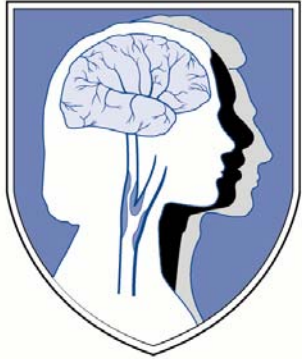


Message to the CREST Principal Investigators

At the request of the NEJM, and until our primary article is published (hopefully), we have agreed to present and discuss only the data contained in these slides, the slides presented at the International Stroke Conference

Thanks for your patience, Tom (and thanks for all of your hard work on CREST...I know that Bob would be proud)



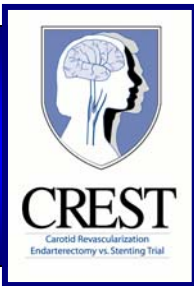
CREST

Carotid Revascularization
Endarterectomy vs. Stenting Trial

Carotid Revascularization Endarterectomy vs. Stenting Trial

Wayne M. Clark, MD

On behalf of the CREST Investigators



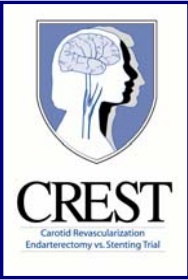
Presenter Disclosure Information

Wayne M. Clark, MD
Carotid Revascularization
Endarterectomy vs. Stenting Trial

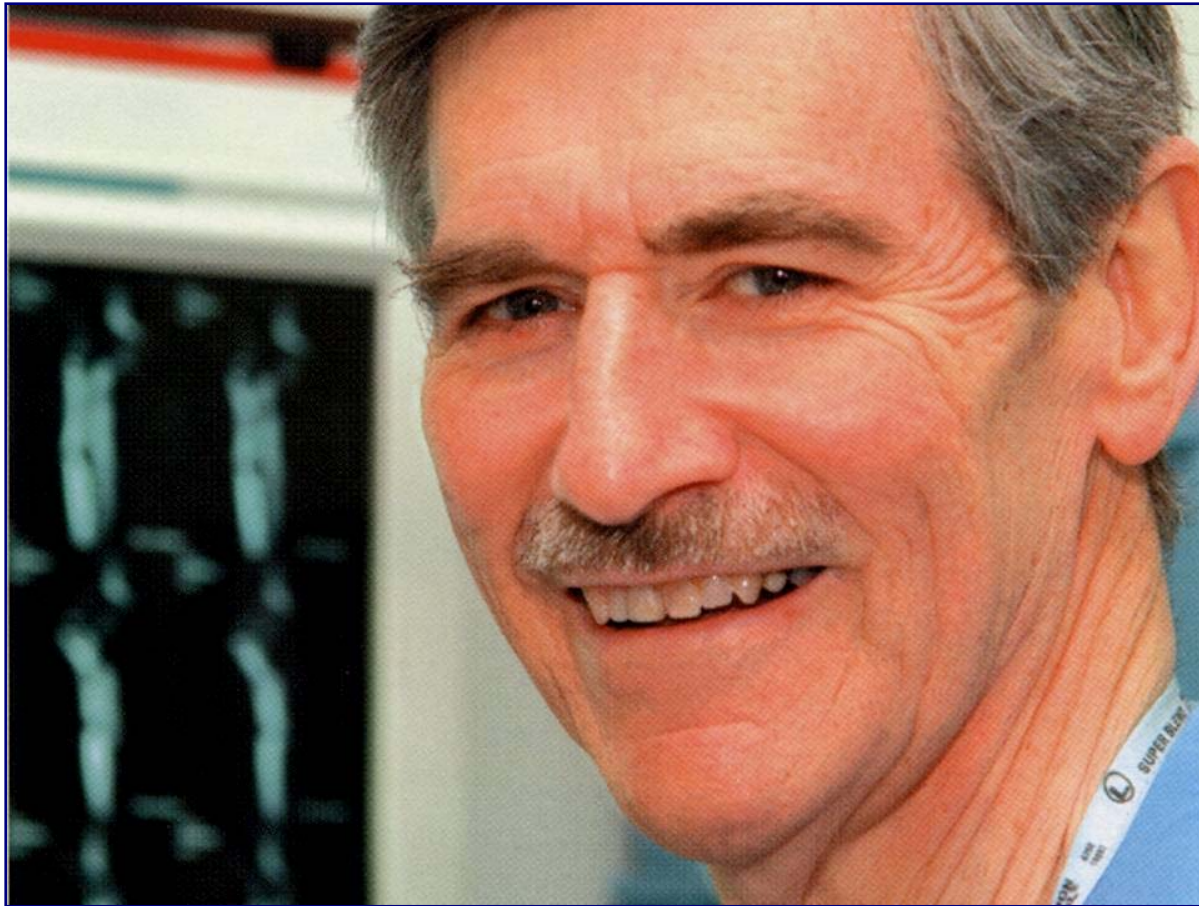
FINANCIAL DISCLOSURE:

No relevant financial relationship exists

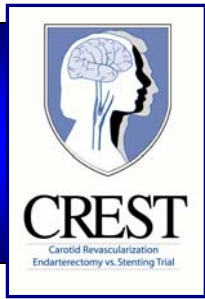
**Grant Sponsorship: NIH – US Public Health Service,
NINDS, R01 NS 038384**



Carotid Revascularization Endarterectomy vs Stenting Trial

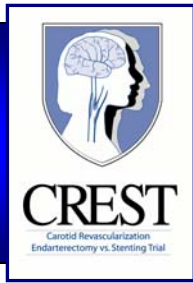


Robert Hobson II MD, PI 1999-2007



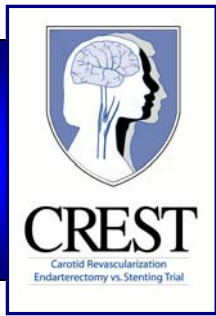
Background

- Carotid artery atherosclerosis causes up to 10% of ischemic strokes
- CEA and CAS are options for revascularization
- By 2000, the safety of CAS demonstrated in case-series justified comparison to CEA



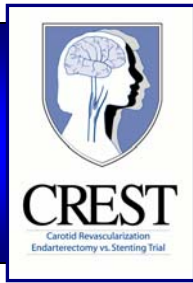
Study Design

- Prospective, multicenter, randomized, controlled trial with blinded endpoint adjudication
- Comparing CEA and CAS in participants with symptomatic and asymptomatic stenosis
- 108 US and 9 Canadian sites
- Team included neurologist, interventionalist, surgeon, and research coordinator at each center



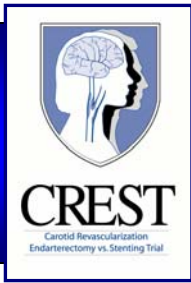
Primary Endpoint

- Peri-procedural
 - a composite of:
 - any Clinical Stroke
 - Myocardial infarction
 - Death
- Post-procedural
 - Ipsilateral stroke up to 4 years



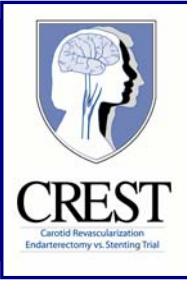
Stroke

- An acute neurological ischemic event of at least 24 hours duration with focal signs and symptoms.
- Adjudicated by at least two neurologists blinded to treatment



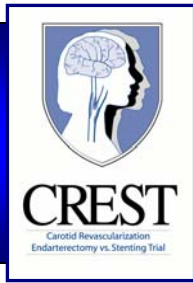
Myocardial Infarction (MI)

- Combination
 - Elevation of cardiac enzymes (CK-MB or troponin) to a value 2 or more times the individual clinical center's laboratory upper limit of normal. **Plus**
 - Chest pain or equivalent symptoms consistent with myocardial ischemia, **or**, ECG evidence of ischemia including new ST segment depression or elevation > 1mm in 2 or more contiguous leads
- Not enzyme-only
- Adjudicated by two cardiologists blinded to treatment



Secondary Aims

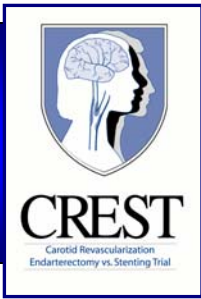
- Differential efficacy by symptomatic status, sex, and age
- Differential restenosis
- Quality of Life and cost effectiveness



