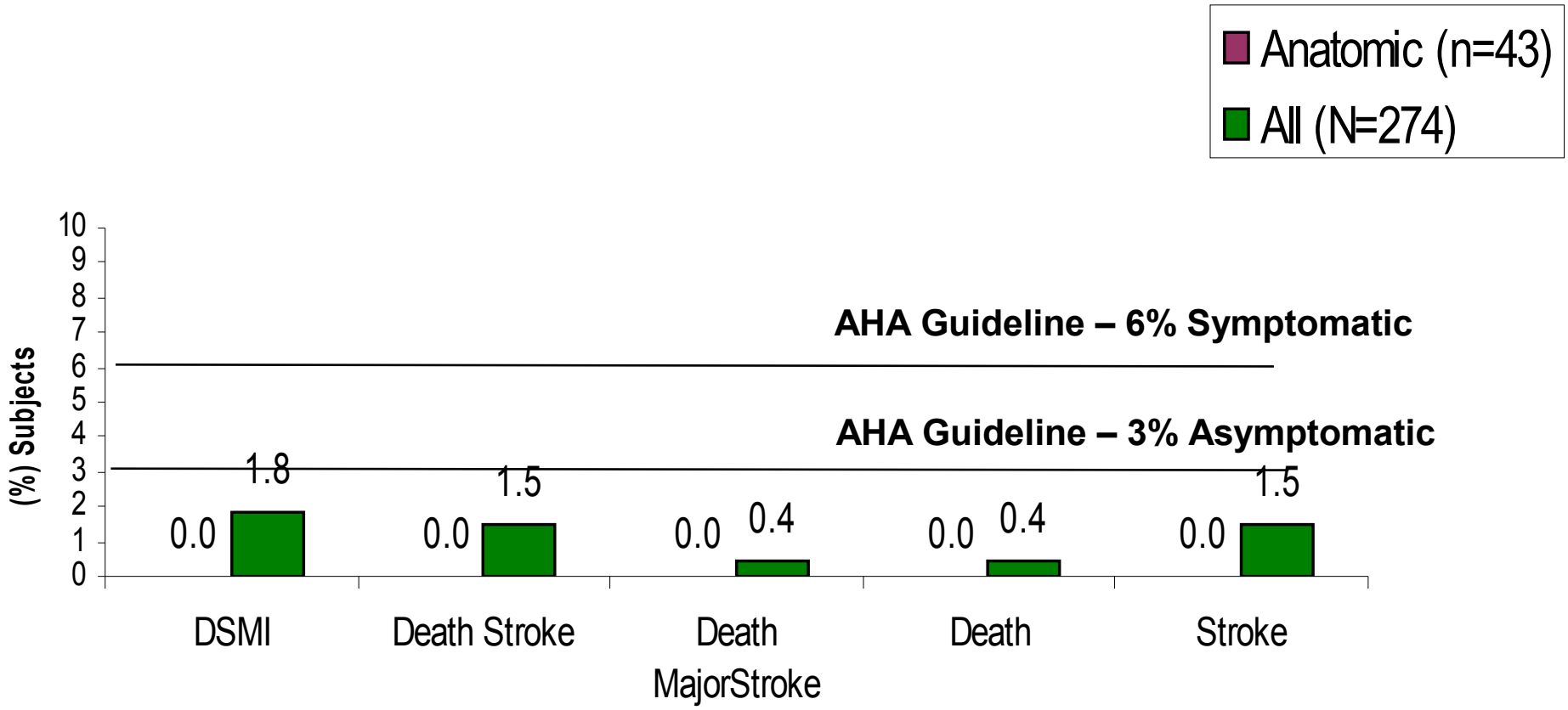
#Non-hierarchical-represents each event even in patients with multiple events

PROTECT
Secondary endpoint: 30-day major adverse events

EVENT Non-Hierarchical	PROTECT (N=274)
TIA and Amaurosis Fugax[#]	2.9%
TIA[#]	2.9%
Amaurosis Fugax[#]	0.4%

