# Approach to the Patient with Carotid Artery Disease

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# Conflict of Interest Statement

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

| Physician Name | Company/Relationship |
| --- | --- |
| Michael R. Jaff | Cordis Endovascular |
| | Boston Scientific |
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| | Medical Simulation Corp |
| | Pathway Medical |
| | Paragon Medical |
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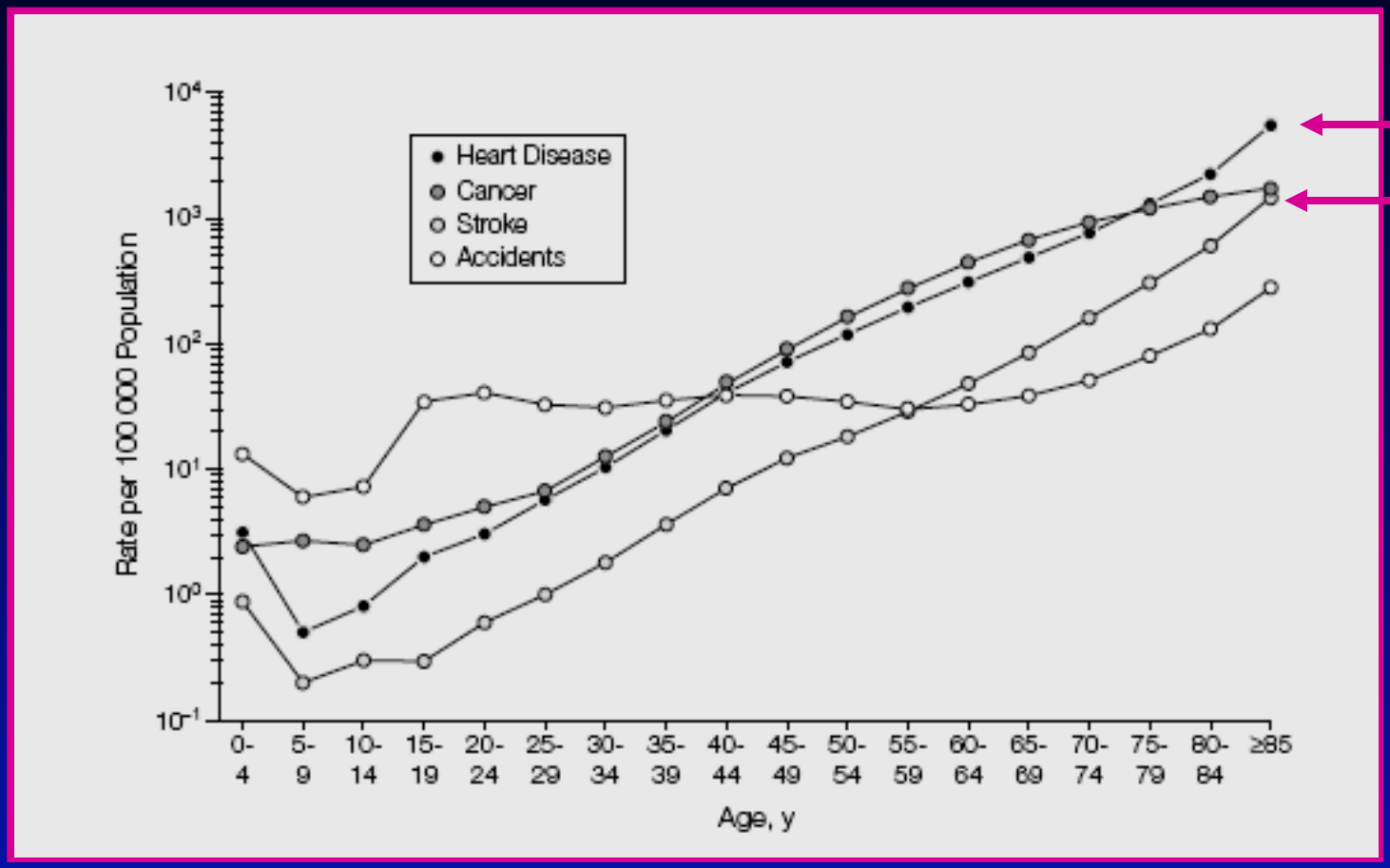
| | Access Closure, Inc |
| | Setagon, Inc. |

# Rate of Deaths Due to Atherosclerosis is Increasing in U.S.




JAMA 2005;294:1255.

# American Heart Association/ American Stroke Association Guidelines

**Guidelines for Prevention of Stroke in Patients With Ischemic Stroke or Transient Ischemic Attack: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association Council on Stroke: Co-Sponsored by the Council on Cardiovascular Radiology and Intervention: The American Academy of Neurology affirms the value of this guideline.**

Ralph L. Sacco, Robert Adams, Greg Albers, Mark J. Alberts, Oscar Benavente, Karen Furie, Larry B. Goldstein, Philip Gorelick, Jonathan Halperin, Robert Harbaugh, S. Claiborne Johnston, Irene Katzan, Margaret Kelly-Hayes, Edgar J. Kenton, Michael Marks, Lee H. Schwamm and Thomas Tomsick

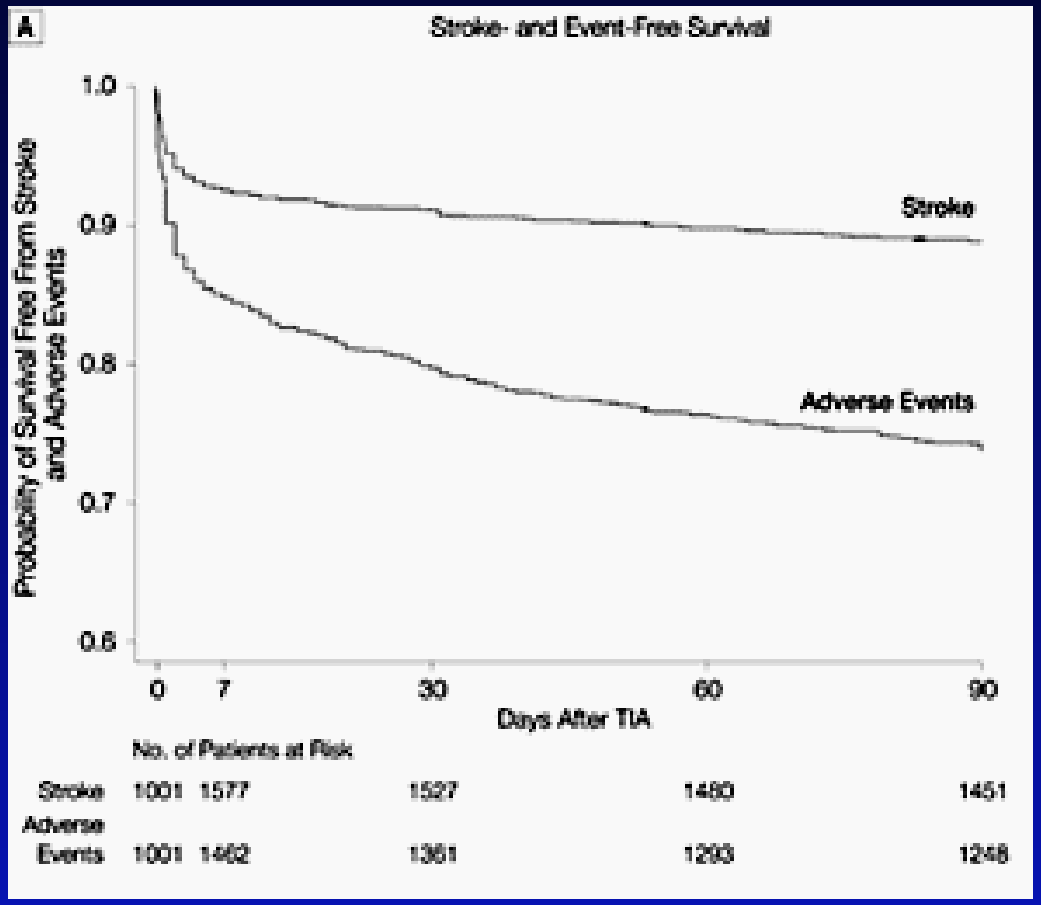
*Stroke* 2006;37;577-617

# Burden of Stroke in the U.S.

- 1 stroke every 45 seconds (700,000 per year)
- 2.4 million non-institutionalized stroke survivors
- Stroke causes 1 in 15 deaths
- Approximately 30 % aged 70-80 have silent brain infarction
- Stroke cost= 58.8 billion/year

# TIAs Cause Early Stroke and Cardiovascular Events

**Follow up of 1707 subjects diagnosed with TIA in ED**




**Risk Factors for Events:**

| | OR |
|---|---|
| Age > 60 y | 1.8 |
| Diabetes | 2.0 |
| >10 Min TIA | 2.3 |
| Weakness | 1.9 |
| Speech | 1.5 |

