Michael Brant-Zawadzki, M.D., F.A.C.R.
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August 16, 2006

Steve Phurrogh, MD, MPA
Director, Coverage & Analysis Group
Office of Clinical Standards & Quality
Department of Health & Human Services
Centers for Medicare & Medicaid
7500 Security Blvd, Mail Stop C1-09-06
Baltimore, Maryland 21244-1850

Dear Dr. Phurrogh:

I understand that CMS is considering expansion of coverage for carotid stenting to patients with asymptomatic disease at high risk for surgery, when stenosis is greater that 80%. I would personally like to write this letter, as opposed to commenting on the web page as requested by one of the vendors, in hopes that a more personal communication will be more likely to be considered as more thorough and objective, rather than prompted by commercial interests

As a neuroradiologist and neurointerventionalist with over 25 years of interest in carotid artery disease and its management, I have welcomed the developments in endovascular treatment for symptomatic carotid occlusive disease. I have carefully evaluated the literature in this area over the years, including that covering surgical and medical management strategy.

Although I welcome the addition of carotid stent angioplasty to our armamentarium for treatment of this disease particularly in symptomatic patients, and use it myself, I am quite concerned about broadening its application for asymptomatic patients. Only 3 studies in the literature address the issue of surgical endarterectomy for asymptomatic disease, 2 of which show a minor benefit in stroke prevention for patients with asymptomatic lesions (reducing stroke risk from a low 2% to 1% per year). Indeed, analysis of the ACAS trial shows we need to do 50 endarterectomies to prevent 1 minor stroke (major stroke rate was statistically similar for both surgical and medical arms). It is not clear that even this benefit would stand up in the face of optimal medical therapy as we would define it today (specifically statin therapy).

Broadening the approach to asymptomatic carotid disease by allowing endovascular interventionalists, and particularly cardiologists to treat disease has some problems. It has been my experience that the definition of 80% is in the eye of the beholder, and depends considerably on the tool used for measurement and the one measuring it. When

surgeons operate on the carotid, other physicians have typically evaluated the patient first, measurements of the stenosis are most likely based on angiograms, although unfortunately ultrasound is still used as the only tool for such measurements (despite the evidence base being in conventional angiography). Nevertheless, there is at least some collaborative oversight by non-operator physicians in such patient management.

Once the tool of stent angioplasty is placed in the hands of clinicians who evaluate the patient, measure the stenosis themselves, and decide on whether or not there is high surgical risk without any additional input from non-incentivized physicians, there exists potential for overuse and abuse. It has been my experience in the pre- clinical trials and post-market studies of the devices to date that some cardiologists planning to perform the procedure may overestimate the degree of stenosis, as well as the risk of conventional surgery in patients that they wish to enroll in such trials. Being the sole determining physicians as to these indications for asymptomatic disease endovascular treatment, allows their unconscious biases to influence patient management decisions. At the very least, CMS might consider a sample audit of the data base available to you with independent observers retrospectively measuring the stenoses in carotids of asymptomatic patients treated by stenting (and also perhaps their surgical risk status).

I would suggest that if indeed coverage is extended to asymptomatic disease in patients at high risk who harbor lesions of 80% or more, which is a reasonable management strategy at this point in time, an independent physician determines the degree of stenosis, and perhaps the degree of surgical risk rather than the physician performing the procedure. Any patient that I personally take to the cath lab for such a procedure has had a surgeon's and often a practicing neurologist's evaluation.

In these days when overuse of medical technology is a concern, and unnecessary expenditures of public funds for healthcare are constantly in the news, CMS should carefully consider loosening the indications for treatment for asymptomatic carotid disease with invasive means, particularly when non-invasive medical therapy has made such great strides, and no double blind trials are available to compare the efficacy of surgical or endovascular interventional therapy against modern day medical management (I would only remind you that numerous trials of statins for heart disease patients demonstrated lowering of stroke risk in such patients by up to 50%).

Thank you so much for your consideration of the above.

Sincerely,

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August 20, 2006

Bram Zuckerman, M.D.
Director, Division of Cardiovascular Devices
Office of Device Evaluation
CDRH Food and Drug Administration
9200 Corporate Blvd.
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Steve Phurrough, M.D., CMS
Director of Coverage Policy
CMS Coverage and Analysis Group
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7500 Security Blvd.
Baltimore, MD 21244-1850

Dear Drs. Zuckerman and Phurrough,

As the principal investigators and scientific leaders of ongoing randomized studies comparing carotid therapies, we are writing to express our serious concerns regarding the potential approval of non-randomized trials or registries of carotid artery stenting (CAS) in patients who are at standard risk for carotid endarterectomy (CEA). Specifically, we understand FDA is in negotiations with a party about the possibility of such a non-randomized study as a means to a standard risk approval. As you are aware, CREST and ACT I, the federally-funded (NIH) and industry-funded randomized clinical trials to which we have committed, were designed to evaluate the safety and efficacy of carotid artery stenting with embolic protection directly compared to carotid endarterectomy in North America. Great efforts were made in these trials to maintain the most rigorous of scientific standards, utilizing randomized, controlled design, in order to produce Level I evidence for the scientific and regulatory communities, and most importantly, for the public. Results from these landmark clinical trials will provide the opportunity to develop the best clinical evidence for decision making in these standard risk patients. Consistent with this, FDA had taken the position that this type of randomized evidence was needed to expand indications to the standard risk population. It is our understanding that CMS has also been seeking this type of Level I evidence. The possible shift in FDA's stance towards non-randomized studies as a means to a standard risk approval would also trigger others to pursue non-randomized studies, with potentially devastating effects on the currently enrolling randomized trials.

