Treatment of Asymptomatic Carotid Disease – What is the Current Data?

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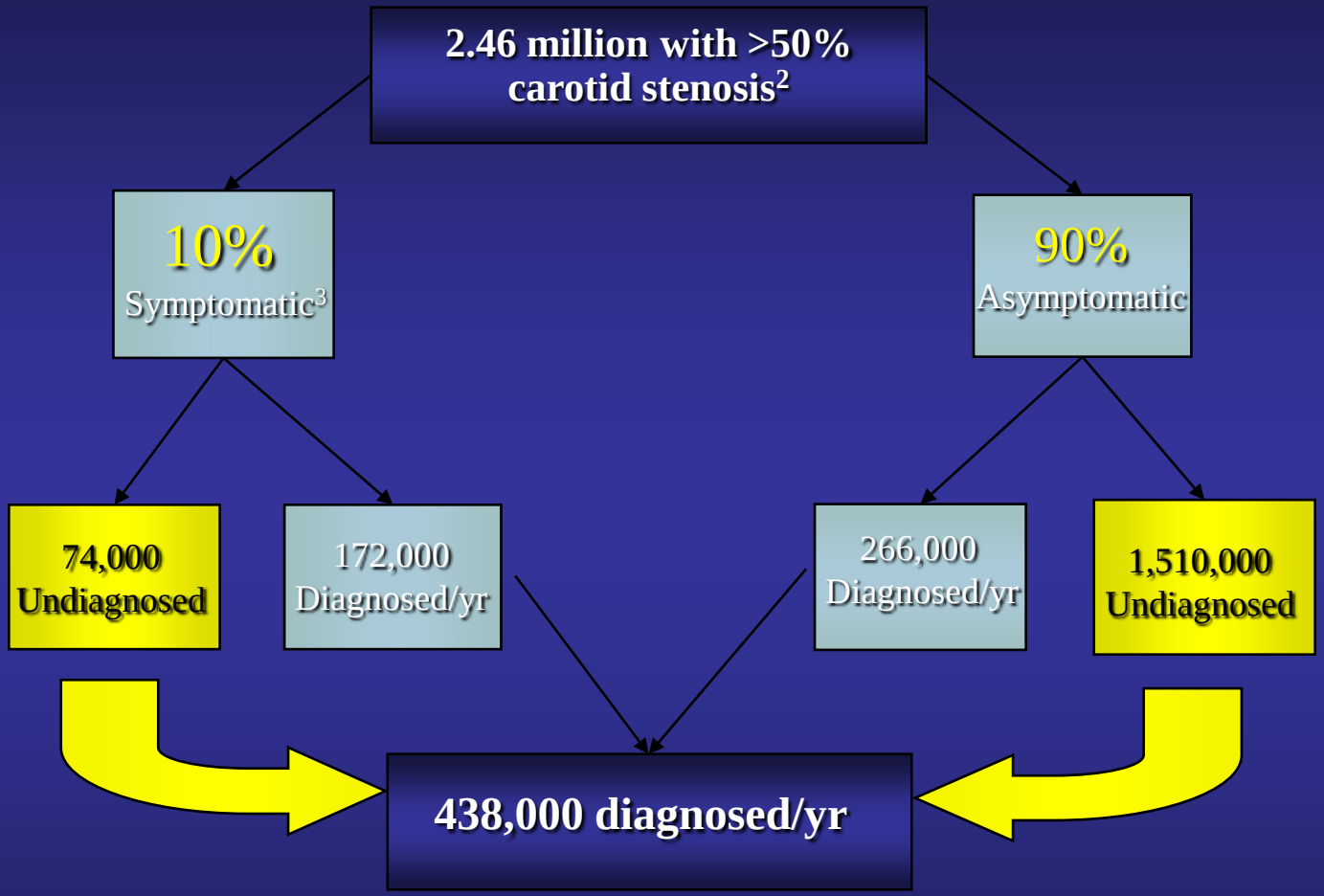
Disclosure

Education & Consulting but NO Compensation:

Abbott Vascular
Medtronic
Spectranetics
MEDRAD

Carotid Disease Epidemiology (United States)



1. Numbers reflect epidemiology of United States only.
2. Primary Prevention of Ischemic Stroke, Circulation, 2001;103:163-182.
3. *Endarterectomy for Asymptomatic Carotid Artery Stenosis, JAMA, 1995. Vol 273, No. 18. P.1421-1428.*
4. *New Insights on Stroke Prevention in Patients without Symptoms. London, Ontario. June 7, 2000.*

- 72 year old male with prior history of coronary artery disease (CABG 8 years ago), hypertension, hyperlipidemia, and diabetes mellitus presents to you for evaluation of asymptomatic severe carotid disease. He denies any prior history of stroke or TIA. He has no chest pain or shortness of breath. He is currently taking aspirin 81mg, simvastatin 40mg, and lisinopril 20mg.

In addition to exercise you recommend:

1) Continued medical therapy until he has a stroke
2) Immediate CEA
3) Immediate carotid stenting
4) Either CEA or stent
5) Add plavix only

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: A Report of the American College of Cardiology

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).

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*)

Carotid endarterectomy for asymptomatic carotid stenosis (Review)

Chambers BR, Donnan G

1983 to 2003

1% per year absolute risk reduction

3% perioperative stroke or death rate,

This is a reprint of a Cochrane review, prepared and maintained
2008, Issue 4

http://www.th

AUTHORS' CONCLUSIONS

Implications for practice

shows that in patients with asymptomatic about a 3% perioperative stroke or death isk of ipsilateral stroke, and any stroke, by three years. However, the absolute risk reduction is small (approximately 1% per annum over the first few wo largest and most recent trials) but nger follow up. Any benefit would be rative complication rate and only those centres with complication rates of 3% or less should contemplate performing CEA in asymptomatic patients. Whilst there is clear benefit for men, CEA did not appear to help women but it is possible that there could be a positive effect with longer follow up. At present, there is insufficient evidence on whether the surgical oucomes are different in older and younger people, and in patients with different degrees of stenosis. Longer follow up of patients in existing trials or recruitment of additional patients should help clarify these points.

Stroke

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Medical (Nonsurgical) Intervention Alone Is Now Best for Prevention of Stroke Associated With Asymptomatic Severe Carotid Stenosis

Results of a Systematic Review and Analysis

Anne L. Abbott, PhD, MBBS, FRACP

(*Stroke*. 2009;40:e573-e583.)

Method

Method

Literature Search

A Medline literature search was performed for prospective studies of direct imaging identified nonoperated, angioplasty/stenting-free, asymptomatic severe (nonsubcategorized 50% to 75%+) proximal ICA stenosis with sufficient original data to calculate an average annual patient rate of stroke (fatal/nonfatal infarct/hemorrhage). To

…..asymptomatic severe (nonsubcategorized 50% to 75% +)….

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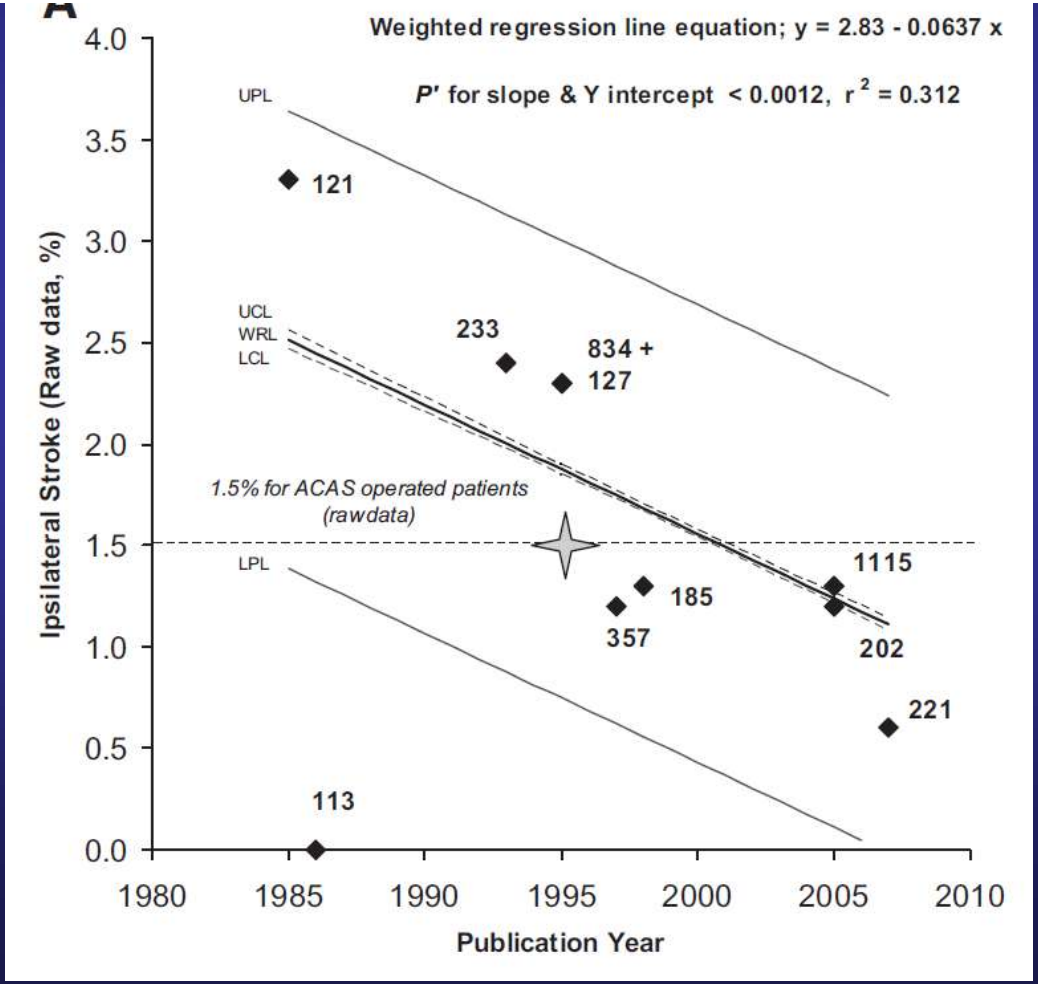