JAMA. 2000;284:2901-2906

# Stroke Subtype Frequency

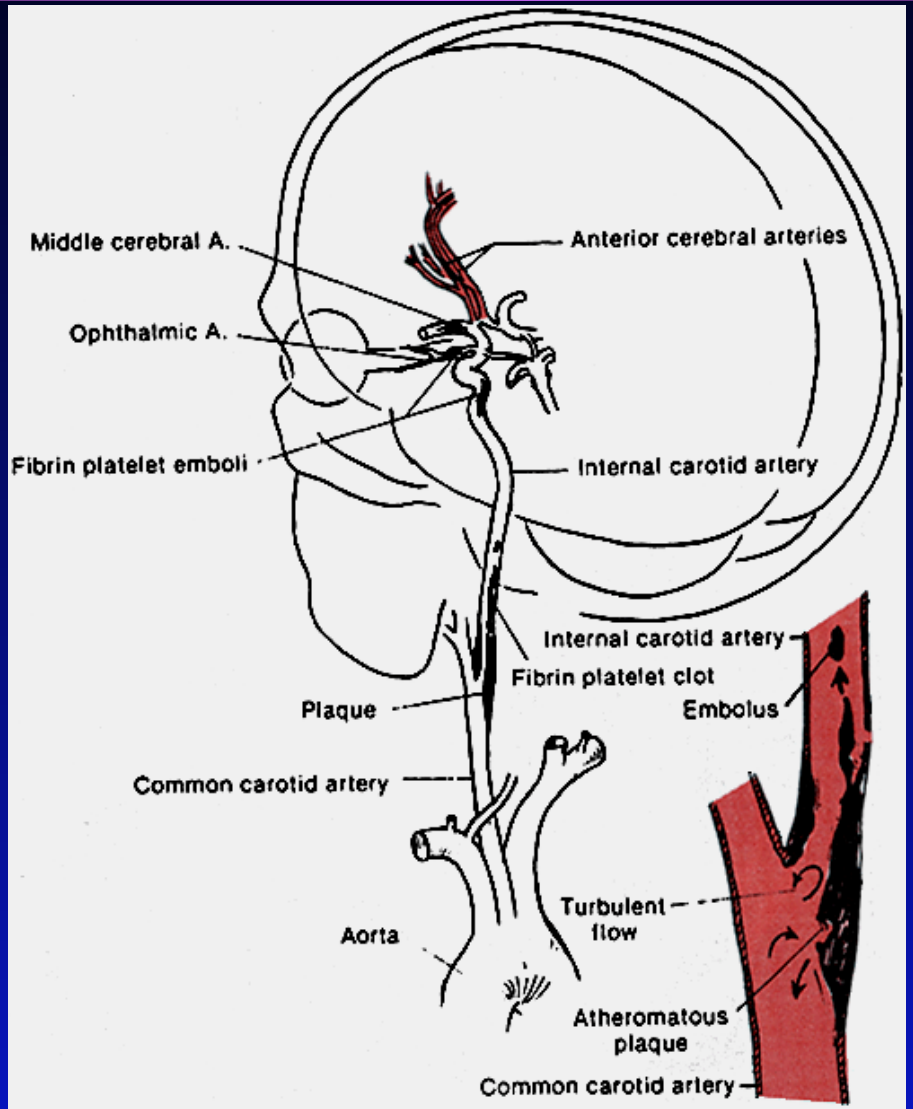
**TABLE 1.** APPROXIMATE DISTRIBUTION OF MAJOR SUBTYPES OF ISCHEMIC STROKE.*

| TYPE OF STROKE | PROPORTION OF STROKES (%) |
|---|---|
| Large-vessel atherothrombotic | 15 |
| Due to internal-carotid-artery stenosis | 9 |
| Small-vessel (lacunar) | 25 |
| Embolic | 60 |
| Due to atrial fibrillation | 15 |
| Other (due to dissection or other causes) | 3 |

*The data are from the Stroke Data Bank of the National Institute of Neurological and Communicative Disorders and Stroke[2] and the Framingham Study.[3] The percentages do not total 100 because of a modification of the categories of stroke used.

Furie KL, Kistler JP, NEJM 2000

# Artery to Artery Embolism



# Does Risk of Stroke Increase with Greater Degrees of ICA Stenosis?

- 696 Patients evaluated with Carotid Duplex Ultrasonography
- 369 Male/327 Female
  - Mean Age 64 years
- Mean Follow-Up 41 months
- Duplex Ultrasonography Categories
  - Mild <50% Stenosis
  - Moderate 50-75% Stenosis
  - Severe >75% Stenosis

Stroke 1991;22:1485

# Vascular Risk of Asymptomatic Carotid Stenosis

| Category | N | TIA | CVA | Cardiac Event | Vascular Death |
|---|---|---|---|---|---|
| <50% | 303 | 1 | 1.3 | 2.7 | 1.8 |
| 50-75% | 216 | 3 | 1.3 | 6.6 | 3.3 |
| >75% | 177 | 7.2 | 3.3 | 8.3 | 6.5 |

***75% of Events were Ipsilateral to the Stenosis***

Stroke 1991;22:1485

# The Diagnosis of Carotid Artery Disease

- Complete neurologic history and physical examination
- Complete medical history and physical examination
- Carotid Duplex Ultrasonography
- (?) Magnetic Resonance Arteriography
- (?) CT Angiography
- (?) Arteriography

# What Can the Physical Exam Tell You About the Etiology of Stroke?

| | |
|---|---|
| Atrial Fib/Flutter, Bradycardia | Likely Cardiogenic Embolus |
| No pulse below knee | Recurrent systemic embolus |
| Carotid Bruit | Severe Extracranial Carotid Stenosis |
| Head/Orbital Bruit | AV Malformation |
| Fever and Acute CVA | Endocarditis and Cardiogenic Embolus |
| Stroke and Altered MS | Check Glucose, EtOH, Narcotics, O/D, other Toxins |

# Cervical Bruit

- Marker of systemic atherosclerosis
- Not indicative of severity of internal carotid artery stenosis
  - NASCET: Sensitivity 63%/Specificity 61%
- Frequency of Cervical Bruits
  - ~1-3% in adults aged 45-54 years
  - ~8% in adults ≥75 years

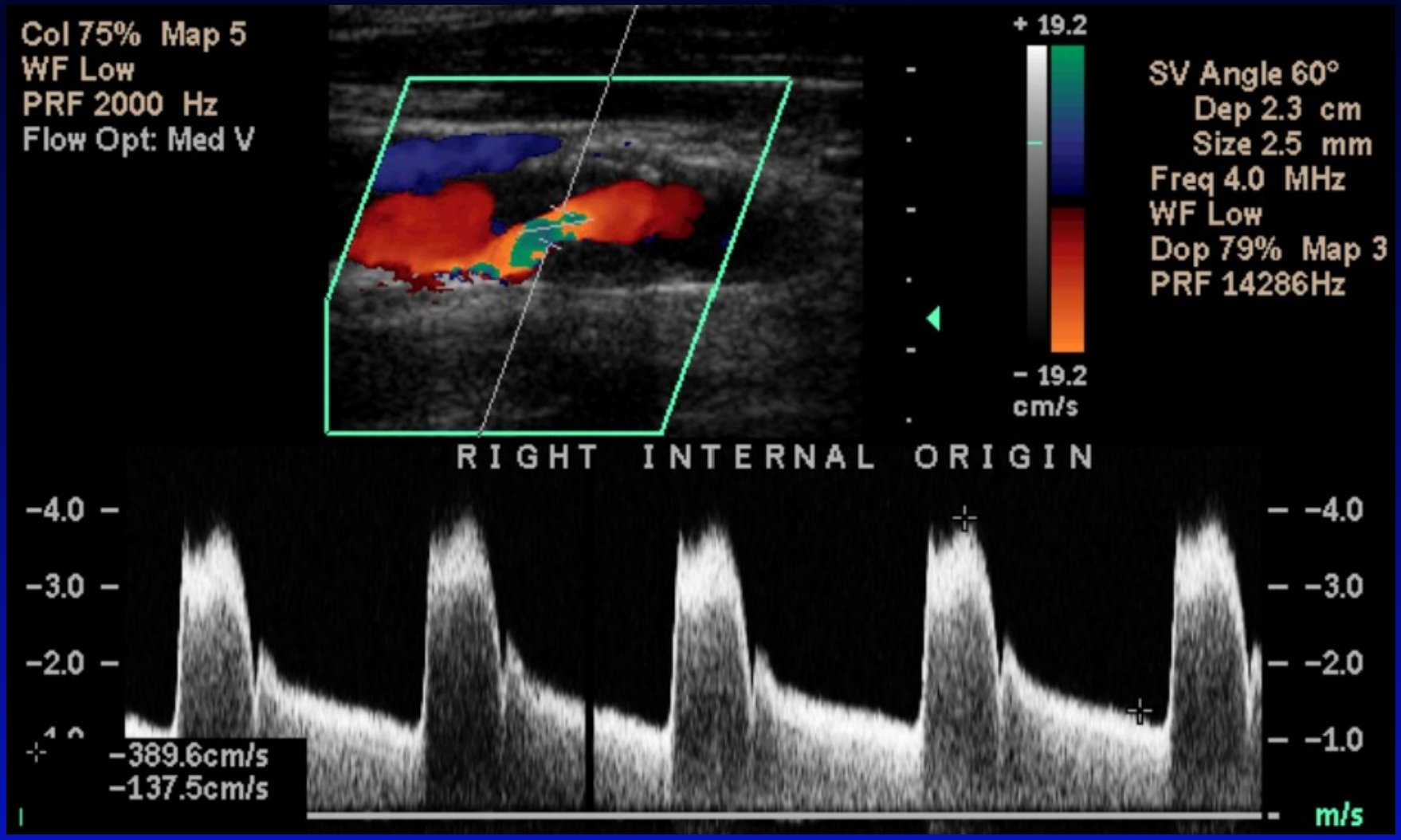
# Causes of Cervical Bruit (Systolic, Diastolic, or Both)

- Carotid atherosclerosis
- Thyrotoxicosis
- Transmitted cardiac murmur
  - Aortic Stenosis (systolic)
  - Aortic Insufficiency (diastolic)
- Arteriovenous Fistula (systolic/diastolic)
- Venous Hum (systolic or systolic/diastolic)

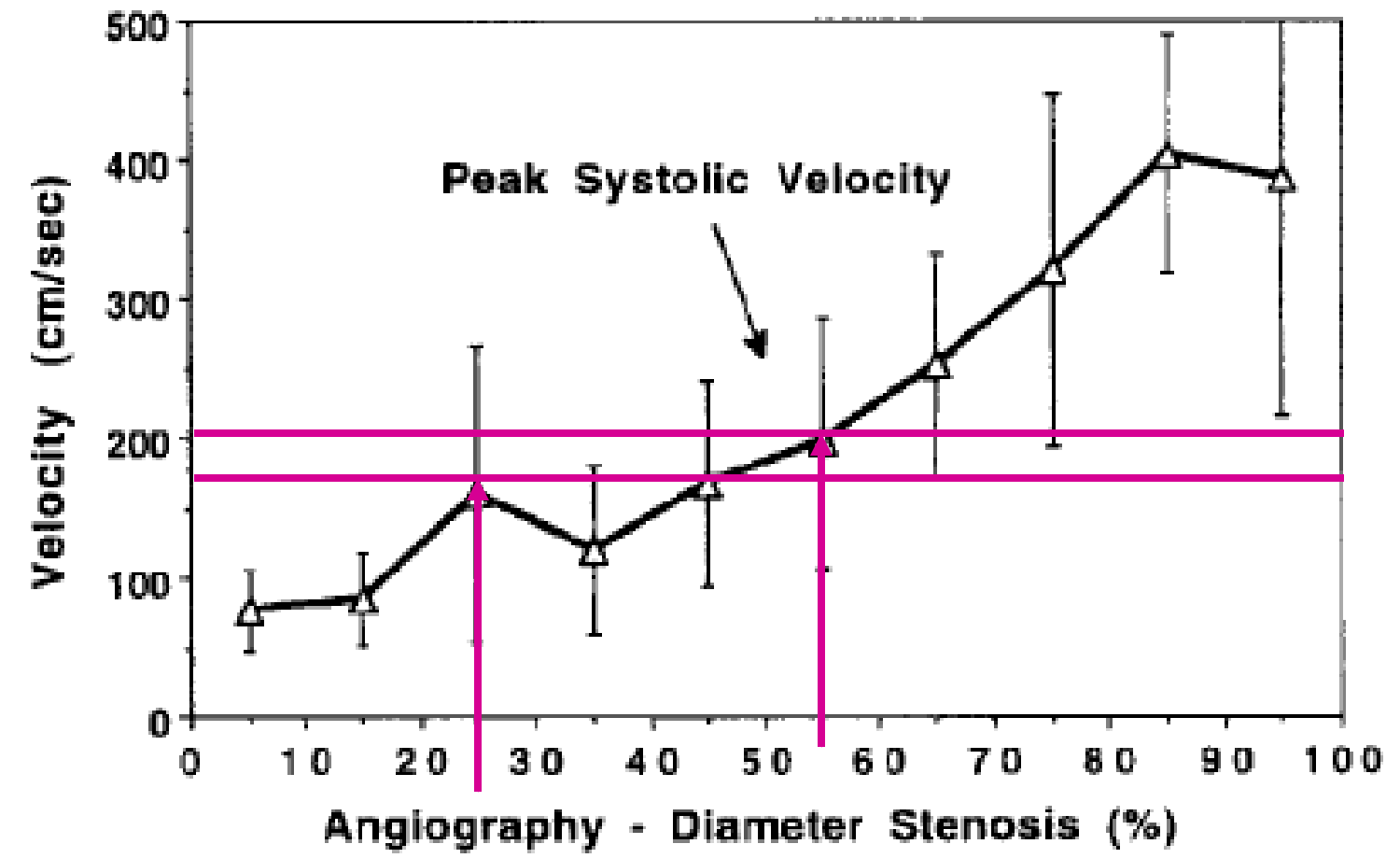
# Indications for Carotid Duplex Ultrasonography