Enrollment is always one of the greatest challenges in large randomized clinical trials. Patients participating in CREST and ACT I must, of course, consent for randomization. Given the perceived differences between CAS and CEA, obtaining informed consent often requires that dedicated investigators provide lengthy explanations and education (in lay terms) regarding the concept of clinical equipoise. The availability of carotid artery stenting in nonrandomized studies, with associated CMS or third party coverage, will severely dampen enrollment in the more rigorously designed, randomized trials, if not make it impossible to complete these essential trials. Given the opportunity, as has been demonstrated time and again, both patients and physicians will preferentially choose to enroll in trials with less rigorous design, in which the parties select either CAS or CEA based on preconceived (non-evidence based) ideas about which therapy is "better" for a given patient. While such non-randomized trials have some value, they do not require that physicians acknowledge the presence of clinical equipoise, nor do they provide the type of Level I evidence that is critical for our understanding of the relative roles of each of these therapies. More importantly, if the availability of non-randomized trials prevents CREST and ACT 1 from completing enrollment (which is likely), the public will have been deprived of what is likely to be the only window of opportunity to answer critical and clinically relevant scientific questions. Furthermore, the federal

government will have undermined its own initiative and position that these trials are essential, and will send a strong signal to clinicians and manufacturers that initiating these type of rigorous trials has little value.

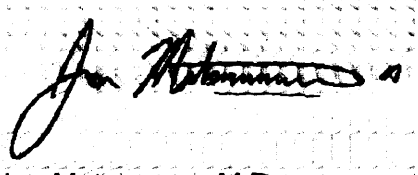
We are not in any way opposed to (and indeed would support) additional trials, whether supported by industry, payers or government, which maintain the same scientific standards that CREST and ACT I incorporate. Indeed, based on precedent, until the questions posed by these randomized trials are resolved, we would expect that FDA would demand similarly rigorous design standards for trials attempting to examine the same issues.

We strongly urge that, in your decision-making for approval and coverage of nonrandomized IDE studies in the standard risk CAS population, you consider the impact on the ability to recruit patients into - and accumulate a more rigorous data set from- existing (and potentially new) trials with randomized controlled design.

Respectfully submitted,

Thomas G. Brott, M.D.,
Professor of Neurology, Mayo Clinic,
National Co-PI CREST

Robert Hobson, M.D
Professor of Surgery UMDNJ
National PI CREST



Jon Matsumura, M.D.,
Associate Professor of Surgery
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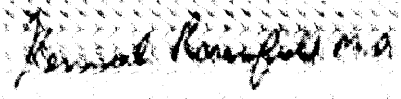

Ken Rosenfield, M.D.,
Section Head, Vascular Medicine and Intervention
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National Co-PI, ACT 1

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RICHARD, I. KIM, M.D.

August 15, 2006

Re: Appeal for Carotid Stenting Reimbursement

To Whom It May Concern:

I am strongly encouraging you to change your reimbursement policy to cover patients who have critical asymptomatic carotid artery stenosis. The basis for this recommendation is really the SAPPHIRE trial. It is the only well-conducted randomized study comparing carotid artery stenting and carotid endarterectomy and it showed a clearcut advantage to carotid stenting in a high risk patient population. It included patients with symptomatic carotid disease greater than 50% stenosis and asymptomatic carotid artery stenosis patients with greater than 80% stenosis, it thus is not logical to reimburse only the symptomatic population since the main inclusion criteria of the study included both of those patient subsets.

Thank you.

With kindest regards as always.

Sincerely,

Farrell O. Mendelsohn, M.D.

J: FMEN0033_5
T: 08/15/2006

Cy: Ms. Susan DeRamos

RE: NCA Tracking Sheet for Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085R3)

I am writing this letter in order to provide comments/ opinions from a practicing clinicians who takes care of patients with carotid artery stenosis.

I believe that carotid artery stenosis and specifically stenting of the carotids is an excellent alternative to the more costly and invasive surgical endarterectomy.

Based on the BEACH, SAPPHIRE and numerous other trials it has been shown that carotid stenting (CAS) is safe, effective and durable procedure. That has been shown without doubt. Hence this should be provided to patients with high surgical risk with either symptomatic or asymptomatic stenosis based on the NASCET critiriea.

More importantly it is imperative that we remove that high surgical risk is determined by "in opinon of surgeon". This is vague and in a field beset with territorial issues frought with problems. We have enough studies to validate what objectively is high surgical risk that we don't need subjective decisions, which sometimes are motivated by personal interest. For example, if a surgeon just beginning to learn the procedure starts obtaining his/her learning curve by treating objectively non-high risk but "in their opinion" high risk patient, would that be acceptable.

Finally if one looks at this from the prespective of cost I think CAS makes sense. As economies of scale set in…i.e. competition between suppliers the costs (most currently on the stent and filter) will come down. Surgery costs will stay the same.
I hope that CMS will think about our patients and let this technology grow.

Utpal H. Pandya, MD

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September 1, 2006

Sarah McClain, MHS
Joseph Chin, MD
Centers for Medicare and Medicaid Services
Department of Health and Human Services
Attention: CAG-00085R3
P.O. Box 8014
Baltimore, MD 21244-8014

Dear Ms. McClain and Dr. Chin:

The American College of Cardiology appreciates the opportunity to comment on the Centers for Medicare and Medicaid Services' (CMS) third reconsideration of its National Coverage Analysis (NCA) on Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085R3). The ACC is a 34,000 member non-profit professional medical society and teaching institution whose mission is to advocate for quality cardiovascular care through education, research promotion, development and application of standards and guidelines, and to influence health care policy.

The American College of Cardiology has been a strong advocate for expanding coverage for clinically appropriate use of carotid artery stent therapy and is intimately involved with the process for developing physician training, education, certification, and creation of a web-based data collection tool based on the strength of the National Cardiovascular Data Registry (NCDR).

In general, the ACC supports the expansion of coverage as outlined in the request from Guidant/Abbott Vascular, Inc., although we believe some changes are necessary before final adoption by CMS. Following are ACC's recommendations for your consideration.

These comments address each of the issues identified in the NCA, and other related issues that pertain to the March 2005 coverage decision by CMS, including:

- Inadequate data on long-term outcomes and durability in CAS;
- No proven ability to transfer the technology and results obtained from the trial sites to a non-trial clinical practice setting; and
- A clarification of the role of stenting in asymptomatic high surgical risk patients with medical comorbidities.

