

# Carotid Artery Disease



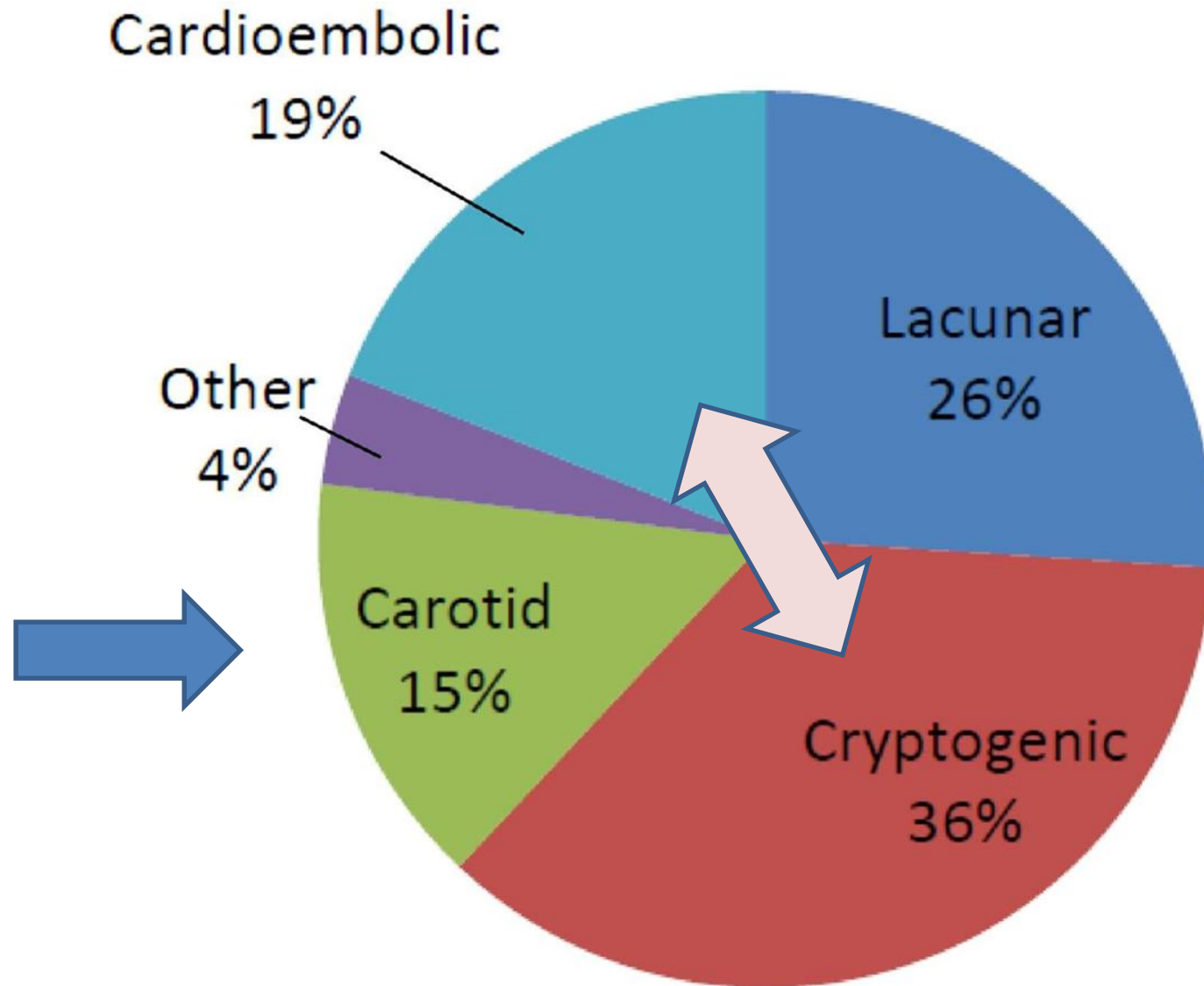
Dr. Arturo Tamayo MD, FAHA, MSc.

# Conflict of interests:

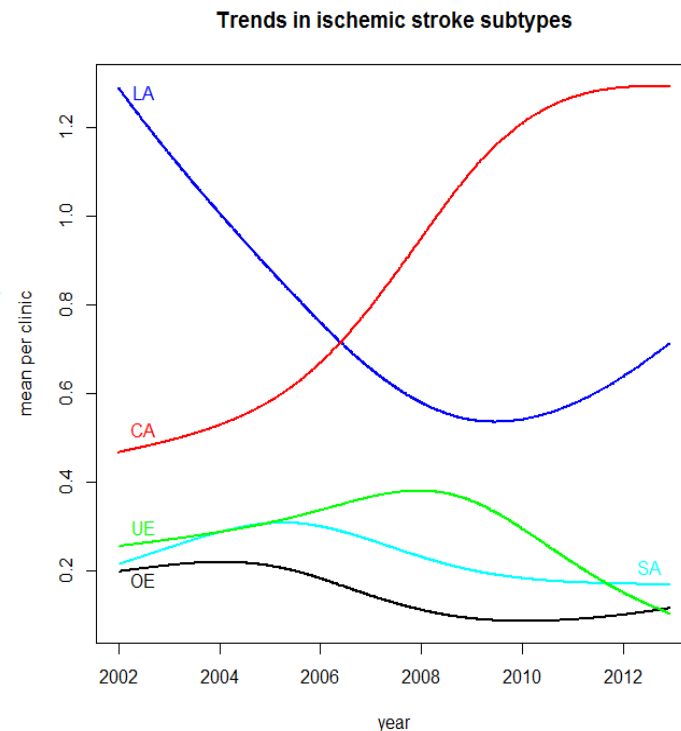
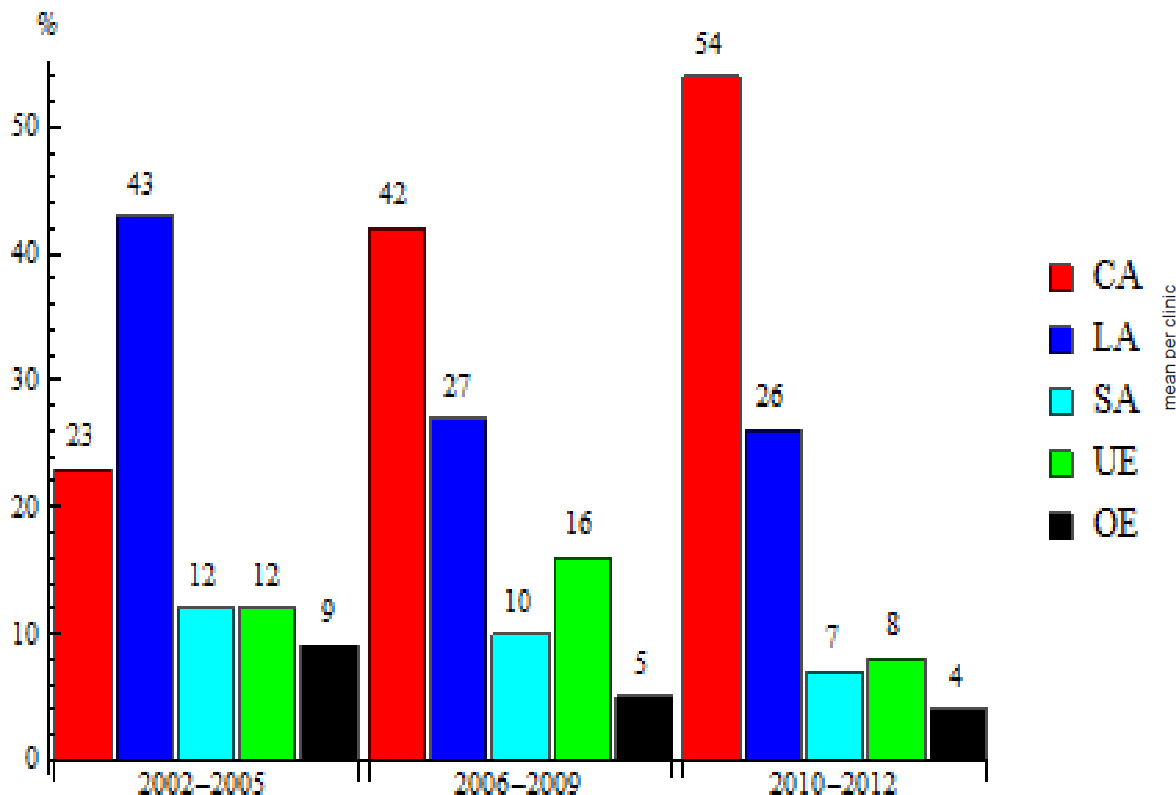
- I do not have any conflict of interest to disclose.