Medical (Nonsurgical) Intervention Alone Is Now Best for Prevention of Stroke Associated With Asymptomatic Severe Carotid Stenosis

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Anne L. Abbott, PhD, MBBS, FRACP

Table 1. Average Annual Stroke +/−TIA Rates of Patients With Asymptomatic Severe (>50%) Carotid Stenosis Managed With Medical Intervention Alone (%)*

		Ipsilateral Stroke		Ipsilateral Stroke/TIA		Any Territory Stroke		Any Territory Stroke/TIA	
Study	Sample Size	Raw Data	KM Estimates	Raw Data	KM Estimates	Raw Data	KM Estimates	Raw Data	KM Estimates
Johnson, 1985[76]	121	3.3	. . .	19.0	. . .	. . .	. . .	. . .	. . .
Toronto, 1986[2]	113	0	. . .	7.9 (all TIA)	. . .	1.9	. . .	10.7	11.0
VACS, 1993[10]	233	2.4	. . .	5.2	. . .	3.0	. . .	6.1	. . .
ACAS, 1995[11]	834	2.3	2.2	4.5	3.8	3.8	3.5	. . .	. . .
ECST, 1995[77]	127	2.3	1.9	. . .	. . .	. . .	. . .	. . .	. . .
ACBS, 1997[78]	357	1.2	1.4	3.4	4.2	2.1	2.5	5.8	. . .
CHS, 1998[82]	185	1.3	1.0	. . .	. . .	2.6	2.3	. . .	. . .
NASCET, 2000[3]	216	. . .	3.2	. . .	. . .	. . .	. . .	. . .	. . .
ACSRS, 2005[79]	1115	1.3	1.7	3.1	3.4	. . .	2.1	. . .	4.1
ASED, 2005[80]	202	1.2	1.0	3.2	3.1	2.4	2.2	5.6	5.1
SMART, 2007[81]	221	0.6	. . .	. . .	. . .	0.7	. . .	. . .	. . .

Severity of Asymptomatic Carotid Stenosis and Risk of Ipsilateral Hemispheric Ischaemic Events: Results from the ACSRS Study

A.N. Nicolaides,[1,4*] S.K. Kakkos,[1] M. Griffin,[1] M. Sabetai,[1] S. Dhanjil,[1] T. Tegos,[1] D.J. Thomas,[2] A. Giannoukas,[1] G. Geroulakos,[1,3] N. Georgiou,[4] S. Francis,[1] E. Ioannidou,[4] C.J. Doré[5] and For the Asymptomatic Carotid Stenosis and Risk of Stroke (ACSRS) Study Group

Objectives. *This study determines the risk of ipsilateral ischaemic neurological events in relation to the degree of asymptomatic carotid stenosis and other risk factors.*

Results. *The relationship between ICA stenosis and event rate is linear when stenosis is expressed by the ECST method, but S-shaped if expres CI 1.21–2.15), history of contralat % CI 1.23–3.65) were independent r p (7.3% annual event rate and 4.3% stroke rate).*

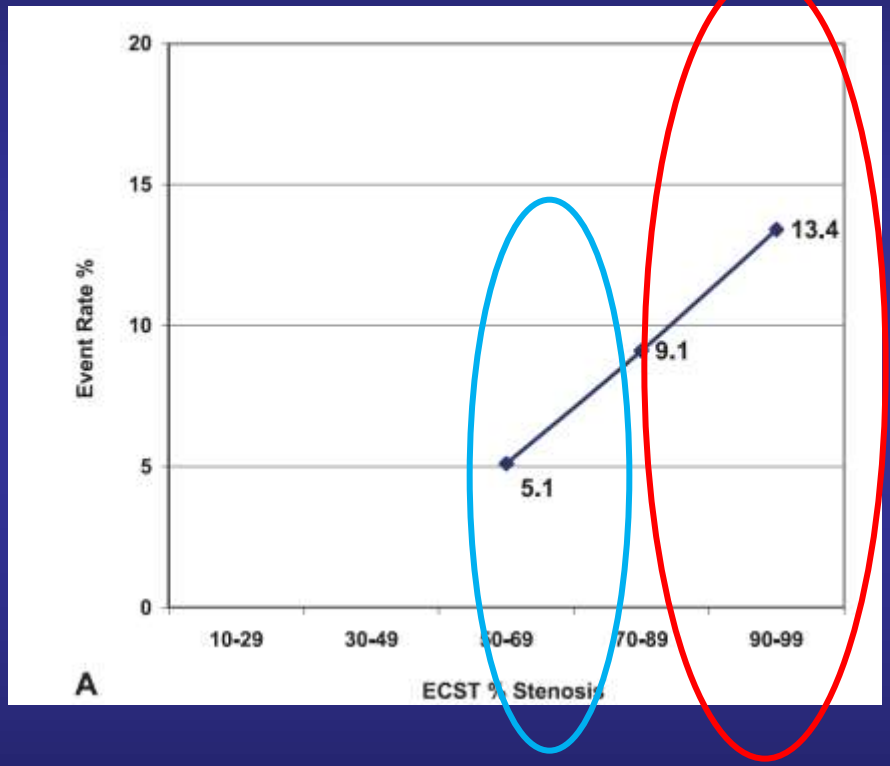
-3 risk factors:

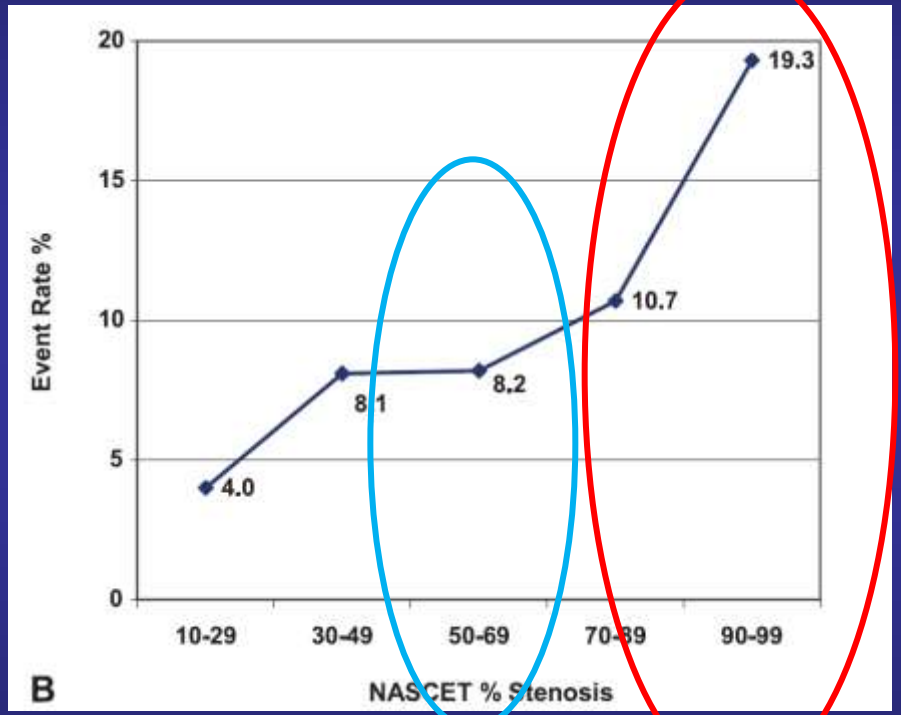
- -ECST grade of stenosis
- -Hx of contralateral TIAs
- -Serum creatinine

-The combination of these three risk factors can identify a high-risk group (7.3% annual event rate and 4.3% annual stroke rate) and a low risk group (2.3% annual event rate and 0.7% annual stroke rate).

Eur J Vasc Endovasc Surg **30**, 275–284 (2005)

The incidence of ipsilateral ischemic hemispheric events





Eur J Vasc Endovasc Surg **30**, 275–284 (2005)

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Medical (Nonsurgical) Intervention Alone Is Now Best for Prevention of Stroke Associated With Asymptomatic Severe

..... I encourage everyone to read the paper .....

..... Many of you will be horrified with what you find; small, poorly controlled studies of patients with no neurological examination, lots of crossovers, unclear duplex findings, and many minor carotid lesions. We are being told that the answer has been "discovered" through a review of these earlier studies.