Although yet to appear in peer-reviewed journals, both the SAPPHIRE and ArCHER trials have completed 3-year follow-up of pivotal patients. Data presented at National meetings have demonstrated low stroke and death rates when compared to surgical carotid endarterectomy (CEA). For example, submitted ArCHER data demonstrates annual ipsilateral stroke rates of 1.2% followed out to 36 months. These data support the durability of CAS in high risk patients.

There are no new randomized data evaluating high-risk patients with moderate carotid artery stenosis and symptoms. However, the SAPPHIRE study did include such patients, with similar stroke and death rates among patients treated with CAS and CEA. Current standard of care recommends CEA in patients with symptoms and ≥50% internal carotid artery stenosis, based on the NASCET data. We strongly support providing CAS as an option for symptomatic patients with ≥50% internal carotid artery stenosis who are viewed to be at high risk for surgical therapy.

Since the prior March 2005 CMS decision, there are no new randomized trial data in CAS or CEA in asymptomatic high surgical risk patients. There is post-hoc analysis data from the SAPPHIRE trial suggesting a statistically significant (p=0.04) reduction in the primary endpoint at 12-months in asymptomatic high surgical risk patients treated with CAS vs. CEA.

In addition, there are important data to consider both on the natural history of asymptomatic patients by both stenosis severity and comorbidities as well as the influence of medical therapy in this group.

The Asymptomatic Carotid Stenosis and Risk of Stroke Study (ACSRS), an observational international multi-center trial examining the outcomes of patients with significant stenosis, published its results in 2005 (Nicolaides AN, Kakkos SK, Griffin M, et al. Severity of asymptomatic carotid stenosis and risks of ipsilateral hemispheric events: results from the ACSRS study. Eur J Vasc Endovasc Surg 2005; 30: 275-284). The study followed 1115 patients who were asymptomatic with ≥50% internal carotid artery stenosis. Patients were followed for a mean of 37 months. In this prospective observational study, patients with more severe ipsilateral carotid stenosis, contralateral transient cerebral ischemia, and impaired renal function were found to be at significant risk for ipsilateral stroke and death (7.3%/year) and 4.3% stroke risk/year.

The influence, and superiority, of medical therapy over revascularization for stroke reduction *specifically in patients with established asymptomatic carotid artery stenosis*

has not been demonstrated and has not been further studied since the previous CMS coverage decision. Two recent studies relevant to this question shed some light in the application of risk factor modification in broader atherosclerotic populations have supplied data new since the prior coverage decision.

- The Heart Protection Study (Collins R, Armitage J, Parish S, Sleight P, Peto R. Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20,536 people with cerebrovascular disease or other high-risk conditions. Lancet. Mar 6, 2004.363; 9411; 757) examined the effect of statins on the incidence of stroke in over 20,000 patients (average age ~64 years) with significant cardiovascular risk, and found a reduction in all stroke at 5 years compared to placebo in this population (4.3% vs. 5.7%, $p<0.0003$). However, when the population with established cerebrovascular disease was analyzed, statin benefit was lost. Worth noting is the low 5 year rate of ipsilateral stroke, again confirming that stroke risk is dependent on severity of presenting atherosclerosis and comorbidities, and that normal risk patient event rates (i.e., ACAS and ACST) can not be definitively applied to the aged population with high risk co-morbidities under consideration by CMS.
- The SPARCL study (Amarenco P, Bogousslovsky J, Callahan A, et al. High-dose atorvastatin after stroke or transient ischemic attack. The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) investigators. N Engl J Med 2006; 355: 549-59.) randomized 4731 patients with recent TIA or stroke to 80 mg of atorvastatin or placebo. After 5 years, there was an absolute stroke reduction of 2.2% (11.2% vs. 13.1%, P=0.05) among patients receiving atorvastatin. Unfortunately, although 70% of patients were enrolled with stroke as the qualifying event, and ~65% of those were ischemic, there is no mention of concomitant carotid artery disease. Therefore, extrapolation of this data to a population with carotid disease is difficult at best.

We continue to support the notion that the risk of ipsilateral stroke is related to both stenosis severity and comorbidities. Although risk factor modification is an important component of the management of these patients, medical therapy has not been demonstrated to have a significant effect on stroke reduction in patients with established carotid artery disease. For asymptomatic patients with severe (≥80%) internal carotid artery stenosis viewed to be at high-risk for surgical therapy, we support the approval of CAS as a therapeutic alternative.

The language suggesting that "…a patient should be determined to be a poor candidate for carotid endarterectomy (CEA) 'in the opinion of a surgeon'" has been, in our opinion, misinterpreted. Although this issue of "high surgical risk" is central to the coverage decision, it does not require a surgical opinion. The medical and anatomic factors which result in high surgical risk have been clearly described, and physicians with internal medicine and cardiovascular medicine training and expertise are the most qualified to determine "high surgical risk." We support deleting this language.

In response to the CMS question regarding "…establishing more formal accreditation and recertification processes for CAS facilities, including those developed by national

professional societies," the ACC has led this pathway with the development of the NCDR™ CARE Registry™. The CARE Registry™, which stands for Carotid Artery Revascularization and Endarterectomy, has been developed in partnership with the Society for Cardiovascular Angiography and Interventions. It uses standardized data elements, developed from evidence-based guidelines and published literature, to accurately capture and report outcomes and performance measures for patients receiving carotid artery stenting procedures (CAS). Some of the key benefits it offers hospitals and CMS include:

- Annual on-site audit program;
- Quarterly benchmarking reports comparing individual hospital outcomes with those of peer groups and the national experience;
- Optional data collection for carotid endarterectomy procedures;
- Design that was developed collaboratively by a multidisciplinary physician team that included representation from cardiology, neurology, invasive radiology, vascular surgery, vascular medicine and other specialties;
- Independent neurologic (e.g. stroke) assessment; and
- Accurate assessment of adverse outcomes, including for 30 day patient follow-up.

The CARE Registry™ may be used by an accrediting program because some facilities will be using it to meet the CMS data collection requirements.