Major Eligibility Criteria: Symptomatic

Conventional-risk (not low risk) patients with symptomatic carotid stenosis

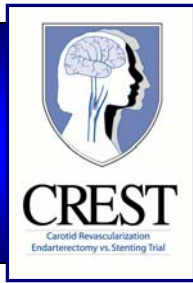
- $\geq 50\%$ by angiography
- $\geq 70\%$ by ultrasound, or
- $> 70\%$ by CTA/MRA if ultrasound is 50-69%



Major Eligibility Criteria: Asymptomatic

Asymptomatic carotid stenosis:

- $\geq 60\%$ by angiography
- $\geq 70\%$ by ultrasound, or
- $> 80\%$ by CTA/MRA if ultrasound is 50-69%

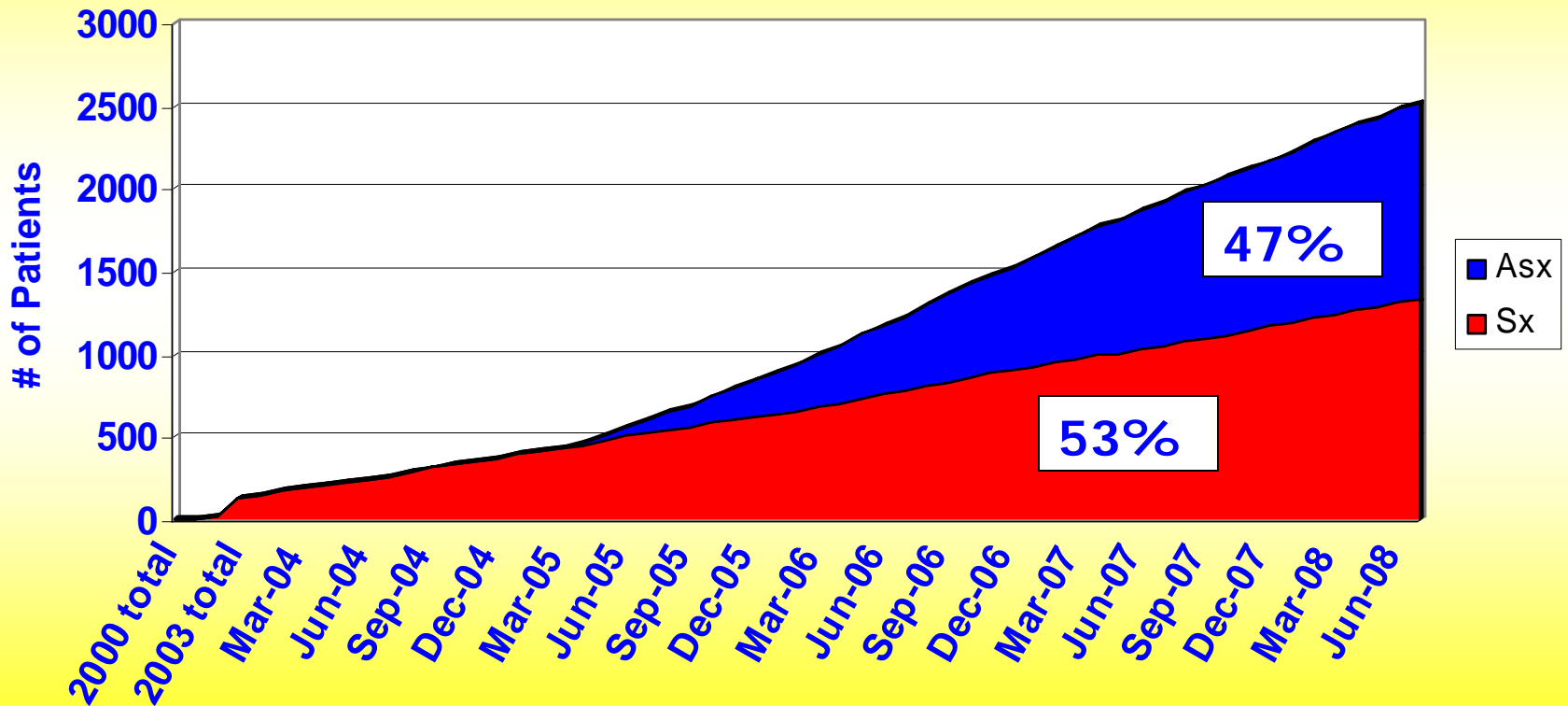


Major Eligibility Criteria: selected exclusions

- Evolving stroke or major stroke likely to confound study endpoints
- Chronic atrial fibrillation
- MI within the previous 30 days
- Unstable angina

CREST Cumulative Randomizations

2000 through July 2008



	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

	CAS (n=1262)	CEA (n=1240)
Cardiovascular disease - %	41	43
Systolic BP, mean mmHg	142	141
% stenosis \geq 70%	85	87
Days from randomization to treatment	6	7