P. Schneider
Honolulu, United States
E-mail address: Peterschneidermd@aol.com

Eur J Vasc Endovasc Surg (2010) **40**, 678–680

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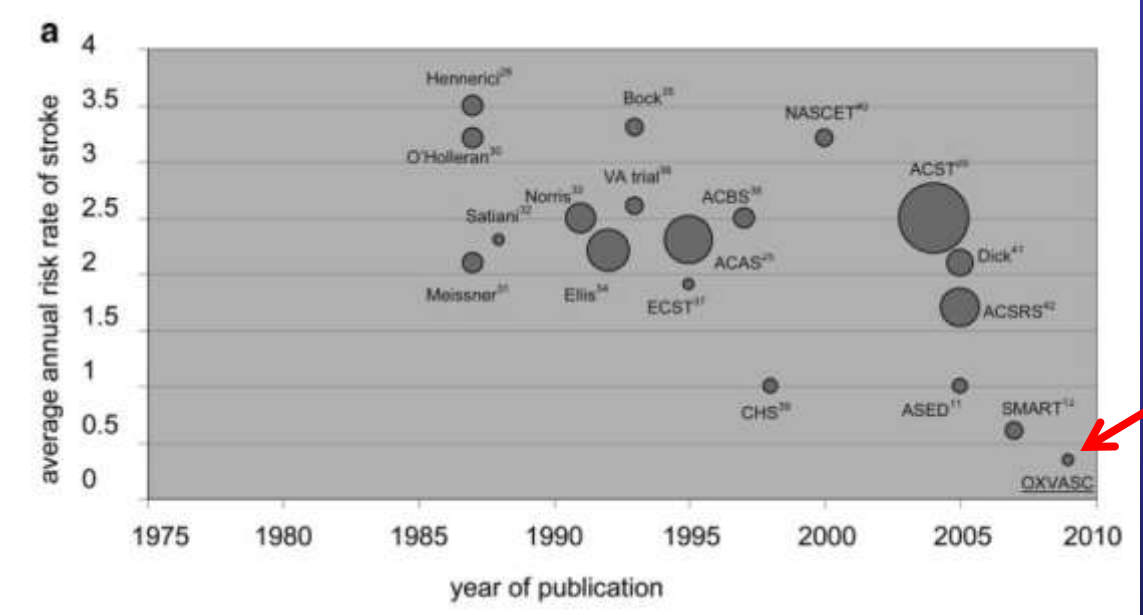
Low Risk of Ipsilateral Stroke in Patients With Asymptomatic Carotid Stenosis on Best Medical Treatment : A Prospective, Population-Based Study

Lars Marquardt, Olivia C. Geraghty, Ziyah Mehta and Peter M. Rothwell

Conclusions—In the first study of the prognosis of ≥50% asymptomatic carotid stenosis to be initiated in the last 10 years, the risk of stroke on intensive contemporary medical treatment was low. Larger studies are required to determine whether this apparent improvement in prognosis is generalizable. **(*Stroke*. 2010;41:e11-e17.)**



(*Stroke*. 2010;41:e11-e17.)

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Low Risk of Ipsilateral Stroke in Patients With Asymptomatic Carotid Stenosis on Best Medical Treatment : A Prosp[illegible]ased Study

Lars Marquardt, Olivia C. G[illegible] Rothwell

Of the 1153 imaged [illegible] stenosis of at least 1 carotid bi[illegible] had ≥50% symptomatic carotid s[illegible] 0% asymptomatic carotid steno[illegible]nts, 75 present-

33 patients

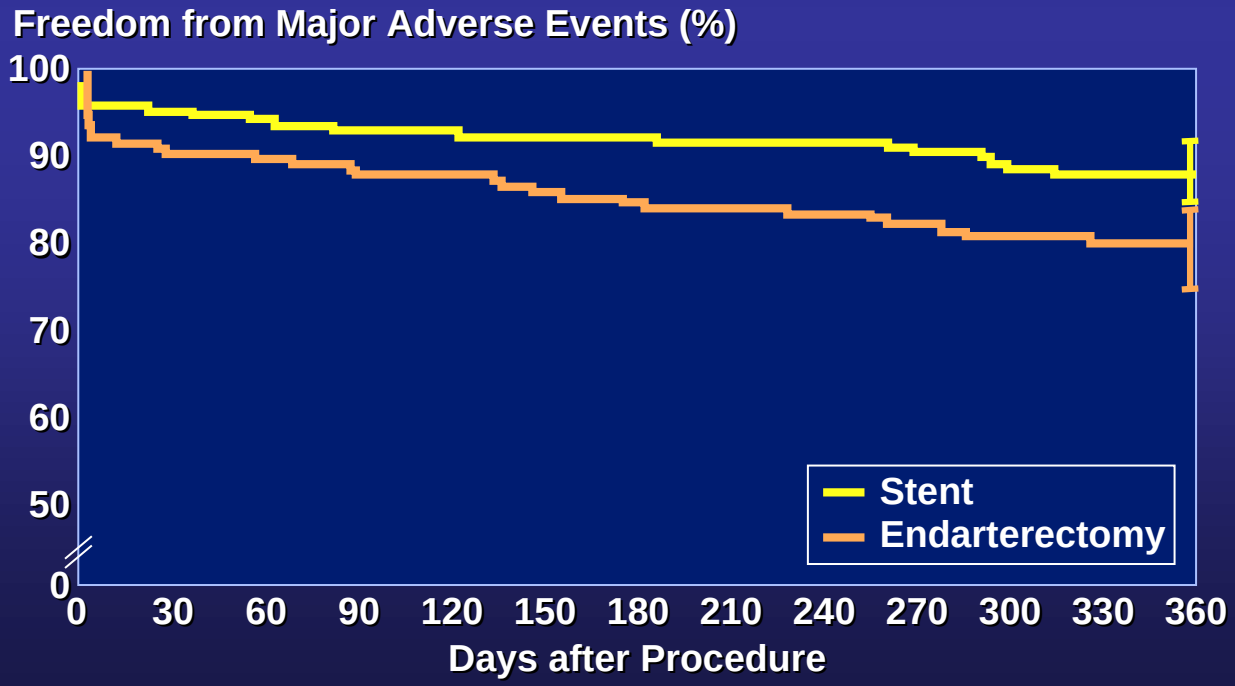
..... the majority of pa[illegible]nts had only 50% to 69% stenosis, with about a third of our patients having an asymptomatic carotid stenosis of 70% to 99%.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 7, 2004 VOL. 351 NO. 15

Protected Carotid-Artery Stenting versus Endarterectomy in High-Risk Patients

the luminal diameter, and patients with asymptomatic carotid-artery stenosis were required to have a stenosis of at least 80 percent on color duplex ultrasonography. Each center had a vascular laboratory



The NEW ENGLAND JOURNAL of MEDICINE

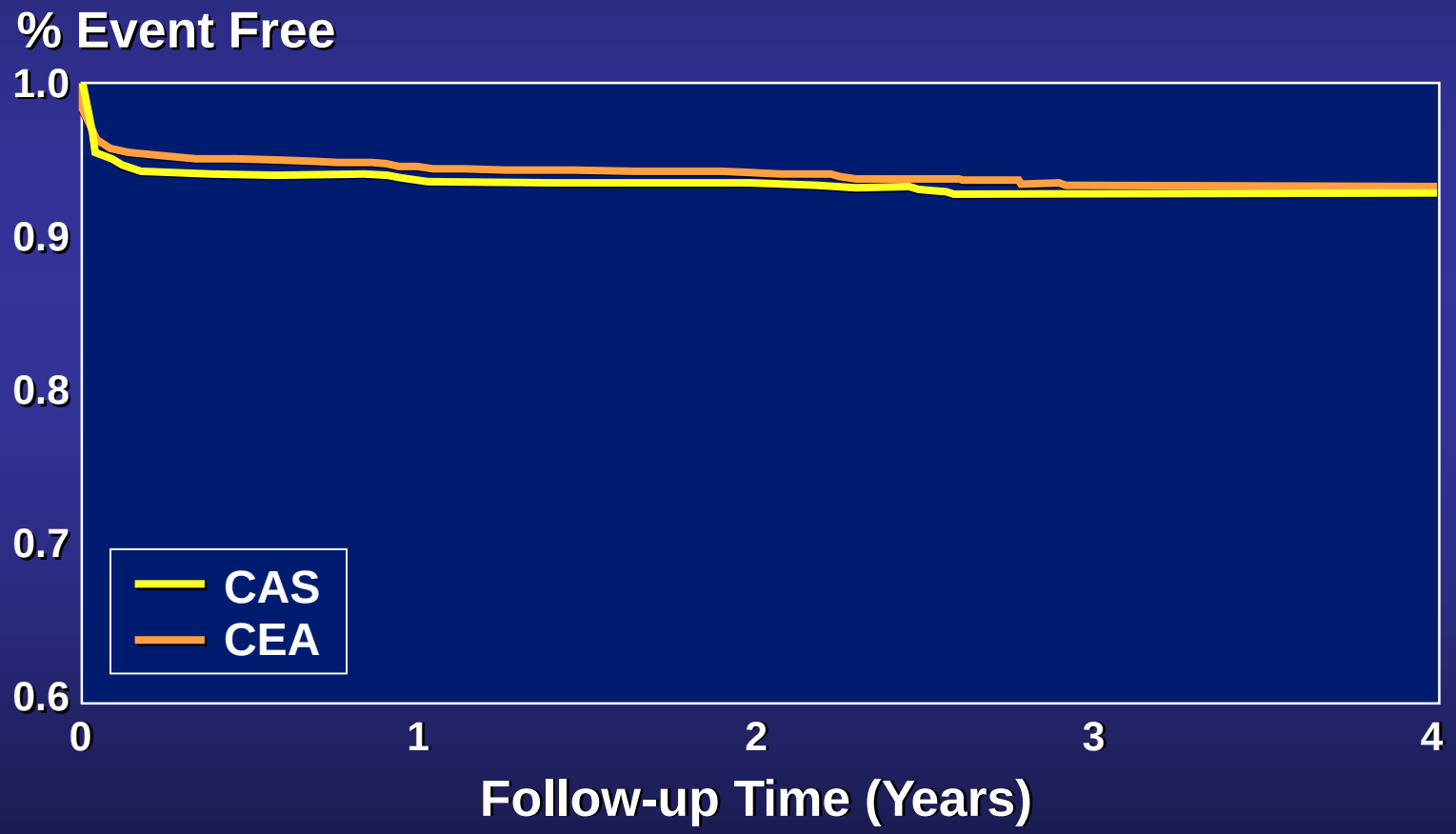
ESTABLISHED IN 1812 JULY 1, 2010 VOL. 363 NO. 1