The NCDR™ supports CMS's requirement that facilities collect data on all CAS procedures performed at that facility in order to receive Medicare payment. The CARE Registry™ offers healthcare providers a robust tool for collecting data and measuring quality of care for patients with cardiovascular disease, using standardized data elements and definitions. This will enable individual facilities to systematically analyze their data in a rigorous and methodological fashion, and use it to improve patient care.

In an issue related to this NCA, we echo the Society for Cardiovascular Angiography and Interventions' (SCAI) concerns regarding the existing NCD's inflexibility in not covering carotid stenting procedures where embolic protection is attempted, but not deployed successfully. By not covering this procedure under such circumstances, the NCD can force providers into the ethical dilemma of having to choose between two risky options:

1. Proceed with the procedure and risk non-payment; or
2. Terminate the procedure altogether—which may not be in the best interests of the patient, especially where the patient requires the placement of a stent irrespective of whether embolic protection is successfully employed during the procedure.

We do not believe this was intended when the NCD was originally issued, and recommend that this dilemma can be best avoided with a coverage decision which allows coverage when embolic protection is attempted but unsuccessful.

In conclusion, the ACC strongly supports expansion of coverage for carotid artery stent deployment for patients at high risk for surgical therapy of extra-cranial carotid artery disease:

- With symptoms and stenosis ≥50%
- Without symptoms and stenosis ≥80%.

We do not view CAS as exclusive therapy for carotid stenosis. There are many clinical scenarios in which CEA or medical therapy might be appropriate, and there are centers that provide excellent surgical therapy for high risk patients. However, approval of CAS provides a reasonable and scientifically sound alternative in appropriate patients, when the procedure is performed by skilled interventionists in credentialed centers. This is a responsible approach to a population of patients with multiple co-morbidities and challenges, and is appropriate. In addition, post-marketing surveillance data will aid in demonstrating safety and efficacy of both treatments in community and academic institutions, providing reassurance to Federal government, physicians, and most importantly, our patients.

Again, the ACC appreciates the opportunity to comment on CMS' NCA on PTA of the Carotid Artery Concurrent with Stenting. We would be happy to work with you on any of our recommendations. If you have any questions, please contact Rebecca Kelly, Director of Regulatory Affairs at 301.493.4398, or by e-mail at rkelly@acc.org.

Sincerely,

Steven E. Nissen, MD, F.AC.C.
President

Michael R. Jaff, MD, F.A.C.C.

SOCIETY OF INTERVENTIONAL RADIOLOGY
Enhanced care through advanced technology℠

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September 1, 2006

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Comments submitted electronically via CMS Web site and Email, http://www.cms.hhs.gov/mcd/viewtrackingsheet.asp?id=194 and joseph.chin@cms.hhs.gov, respectively.

RE: NCA Tracking Sheet for Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085R3)

Dear Dr. Chin:

The Society of Interventional Radiology (SIR) is a physician association with over 4,300 members that represents the majority of practicing vascular and interventional radiologists in the United States.

SIR having reviewed the proposed revisions to the national coverage determination policy "Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085R3)" offers the following general and specific comments:

CAS comparable to CEA
SIR finds that carotid endartectomy (CEA) remains the gold standard for treating carotid stenosis. However, one-year published data (Yadav, 2004) and three-year trial data, which have been presented, show that carotid stenting (CAS) is durable as compared to CEA; in addition, there may be advantage to CAS over CEA in high risk patients, with a smaller restenosis rate and less morbidity (SAPPHIRE 2002, ARCHER-Gray 2006, SECURITY 2003, BEACH 2005, MAVErIk 2004 and CABERNET 2004). SIR supports that CMS continue to examine the efficacy for both CEA and CAS as treatment options for carotid disease as compared to medical treatment without intervention by continuing to support cases being entered into national registries and continued support of post market studies already initiated.

Coverage for Symptomatic Patients
Those at highest risk for stroke from carotid disease are symptomatic. SIR supports the expansion of coverage of CAS for high risk symptomatic patients with severe stenosis of ≥ 50% as proposed, based on outcomes from one-year published data (Yadav, 2004) and three-year trial data, which have been presented (SAPPHIRE 2002, ARCHER-Gray 2006, SECURITY 2003, BEACH 2005, MAVErIk 2004 and CABERNET 2004).

Coverage for Asymptomatic Patients
Although asymptomatic patients will continue to need further study, we would support CMS' decision in regards to this group of patients. We believe this group of patients will need to continue to be evaluated through national registries and post market studies. SIR also finds that the collection of 30-day post procedure data is insufficient to effectively evaluate these procedures for asymptomatic patients and supports the collection of, at minimum, one-year post procedure data. SIR supports coverage for high risk asymptomatic patients treated with CAS or CEA when provided within the context of an approved clinical trial.

Registry Participation as a Requirement of Site Approval
SIR supports that site approval for the performance of CAS, as well as CEA, require that all these procedures be tracked through a national registry in support of the continued compilation of data. All such registries should be monitored and have audit mechanisms in place.

Embolic Protection Device
SIR finds that there is a small subset of patients in whom use of an embolic protection device (EPD) makes CAS higher risk than CAS without EPD. In these patients who otherwise meet the required coverage criteria, there is sufficient evidence to support the performance of CAS with or without the placement of an embolic protection device. This position is supported by the findings of Sztriha, Vörös, Sas, et al (2004), which concluded that "Carotid artery stenting without protection devices appears to be safe". We believe that the decision to use or not use EPD needs to be left to the qualified treating physician, and that coverage should not be limited to CAS with EPD.

If you have any questions pertaining to the comments presented or regarding any other interventional radiology procedures or services, please feel free to contact Tricia McClenny, associate executive director at (800) 488-7284, ext. 588, or McClenny@SIRweb.org.

Sincerely,

[Endorsed copy mailed this day.]

Katharine L. Krol
President

Cc: David Sacks, MD
Michael Edwards, MD
Robert Raabe, MD
John J. Connors, MD
Richard A. Baum, MD
Tricia McClenny
Dawn Hopkins

References Citied

Yadav, JS, Wholey, MH, Kuntz, RE, et al. Protected Carotid-Artery Stenting versus Endardectomy in High-Risk Patients. NEJM. 2004; 351:1493-1501.