# Common Subtypes of Ischemic Stroke



# Cardioembolic strokes are increasing with decline in LA .



LAA: Large Artery Atherosclerosis, CAE: Cardioembolic, SVD: Small Vessel Disease, Other: Other Determined Etiology, UE Undetermined

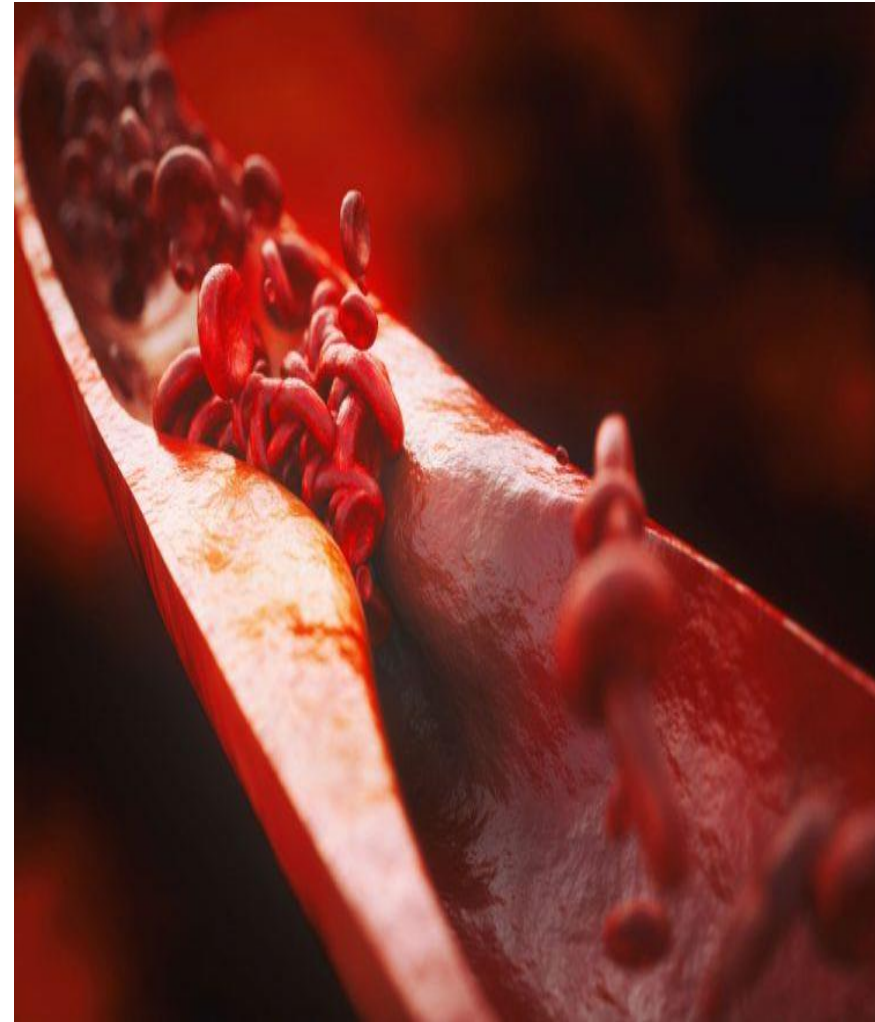
# Prevalence of carotid stenosis

Who is at risk?

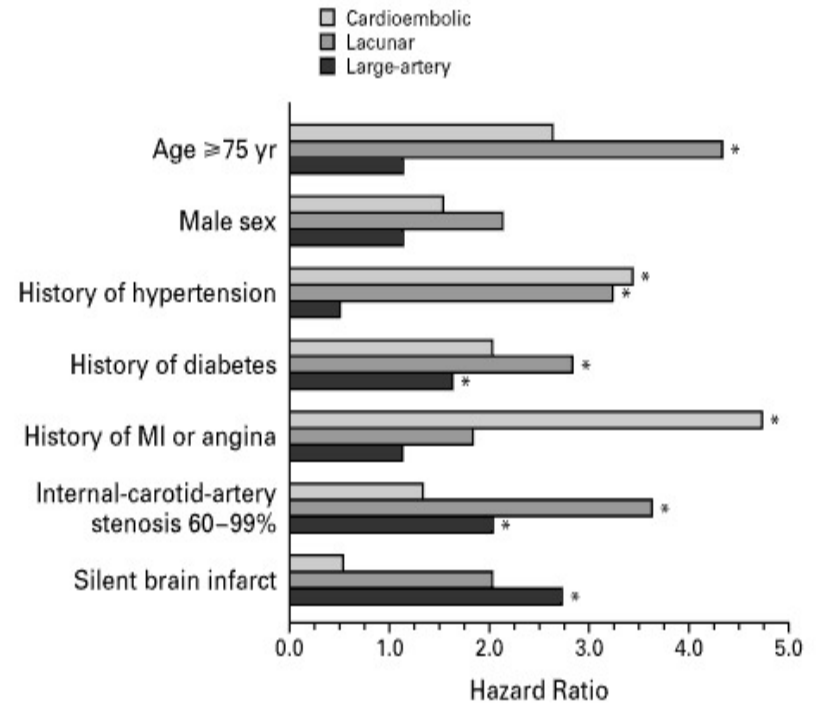
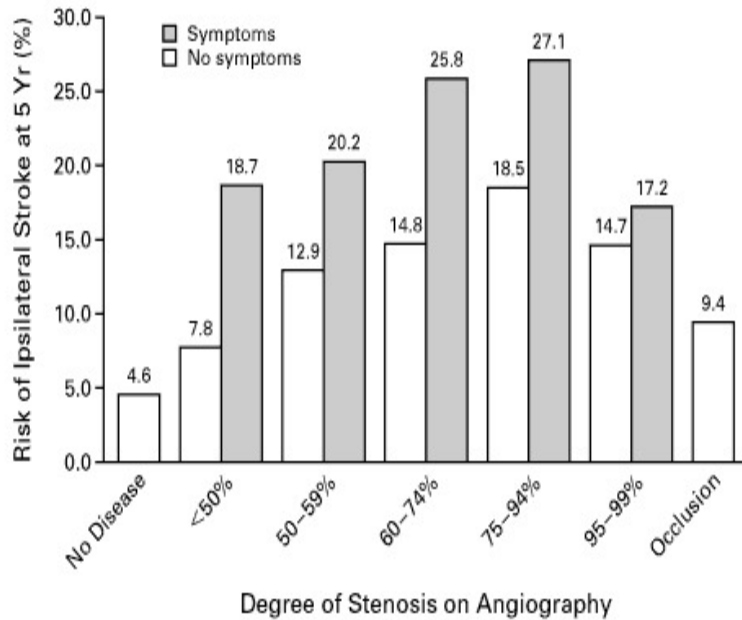
	<u>Prevalence</u>	
Canadian Population	?	} Prevalence of stenosis >75%
Over age 65	0.5 – 1 %	
Bruit	1.2%	
Risk Factors	14%	
RF + Bruit	25%	

# Asymptomatic vs Symptomatic

- What contributes to it?