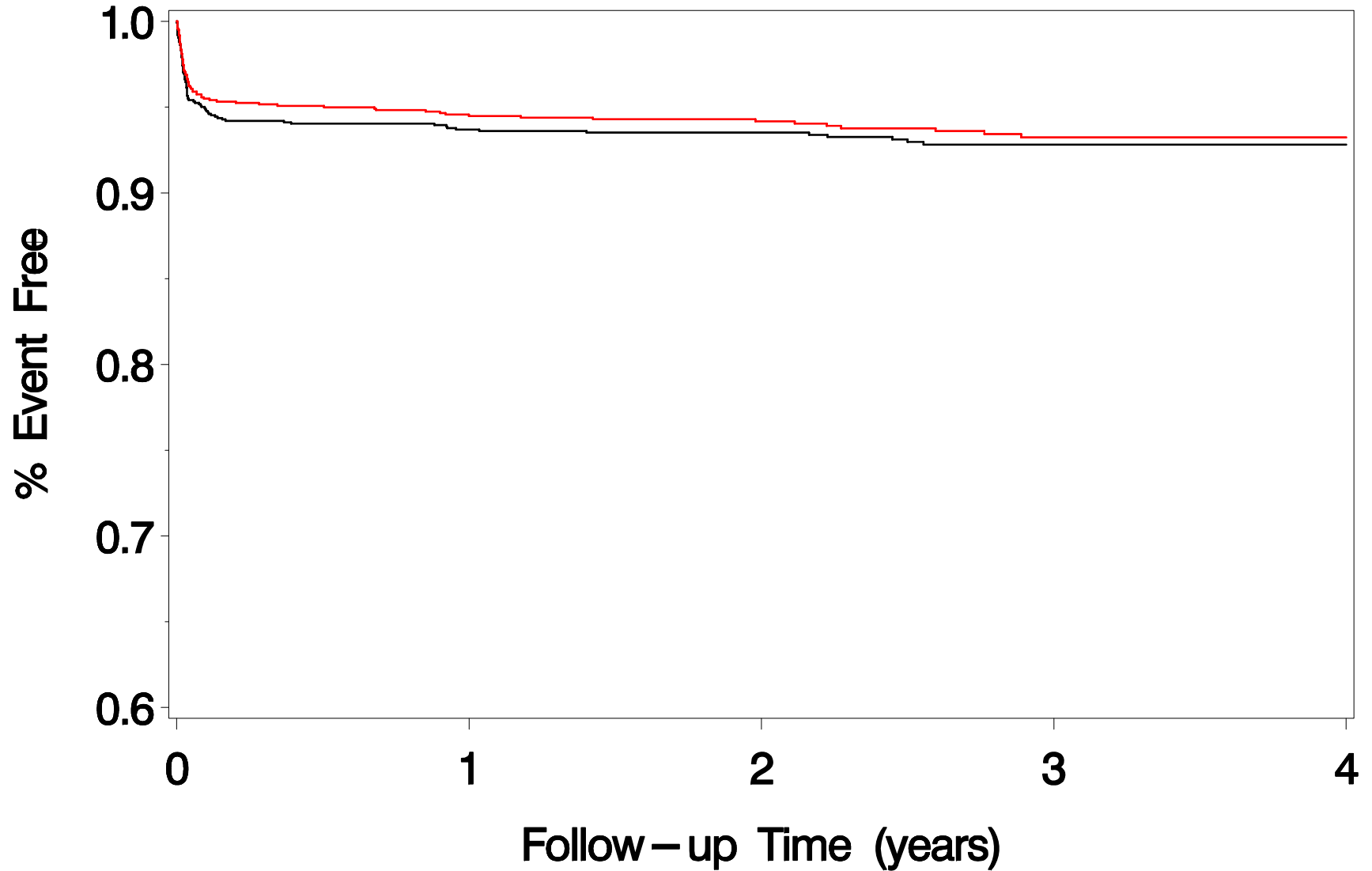
Primary Endpoint \leq 4 years

(any stroke, MI, or death within peri-procedural period plus ipsilateral stroke thereafter)

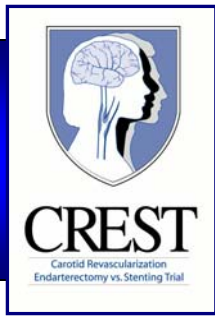
CAS vs. CEA	Hazard Ratio, 95% CI	P-Value
7.2 vs. 6.8%	HR = 1.11; 95% CI: 0.81-1.51	0.51