Stenting versus Endarterectomy for Treatment of Carotid-Artery Stenosis

Table 1. Baseline Characteristics of the Study Population, According to Treatment Group.*

Characteristic	Carotid-Artery Stenting (N = 1262)	Carotid Endarterectomy (N = 1240)
Percent stenosis at randomization		
Moderate (<70%)	13.1	14.9
Severe (≥70%)	86.9	85.1

CREST
Primary Endpoint –All Stroke



Ipsilateral Stroke After Peri-procedural Period ≤ 4 years

CAS vs. CEA	Hazard Ratio, 95% CI	P value
2.0 vs. 2.4%	0.94 (0.50-1.76)	0.85

Primary Endpoint Peri-procedural Components

Any death, stroke, or MI within peri-procedural period

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

Primary Endpoint ≤ 4 Years

Any stroke, MI, or death within peri-procedural period plus ipsilateral stroke thereafter

CAS vs. CEA	Hazard Ratio, 95% CI	P value
7.2 vs 6.8%	1.11 (0.81-1.51)	0.51

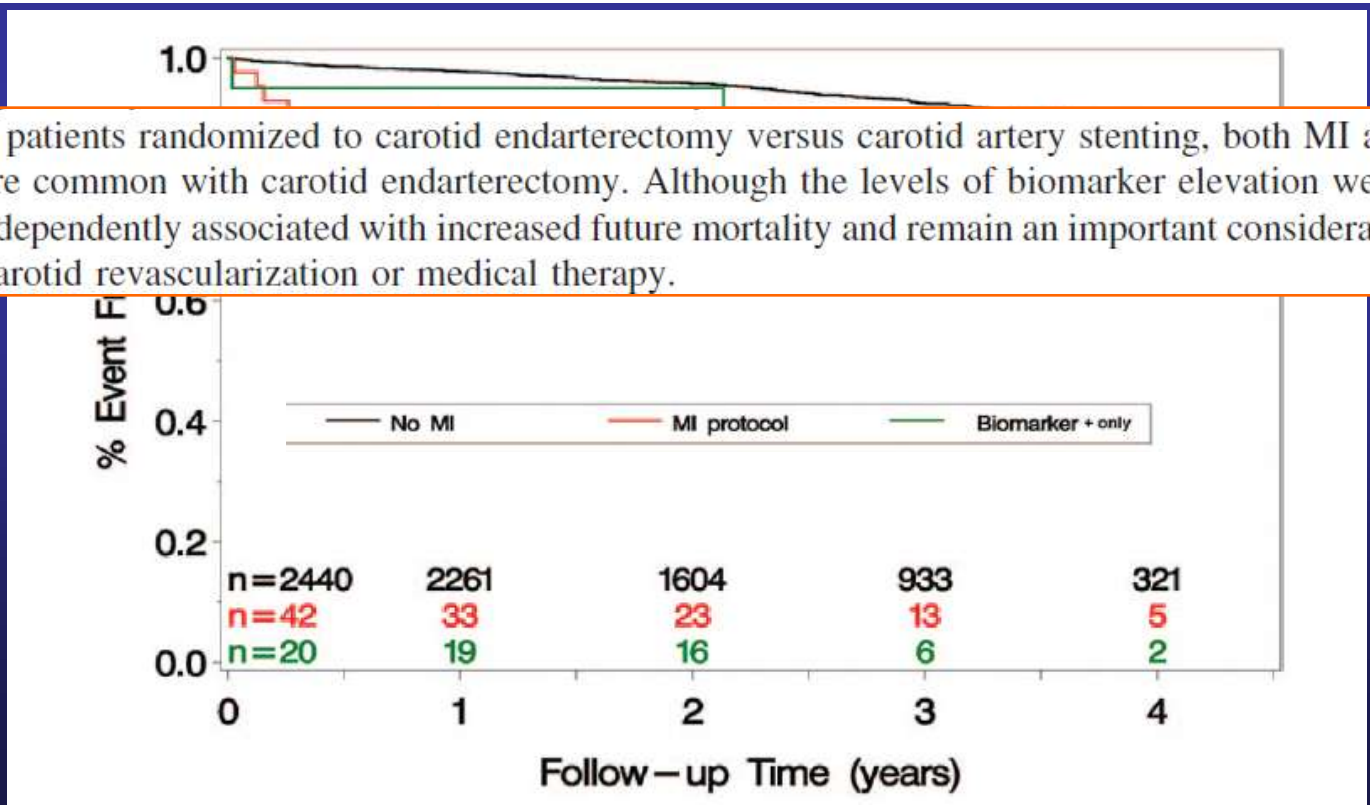
Components of the Primary Endpoint

	CAS vs. CEA	Hazard Ratio, 95% CI	P value
All Stroke	4.1 vs. 2.3%	1.79 (1.14-2.82)	0.01
Major Stroke	0.9 vs. 0.7%	1.35 (0.54-3.36)	0.52
MI	1.1 vs. 2.3%	0.50 (0.26-0.94)	0.03

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Myocardial Infarction After Carotid Stenting and Endarterectomy : Results From the Carotid Revascularization Endarterectomy Versus Stenting Trial

Joseph L. Blackshear, Donald E. Cutlip, Gary S. Roubin, Michael D. Hill, Pierre P. Leimgruber, Richard J. Begg, David J. Cohen, John F. Eidt, Craig R. Narins, Ronald J. Prineas, Stephen P. Glasser, Jenifer H. Voeks, Thomas G. Brott and for the CREST Investigators



Conclusions—In patients randomized to carotid endarterectomy versus carotid artery stenting, both MI and biomarker+ only were more common with carotid endarterectomy. Although the levels of biomarker elevation were modest, both events were independently associated with increased future mortality and remain an important consideration in choosing the mode of carotid revascularization or medical therapy.

CAROTID STENOSIS: TO REVASCULARIZE, OR NOT TO REVASCULARIZE: THAT IS THE QUESTION

Bart M. Demaerschalk, Scottsdale, AZ; George Howard, Birmingham, AL; Thomas G. Brott, Jacksonville, FL: In their editorial, Drs. Marquardt

However, we found no evidence of treatment effect by symptomatic status for stroke and death.

.....

Our conclusions differ substantially from those of Drs. Marquardt and Barnett. Both endarterectomy and stenting have an important role to play in the management of carotid stenosis. Clinicians and their patients now have 2 safe and effective options[3] for revascularization of the carotid artery.

Neurology 78 January 24, 2012

The Path to Personalized Medicine

Margaret A. Hamburg, M.D., and Francis S. Collins, M.D., Ph.D.