# Predictors for stroke/TIA in ASX carotid stenosis

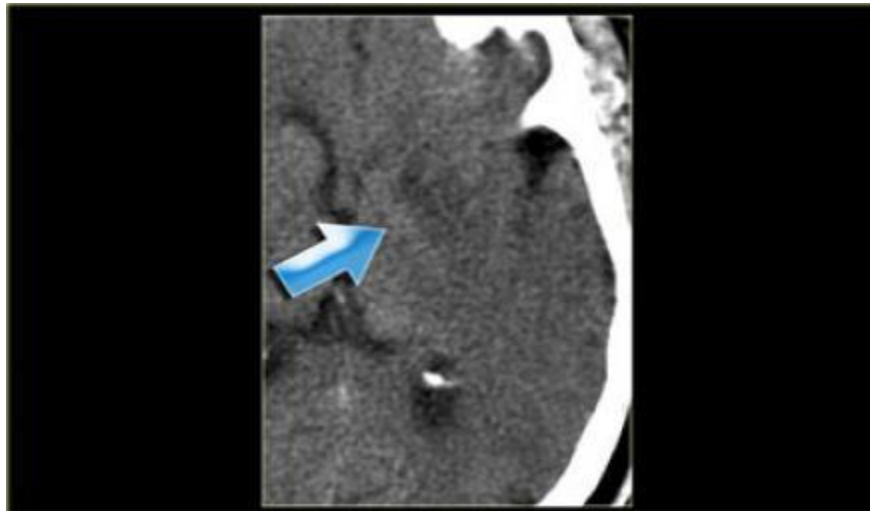


DM (RR 1.2)  
 Prior contralateral SX (RR 1.5)  
 Progression stenosis (RR 1.4,4.0,7.6)

Inzitari D, Eliasziw M, Gates P, et al. The causes and risk of stroke in patients with asymptomatic internal carotid artery stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med. 2000;342:1693-1700

# Silent infarct on CT

- 10-18% w Asx carotid stenosis have silent infarcts
- Annual stroke risk 3.6% vs 1.0%,  $p=0.002$



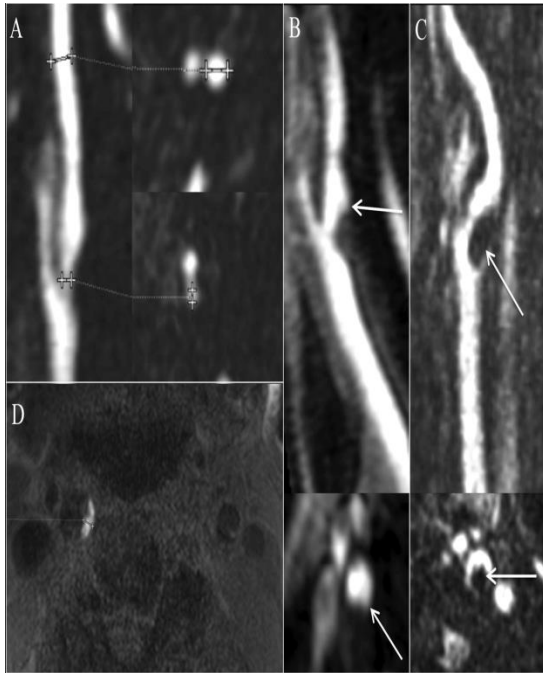
\*Martin JD, Valentine RJ, Myers SI, Rossi MB, Patterson CB, Clagett GP. Is routine CT scanning necessary in the preoperative evaluation of patients undergoing carotid endarterectomy? *J Vasc Surg.* 1991;14:267-270.

\*Cao P, Zannetti S, Giordano G, De Rango P, Parlani G, Caputo N. Cerebral tomographic findings in patients undergoing carotid endarterectomy for asymptomatic carotid stenosis: short-term and long-term implications. *J Vasc Surg.* 1999;29:995-1005.

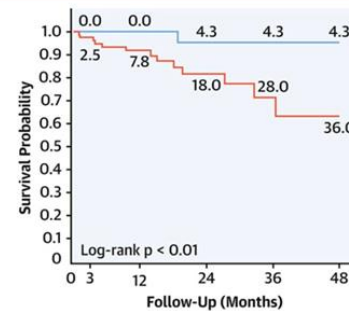
\*Kakkos SK, Sabetai M, Tegos T, Stevens J, Thomas D, et al; Asymptomatic Carotid Stenosis and Risk of Stroke (ACRS) Study Group. Silent embolic infarcts on computed tomography brain scans and risk of ipsilateral hemispheric events in patients with asymptomatic internal carotid artery stenosis. *J Vasc Surg.* 2009;49:902-909.



# Prediction of Stroke risk by detection of hemorrhage in carotid plaques (triples risk!)



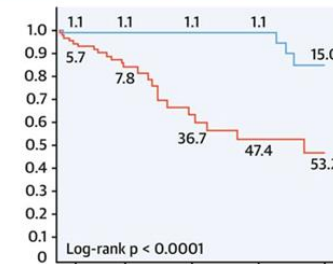
**A Cumulative Risk (%)**



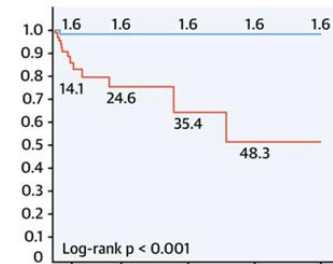
Number at risk (number of individuals with stroke in preceding year):

IPH-	103	103 (0)	28 (0)	17 (1)	8 (0)	3 (0)
IPH+	84	74 (2)	41 (4)	23 (4)	9 (2)	1 (1)

**B Cumulative Risk (%)**      **C Cumulative Risk (%)**



IPH-	97	88 (1)	56 (0)	41 (0)	25 (0)	16 (3)
IPH+	95	76 (5)	37 (7)	20 (7)	12 (3)	7 (1)

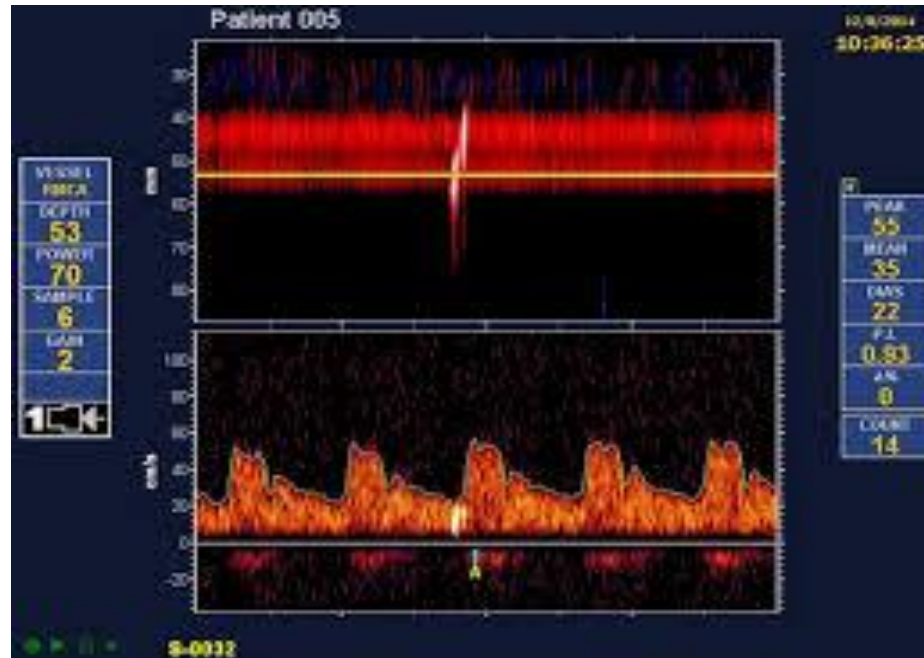


IPH-	71	39 (1)	22 (0)	12 (0)	4 (0)	2 (0)
IPH+	110	30 (9)	16 (3)	6 (1)	3 (1)	