Sztriha, LK, Voros, E, Sas, K, et al. Favorable Early Outcomes of Carotid Artery Stenting Without Protection Devices. Stroke. 2004; 35:2862-2866.

Alamowitch, S, Eliasziw, M, Barnett, HJM. North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the ASA and Carotid Endarterectomy (ACE) Trial Groups: The Risk and Benefit of Endarterectomy in Women with Symptomatic Internal Carotid Artery Disease. Stroke. 2005; Jan;36(1):27-31

Gray WA, Hopkins LN, MD, Yadav S, et al for the ARCHeR Trial Collaborators. Protected carotid stenting in high-surgical-risk patients: The ARCHeR results. J Vasc Surg 2006;44:258-269.

SAPPHIRE 2002: Stenting and Angioplasty with Protection in Patients and High Risk for Endarterectomy– unpublished data, trial halted due to low enrollment; presented in February 2003.

MAVErIC (Evaluation of the Medtronic AVE Self-Expanding Carotid Stent System with D Protection in the treatment of carotid stenosis)– unpublished data, presentation at the Transcatheter Cardiovascular Therapeutics meeting 2004.

SECURITY: Carotid artery stenting with a distal-protection device safe in high-risk patients- unpublished data, presented by Patrick L Whitlow at the Transcatheter Cardiovascular Therapeutics meeting 2003.

BEACH: Boston Scientific EPI-A Carotid Stenting Trial for High Risk Surgical Patients– unpublished data, presented at the 2005 International Stroke Conference 2005.

CABERNET: Carotid Artery Revascularization Using the Boston Scientific FilterWire and the EndoTex NexStent– unpublished data, presented at the 2005 International Stroke Conference 2005.

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September 1, 2006

The Honorable Mark McClellan, MD, PhD
Administrator
Centers for Medicare and Medicaid Services
Department of Health and Human Services
Room 445-G
Hubert H. Humphrey Building
200 Independence Avenue, SW
Washington, DC 20201

Re: Proposed Expansion of National Coverage for Carotid Artery Stenting in High Surgical Risk Patients (CAG – 00085R2)

Dear Dr. McClellan:

Boston Scientific Corporation's Peripheral Interventions Division appreciates the opportunity to present these comments and policy recommendations on the Centers for Medicare and Medicaid Services' (CMS) reconsideration of its coverage policy for carotid artery stenting.

As the world's largest company dedicated to the development, manufacturing, and marketing of less-invasive therapies, Boston Scientific supplies medical devices and technologies used by physicians representing cardiac rhythm management, cardiovascular (including peripheral interventions and vascular surgery), endosurgery, and neuromodulation.

Executive Summary

Boston Scientific strongly supports the expansion of Medicare coverage for carotid artery stenting (CAS) in patients who are at high risk for carotid endarterectomy (CEA) and who are either symptomatic with stenosis of 50%-69% or asymptomatic with stenosis ≥80%. Coverage expansion is justified by the wealth of available clinical data for CAS in these patient populations, and it would align Medicare coverage with FDA-approved labeling for commercially available carotid stent systems.

The incidence and prevalence of carotid artery disease (CAD) is well-known. Approximately 30% of ischemic strokes result from CAD, resulting in estimated direct and indirect costs of $57.9 billion for 2006.[1] The mean lifetime cost of ischemic stroke in the United States is estimated at $140,048.[2] CEA is the most frequently performed surgical procedure to prevent stroke.[3,4] In the past several years, CAS has

[1] Thom T, *et al*. Heart Disease and Stroke Statistics – 2006 Update: A Report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2006;113;85-151.
[2] Ibid.
[3] Ibid.
[4] As cited in Gray WA, *et al*. Protected carotid stenting in high-surgical-risk patients: The ARCHeR results. *J Vasc Surg*. 2006;44:258-69.

emerged as an alternative to CEA for patients who are at high risk for complications from surgery. Currently available CAS systems have been approved by the FDA for use in high surgical risk, symptomatic patients with stenosis ≥50% and high surgical risk, asymptomatic patients with stenosis ≥80%.

CMS, through both its coverage and payment policies, has acknowledged the growing acceptance among clinicians of CAS as a safe and effective treatment option for high surgical risk patients, stating, "We note that the number of procedures has increased…, thus indicating acceptance of this procedure by the medical community as a main-stream surgical alternative."[5] In March 2005, CMS issued a national coverage determination (NCD) providing coverage for high surgical risk, symptomatic patients who have carotid artery stenosis of ≥70%. Thus high surgical risk, symptomatic patients with stenosis 50%-69% and high surgical risk, asymptomatic patients with stenosis ≥80%, a substantial portion of the population described in the FDA labeling for carotid stenting systems, are left without coverage outside of post-market studies and IDE trials.

Boston Scientific believes that CMS's March 2005 decision to cover only high surgical risk, symptomatic patients with ≥70% stenosis was based on a flawed comparison to safety and efficacy data on CEA in both high surgical risk and non-high risk patients with stenosis ≥50%. In the North American Symptomatic Carotid Endarterectomy Trial (NASCET), CEA was found to provide only marginal benefit for patients with 50%-69% stenosis. However, the patients studied had varying levels of risk for surgery, whereas CAS is only indicated in patients who are defined as being at high risk for surgery and indeed would not qualify to participate in NASCET. Therefore, Boston Scientific urges CMS to evaluate the safety and efficacy of CAS based on data specific to the high surgical risk, symptomatic patient population with stenosis ≥50% and the high surgical risk, asymptomatic patient population with stenosis ≥80%.