Dynamic Approach

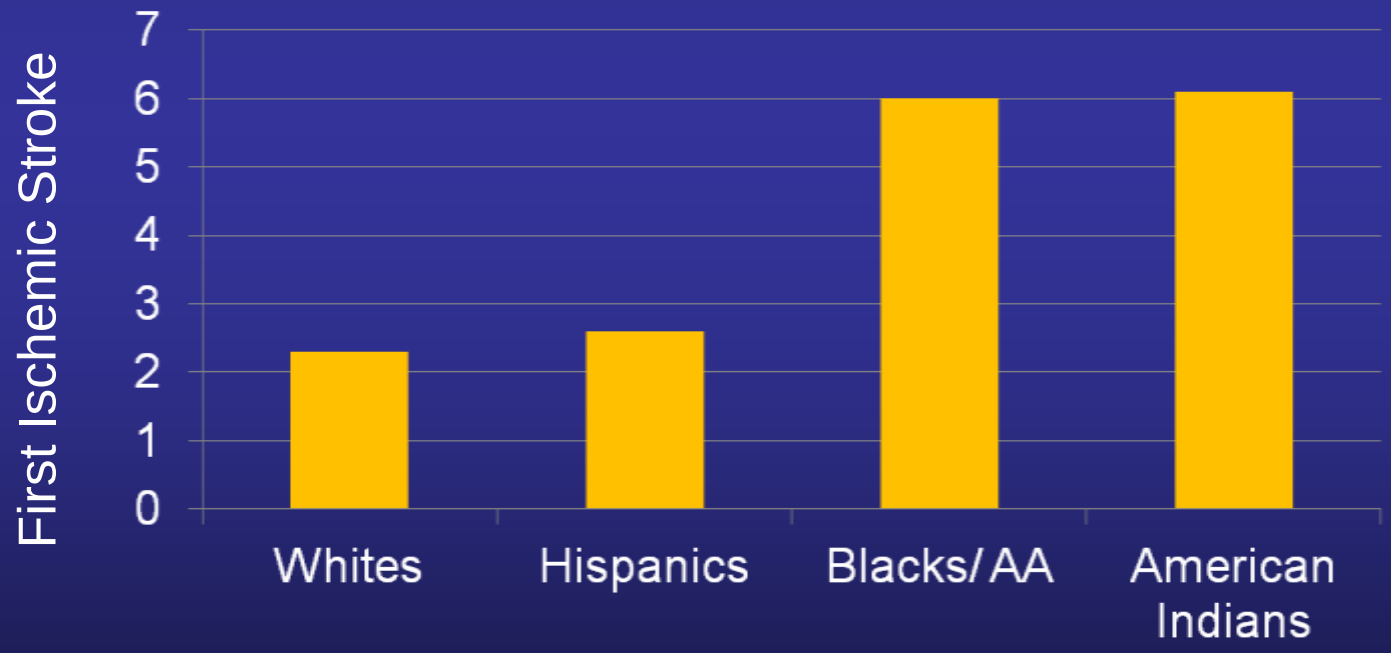
Utilizing

Every Piece of Information

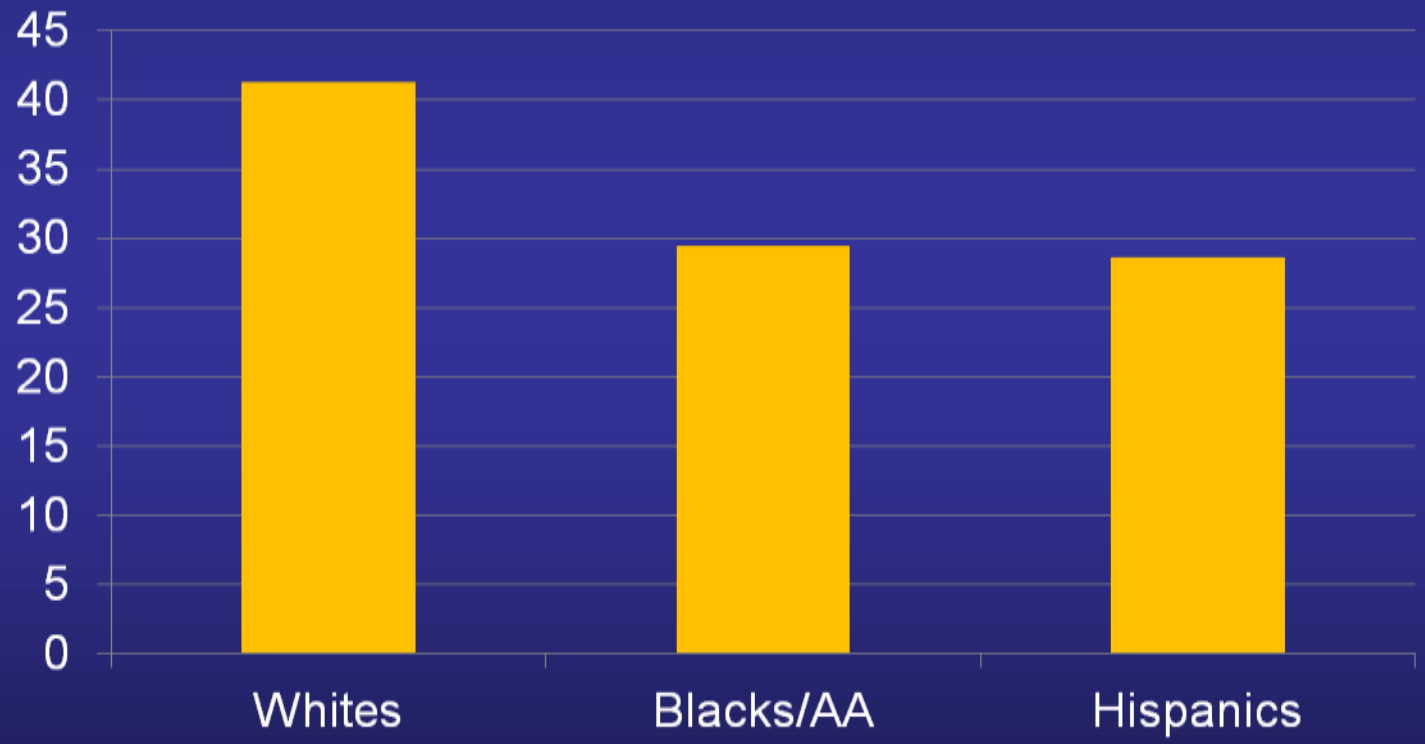
Stroke
JOURNAL OF THE AMERICAN HEART ASSOCIATION
American Stroke Association
A Division of American Heart Association

Racial-Ethnic Disparities in Stroke Care: The American Experience : A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

Salvador Cruz-Flores, Alejandro Rabinstein, Jose Biller, Mitchell S.V. Elkind, Patrick Griffith, Philip B. Gorelick, George Howard, Enrique C. Leira, Lewis B. Morgenstern, Bruce Ovbiagele, Eric Peterson, Wayne Rosamond, Brian Trimble and Amy L. Valderrama



The proportion of respondents who were able to identify 5 stroke warning signs and recognize the need to call 9-1-1 (n=72,000)



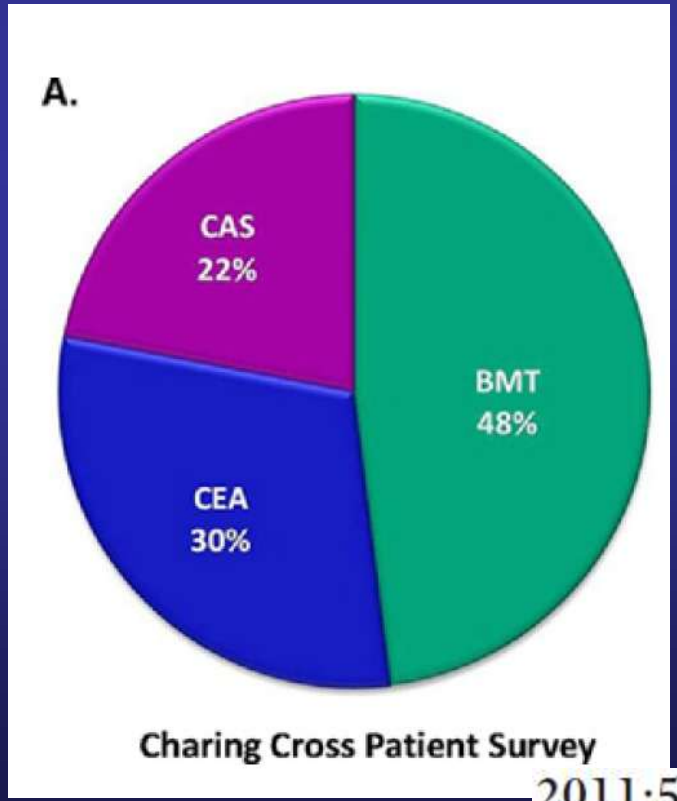
Centers for Disease Control and Prevention. Awareness of stroke warning symptoms: 13 states and the District of Columbia, 2005. *MMWR Morb Mortal Wkly Rep.* 2008;57:481–485.

Patient preference survey in the management of asymptomatic carotid stenosis

Gayani S. Jayasooriya, BSc, MBBS, Joseph Shalhoub, BSc, MBBS, MRCS,
Ankur Thapar, BSc, MBBS, MRCS, and Alun H. Davies, MA, DM, FRCS, *London, United Kingdom*

disease. Patients were asked to imagine their duplex revealed a 70% unilateral carotid stenosis. Five-year stroke or death risks of 11% were quoted for best medical therapy. The perioperative stroke or death rates quoted were 3% for endarterectomy and 3% to 5% for stenting, based on best current evidence. No physician interaction was allowed to minimize clinician bias. Responses for treatment preference and reasoning were analyzed using appropriate statistical

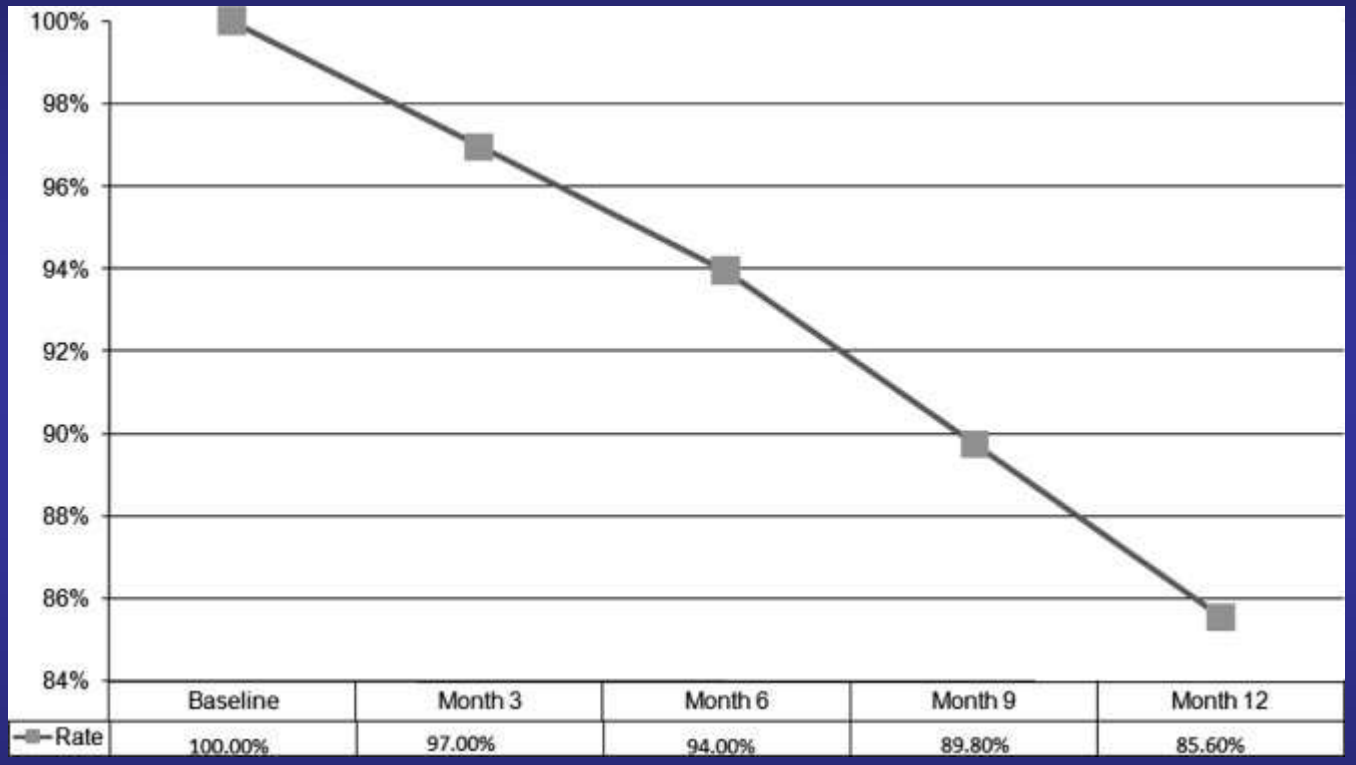
	Death & Stroke
Medical Therapy:	**11%**
CEA:	**3%**
CAS:	**3-5%**



2011;53:1466-72.)