— IPH+ — IPH-

A: Mild. B: Moderate. C: Severe

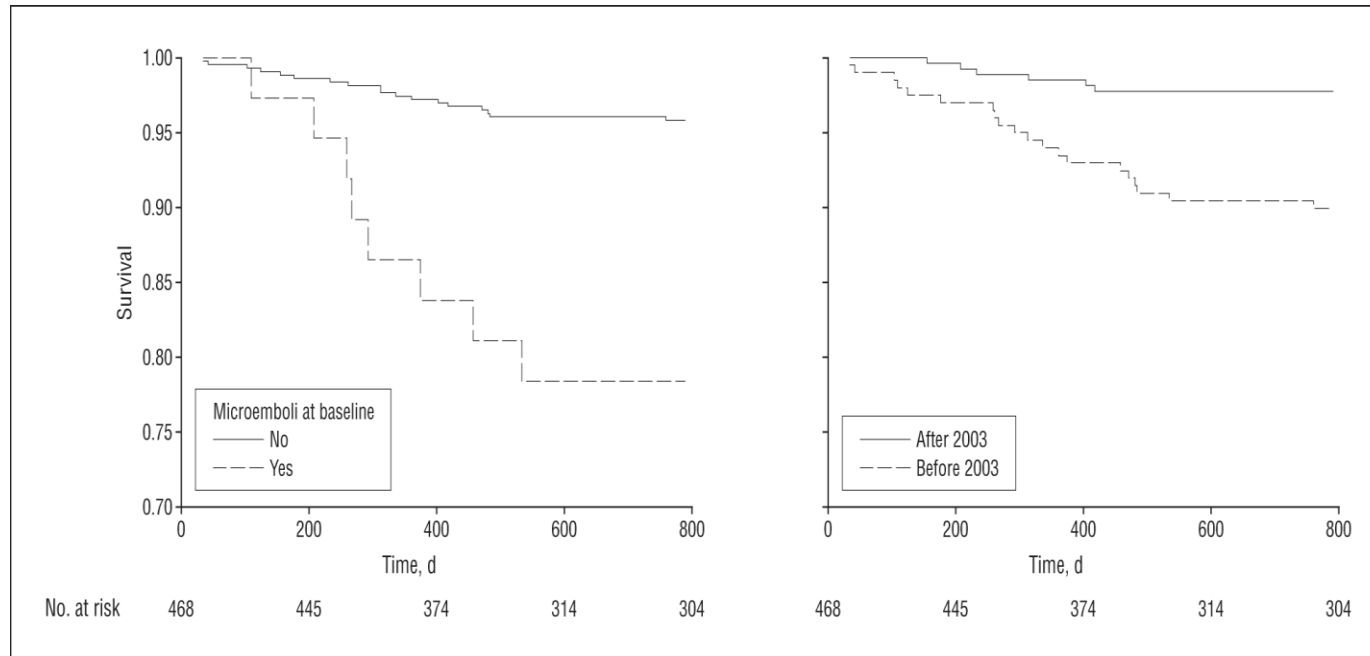
# Embolitic signals on TCD



- OR 6.6 (95% CI 2.9-15.4)
- Stroke risk 8.7% vs 1.4% w/ embolic signals

\*King A, Markus HS. Doppler embolic signals in cerebrovascular disease and prediction of stroke risk: a systematic review and meta-analysis. Stroke. 2009;40:3711-3717.  
Spence JD, Tamayo A et al. Arch Neurol. 2010;67(2):180-186

# Effects of Intensive medical therapy on microemboli and cardiovascular risk in asymptomatic carotid stenosis.

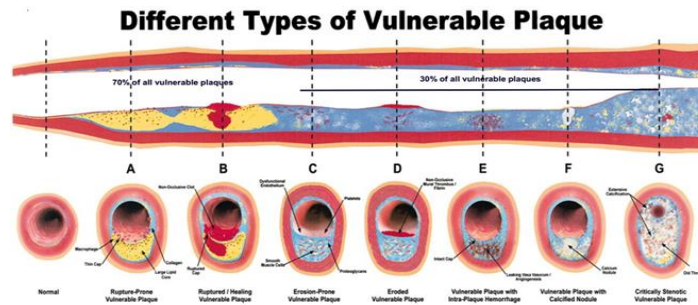
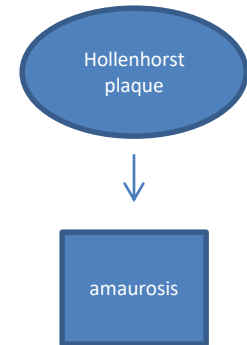


# Symptomatic Carotid stenosis

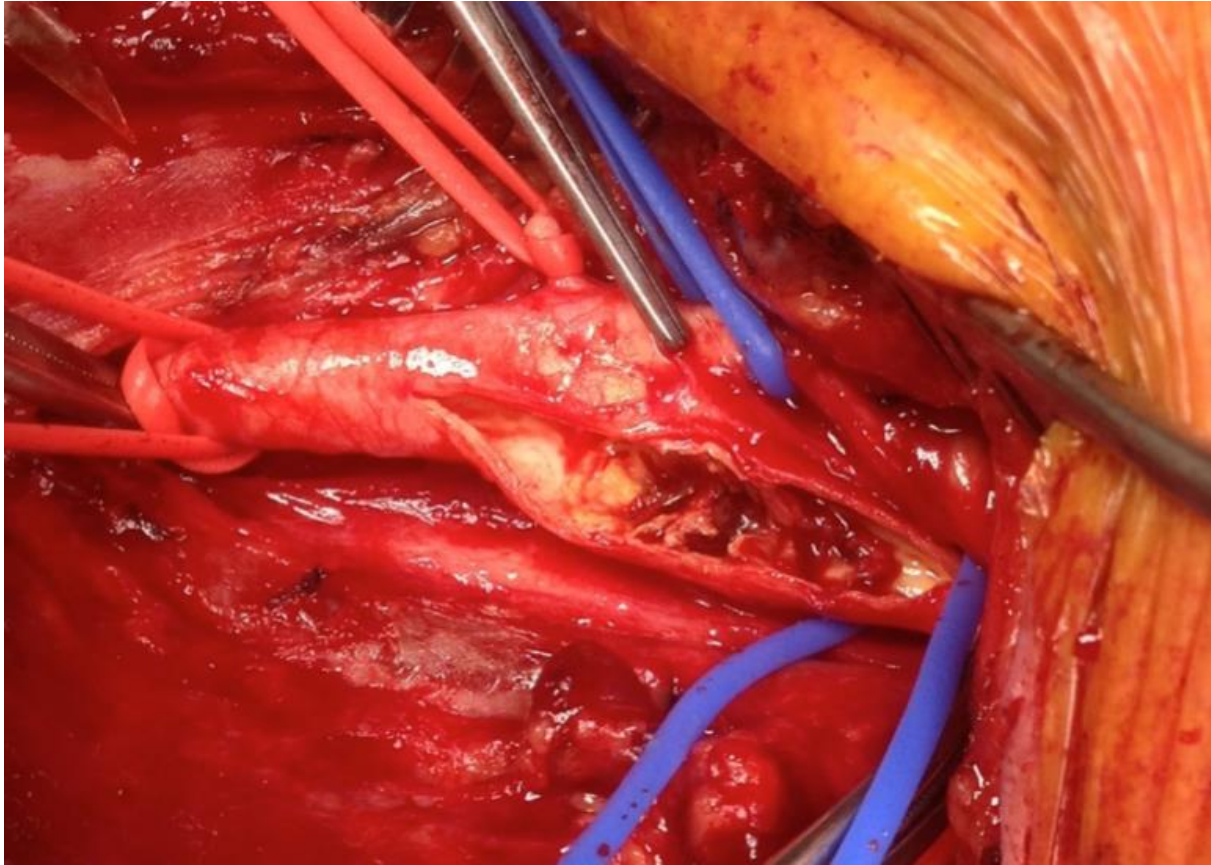
Stroke risk as high as 43% (HTIA) vs. 16% (RTIA) at 2 years (>3months) .

**F**ACE is it drooping?  
**A**RM can you raise both?  
**S**PEECH is it slurred or jumbled?  
**T**IME to call 9-1-1 right away.

© Heart and Stroke Foundation of Canada, 2014.

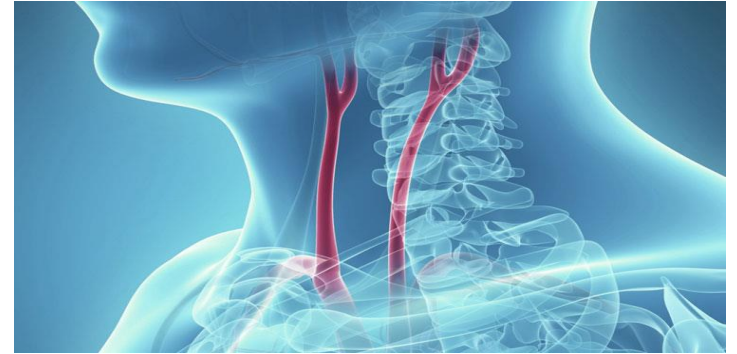


# Carotid endarterectomy



NASCET

ECST



## NASCET 1987-1996

North American Symptomatic Carotid Endarterectomy Trial (NASCET)

- 2885 patients enrolled: TIA/stroke 120 days  
1583 patients (54.9%)—TIA  
1302 patients (45%)—Nondisabling stroke
- Carotid stenosis; angio confirmed  
moderate (30-69%); severe (70-99%)
- Established CEA over medical RX in patients with high grade stenosis (>70%)

N Engl J Med 1991;325:445-53

# NASCET

	Medical	Surgical	Absolute Difference	RRR	NNT
70-99%	26.0%	9.0%	17%	65%	8
50-70%	22.0%	16%	6%	39%	15