[#]Non-hierarchical-represents each event even in patients with multiple events

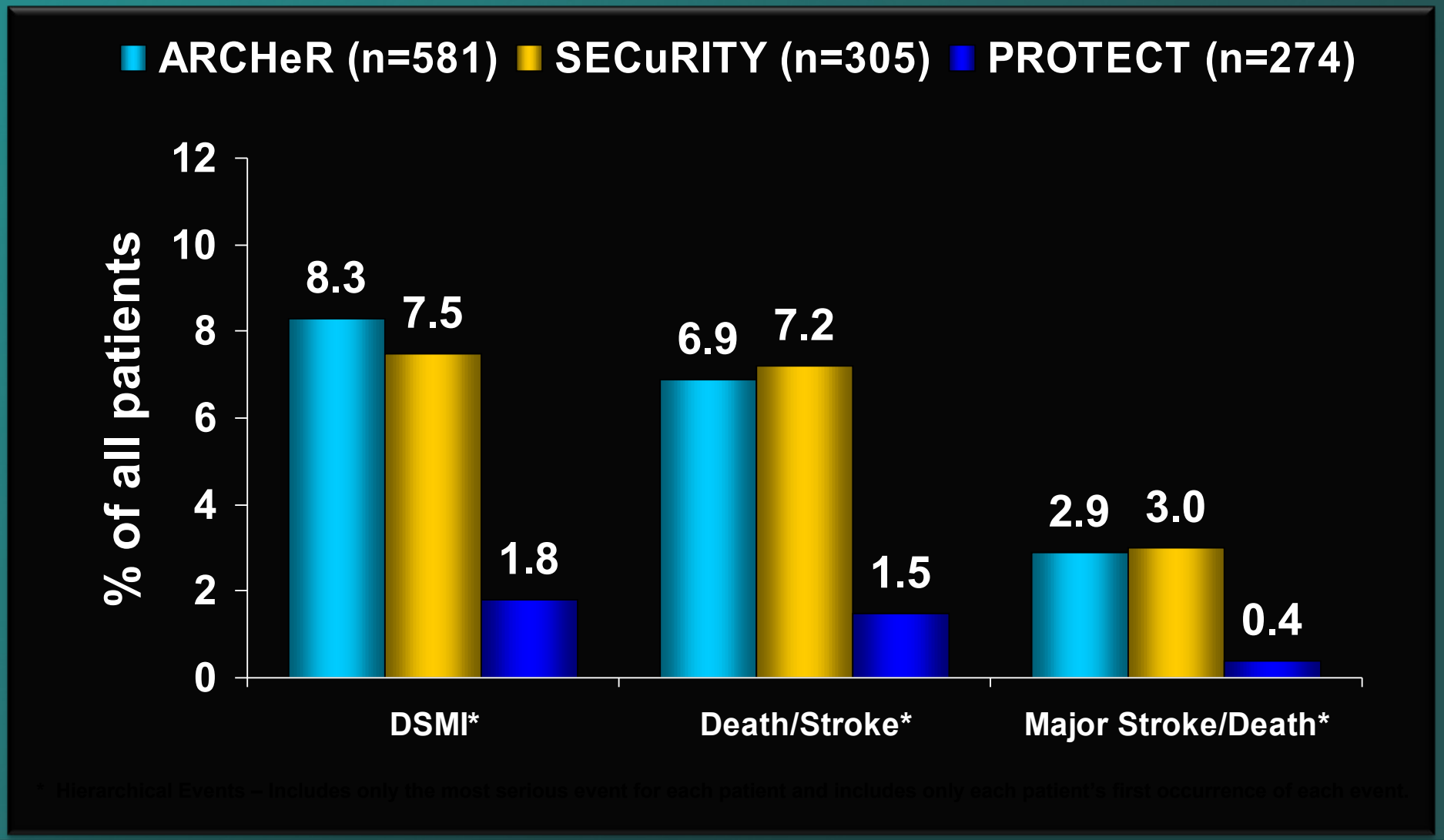
Total and anatomic subset vs. AHA guidelines for CEA



The anatomic subgroup does not include co-morbidities.