Reality of Medical Therapy

Percent on Dual Anti-platelet Therapy



Months after ACS and Coronary Stenting

(*Circulation*. 2010;122:1017-1025.)

The Path to Personalized Medicine

Margaret A. Hamburg, M.D., and Francis S. Collins, M.D., Ph.D.

- Clinical characteristics
- Anatomy
- Operator experience
- Degree of stenosis (>80% angiographically)
- Life expectancy
- Prior history of TIA or stroke

Medical Therapy and Revascularization Should Compliment Each Other and not Compete

Thank you!

Carotid Artery Stenting Versus CEA

Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis

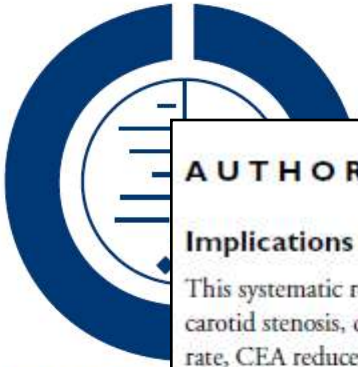
P M Rothwell, M Eliasziw, S A Gutnikov, A J Fox, D W Taylor, M R Mayberg, C P Warlow, H J M Barnett, for the Carotid Endarterectomy Trialists' Collaboration

Trial	ECST		NASCET		VA309		Total		p*
Outcome									
Stroke or death									
⩾70%	17/249	6·8% (4·0–10·7)	14/261	5·4% (3·0–8·8)	5/71	7·0% (2·3–15·7)	36/581	6·2% (4·4–8·5)	0·58
<50%	73/1044	6·9% (5·4–8·6)	43/663	6·5% (4·7–8·6)	0/0	..	116/1707	6·7% (5·6–8·0)	0·52
50–69%	37/371	10·0% (6·9–13·1)	30/421	7·1% (4·8–10·0)	2/20	10·0% (1·2–3·2)	69/812	8·4% (6·6–10·5)	0·16
⩾70%	17/249	6·8% (4·0–10·7)	14/261	5·4% (3·0–8·8)	5/71	7·0% (2·3–15·7)	36/581	6·2% (4·4–8·5)	0·58
Near-occlusion	3/78	3·8% (0·8–10·8)	5/70	7·1% (2·4–15·0)	0/0	..	8/148	5·4% (2·4 –10·4)	0·48
Total	130/1742	7·5% (6·3–8·8)	92/1415	6·5% (5·3–7·9)	7/91	7·7% (3·1–15·2)	229/3248	7·1% (6·3–8·1)	0·30
Death									
<50%	10/1044	0·9% (0·5–1·7)	7/663	1·1% (0·4–2·2)	0/0	..	17/1707	1·0% (0·6–1·6)	0·80
50–69%	6/371	1·5% (0·6–3·3)	6/421	1·4% (0·5–3·1)	0/20	0% (0–16·8)	12/812	1·4% (0·8–2·5)	0·83
⩾70%	1/249	0·4% (0–12·2)	1/261	0·4% (0–2·1)	3/71	4·2% (0·8–11·9)	5/581	0·9% (0·3–2·0)	0·97
Near-occlusion	0/78	0% (0–4·6)	1/70	1·4% (0–7·7)	0/0	..	1/148	0·7% (0–3·7)	0·29
Total	17/1742	1·0% (0·6–1·6)	15/1415	1·1% (0·6–1·7)	3/91	3·3% (0·7–9·3)	35/3248	1·1% (0·8–1·5)	0·86

Data are number/events/number/patients, and percentage risk (95% CI). *Heterogeneity.

Carotid endarterectomy for asymptomatic carotid stenosis (Review)

Chambers BR, Donnan G



THE CO

This is a reprint of a Cochrane review, prepared and maintained
2008, Issue 4

http://www.th

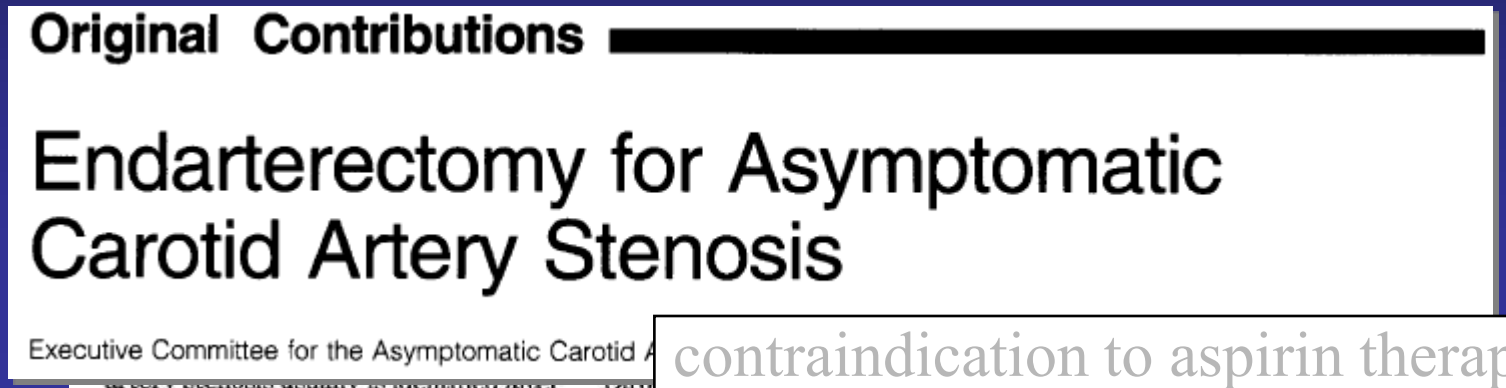
AUTHORS' CONCLUSIONS

Implications for practice

This systematic review shows that in patients with asymptomatic carotid stenosis, despite about a 3% perioperative stroke or death rate, CEA reduces the risk of ipsilateral stroke, and any stroke, by approximately 30% over three years. However, the absolute risk
nately 1% per annum over the first few
o largest and most recent trials) but
ger follow up. Any benefit would be
negated by a higher perioperative complication rate and only those centres with complication rates of 3% or less should contemplate performing CEA in asymptomatic patients. Whilst there is clear benefit for men, CEA did not appear to help women but it is possible that there could be a positive effect with longer follow up. At present, there is insufficient evidence on whether the surgical oucomes are different in older and younger people, and in patients with different degrees of stenosis. Longer follow up of patients in existing trials or recruitment of additional patients should help clarify these points.

3% perioperative stroke or death rate,

Moderate to High Risk Patients Were Excluded from CEA Randomized Trials



Original Contributions

Endarterectomy for Asymptomatic Carotid Artery Stenosis

Executive Committee for the Asymptomatic Carotid A

transient ischemic attack (TIA), but for many patients, cerebral infarction caused by artery-to-artery embolism or carotid occlusion is the initial event. Progression of asymptomatic carotid artery stenosis to occlusion is unpredictable and can be disastrous; at the time of occlusion, dis-

A complete list of the collaborators in the Asymptomatic Carotid Atherosclerosis Study appears at the end of this article.

Reprint requests to Stroke Center and Department of Neurology, Bowman Gray School of Medicine of Wake Forest University, Medical Center Blvd, Winston-Salem, NC 27157-1068 (James F. Toole, MD).

JAMA, May 10, 1995—Vol 273, No. 18

contraindication to aspirin therapy: a disorder that could seriously complicate surgery; or a condition that could prevent continuing participation or was likely to produce disability or death within 5 years. (Detailed information regarding eligibility and exclusion is available on request from the corresponding author.)

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Medical Complications Associated With Carotid Endarterectomy

Maurizio Paciaroni, Michael Eliasziw, L. Jaap Kappelle, Jane W. Finan, Gary G. Ferguson and Henry J. M. Barnett

Stroke 1999;30;1759-1763

	Surgical Arm (n=1415)				Medical Arm (n=1433)
	Mild	Moderate	Severe	Total (%)	Total (%)
Cardiovascular disorders				115 (8.1)	17(1.2)
Hypertension	19	1	...	20	0
Hypotension	23	1	...	24	0
Sudden death	...	...	2	2	0

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The North American Symptomatic Carotid Endarterectomy Trial : Surgical Results in 1415 Patients

Gary G. Ferguson, Michael Eliasziw, Hugh W. K. Barr, G. Patrick Clagett, Robert W. Barnes, M. Christopher Wallace, D. Wayne Taylor, R. Brian Haynes, Jane W. Finan, Vladimir C. Hachinski and Henry J. M. Barnett

Stroke 1999;30;1751-1758

TABLE 3. Summary of Perioperative Wound Complications

	Severity			
Complication	Mild	Moderate	Severe	Total
Risk (n=1415)	5.4%	3.7%	0.3%	9.3%

TABLE 4. Summary of Perioperative Cranial Nerve Injuries

	Severity			
Injury	Mild	Moderate	Severe	Total
Risk (n=1415)	7.9%	0.7%	---	8.6%

Stroke
JOURNAL OF THE AMERICAN HEART ASSOCIATION
American Stroke Association
A Division of American Heart Association

The North American Symptomatic Carotid Endarterectomy Trial : Surgical Results in 1415 Patients