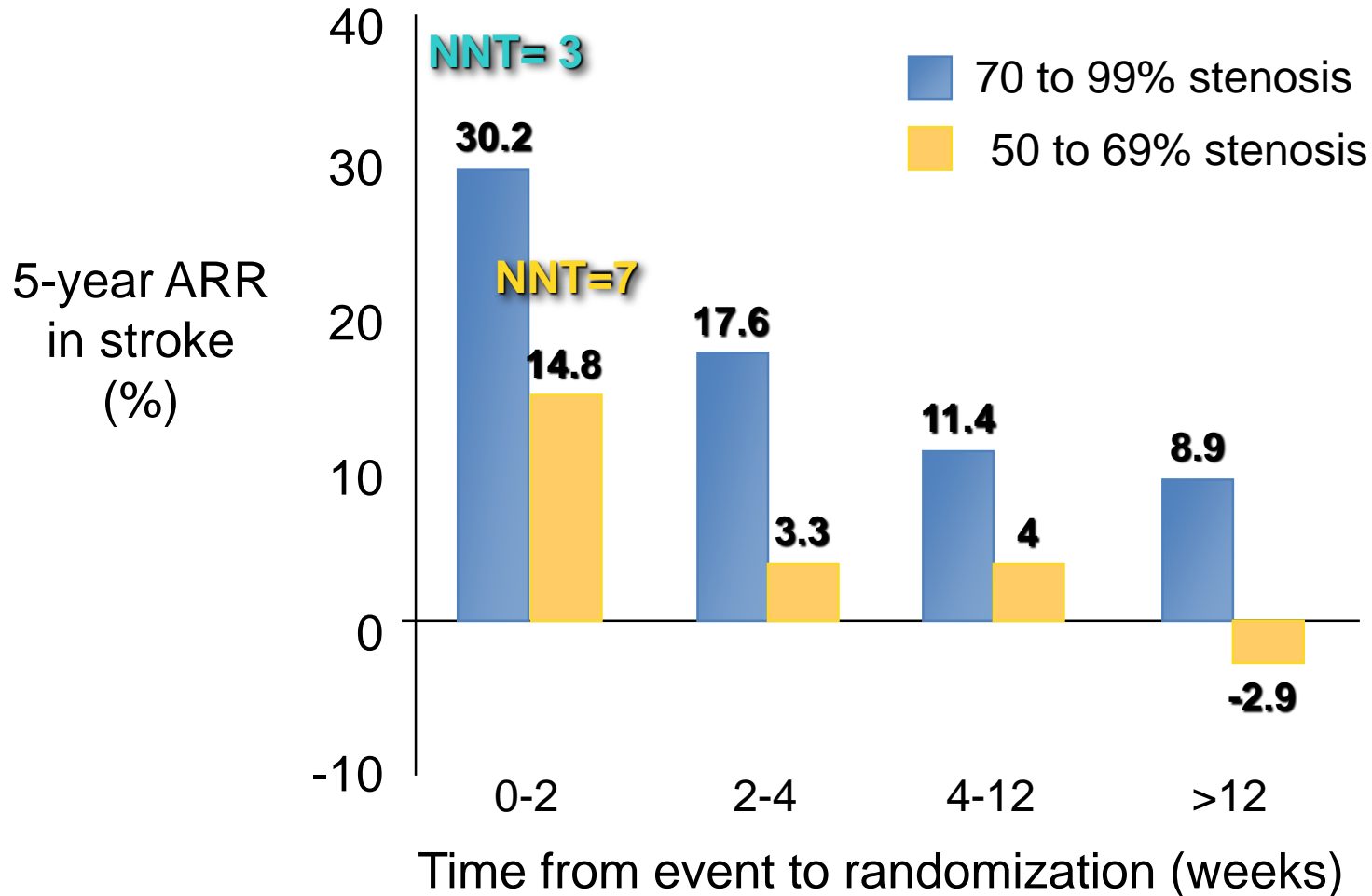
Cumulative risk for ipsilateral stroke in symptomatic carotid trials at 2 years

<50%, CEA not better than ASA (aspirin)

N Engl J Med 1991;325:445-53

# Timing of Surgical Intervention

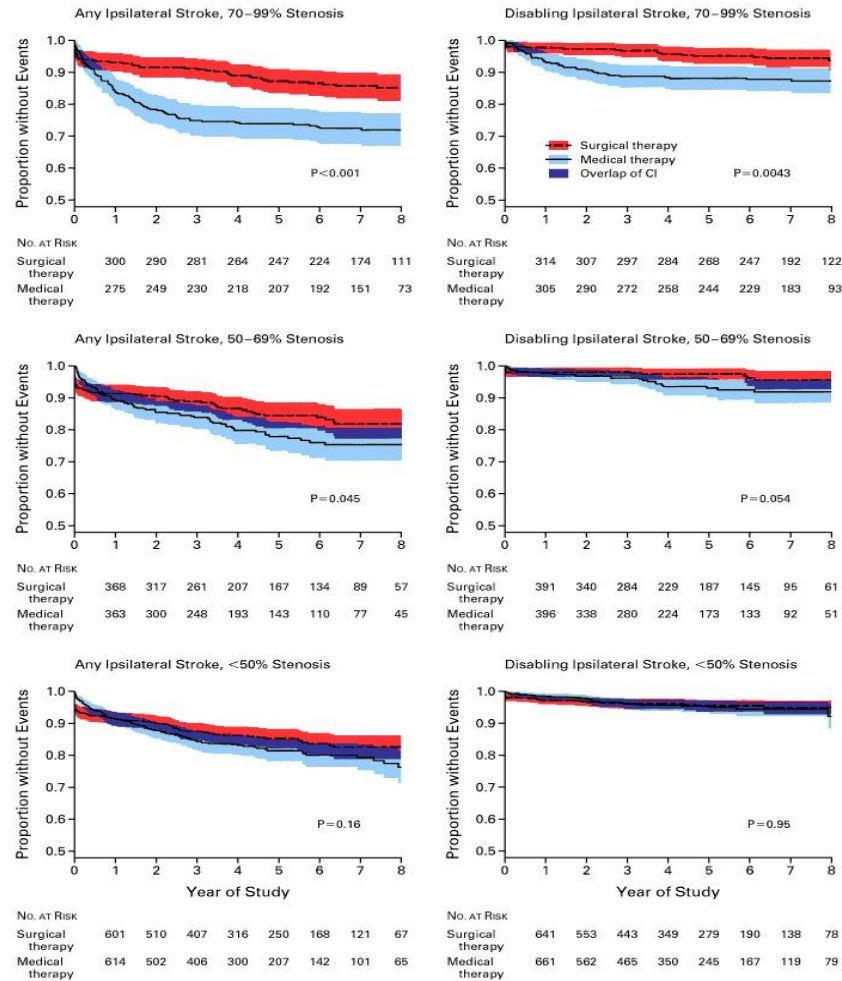
## The NASCET and ECST Studies



Rothwell PM et al. Stroke 2004;35:2855-2861.  
Lancet 2004;363:915-24



# NASCET



Barnett H. et. al. Benefit of Carotid Endarterectomy in Patients with Symptomatic Moderate or Severe Stenosis. NEJM, 1998; 339: 1415-1425.

# Carotid artery stenting

EVA-3S

ICSS

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

Jay S. Yadav, M.D., Mark H. Wholey, M.D., Richard E. Kuntz, M.D., M.Sc., Pierre Fayad, M.D., Barry T. Katzen, M.D., Gregory J. Mishkel, M.D., Tanvir K. Bajwa, M.D., Patrick Whitlow, M.D., Neil E. Strickman, M.D., Michael R. Jaff, D.O., Jeffrey J. Popma, M.D., David B. Sneed, Ph.D., Donald E. Cutlip, M.D., Brian G. Firth, M.D., Ph.D., and Kenneth Ouriel, M.D., for the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators\*

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Long-Term Results of Carotid Stenting versus Endarterectomy in High-Risk Patients

Hitinder S. Gurm, M.D., Jay S. Yadav, M.D., Pierre Fayad, M.D., Barry T. Katzen, M.D., Gregory J. Mishkel, M.D., Tanvir K. Bajwa, M.D., Gary Ansel, M.D., Neil E. Strickman, M.D., Hong Wang, M.D., M.P.H., Sidney A. Cohen, M.D., Ph.D., Joseph M. Massaro, Ph.D., and Donald E. Cutlip, M.D., for the SAPPHERE Investigators\*