CMS CAS Coverage Reconsideration Should Compare Similar Populations

In its March 2005 decision, CMS cited findings in NASCET suggesting that CEA in patients with symptomatic moderate carotid stenosis of 50%-69% yielded only a moderate reduction in the risk of stroke.[6] The agency also referenced the "restraint" of investigators in both the Asymptomatic Carotid Atherosclerosis Study (ACAS) and the Asymptomatic Carotid Surgery Trial (ACST) involving CEA in asymptomatic patients as a rationale for non-coverage of CAS in high surgical risk, asymptomatic patients.[7]

CMS appears to have reached its decision by using the "transitive" property, applying data on one procedure in one population to make decisions on the use of another procedure in another patient population with different characteristics and risk factors. CMS's approach compared patient groups based on the presence of symptoms and the degree of stenosis and did not consider that CAS patients are at high risk for surgery and the majority of CEA patients studied are not at high risk. Such a comparison is inappropriate because high surgical risk and non-high surgical risk patients have different underlying adverse event risks.[8,9] In particular, it is not appropriate to assume that because CEA had marginal benefits in mixed-risk, symptomatic patients with stenosis 50%-69%, CAS would offer only marginal benefits for high surgical risk, symptomatic patients with stenosis 50%-69%.

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[5] 42 CFR Parts 409, 410, 412, *et al*. Revision to Hospital Inpatient Prospective Payment Systems—2007 FY Occupational Mix Adjustment to Wage Index; Implementation; Final Rule, p. 47943.

[6] Barnett HJM, *et al*. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. *N Engl J Med* 1998;339:1415-25.

[7] CMS. Decision Memo for Carotid Artery Stenting (CAG-00085R), p. 28.

[8] Barnett HJM, *et al*. (NASCET).

[9] Gray WA, *et al*. (ARCHeR).

In the March 2005 coverage analysis, although CMS noted the need for additional studies, the agency did not go so far as to suggest that coverage should be dependent upon randomized, controlled trials (RCTs) comparing CAS to CEA in high surgical risk populations. As CMS reconsiders coverage for CAS for high surgical risk patients, Boston Scientific urges CMS not to delay coverage by requiring RCTs for the symptomatic and asymptomatic high risk populations. Large-scale RCTs comparing CAS to CEA in high surgical risk populations would be difficult, if not impossible, from both an ethical and enrollment standpoint. It would be extremely challenging and perhaps unethical to enroll patients who are known to be at high risk for surgery in a trial where they may be randomized to a riskier procedure, and institutional review boards (IRBs) may be reluctant to approve participation in such a study.

Rather than trying to draw conclusions about the appropriateness of CAS in high surgical risk populations through comparisons to CEA in mixed surgical risk populations or requiring RCTs, CMS should make its coverage determination based on whether the data on CAS in high risk patient populations demonstrates safety, efficacy and durability of stroke prevention on its own or when compared to CEA data from like populations (as in SAPPHIRE and ARCHeR). Samples of recent studies which can facilitate coverage evaluation are highlighted on the following pages and a summary table is provided as an attachment (Appendix I). It is important to note that findings are similar across the many studies of CAS in the high surgical risk population, further supporting the validity of these results.

Based on the evidence discussed below, we urge CMS to consider the weight of the CAS evidence, making comparisons and drawing conclusions from data only with like patient populations, and the need for stroke prevention options for patients who are at high risk for CEA as the primary rationale for expanding coverage for CAS.

New Data Affirm the Role of CAS as an Alternative for Patients at High Surgical Risk
Since the last reconsideration of the NCD for carotid stenting was published in March 2005, new data are available, much of which have been published. Together, these data represent the study of over 3,500 CAS patients in addition to the 747 patients participating in SAPPHIRE. The outcomes from these studies consistently demonstrate safety, effectiveness and durability, and strongly support expansion of coverage to include all FDA-labeled high surgical risk patients.

The new data include:

• *ARCHeR (published in the Journal of Vascular Surgery, August 2006[10])*
ARCHeR is a sequential series of three prospective, non-randomized, multicenter studies that consecutively enrolled 581 patients from May 2000 to September 2003. In this trial, CAS was compared to a historical control derived from a review of literature on the results of CEA in a similar high surgical risk population. The following key findings from the ARCHeR study demonstrate that CAS is 1) not inferior to the historical results of CEA among high surgical risk patients and 2) safe, effective and durable as a stroke prevention alternative to CEA for patients who are at high risk for surgery.

- CAS had a 9.6% major adverse event (MAE) rate (30 day death, stroke, MI, and 1-year ipsilateral stroke) compared to 14.4% for the CEA historical control, suggesting that high surgical risk CAS patients have a 33% lower risk of stroke, death and MI than if they underwent a CEA procedure (it is important to note that the primary endpoint for CAS would have been even lower had patients with a concurrent need for open heart surgery within 30 days after the stenting procedure been excluded from the study as they have in other studies).
    - Symptomatic CAS patients: 30-day all-cause death, stroke, MI: 13.1%
    - Asymptomatic CAS patients: 30-day all-cause death, stroke, MI: 6.8%

[10] Gray WA, *et al*. Protected carotid stenting in high-surgical-risk patients: The ARCHeR results. *J Vasc Surg*. 2006;44:258-69.

- At 30 days, the rate of major ipsilateral stroke among symptomatic patients in ARCHeR was 4.3%, which is similar to the endpoint reported in the surgical arm of the NASCET trial (2.1%), particularly when accounting for the high risk profiles of patients participating in ARCHeR.
- 2.2% target lesion revascularization (TLR) for CAS at 1 year is lower than rates in well-conducted surveys of restenosis after endarterectomy.[11]

These data are important, given that peri-operative morbidity and mortality rates for high-risk patients after CEA range from 10% to 20%.[12]

CAPTURE (presented at the 2006 meeting of the American College of Cardiology [ACC])
CAPTURE is an ongoing, FDA-mandated post-approval study of CAS involving 2,500 patients in multiple centers. Procedures were performed by physicians with varying levels of experience with CAS. The results presented at ACC validate findings from SAPPHIRE and ARCHeR. A smaller percentage of participants are symptomatic in CAPTURE (9.3% versus 23.8% in ARCHeR), however the findings are similar to those described for ARCHeR:

- CAS had a 5.7% 30 day death, stroke and MI rate (compared to 8.3% in ARCHeR).
    - Symptomatic CAS patients (stenosis ≥50%): 14.2% versus 13.1% in ARCHeR
    - Asymptomatic CAS patients (stenosis ≥80%): 4.9% versus 6.8% in ARCHeR
- At 30 days, the rate of major stroke among symptomatic patients was 5.2% (versus 4.3% in ARCHeR); and among asymptomatic patients 1.3% (versus 0.7% in ARCHeR).
- One of the key findings from this initial phase is that rollout of CAS to physicians with varying levels of experience achieved excellent results comparable to ARCHeR, thereby addressing one of CMS's concerns regarding whether the success of CAS in trials could be extrapolated to ordinary practice.