Gary G. Ferguson, Michael Eliasziw, Hugh W. K. Barr, G. Patrick Clagett, Robert W. Barnes, M. Christopher Wallace, D. Wayne Taylor, R. Brian Haynes, Jane W. Finan, Vladimir C. Hachinski and Henry J. M. Barnett

Stroke 1999;30;1751-1758

Characteristics	Moderate Stenosis (n=1087)	Severe Stenosis (n=328)	All Patients (n=1415)
Anesthetic technique			
General	92%	96%	93%
			7%
			3.0
			51%
Electroencephalography	29%	39%	31%
Carotid stump pressure	16%	9%	14%
Evoked potentials	8%	5%	7%
Transcranial Doppler	3%	2%	3%
Intraluminal shunting	43%	34%	41%
Clamp time in unshunted patients, min			
Lowest	6	9	6
Median	31	31	31
Highest	95	83	95

Carotid Stent–Supported Angioplasty: A Neurovascular Intervention to Prevent Stroke

Gary S. Roubin, MD, PhD, Sanjay Yadav, MD, Sri S. Iyer, MD, and Jirri Vitek, MD

Obstructive carotid artery disease is responsible for 60% of strokes in the United States and is the third major cause of death. Stent-supported carotid artery angioplasty has the potential to prevent stroke in thousands of patients and offers a number of potential advantages over surgical revascularization (carotid endarterectomy). Results of the prospective observational study at the University of Alabama at Birmingham indicate that carotid stent–supported angioplasty is safe and probably effective in reducing stroke in patients with high-risk cerebrovascular disease. Technical success was achieved in 99% of 146 procedures; 210 stents were placed in 152 vessels, with only 1 instance of stent thrombosis. The rate of major in-hospital complications was unexpectedly low—only 1 death and 2 major strokes. Seven patients suffered minor strokes, but only 2 were left with minor weakness. When compared with a projected complication rate of 6% had these patients undergone carotid endarterectomy, stenting resulted in fewer major events. At 6-month follow-up, 69 of 74 patients were evaluated by angiography or ultrasound, which detected 8 cases of stent deformation and a restenosis rate of <5%. Because of these instances of stent deformation, use of the Palmaz (biliary) stent was discontinued. Although 1 patient had a transient ischemic attack, no strokes occurred during follow-up. To date, carotid stenting is an investigational procedure. Cardiovascular interventionalists, industry, and the FDA are encouraged to validate this approach through clinical testing. However, improvements in technique, devices, and adjunctive therapies are needed before the method can be tested in randomized trials.

(Am J Cardiol 1996;78(suppl 3A):8–12)

ICSS
United Kingdom

SPACE

SAPPHIRE
United States (Cleveland)

CREST
NIH

EVA-3S
Europe (France)

	Year	n*	Lifetime endovascular requirements
CAVATAS			plasty ery);
SAPPHIRE			review or ssisted
SPACE[6,7]			e of a done at
EVA-3S[8]			s of ic trunks; s not
ICSS[9]	2010	1710	A minimum of 50 total stenting procedures, of which at least ten should be in the carotid artery; tutor-assisted procedures allowed for interventionalists with insufficient experience

CAS=carotid
Angioplasty
Symptomati
SAPPHIRE=St
Endarterecto
(SPACE) stud
endarterecto

Table: Requ
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Carotid artery stenting versus surgery: adequate comparisons?

A moratorium on carotid artery stenting (CAS) has been recently

Marco Roffi, Horst Sievert, William A Gray, Christopher J White, Giovanni Torsello, Piergiorgio Cao, Bernhard Reimers, Klaus Mathias, Carlo Setacci, Claudio Schönholz, Daniel G Clair, Martin Schillinger, Iris Grunwald, Marc Bosiers,

Lancet, Vol 9, April 2000

Clinical trial protocols

Design of the Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST)

A.J. Sheffet[1], G. Roubin[2], G. Howard[3], V. Howard[3], W. Moore[4], J.F. Meschia[5], R.W. Hobson, II[1†], and T.G. Brott[1,5*]

Rationale Carotid endarterectomy (CEA) and medical therapy were shown superior to medical therapy alone for symptomatic (≥50%) and asymptomatic (≥60%) stenosis. Carotid angioplasty stenting (CAS) offers a less invasive alternative. Establishing safety, efficacy, and durability of CAS requires rigorous comparison with CEA in symptomatic and asymptomatic patients.

Aims The objective is to compare the efficacy of CAS versus CEA in patients with symptomatic (≥50%) or asymptomatic (≥60%) extracranial carotid stenosis.

Design The Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST) is a prospective, randomized, parallel, two-arm, multi-center trial with blinded endpoint adjudication. Primary endpoints are analyzed using standard time-to-event statistical modeling with adjustment for major baseline covariates. Primary analysis is on an intent-to-treat basis.

Study Outcomes The primary outcome is the occurrence of any stroke, myocardial infarction, or death during a 30-day peri-procedural period, and ipsilateral stroke during follow-up of up to four years. Secondary outcomes include restenosis

Introduction

Carotid endarterectomy (CEA) is a standard treatment for prevention of stroke depending upon severity of carotid stenosis and other preoperative factors (1, 2). Carotid artery stenting (CAS) is an alternative to CEA, but the relative efficacy of these procedures is not well described. Early randomized clinical trials (RCTs) were criticized for inadequate sample size, sub-optimal interventionalist experience, inconsistent use of anti-platelet medications, absence of an anti-embolic device, and incomplete enrollment (3–5). The Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST) was designed to minimize the impact of these issues, and is the only RCT to enroll symptomatic and asymptomatic patients.

Method

Design

CREST is a prospective, randomized, multi-center trial, with blinded endpoint adjudication, designed to compare the

CREST Trial

	CAS (n=1262)	CEA (n=1240)
Age	69	69
Female (%)	36	34
Asymptomatic (%)	47	47
Hypertension (%)	86	86
Diabetes (%)	30	30
Dyslipidemia (%)	82	85
Current Smoker (%)	26	26
CVD (%)	41	43
Systolic BP, mean mmHg	142	141
% stenosis > 70%	85	87
Days from qualifying event (for symptomatic subjects)	20	25

Primary Endpoint Peri-procedural Components

Any death, stroke, or MI within peri-procedural period

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

Primary Endpoint ≤ 4 Years

Any stroke, MI, or death within peri-procedural period plus ipsilateral stroke thereafter

CAS vs. CEA	Hazard Ratio, 95% CI	P value
7.2 vs 6.8%	1.11 (0.81-1.51)	0.51

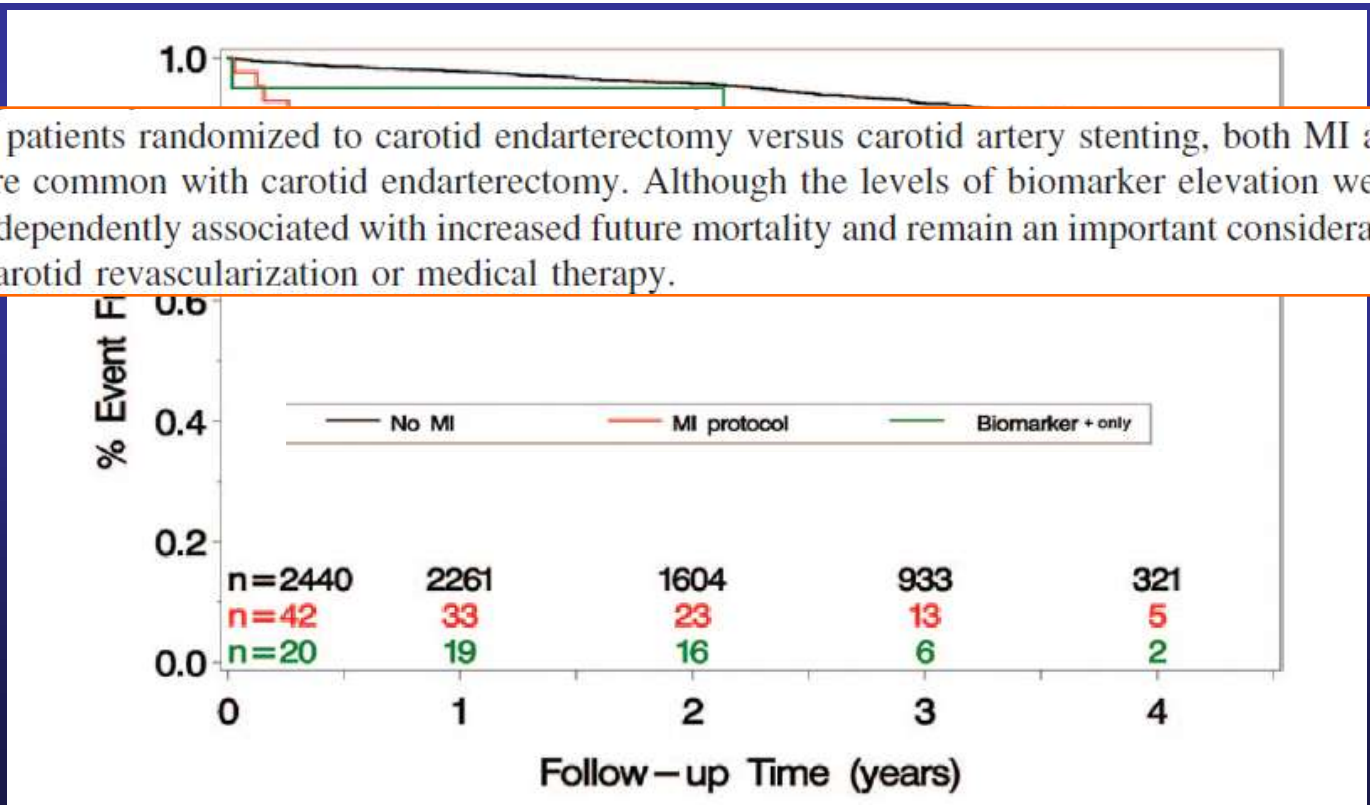
Components of the Primary Endpoint

	CAS vs. CEA	Hazard Ratio, 95% CI	P value
All Stroke	4.1 vs. 2.3%	1.79 (1.14-2.82)	0.01
Major Stroke	0.9 vs. 0.7%	1.35 (0.54-3.36)	0.52
MI	1.1 vs. 2.3%	0.50 (0.26-0.94)	0.03