SAPPHERE I - 2



EPD

THE LANCET

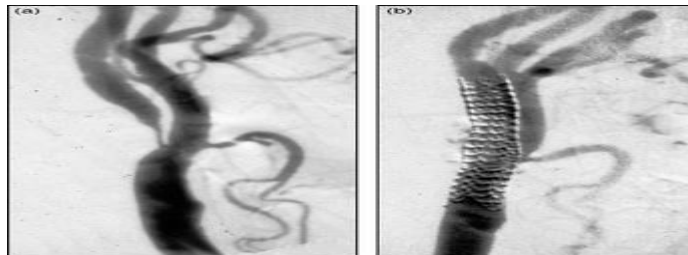
30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial

The SPACE Collaborative Group\*

THE LANCET

Results of the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) study to treat symptomatic stenoses at 2 years: a multinational, prospective, randomised trial

SPACE 1 -2

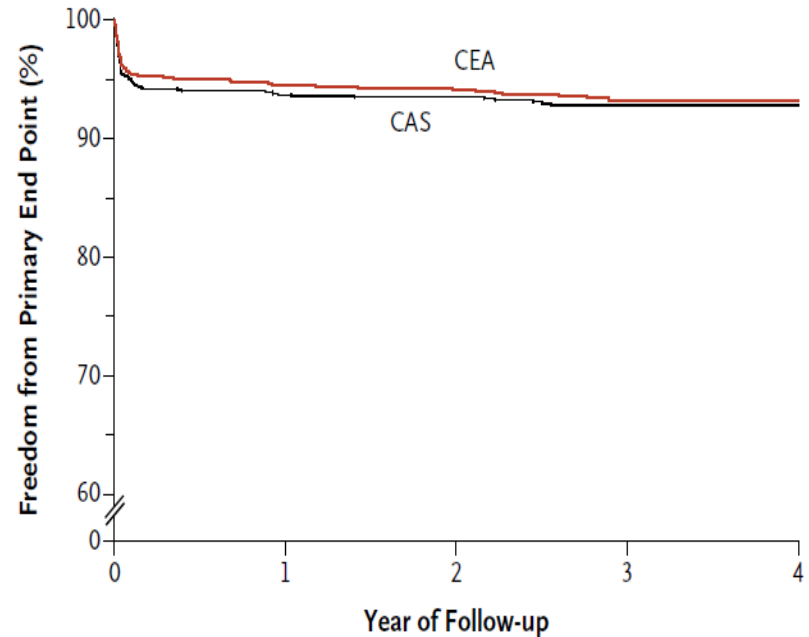


# CREST



## Stenting versus Endarterectomy for Treatment of Carotid-Artery Stenosis

Thomas G. Brott, M.D., Robert W. Hobson, II, M.D.,\* George Howard, Dr.P.H., Gary S. Roubin, M.D., Ph.D., Wayne M. Clark, M.D., William Brooks, M.D., Ariane Mackey, M.D., Michael D. Hill, M.D., Pierre P. Leimgruber, M.D., Alice J. Sheffet, Ph.D., Virginia J. Howard, Ph.D., Wesley S. Moore, M.D., Jenifer H. Voeks, Ph.D., L. Nelson Hopkins, M.D., Donald E. Cutlip, M.D., David J. Cohen, M.D., Jeffrey J. Popma, M.D., Robert D. Ferguson, M.D., Stanley N. Cohen, M.D., Joseph L. Blakeshear, M.D., Frank L. Silver, M.D., J.P. Mohr, M.D., Brajesh K. Lal, M.D., and James F. Meschia, M.D., for the CREST Investigators†



Primary end point - composite of stroke, MI, or death from any cause during the periprocedural period or ipsilateral stroke within 4 years after randomization

NEJM 2010;363:11-23

# CREST

- 2502 pts
- **Symptomatic** stenosis (>50% ECST; >70% on USG; >70% on CT/MRI if 50-69% on USG) – 1321 pts
- **Asymptomatic** stenosis (>60% ECST ; >70% on USG; >80% on CT/MRI if 50-69% on USG) – 1181 pts
- Standard stroke detection protocol in follow-up
- EPD use mandatory whenever feasible – used in 96.1%

# CREST 10 yrs

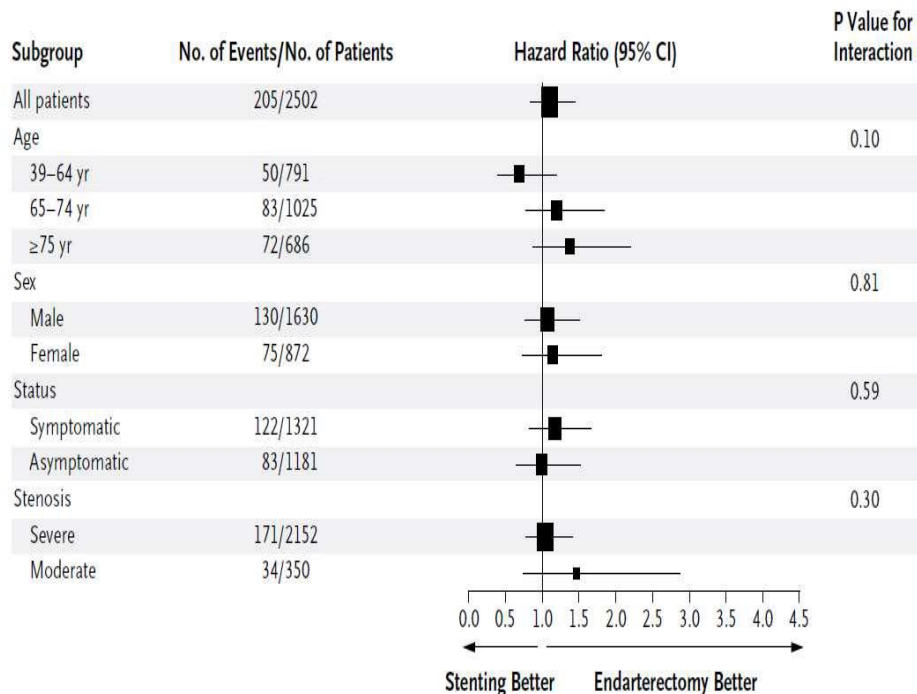
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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Thomas G. Brott, M.D., George Howard, Dr.P.H., Gary S. Roubin, M.D., Ph.D., James F. Meschia, M.D., Ariane Mackey, M.D., William Brooks, M.D., Wesley S. Moore, M.D., Michael D. Hill, M.D., Vito A. Mantese, M.D., Wayne M. Clark, M.D., Carlos H. Timaran, M.D., Donald Heck, M.D., Pierre P. Leimgruber, M.D., Alice J. Sheffet, Ph.D., Virginia J. Howard, Ph.D., Seemant Chaturvedi, M.D., Brajesh K. Lal, M.D., Jenifer H. Voeks, Ph.D., and Robert W. Hobson II, M.D.,\* for the CREST Investigators†

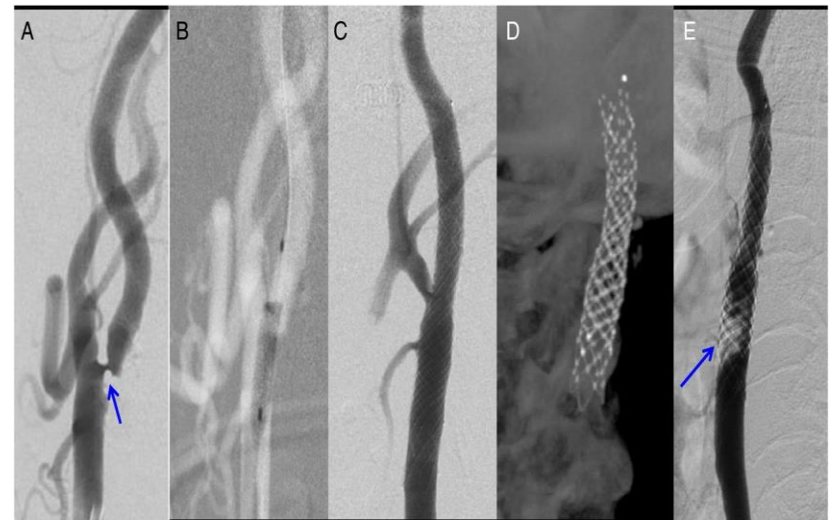
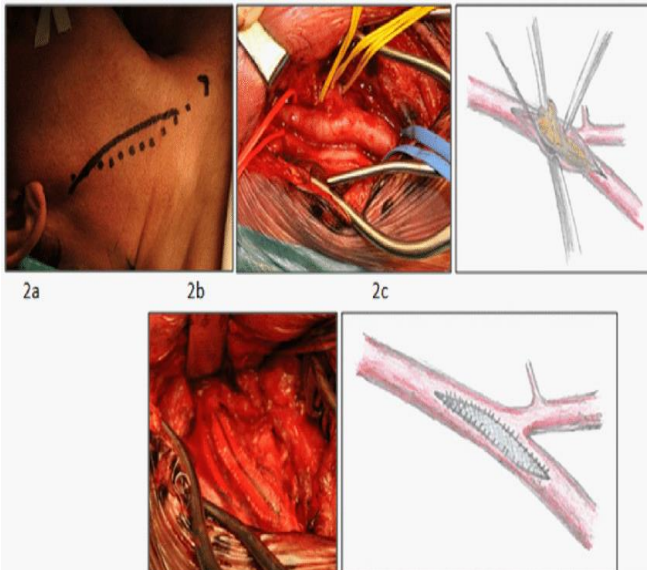
### A Primary Composite End Point