- Cervical bruit in an asymptomatic individual
- Amaurosis Fugax
- Transient Ischemic Attack
- Stroke in a potential candidate for CE or stent
- Follow-up of known stenosis (>20%) in asymptomatic individuals
- Follow-up after carotid endarterectomy or stent
- Intraoperative assessment of carotid endarterectomy
- Drop attacks (rare)

# 80-99% Internal Carotid Artery Stenosis

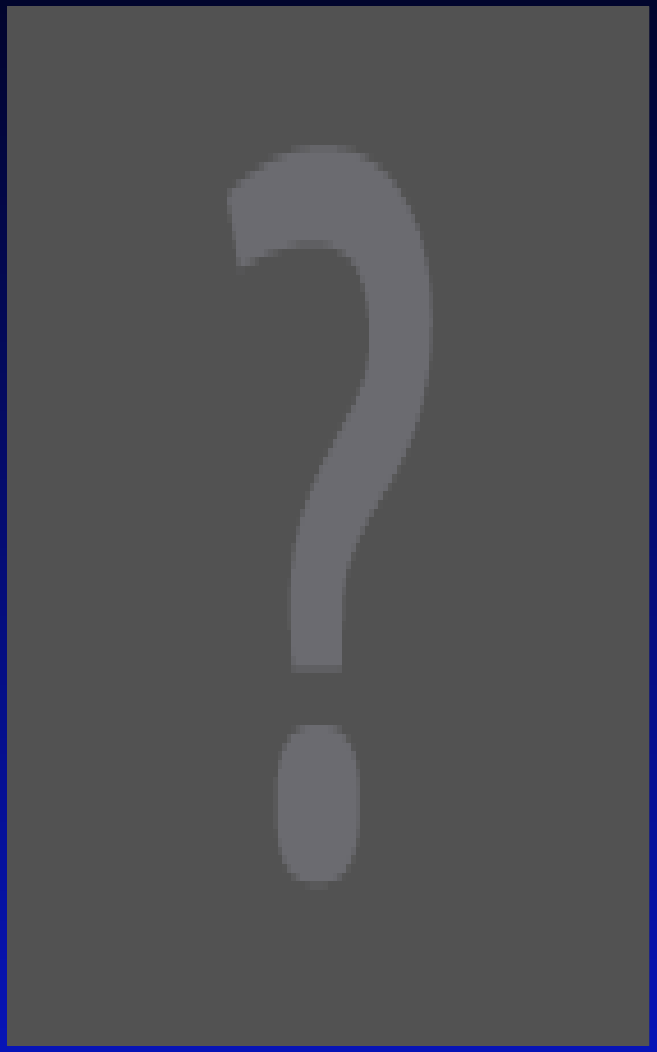


# What is the Relationship Between PSV and Carotid Stenosis?




Radiology 2000;214:247-252

# Carotid MRA



# Carotid Duplex Ultrasonography Ipsilateral to Bruit

# CT Angiogram

# What is the Best Imaging Strategy in Carotid Artery Disease?

- Meta analysis of studies published between 1980-2004
- 41 studies
- 2541 patients/4876 arteries

Lancet 2006;367:1503-12

# Optimal Imaging for Carotid Stenosis

| | DUS | CTA | MRA | CEMRA |
|---|---|---|---|---|
| **70–99% stenosis** | | | | |
| Sensitivity (95% CI) | 0·89 (0·85–0·92 | 0·77 (0·68–0·84) | 0·88 (0·82–0·92) | 0·94 (0·88–0·97) |
| Specificity (95% CI) | 0·84 (0·77–0·89) | 0·95 (0·91–0·97) | 0·84 (0·76–0·97) | 0·93 (0·89–0·96) |
| **50–69% stenosis** | | | | |
| Sensitivity (95% CI) | 0·36 (0·25–0·49) | 0·67 (0·30–0·90) | 0·37 (0·26–0·49) | 0·77 (0·59–0·89) |
| Specificity (95% CI) | 0·91 (0·87–0·94) | 0·79 (0·63–0·89) | 0·91 (0·78–0·97) | 0·97 (0·93–0·99) |
| **0–49% stenosis or 100% occluded** | | | | |
| Sensitivity (95% CI) | 0·83 (0·73–0·90) | 0·81 (0·59–0·93) | 0·81 (0·70–0·88) | 0·96 (0·90–0·99) |
| Specificity (95% CI) | 0·84 (0·62–0·95) | 0·91 (0·74–0·98) | 0·88 (0·76–0·95) | 0·96 (0·90–0·99) |

Lancet 2006;367:1503-12

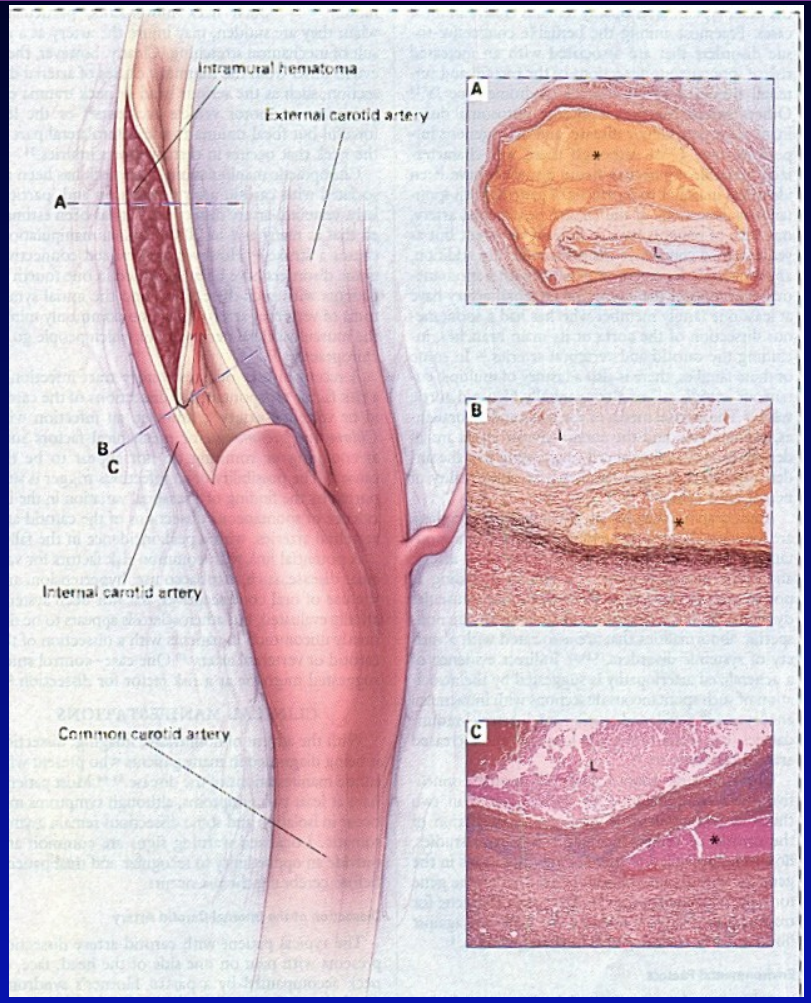
# What is the Best Imaging Strategy in Carotid Artery Disease?

- Meta analysis of studies published between 1980-2004
- 41 studies
- 2541 patients/4876 arteries
- In analyzing 70-99% stenosis, CE MRA had the greatest sensitivity/specificity