BEACH (White, CJ, et al. Carotid Stenting with Distal Protection in High Surgical Risk Patients: The BEACH Trial 30 Day Results. Cath Cardiovasc Interv. 2006;67:503-512)
The BEACH trial enrolled 747 patients at high risk for CEA due to prespecified anatomical criteria and/or medical comorbidities. The trial included both symptomatic (≥50% carotid artery stenosis; 23.5% of the pivotal patients) as well as asymptomatic (≥80% carotid artery stenosis) high surgical risk patients. The 30 day composite MAE rate for the entire cohort of 747 patients was 5.8% (symptomatic, 7.9%; asymptomatic 5.0%). These data were published in April 2006.

The primary endpoint for the BEACH trial (stroke, death, MI at 30 days + ipsilateral stroke and neurological death at 1 year) across all patients studied was 9.1%. Recent analyses of pivotal primary endpoint data for the patient populations being considered for expanded coverage yield the following findings:

- One year morbidity and mortality (primary endpoint) for high surgical risk, symptomatic patients with stenosis 50%-69%: 8.6%
- One year morbidity and mortality for high surgical risk, asymptomatic patients with stenosis ≥80%: 8.0%[13]

• *SAPPHIRE (published in the New England Journal of Medicine, October 2004)*[14]
SAPPHIRE remains the one randomized clinical trial of CAS and CEA that addresses the question of

[11] Ibid.
[12] As cited by Gray WA, *et al*. Protected carotid stenting in high-surgical-risk patients: The ARCHeR results. *JVasc Surg*. 2006;44:258-69.
[13] Boston Scientific Corporation, Data on File.
[14] Yadav JS, *et al*. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med*. 2004;351:1493-501.

safety and efficacy of CAS versus CEA in the patient group that CMS is currently considering for expanded coverage. In this study, the data showed that the rate of death, stroke or MI at 30 days plus ipsilateral stroke or death from neurologic causes within 31 days to 1 year for CAS was 12.0% versus 20.1% for CEA. The study concluded that in high surgical risk patients, CAS is not inferior to CEA. Moreover, among CAS patients the cumulative incidence of stroke, death and MI at 30 days (4.4%), as well as the cumulative incidence of cranial-nerve palsy (0%) and TLR (0.7%) at one year, were lower than among CEA patients (9.9%), (5.3%) and (4.6%), respectively.

• *Additional Trials and Studies of Interest*

There are several recent publications of data from smaller studies that provide additional evidence that CAS offers an appropriate alternative to CEA for high surgical risk, symptomatic patients with stenosis 50%-69% and high surgical risk, asymptomatic patients with stenosis ≥80%. They include:

- Derubertis *et al*. considers indications for CAS versus CEA, and states that: "CAS is now considered an appropriate and equivalent alternative to CEA in…high surgical risk patients, defined by the presence of severe cardiac, pulmonary, or renal disease or by the presence of local factors…"[15]
- In ACSRS study, a study of natural history in asymptomatic patients with carotid artery stenosis, patients with ≥82% stenosis had an overall stroke risk of about 6% per year in a pooled group of patients with and without comorbidities and an ipsilateral stroke risk as high as 6% per year when significant clinical comorbidities were present. These rates are much higher than previously found in ACAS or ACST and suggest a greater need for intervention.[16]
- Other, smaller studies corroborate the larger, multi-center trials and registry studies:
    - Park *et al*. reported that findings from a non-randomized retrospective study of CAS versus CEA that largely mirror the findings from SAPPHIRE.[17]
    - Brooks *et al*., in a single-center, randomized trial, indicate that "CAS and CEA may be equally effective and safe in treating individuals with asymptomatic carotid stenosis."[18]
    - Bush *et al*. found that, in a retrospective study of CAS and CEA, the 30-day stroke and death rates were 3.2% (CAS) and 3.7% (CEA). The 131 patients in the CAS arm were considered to be at high risk for CEA.[19]
    - Yen *et al*. prospectively followed 172 patients after CAS, and found that rates of combined stroke or death were similar for both symptomatic and asymptomatic high surgical risk patients at 30 days (3.2% symptomatic group versus 3.6% asymptomatic) and at 6 months (4.8% symptomatic group versus 5.4% asymptomatic).[20]

The data from these studies provide a wealth of evidence that CAS is a safe, efficacious and durable treatment option for symptomatic patients with stenosis 50%-69% and asymptomatic patients with stenosis ≥80% who are at high risk for surgery. Given this evidence, and the fact that CMS currently covers CEA in the considered patient populations despite the risks associated with surgery, it is logical

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[15] Derubertis BG, *et al*. Evolution of the treatment of carotid occlusive disease: indications for carotid angioplasty and stenting versus carotid endarterectomy. *J Cardiovasc Surg*. 2006;47:297-303.

[16] Kakkos SK, *et al*. Factors associated with mortality in patients with asymptomatic carotid stenosis: Results from the ACSRS study. *Int Angiol*. 2005;24(3):221-30.

[17] Park B, *et al*. Clinical outcomes and cost comparison of carotid artery angioplasty with stenting versus carotid endarterectomy. *J Vasc Surg*. 2006;44:270-6.

[18] Brooks WH, *et al*. Carotid angioplasty and stenting versus carotid endarterectomy for treatment of asymptomatic carotid stenosis: a randomized trial in a community hospital. *Neurosurgery*. 2004;54:318-325.

[19] Bush RL, *et al*. A comparison of carotid artery stenting with neuroprotection versus carotid endarterectomy under local anesthesia. *The American Journal of Surgery*. 2005;190:696-700.