NEJM 2016;374:1021-31

# CREST 2

- Undergoing (expected to finish: December 2020)



# Risk Factors



- Age > 60
- HTN
- CAD
- Smoking
- Family h/o CVA

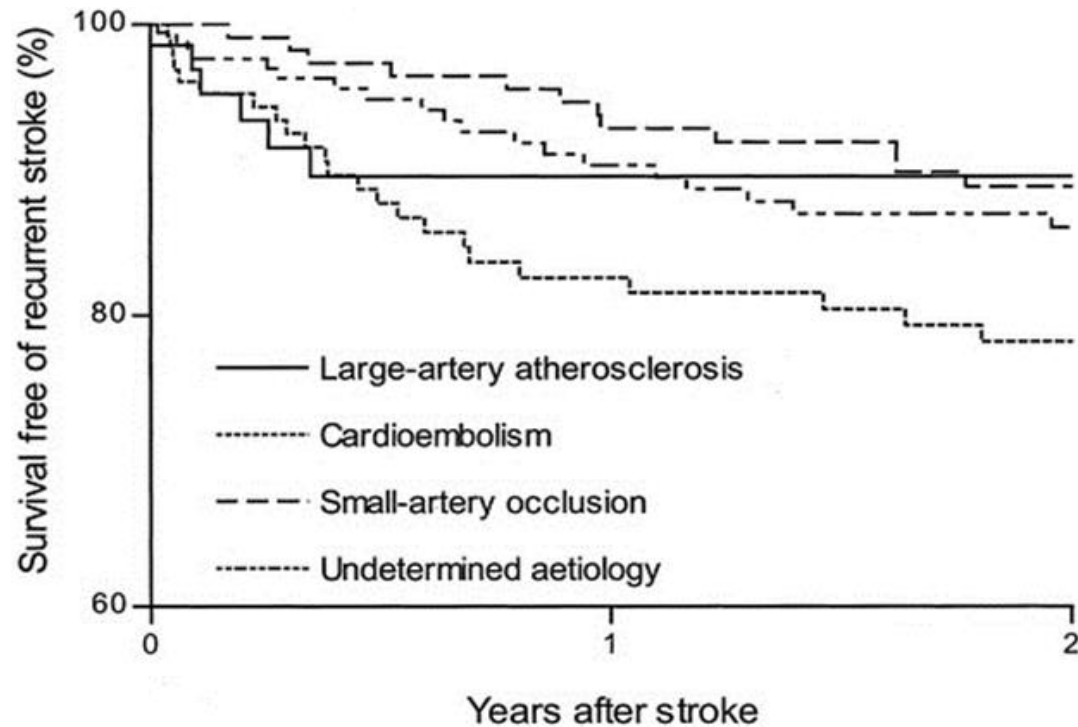
<u># RF</u>	<u>Prevalence</u>
0	2%
1	6%
2	14%
3	16%
4	67%

<u>Risk Factor</u>	<u>OR</u>
• Age > 65	4.1
• Smoking	2.0
• CAD	2.4
• Hyperlipidemia	1.9

Jacobowitz GR, Rockman CB, Gagne PJ, Adelman MA, Lamparello PJ, Landis R, et al. A model for predicting occult carotid artery stenosis: screening is justified in a selected population. *J Vasc Surg.* 2003;38:705-709.

\*Qureshi AI, Janardhan V, Bennett SE, Luft AR, Hopkins LN, Guterman LR. Who should be screened for asymptomatic carotid artery stenosis? Experience from the Western New York Stroke Screening Program. *J Neuroimaging.* 2001;11:105-111.

# Stroke recurrence by etiology



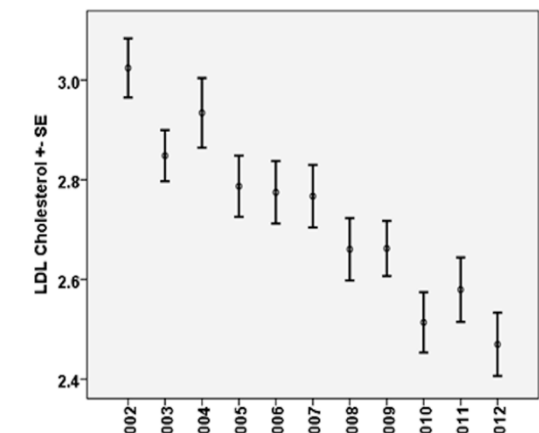
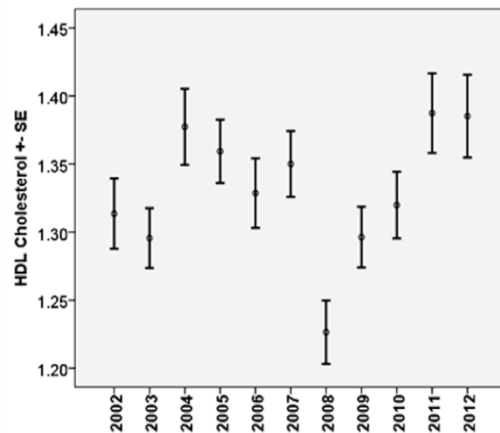
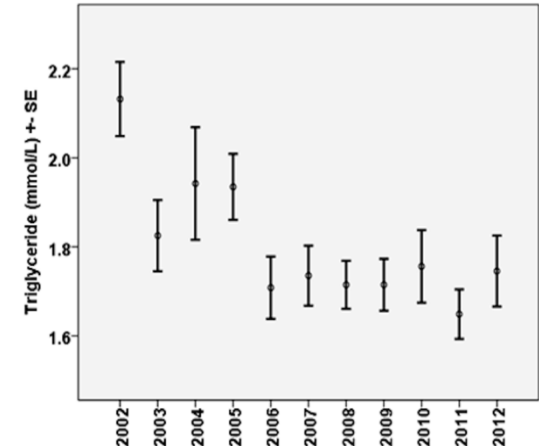
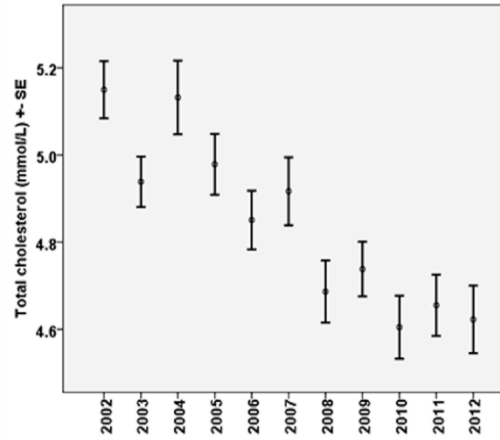
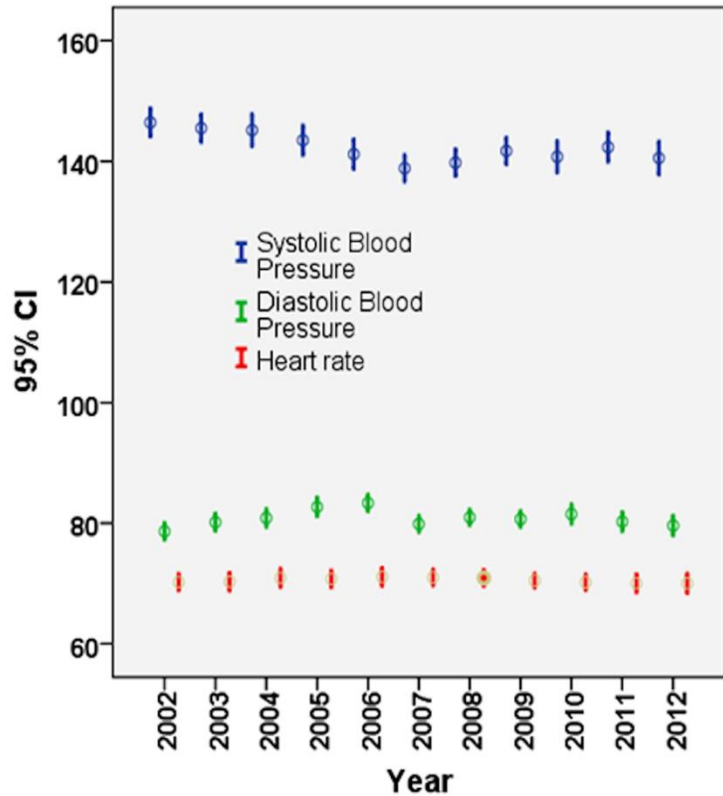
- 2 years  
CE 22% (95% CI 14-30)  
LAA 10% (95% CI 2-18)