Lancet 2006;367:1503-12

# What Does This Arteriogram Reveal?

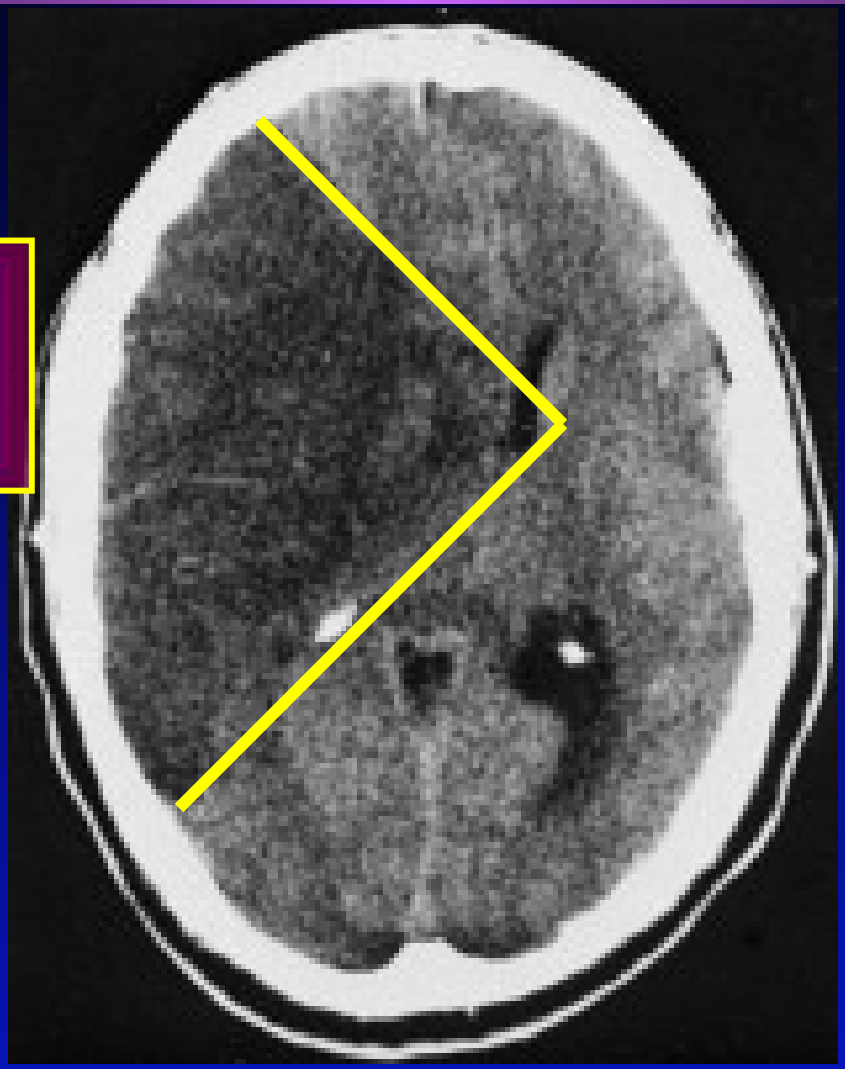
# Spontaneous Carotid Dissection




N Engl J Med 2001;344:898-906

# Once in an ED, You Must Get an Imaging Test IMMEDIATELY!

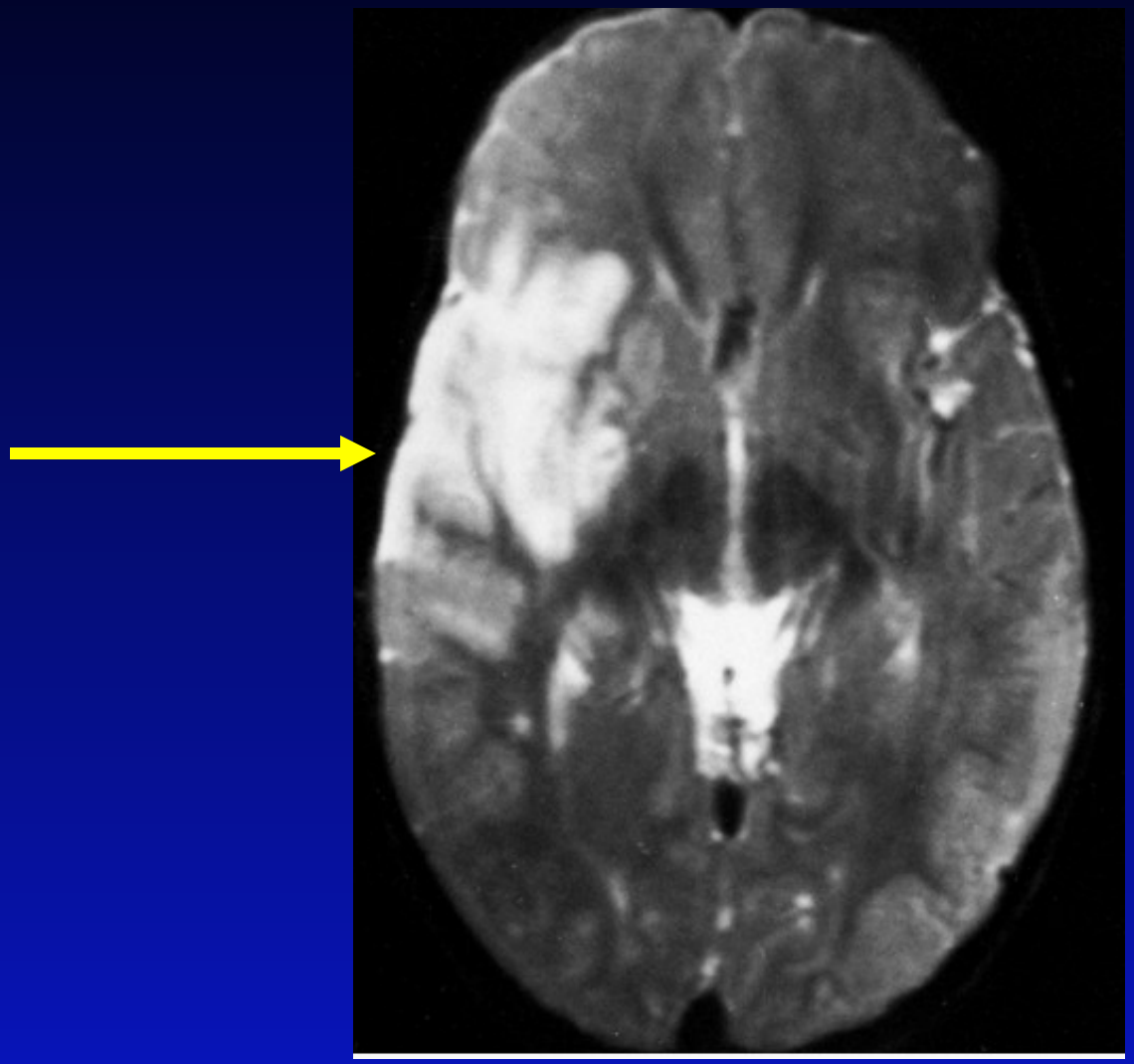
Classic Wedge-Shaped Acute Right MCA Stroke



# Important Characteristics of the CT Scan

- Within 3 hours of onset of ischemia, the CT *without contrast* is virtually normal
- After 6-12 hours, there is evidence of hypodensity with brain edema
- Hemorrhage
  - Appearance will describe type
    - Subdural Hematoma: Crescent shape below dura
    - Subarachnoid Hemorrhage: Diffuse blood pattern along surface of brain in subarachnoid space
      - 5% of SAH have NORMAL CT!!! MUST perform Lumbar Puncture
      - Discern between SAH and traumatic LP
      - RBC Count in 4 tubes all similar
      - Xanthochromic Supernatant---old RBCs consistent with SAH

# MRI Demonstrating Acute Right MCA CVA



# National Institutes of Health Stroke Scale (NIHSS)

- Systematic clinical assessment tool
- Designed in 1983 to standardize and document a reliable, valid neuro assessment
- Measures neurologic deficits
  - Does not assess function
- 5-8 minutes to complete
- Scores range from 0-42
- 11 items tested

http://www.ninds.nih.gov/doctors/stroke_scale_training.htm

# What if Patient Has Altered Mental Status?

## Glasgow Coma Scale

- Eye Opening
  - Spontaneous…4
  - In response to speech…3
  - In response to pain…2
  - None…1
- Best Verbal Response
  - Oriented…5
  - Confused…4
  - Inappropriate Words…3
  - Incomprehensible…2
  - None…1
- Best Motor Response
  - Obeys…6
  - Localizes…5
  - Withdraws…4
  - Abnormal Flexion…3
  - Abnormal Extension…2
  - None…1

# Glascow Coma Scale

| | |
|---|---|
| *Eyes open* | |
| Never | 1 |
| To pain | 2 |
| To verbal stimuli | 3 |
| Spontaneously | 4 |
| *Best verbal response* | |
| No response | 1 |
| Incomprehensible sounds | 2 |
| Inappropriate words | 3 |
| Disoriented and converses | 4 |
| Oriented and converses | 5 |
| *Best motor response* | |
| No response | 1 |
| Extension (decerebrate rigidity) | 2 |
| Flexion abnormal (decorticate rigidity) | 3 |
| Flexion withdrawal | 4 |
| Localizes pain | 5 |
| Obeys | 6 |
| Total | 3–15 |

# Stroke Prevention Strategies

- Reduction in Blood Pressure
- Cessation of Tobacco Use
- Reduction in Serum Cholesterol
- Aggressive Glycemic Control
- Antiplatelet Therapy
- Revascularization of Carotid Stenosis

# Risk of CVA Among Women Who Smoke and Have Partners Who Smoke

## 5379 Women Who Smoke Followed for 8.5 Years

| Participants | Sample Size | No. of Events | Event Rate/100 | Age-Adjusted RR (95% CI) | Multivariate-Adjusted RR (95% CI) | *P* |
|---|---|---|---|---|---|---|
| Cardiovascular diseases | | | | | | |
| Cigarette-smoking women with nonsmoking spouse | 443 | 28 | 6.3 | Reference | Reference | Reference |
| Cigarette-smoking women with cigarette-smoking spouse | 1904 | 174 | 9.1 | 1.4 (0.95–2.1) | 1.4 (0.9–2.0) | 0.1 |
| All strokes | | | | | | |
| Cigarette-smoking women with nonsmoking spouse | 443 | 2 | 0.5 | Reference | Reference | Reference |
| Cigarette-smoking women with cigarette-smoking spouse | 1904 | 49 | 2.6 | 5.7 (1.4–24) | 5.7 (1.4–24) | 0.02 |
| Ischemic stroke | | | | | | |
| Cigarette-smoking women with nonsmoking spouse | 443 | 2 | 0.5 | Reference | Reference | Reference |
| Cigarette-smoking women with cigarette-smoking spouse | 1904 | 43 | 2.3 | 5.1 (1.2–21) | 4.8 (1.2–20) | 0.03 |

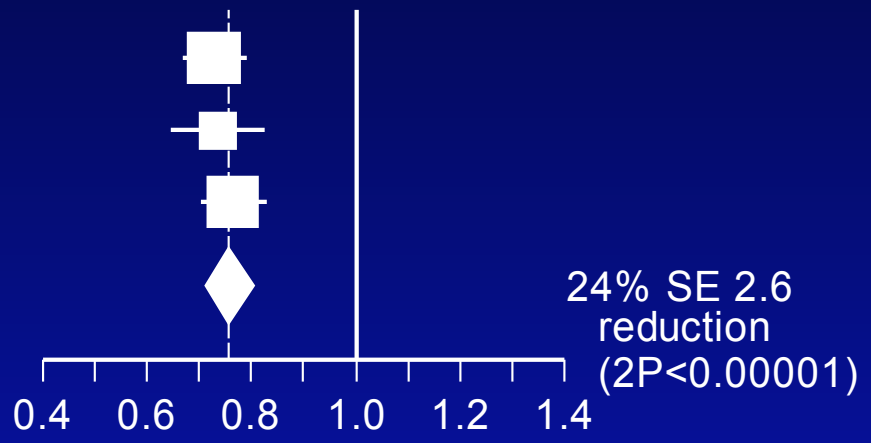
Stroke 2005;36:e74-e76

# Statins Decrease the Risk of Stroke in High Risk Patients:

***Heart Protection Study***

## SIMVASTATIN: MAJOR VASCULAR EVENTS

| Vascular event | STATIN (10269) | PLACEBO (10267) |
|---|---|---|
| Total CHD | 914 | 1234 |
| Total stroke | 456 | 613 |
| Revascularisation | 926 | 1185 |
| ANY OF ABOVE | 2042 (19.9%) | 2606 (25.4%) |