Primary Endpoint

ITT analysis



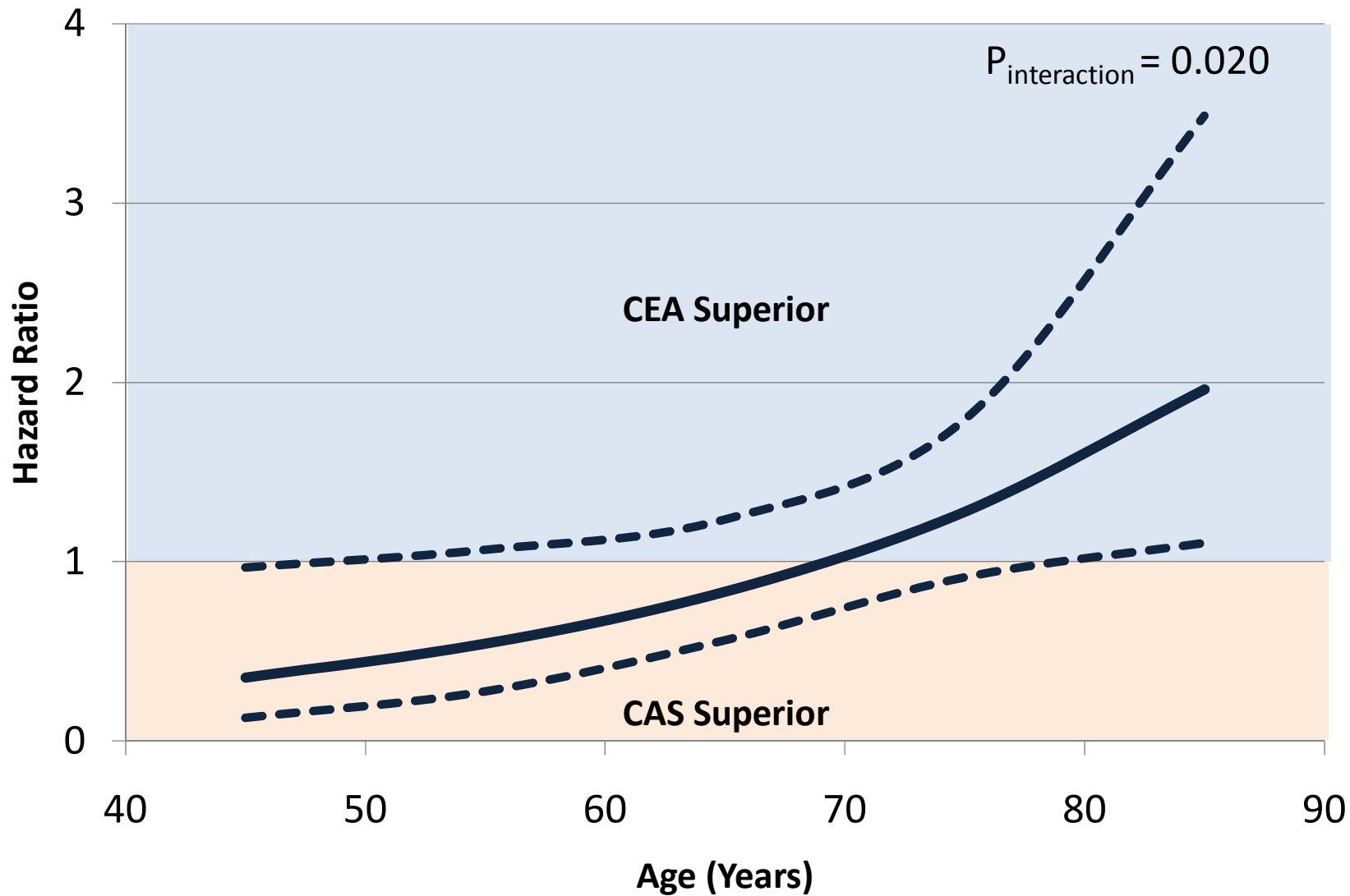
Assignment — CAS — CEA



Interaction with Primary Endpoint

- No effect detected for symptomatic status or sex
- Interaction suggested for age

Primary outcome – 4 year



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%	HR = 1.18; 95% CI: 0.82-1.68	0.38

Peri-procedural Stroke and MI

	CAS vs. CEA	Hazard Ratio 95% CI	P-Value
Stroke	4.1 vs. 2.3 %	HR = 1.79; 95% CI: 1.14-2.82	0.01
MI	1.1 vs. 2.3 %	HR = 0.50; 95% CI: 0.26-0.94	0.03

Peri-procedural Stroke

	CAS vs. CEA	Hazard Ratio 95% CI	P-Value
All Stroke	4.1 vs. 2.3 %	HR = 1.79; 95% CI: 1.14-2.82	0.01
Major Stroke	0.9 vs. 0.6 %	HR = 1.35; 95% CI: 0.54-3.36	0.52

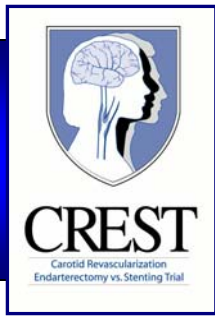
Cranial Nerve Palsies

Peri-procedural

CAS vs. CEA	Hazard Ratio, 95% CI	P-Value
0.3 vs. 4.7%	HR = 0.07; 95% CI: 0.02-0.18	<0.0001

**Ipsilateral Stroke
after
Peri-procedural Period
 ≤ 4 years**

CAS vs. CEA	Hazard Ratio, 95% CI	P-Value
2.0 vs. 2.4%	HR = 0.94; 95% CI: 0.50-1.76	0.85