Peter L. Kolominsky-Rabas. Stroke. Epidemiology of Ischemic Stroke Subtypes According to TOAST Criteria. Stroke.2001;32:2735-2740



# Decline in risk factors 2002-2012



Significant decrease in blood pressure, cholesterol, smoking, total plaque area, homocysteine, glucose (p<0.05)]

# How Does Pharmacotherapy impact ?

- Medical Therapy

- HBP

Each 10 mmHG drop in BP decreases stroke risk by 33%

- Smoking cessation

- Current smokers RR 4
- Ex-Smokers RR 1.7



Lawes CM, Bennett DA, Feigin VL, Rodgers A. Blood pressure and stroke: an overview of published reviews. Stroke 2004;35:776-785  
Wannamethee SG, Shaper AG, Whincup PH, Walter M. Smoking cessation and the risk of stroke in middle-aged men. JAMA 1995;274:155-160

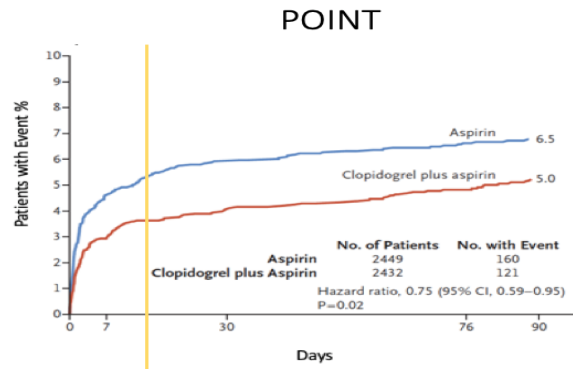
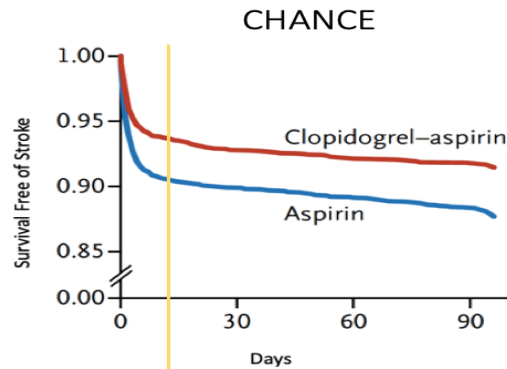
# Antiplatelets

Aspirin: Secondary prevention:



OR 0.77, CI: 0.69-0.86, 2P->0.0001.  
 (3.1 to 2.4%).  
 7 ischemic strokes were avoided for every  
 1000 patients

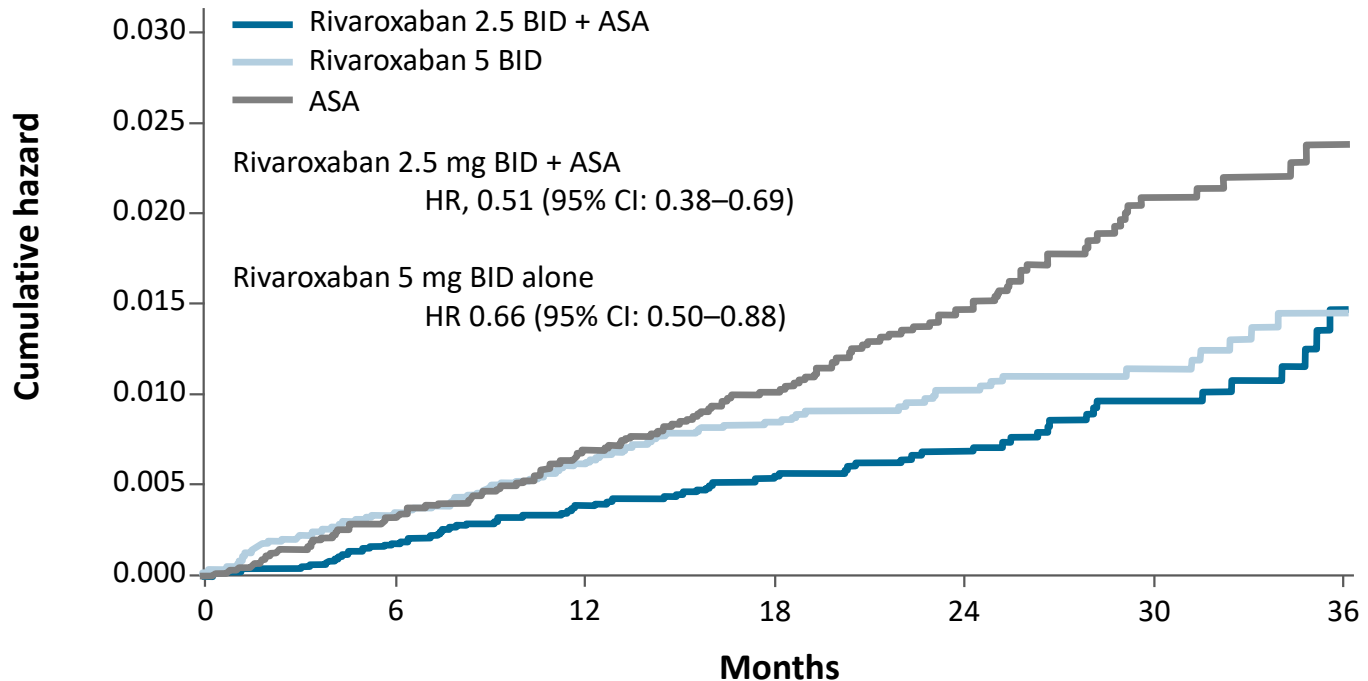
## POINT and CHANCE Trials



RRR=26%  
 ARR=1.7%  
 NNT=59  
 NNH=200

Johnston C, et al. Clopidogrel and aspirin in acute ischemic stroke and high risk TIA N Engl J Med 2018;379:215-225  
 Wang Yongjun et al. Clopidogrel and aspirin in acute minor stroke or transient ischemic attack. N Engl J Med 2013;369:11-19

# COMPASS TRIAL: 49% REDUCTION IN ISCHEMIC/UNCERTAIN STROKE WITH RIVAROXABAN + ASA vs. ASA



**Number at risk**

Rivaroxaban 2.5 BID + ASA	6152	9069	7973	6374	3975	2259	673
Rivaroxaban 5 BID	9117	9016	7893	6291	3943	2228	691
ASA	9126	9022	7874	6251	3951	2231	693

ASA, acetylsalicylic acid; BID, twice daily; HR, hazard ratio; CI, confidence interval;  
 Riva, rivaroxaban  
 Sharma M *et al.* Presented at the International Stroke Conference 2018 (late-breaker presentation LB7).

# Conclusions

- The complex management of carotid artery disease has evolved over the last 20 years.
- Medical management continues to be the pillar
- Untreated risk factors play an etiological role in symptomatic artery transformation.
- Symptomatic carotids with severe and moderate stenosis benefit from early CAE or Stenting along with intensive medical treatment.
- CREST-2 will provide further answers with asymptomatic arteries. **Stay tuned Dec 2020!**

Thank you !!



Any questions?