**50% reduction in CEA or angioplasty**
(simvastatin 42 [0·4%] *vs* placebo 82 [0·8%]; P=0·0003)

MRC/BHF HPS Investigators Lancet 2002; 360 (9326): 7

# The Ultimate Lipid Trial in Stroke: SPARCL

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 10, 2006 VOL. 355 NO. 6

## High-Dose Atorvastatin after Stroke or Transient Ischemic Attack

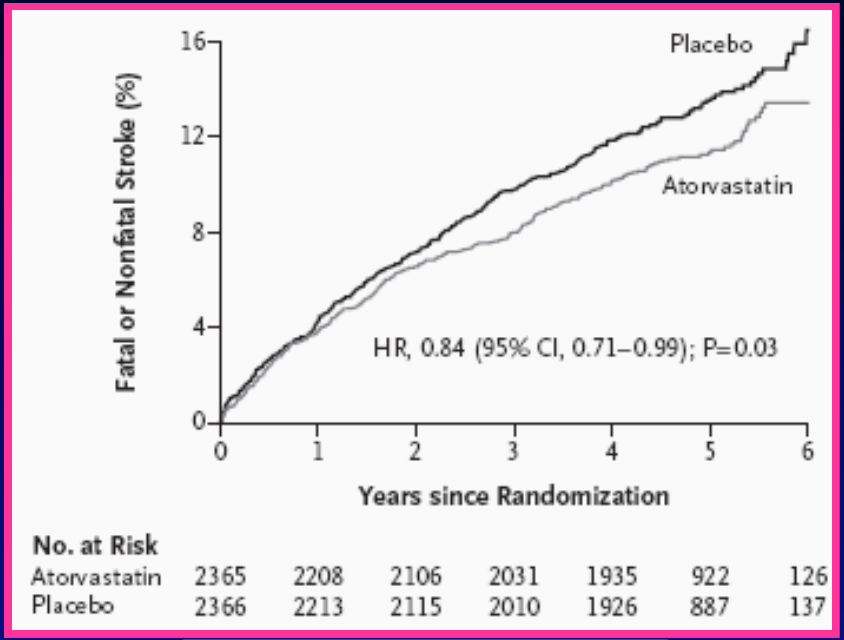
The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators*

# SPARCL

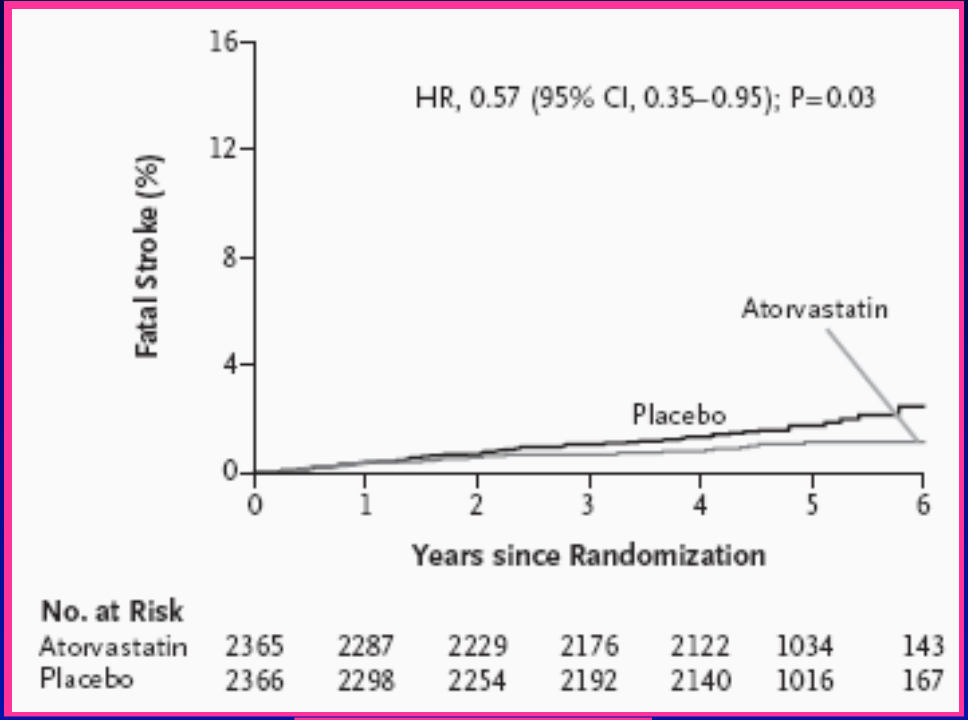
- 4731 patients with recent CVA/TIA (1-6 months before randomization)
- NO KNOWN CAD
- LDL-C 100-190 mg/dL
- Randomized to Placebo vs Atorvastatin 80 mg/d
- Primary Endpoint:
  **First non-fatal or fatal stroke**