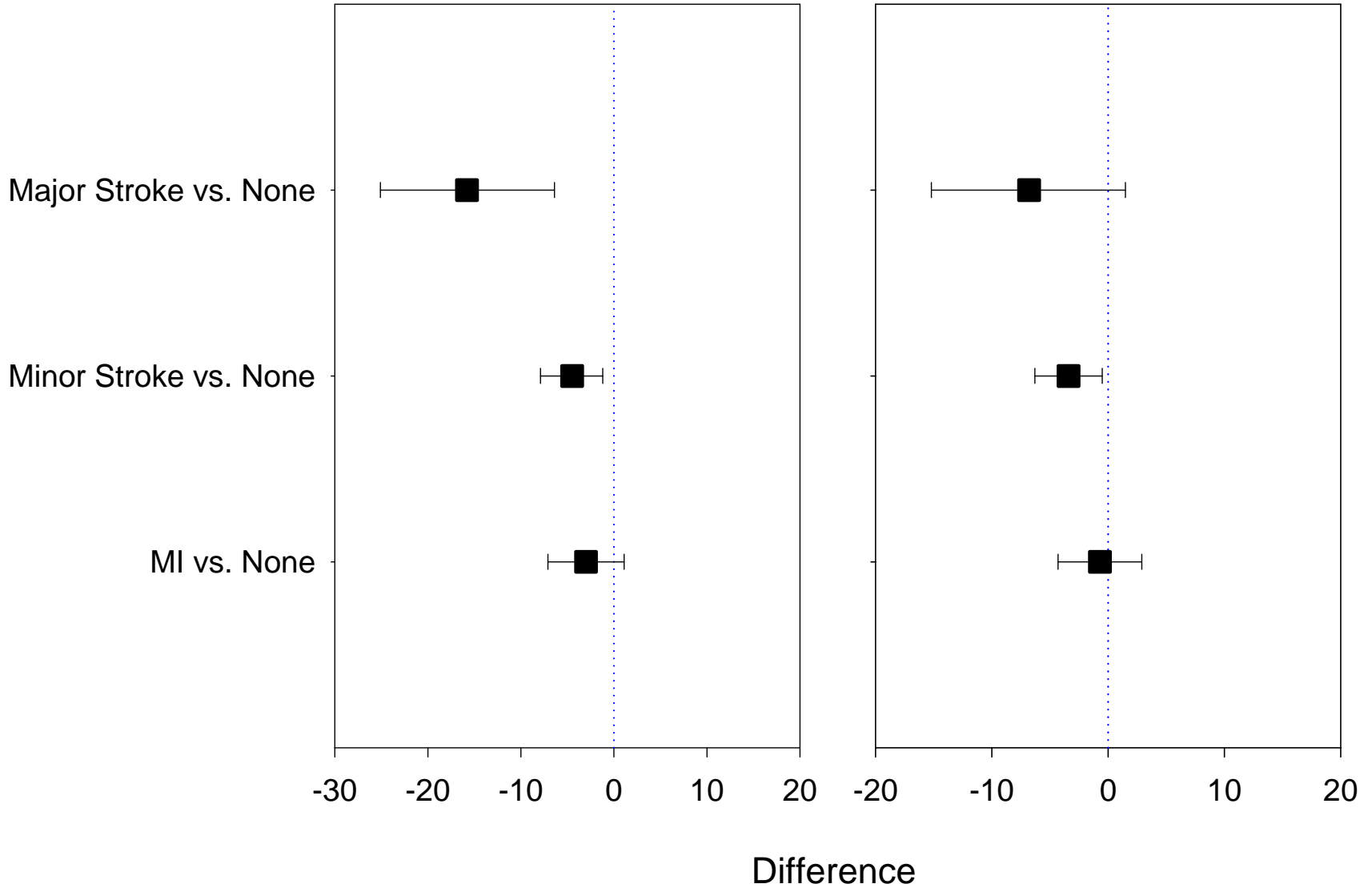


Summary

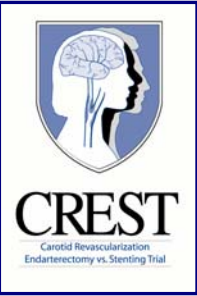
- Similarity in the Primary Endpoint driven by differences in perioperative stroke and MI
- More MIs after CEA
- More strokes after CAS

Physical Component Scale

Mental Component Scale

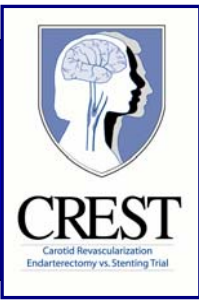


Impact of periprocedural events (stroke/MI) on SF-36 at 1 year adjusting age, sex, symptomatic cerebrovascular disease and baseline SF-36 measures – Growth Curve Modeling.