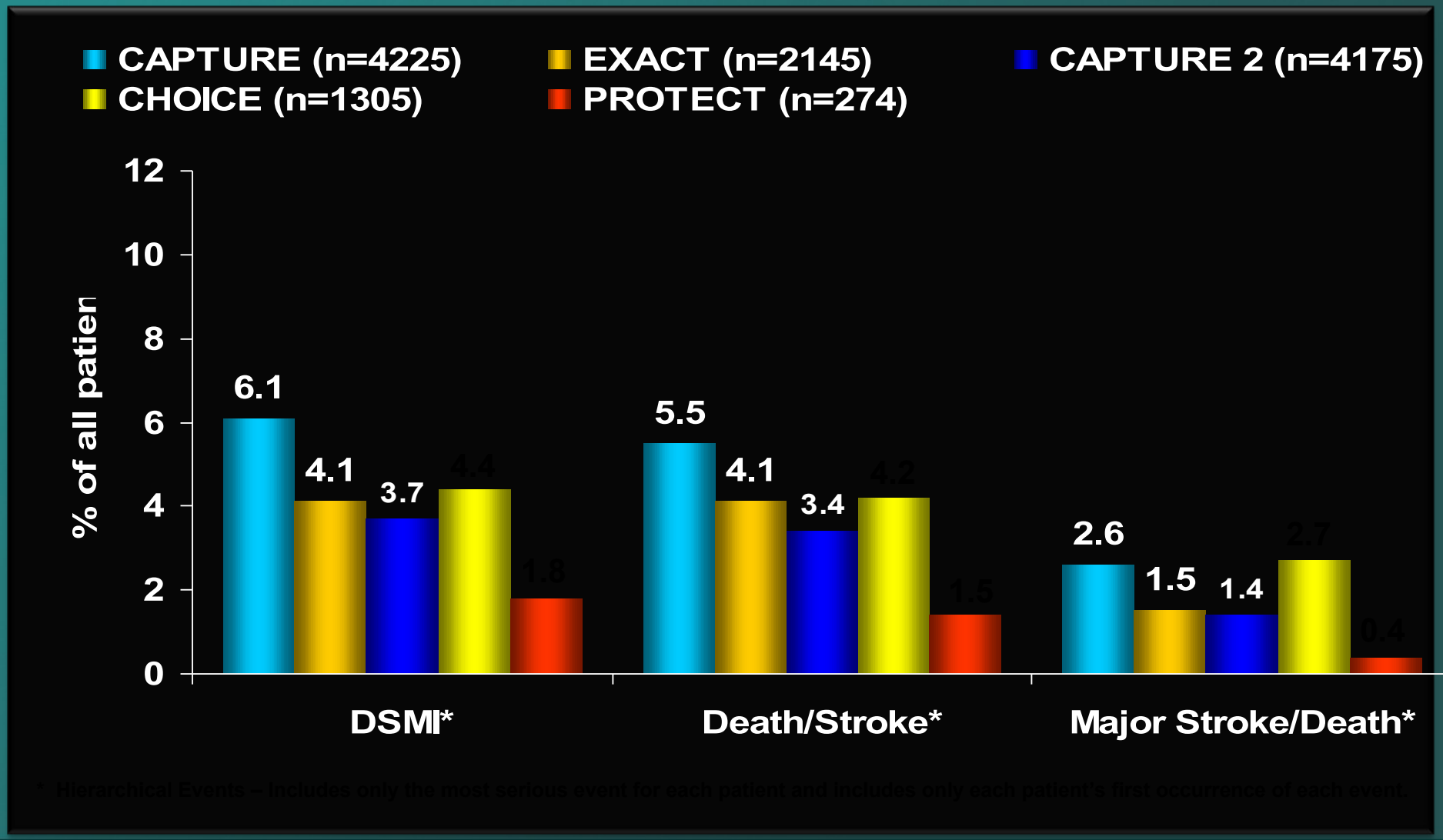
All age included.

Pivotal (IDE) trial 30 day outcomes ARCHeR, SECuRITY, and PROTECT



*. Hierarchical Events – Includes only the most serious event for each patient and includes only each patient's first occurrence of each event.

Post-market approval studies vs. PROTECT: 30 day outcomes



*. Hierarchical Events – Includes only the most serious event for each patient and includes only each patient's first occurrence of each event.

PROTECT: Conclusions

- 30 day primary outcome for PROTECT demonstrate non-inferiority with pre-specified OPC comparator
  - Next generation embolic protection proven safe and effective in preventing peri-procedural stroke
- PROTECT enrolled similar subjects compared to prior IDE studies, except with fewer symptomatic patients

PROTECT: Conclusions

- Total, anatomic and physiologic subsets all achieved/exceeded AHA guidelines established for standard risk CEA
- Continuing improvement in outcomes for IDE studies is demonstrated
  - Improvement is also noted with more contemporary post-market studies