N Engl J Med 2006;355:549-559

# SPARCL



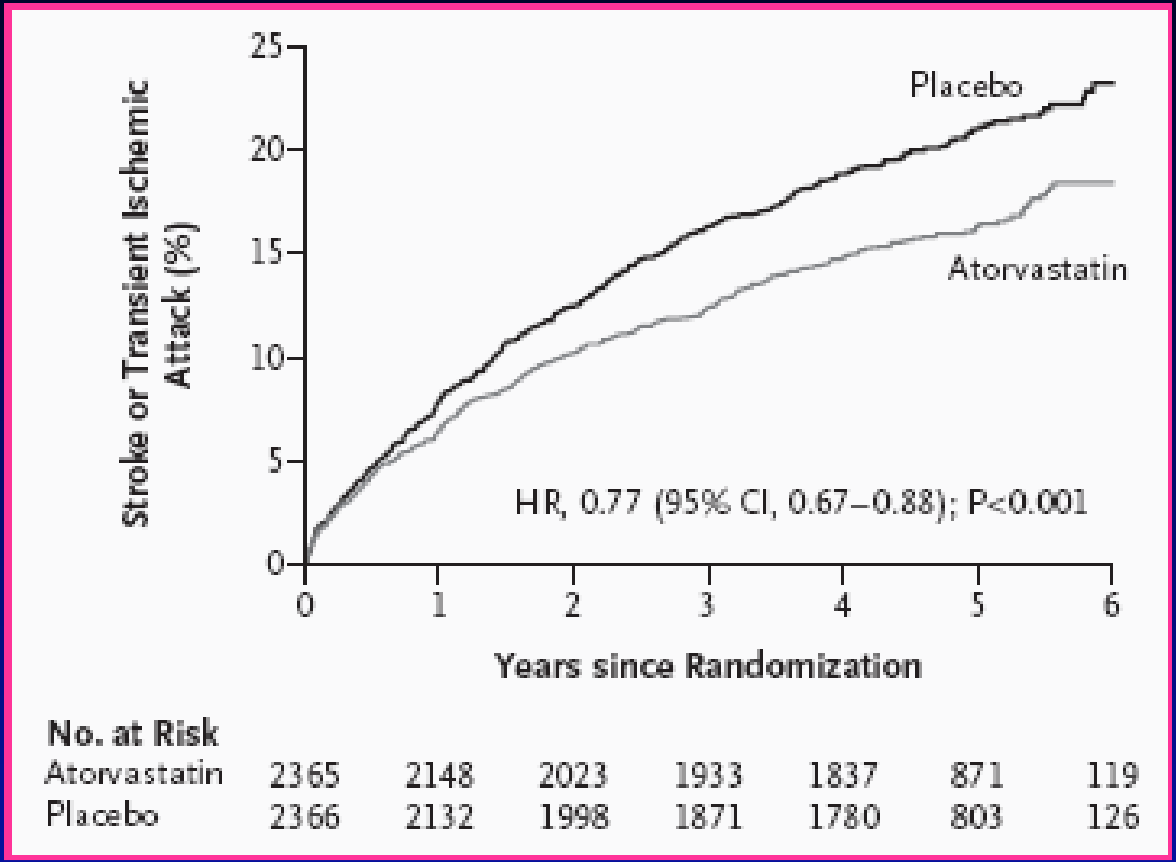

Primary Endpont




Fatal Stroke

N Engl J Med 2006;355:549-559

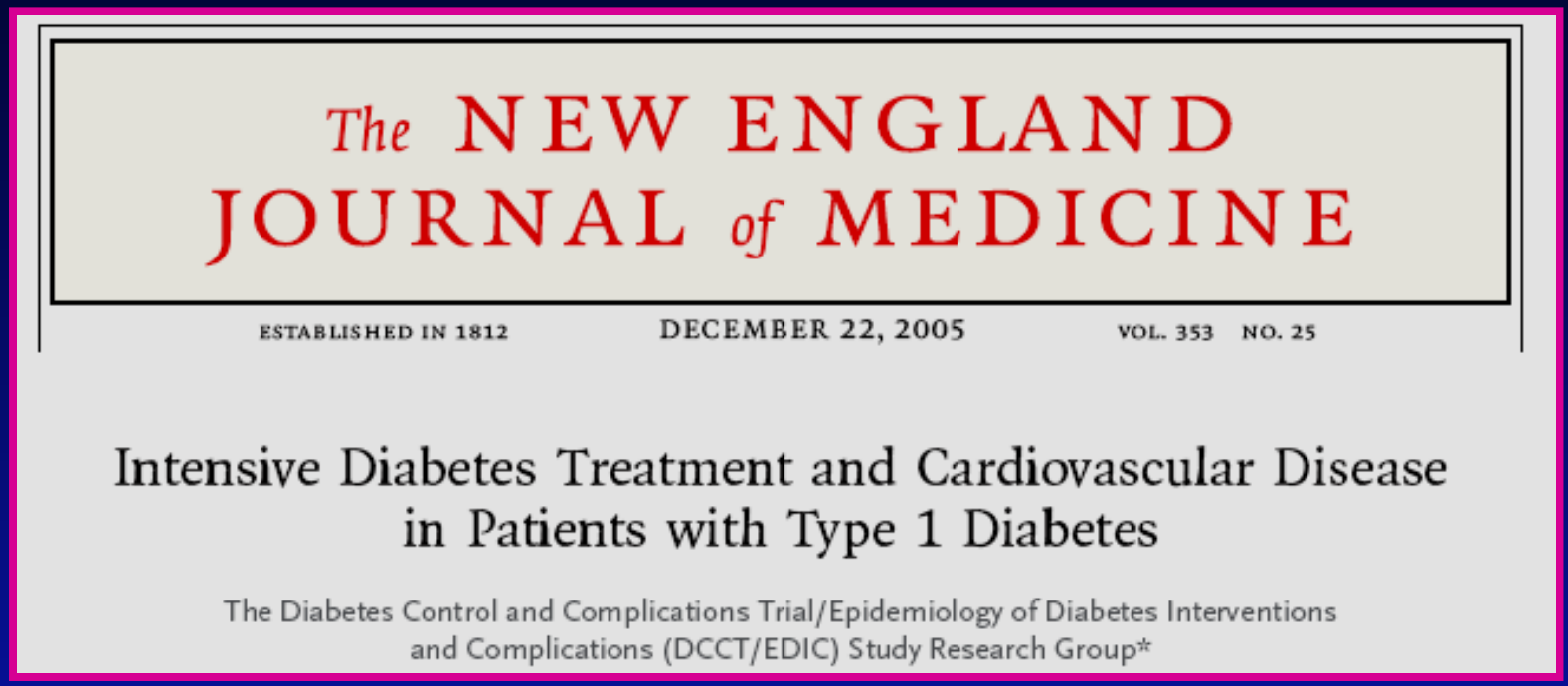
# SPARCL




Stroke or TIA

N Engl J Med 2006;355:549-559

# The Most Important Publication in Diabetes Research in Our Time



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 22, 2005 VOL. 353 NO. 25

## Intensive Diabetes Treatment and Cardiovascular Disease in Patients with Type 1 Diabetes

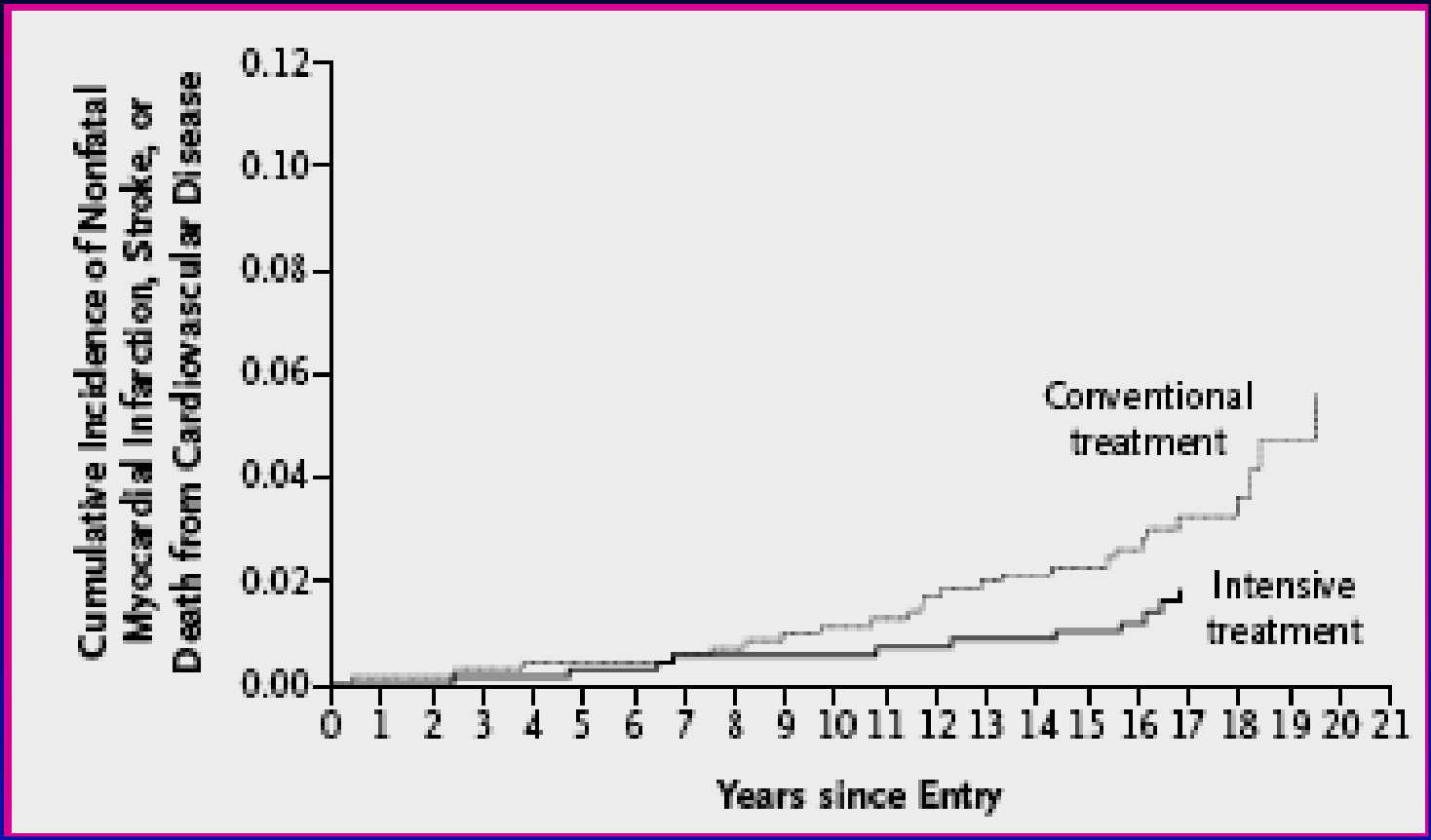
The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group*

# Diabetes Control and CV Events

- The DCCT (**D**iabetes **C**ontrol and **C**omplications **T**rial)
  - 1441 patients with Type 1 DM (1983-1993)
  - Randomized to conventional vs intensive glycemic control
  - Treated for mean of 6.5 years
  - 93% followed until February 2005
- CV Disease defined as: Non-Fatal MI, CVA, Death due to CV Disease, Angina, Need for CABG/PCI)

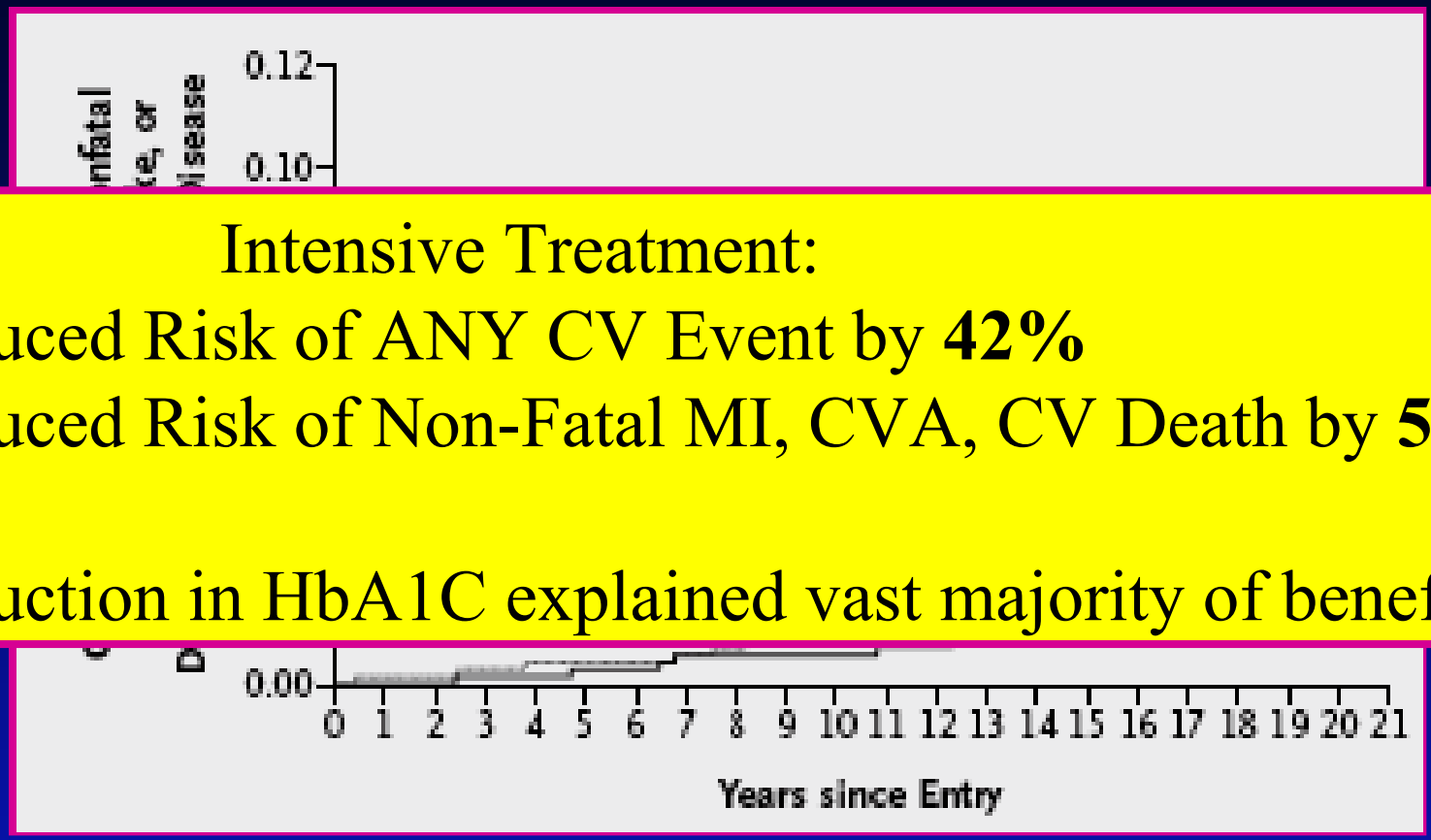
N Engl J Med 2005;353:2643-53.

# Cumulative Incidence of Non-Fatal MI, CVA, CV Death




N Engl J Med 2005;353:2643-53.