Conclusions

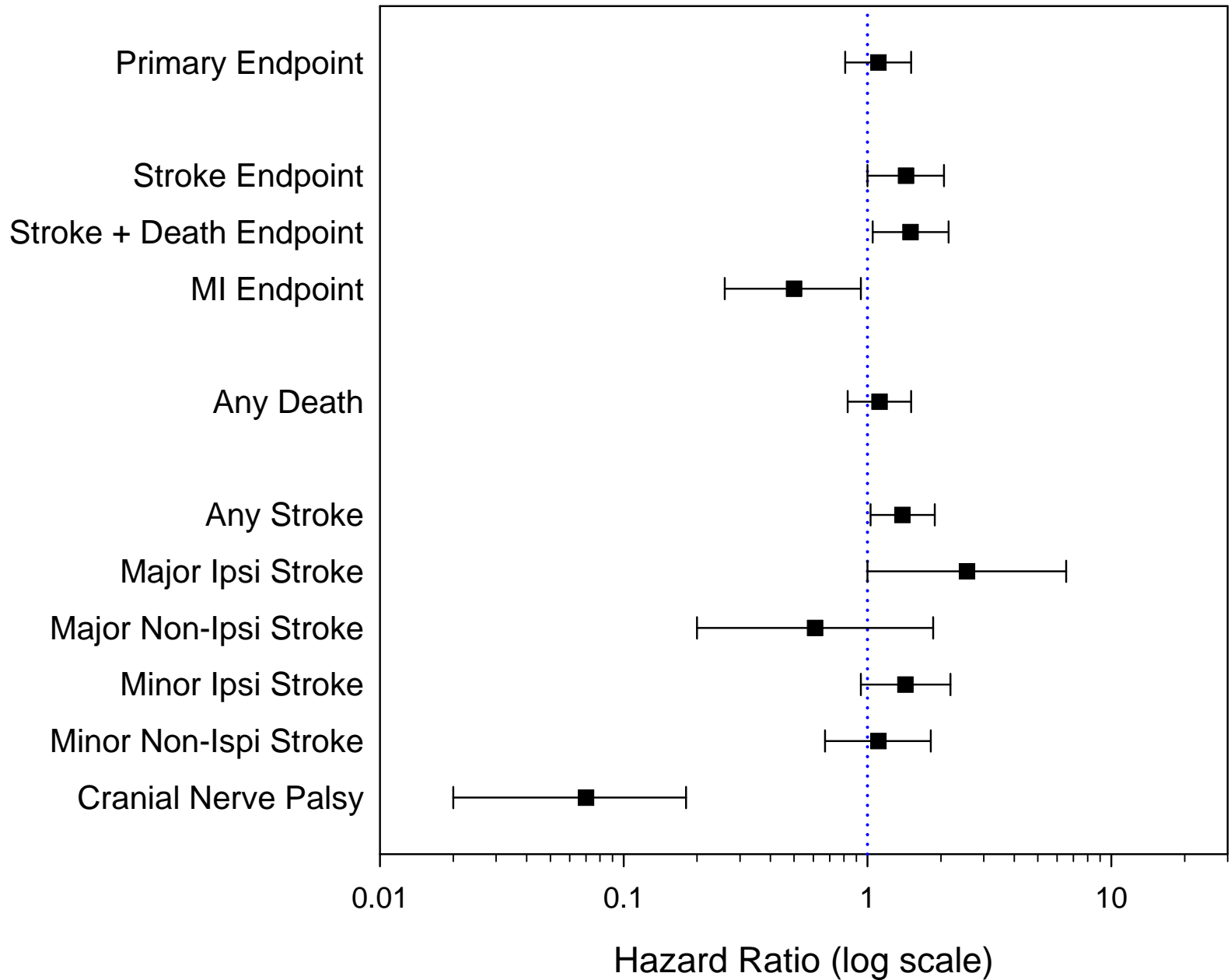
- CEA and CAS have similar net outcomes though the individual risks vary, lower stroke with CEA and lower MI with CAS
- Younger patients may have improved efficacy with CAS and older patients have improved efficacy with CEA



Conclusions

- At experienced centers both CEA and CAS appear to have low perioperative complications and excellent longer-term results
- For the future, both CEA and CAS appear to be useful tools for preventing stroke

← CAS Superior | CEA Superior →



Thank you

- 1565 Lead-in patients
- 2502 Randomized patients
- More than 200 Coordinators
- More than 117 CREST PIs
- Partners at UMDNJ, UAB, HCRI, Mayo
- Three Core Labs
- Quality of Life/Cost Effectiveness Group
- Stroke and MI Adjudication Committees
- Data Safety Monitoring Board (James Marsh, MD, Chair)
- NINDS (Janice Cordell, Wendy Galpern, et al)
- Abbott Vascular, Inc.