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Myocardial Infarction After Carotid Stenting and Endarterectomy : Results From the Carotid Revascularization Endarterectomy Versus Stenting Trial

Joseph L. Blackshear, Donald E. Cutlip, Gary S. Roubin, Michael D. Hill, Pierre P. Leimgruber, Richard J. Begg, David J. Cohen, John F. Eidt, Craig R. Narins, Ronald J. Prineas, Stephen P. Glasser, Jenifer H. Voeks, Thomas G. Brott and for the CREST Investigators

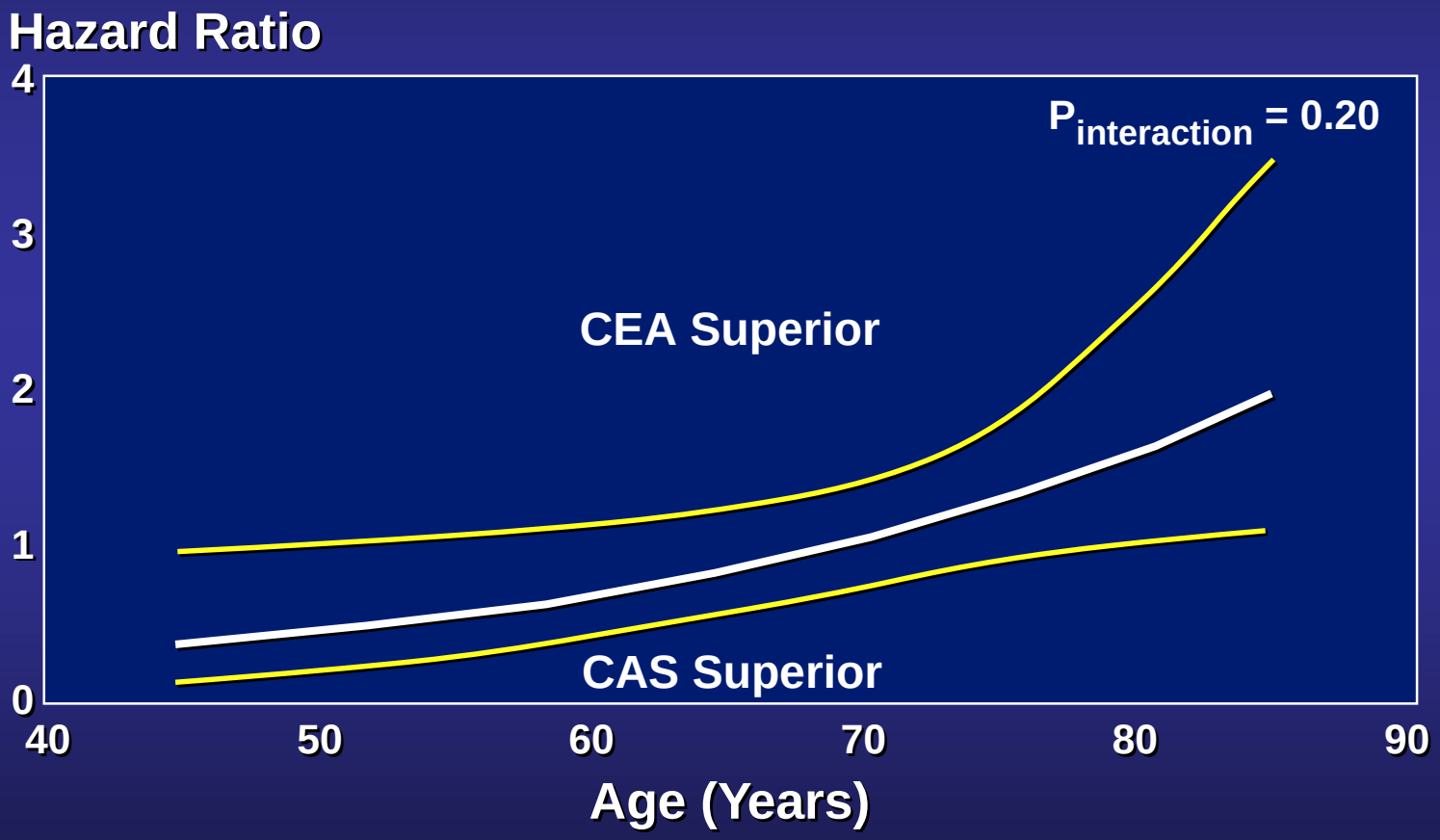


Conclusions—In patients randomized to carotid endarterectomy versus carotid artery stenting, both MI and biomarker+ only were more common with carotid endarterectomy. Although the levels of biomarker elevation were modest, both events were independently associated with increased future mortality and remain an important consideration in choosing the mode of carotid revascularization or medical therapy.

Cranial Nerve Palsies Peri-procedural

CAS vs. CEA	Hazard Ratio, 95% CI	P value
0.3 vs. 4.8%	0.70 (0.02-0.18)	<0.0001

Interaction with Age



N.Y. jet crash called 'miracle on the Hudson'

Pilot Error to Blame in Deadly Flight Accident Last February

NTSB Report Highlights Major Safety Lapses, Sheds Light on Regional Carriers

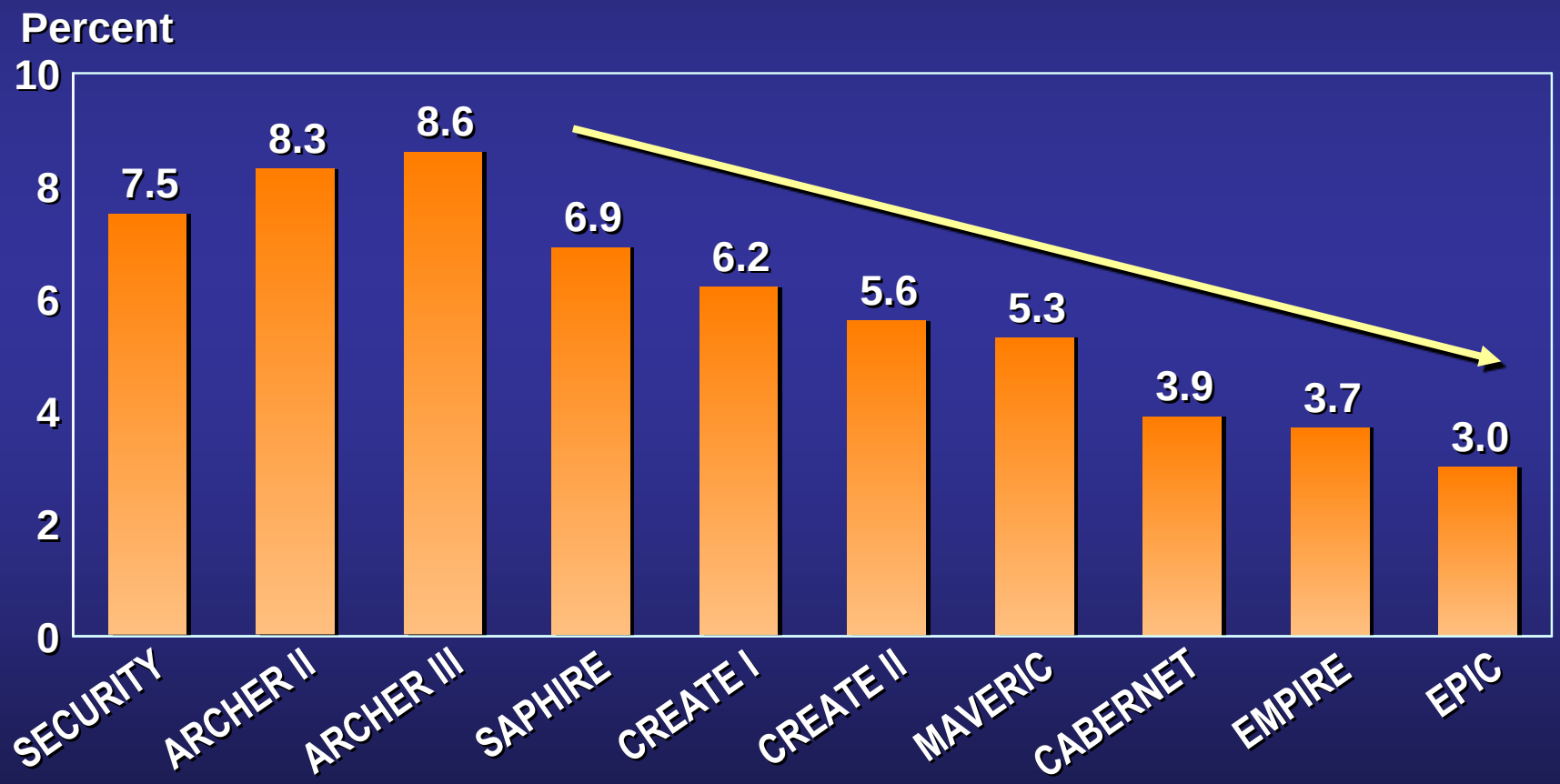
By LISA STARK and HUMA KHAN

Feb. 2, 2010

abc WORLD WITH DIANE

30-Day Event Rates

MACE (Death, CVA, MI) Clinical Trails Comparison



THANK YOU!