# Cumulative Incidence of Non-Fatal MI, CVA, CV Death




Intensive Treatment:

- Reduced Risk of ANY CV Event by **42%**
- Reduced Risk of Non-Fatal MI, CVA, CV Death by **57%**

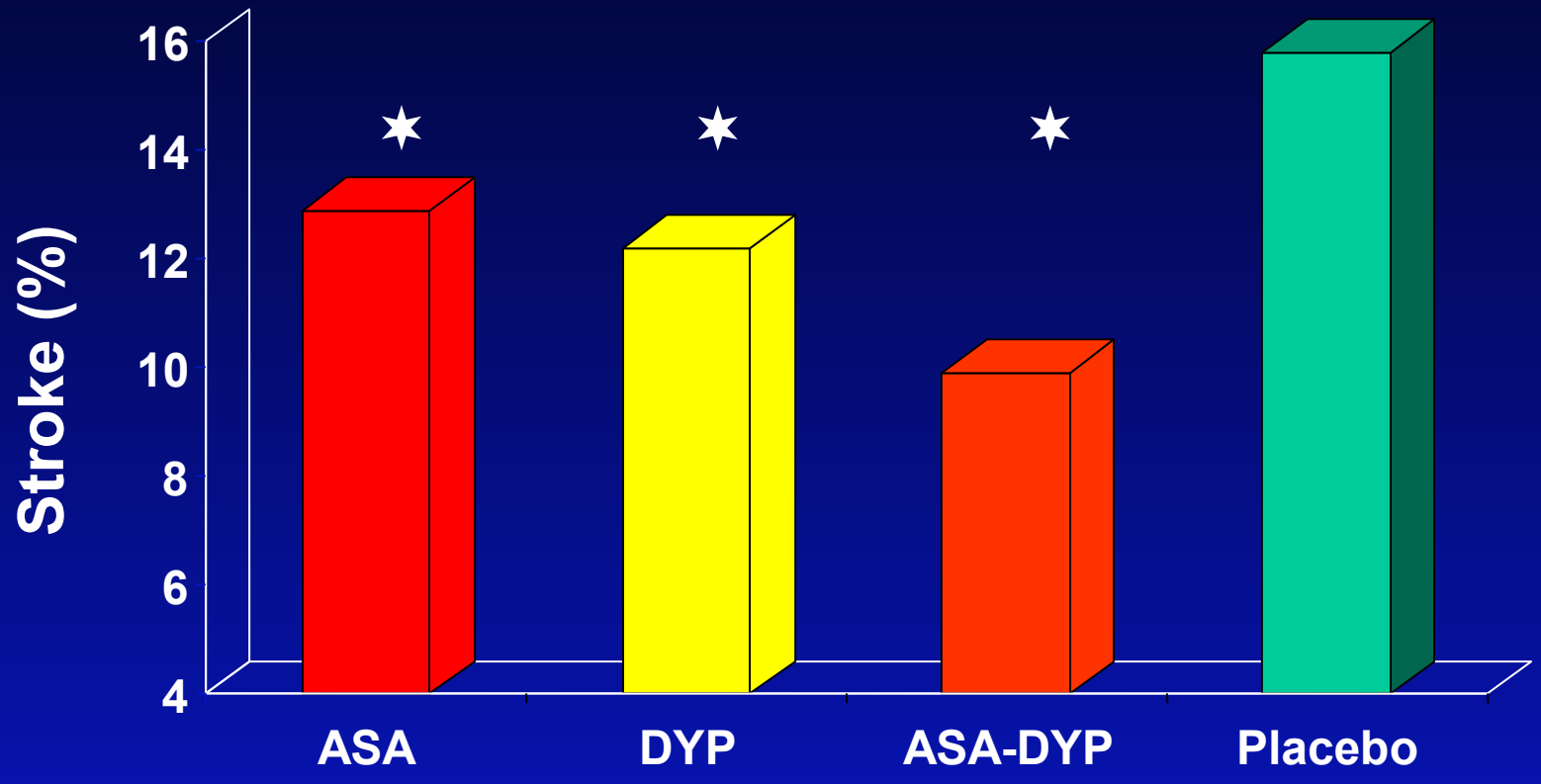
- Reduction in HbA1C explained vast majority of benefit

N Engl J Med 2005;353:2643-53.

# Aspirin & Dypyridamole Decreases Stroke after TIA

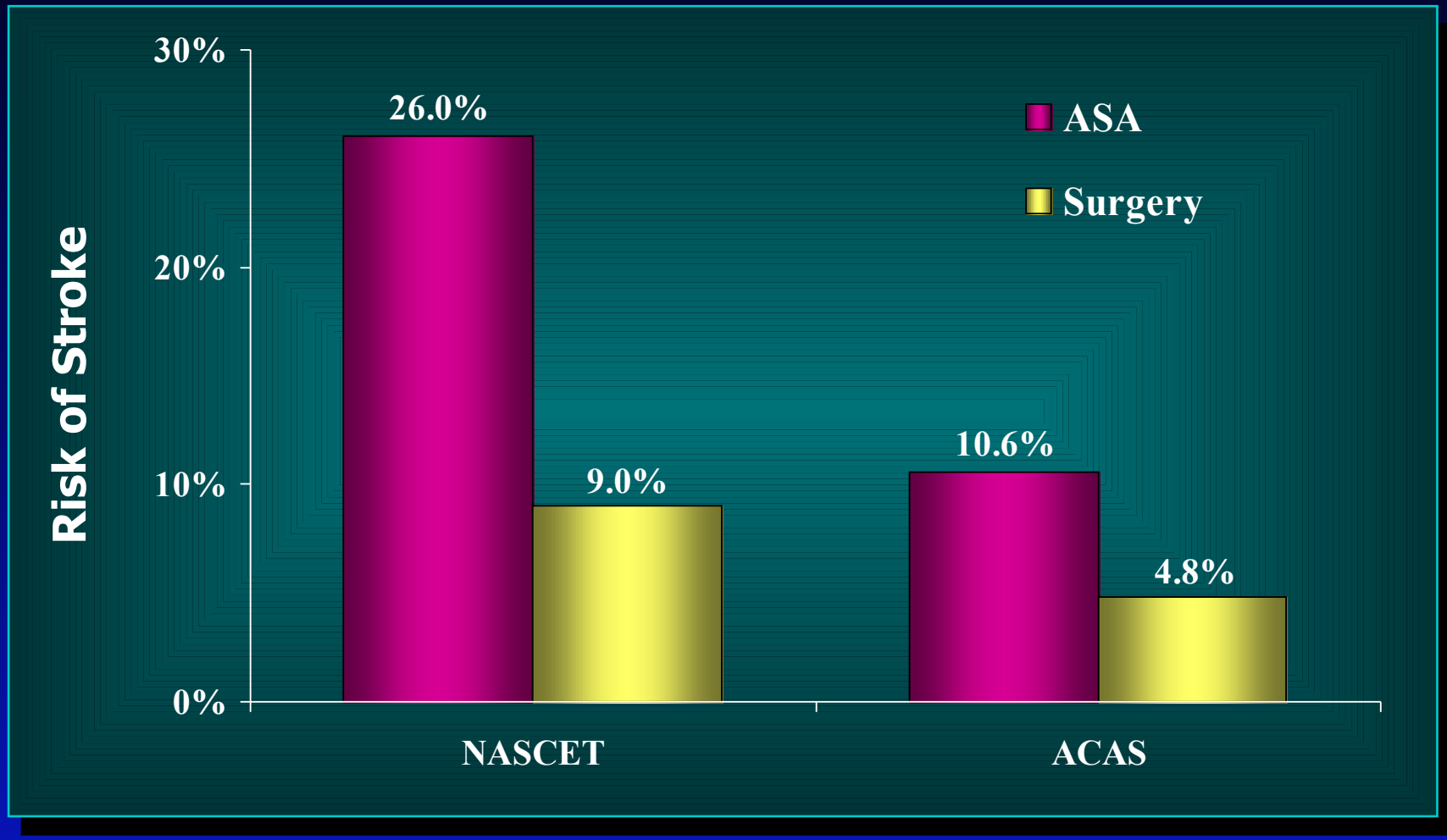
*European Stroke Prevention Study*

**6602 pts with recent TIA or CVA followed for 2 years**




*J Neurol Sci 1996; 143(1-2):1*

# Surgery for Carotid Stenosis



# Early vs Deferred Carotid Endarterectomy in Asymptomatic Patients with >70% ICA Stenosis

- Risk of CVA/Death within 30 days of CEA
  - 3.1%
- 5-year CVA risk
  - 3.8% immediate CEA
  - 11% deferred CEA ($p<0.0001$)
    - Half of all CVAs were disabling
- Combining peri-op and non-peri-op CVA
  - 5-year CVA risk
    - 6.4% vs 11.8% ($p<0.0001$)

ACST Investigators. Lancet 2004;363:1491-1502

# Carotid Endarterectomy

- **Complications**
  - Wound Complications
    - Hematoma 0.7-1.5%
    - Infection/Pseudoaneurysm 0.15%
    - Cranial Nerve Dysfunction
      - Hypoglossal Nerve 5-8%
      - All other Cranial Nerves <2%
    - Perioperative Stroke
      - Cleveland Clinic
        - 1.5% Asymptomatic
        - 2.7% Prior TIA
        - 3.8% Prior CVA

# Carotid Artery Stenting

**Decision Memo for Carotid Artery Stenting (CAG-00085R)**

## Decision Summary

The Centers for Medicare and Medicaid Services (CMS) has determined that the evidence is adequate to conclude that carotid artery stenting (CAS) with embolic protection is reasonable and necessary for the following:

1. Patients who are at high risk for carotid endarterectomy (CEA) and who also have symptomatic carotid artery stenosis ≥ 70%. Coverage is limited to procedures performed using FDA approved carotid artery stenting systems and embolic protection devices;
2. Patients who are at high risk for CEA and have symptomatic carotid artery stenosis between 50% and 70%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the National Coverage Determination on CAS post approval studies (Medicare NCD Manual 20.7);
3. Patients who are at high risk for CEA and have asymptomatic carotid artery stenosis ≥ 80%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the National Coverage Determination on CAS post approval studies (Medicare NCD Manual 20.7).


Who Will Be Covered?

- Patients at **high risk for CEA** with a SYMPTOMATIC carotid artery stenosis ≥70%
- Patients at **high risk for CEA** with a SYMPTOMATIC carotid artery stenosis between 50% and 70% AND are enrolled in a Category B IDE Clinical Trial
- Patients at **high risk for CEA** with an ASYMPTOMATIC carotid artery stenosis ≥80% AND are enrolled in a Category B IDE Clinical Trial

# What is “High Risk”?

- **Serious Co-Morbid Medical Condition**
  - -Congestive heart failure (class III/IV) and/or known severe left ventricular dysfunction LVEF <30%
  - -Open heart surgery needed within six weeks
  - -Recent MI (>24 hrs. and <4 weeks)
  - -Unstable angina (CCS class III/IV)
  - -Severe pulmonary disease

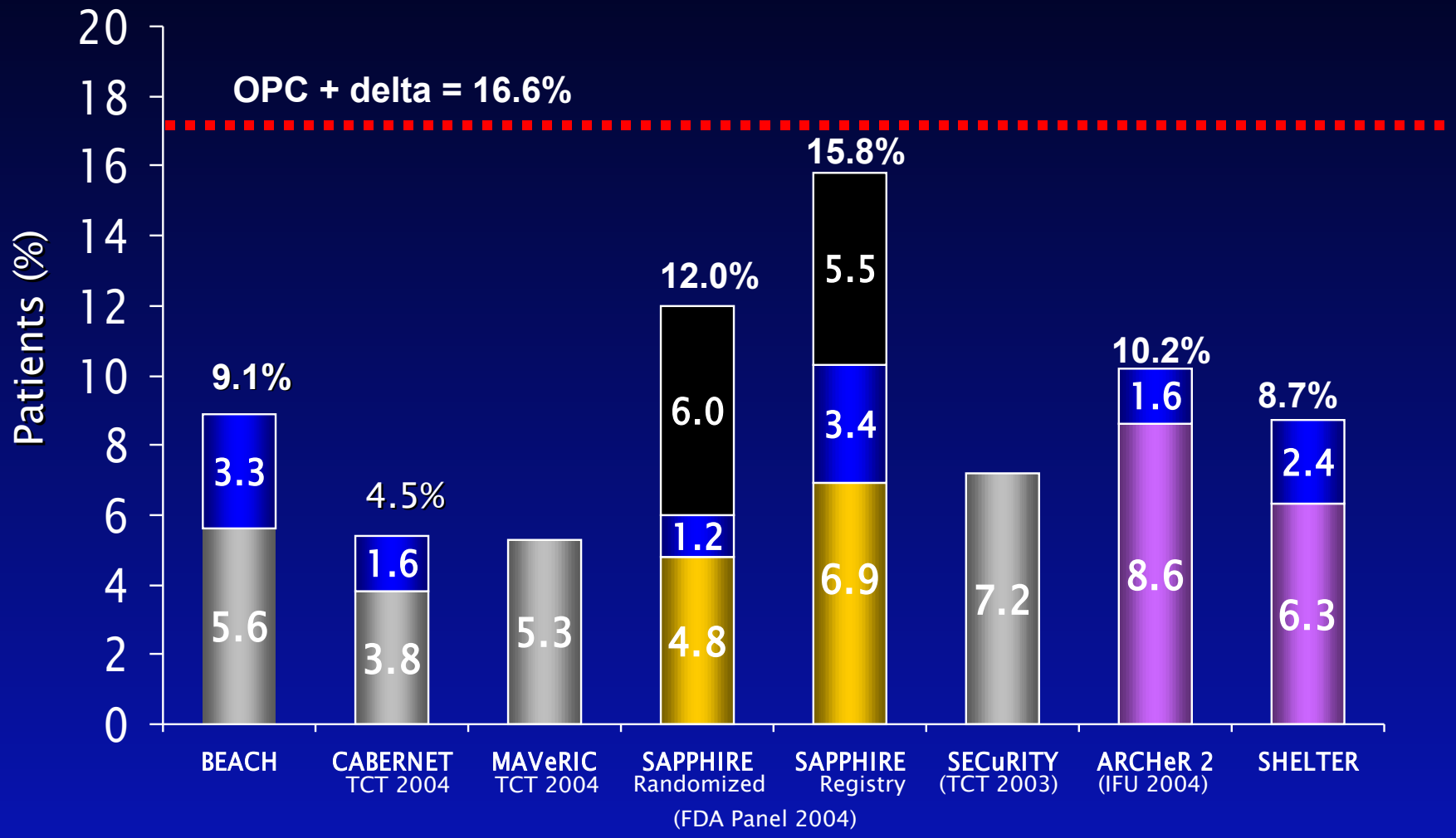
- **Anatomic Challenges**
  - -Contralateral carotid occlusion
  - -Contralateral laryngeal nerve palsy
  - -Radiation therapy to neck
  - - Previous CEA with recurrent stenosis
  - - High cervical ICA lesions or CCA
    lesions below the clavicle
  - - Severe tandem lesions
  - - Age > 80 years

# SAPPHIRE Data

| Event | Intention-to-Treat Analysis | | | Actual-Treatment Analysis | | |
|---|---|---|---|---|---|---|
| | Stenting (N=167) | Endarterectomy (N=167) | P Value | Stenting (N=159) | Endarterectomy (N=151) | P Value |
| | *no. (%)* | | | *no. (%)* | | |
| 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 |

N Engl J Med 2004;351:1493-501.

# 1 Year Composite MAE Endpoint
## Carotid Stenting Trials



# Carotid Revascularization Endarterectomy vs. Stenting Trial

CREST
Carotid Revascularization Endarterectomy vs. Stenting Trial

## Recruitment Goals

- 113 sites in U.S., plus 10 in Canada

- 2500 randomized subjects
  - 1400 symptomatic, 1100 asymptomatic

  - 40% women
  - 12% minorities

- Monitored & reported by:
  - Overall
  - By site
  - By Sex & minority


Gulf of Alaska
ALAS.
Hudson Bay
Labrador Sea
NFLD. AND LAB.
CANADA
BRITISH COLUMBIA
ALBERTA
SASKATCHEWAN
MANITOBA
QUÉBEC
ONTARIO
N.B.
ME.
WASHINGTON
N. DAK.
MONTANA
Montréal
Ottawa
MINNESOTA
Lake Huron
OREGON
IDAHO
SOUTH DAKOTA
WYOMING
New territory
N.Y.
NEBR.
PA.
New York
Philadelphia
Chicago
Washington, D.C.
Pacific Ocean
NEVADA
UTAH
UNITED STATES
VA.
Atlantic Ocean
COLO.
KANSAS
KY.
MO.
CALIFORNIA
Los Angeles
San Diego
ARIZONA
Phoenix
NEW MEXICO
OKLA.
ARKANSAS
S.C.
Dallas
MISS.
ALABAMA
G A.
TEXAS
San Antonio
Houston
Gulf of Mexico
Nassau
THE BAHAMAS
MEXICO
Monterrey
Havana
CUBA
RANDOMIZING SITES N = 104
WORK-UP SITES N= 10
LEAD-IN SITES N= 10

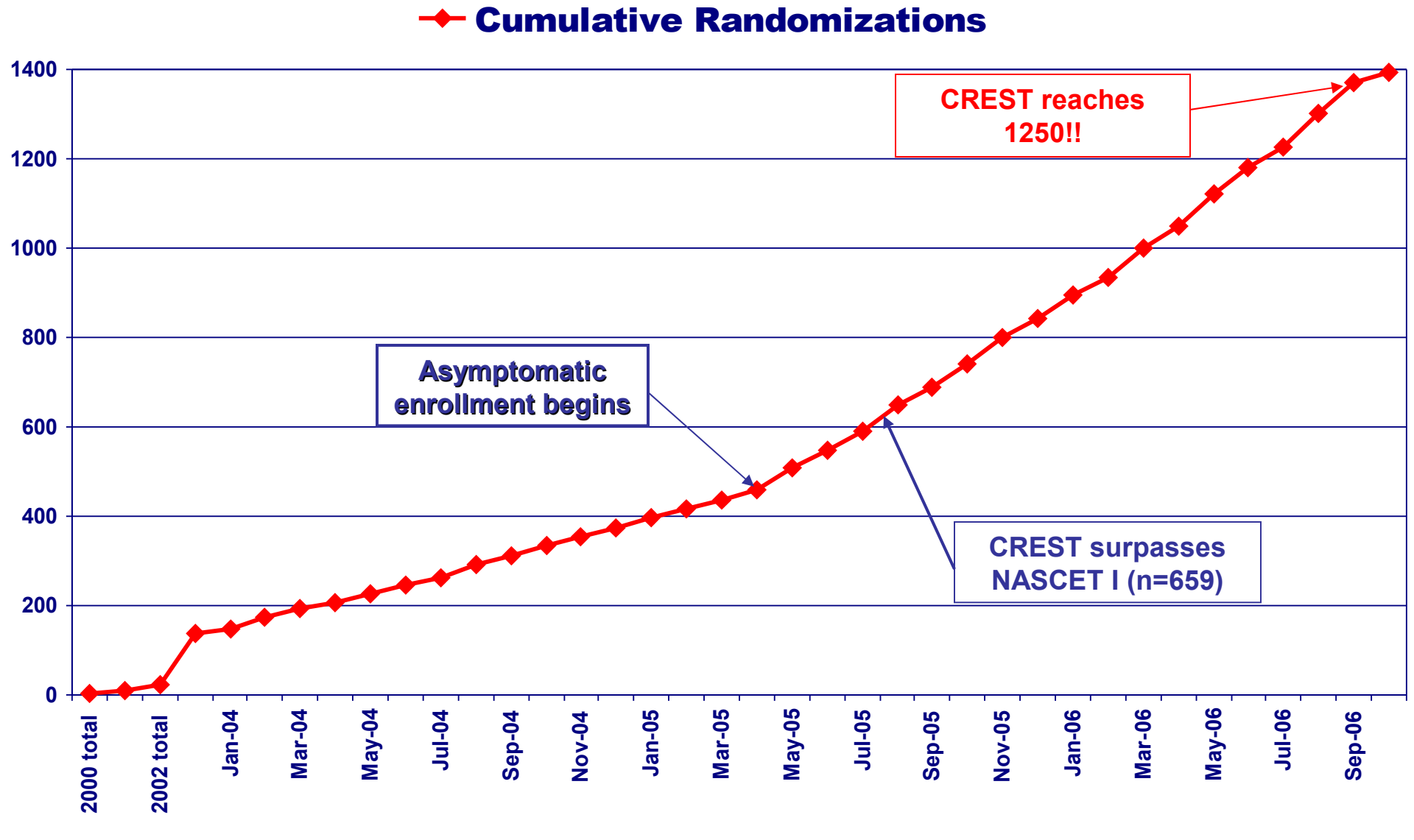
# Carotid Revascularization Endarterectomy vs. Stenting Trial

CREST
Carotid Revascularization Endarterectomy vs. Stenting Trial

## Recruitment in CREST

- Goal - 2500
- Total number of randomized subjects (10/12/06) - 1393
  - Symptomatic – 841
  - Asymptomatic – 552

# Carotid Revascularization Endarterectomy vs. Stenting Trial



# Who Benefits from Carotid Therapy Today?

- Symptomatic patients with >70% ipsilateral carotid artery stenosis deserve revascularization
  - High Risk for CEA: Candidate for CAS
- The jury (CMS) remains out on ANYONE else
- Symptomatic patients with 50-69% ipsilateral carotid artery stenosis
  - Candidates for CEA (CAS if high risk and in trial)
- Asymptomatic patients with >60% carotid stenosis
  - ??? CEA
  - Trial to evaluate CAS
  - Optimize medical therapy?
  - Enroll in TACIT?
- EVERYONE gets optimal
  - Antiplatelet Therapy
  - Antihypertensive Therapy
  - Lipid Lowering Therapy
  - Strategies to Stop Smoking
  - Tight Glycemic Control