[20] Yen MH, *et al*. Symptomatic Patients have Similar Outcomes Compared with Asymptomatic Patients after Carotid Artery Stenting with Emboli Protection. *Am J Cardiol*. 2005 Jan 15;95(2):297-300.

and appropriate to extend coverage for CAS as proposed.

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In closing, rapidly enacting an expansion of Medicare coverage for CAS to include all FDA-indicated high surgical risk patient populations will provide more Medicare beneficiaries with appropriate and immediate access to an important, mainstream treatment option for CAD. We greatly appreciate the opportunity to comment on the proposed expansion of national coverage carotid artery stenting. Please call Tom Meskan at 763-494-2016 or me at 508-652-7492 if you have any questions.

Sincerely,

Parashar Patel
Vice President, Health Economics and Reimbursement

Cc: Steve Phurrough, MD
Joseph Chin, MD
Barry Straube, MD
John Pedersen
Tom Meskan
Scott Reid
Maria Stewart

Boston Scientific Corporation Comments on Proposed Expansion of National Coverage for Carotid Artery Stenting in High Surgical Risk Patients (CAG – 00085R2)

Appendix I: Summary of CAS Studies

Table 1: Multi-Center Carotid Stenting Trials

Trial	Study Design	N pts	Patient Population	30 day M/M (%)	1 year M/M (%)	Primary Endpoint
BEACH[i]	Non-randomized	112	High risk symptomatic, stenosis ≥50%	7.9		24h non-Q MI + 30day death/stroke /Q MI + 1yr ipsi stroke, neuro death
		368	High risk asymptomatic, stenosis ≥80%	5.0		
		41	High risk symptomatic, 50-69% stenosis	6.5	9.6	
CABERNET[ii]	Non-randomized	488 (454 pivotal)	High risk, symptomatic and asymptomatic	3.9	4.5	30day death/stroke/MI + 1yr ipsi stroke, death due to ipsi stroke
SAPPHIRE[iii]	Randomized	724 (310 randomized)	High risk symptomatic and asymptomatic	5.4 (CAS) 10.2 (CEA)	12.0 (CAS) 20.1 (CEA)	30day death/stroke/MI + 1yr ipsi stroke, neuro death
ARCHER 1[iv]	Non-randomized	209 (158 pivotal)	High risk symptomatic and asymptomatic	7.6	8.3	30day death/stroke/MI + 1yr ipsi stroke
ARCHER 2	Non-randomized	303 (278 pivotal)	High risk symptomatic and asymptomatic	8.6	10.2	30day death/stroke/MI + 1yr ipsi stroke
ARCHER 3[v]	Non-randomized	581	High risk symptomatic and asymptomatic	8.3	9.6	30day death/stroke/MI + 1yr ipsi stroke
		138	High risk symptomatic	13.1	Not Provided	
		443	High risk asymptomatic	6.8	Not Provided	
CAPTURE[vi]	Non-randomized	2500	High risk symptomatic and asymptomatic	5.7	NA	30day death/stroke/MI
		233	High risk symptomatic	14.2	NA	
		2267	High risk asymptomatic	4.9	NA	
MAVErIC I & II[vii]	Non-randomized	99 (Phase I) 399 (Phase II)	High risk symptomatic and asymptomatic	5.1 5.3	NA	30day death/stroke/MI
MAVErIC International[viii]	Non-randomized	51	High risk symptomatic and asymptomatic	5.9	NA	30day death/stroke/MI

Trial	Study Design	N pts	Patient Population	30 day M/M (%)	1 year M/M (%)	Primary Endpoint
CREATE[ix]	Non-randomized	419	High risk symptomatic and asymptomatic	6.2	NA	30day death/stroke/MI
SECuRITY[x]	Non-randomized	398 (305 pivotal)	High risk symptomatic and asymptomatic	7.5	8.5	30day death/stroke/MI
CaRESS[xi]	Non-randomized 2 CEA : 1 CAS	143 (CAS) 254 (CEA)	Mixed risk symptomatic and asymptomatic	2.1 (CAS) 4.4 (CEA)	10.9 (CAS) 14.3 (CEA)	1yr death/stroke/MI

Table 2: Single Center Carotid Stenting Trials[xii]

Study	Study Design	N pts	ASx %	30 day M/M	Deaths / Mortality (%)	Major / minor Stroke (%)	Restenosis
Brooks 2004[xiii]	Prospective, randomized study of CAS and CEA	43 (CAS) 42 (CEA)	100 (CAS / CEA)	0 (CAS / CEA)	0 (CAS / CEA)	0 (CAS / CEA)	Not provided
Bush 2005[xiv]	Retrospective, non-randomized review of CAS and CEA from 2001-2004 (30 days)	152 (CAS) 221 (CEA)	68 (CAS) 66 (CEA)	3.2 (CAS) 3.7 (CEA)	0.7 (CAS) 0.9 (CEA) (30 days)	Major Stroke: 0.7 (CAS) 1.8 (CEA) Minor Stroke (TIA): 2.0 (CAS) 0.9 (CEA) (30 days)	4.6 (CAS) 2.3 (CEA) (30 days)
Yen 2005[xv]	Prospective, Non-randomized (CAS only) (6 months)	174	64	3.2 (symptomatic) 3.6 (asympto-matic)	4% (6months)	1.1% (6 months)	Not provided
Park 2006[xvi]	Prospective, non-randomized study of CAS and CEA	46 (CAS) 48 (CEA)	22 (CAS) 38 (CEA)	2 (CAS) 10 (CEA)	0 (CAS 2 (CEA)	2 (CAS) 4 (CEA)	Not provided

[i] BEACH Report of One-year Results. Data on file Boston Scientific Corporation.

[ii] CABERNET One-year results presented at TCT 2005 (L. Nelson Hopkins MD).

[iii] Yadav JS, *et al*. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med.* 2004;351:1493-501.

[iv] RX ACCULINK™ Carotid Stent System Information for Prescribers.

[v] Gray WA, *et al*. Protected carotid stenting in high-surgical-risk patients: The ARCHeR results. *J Vasc Surg*. 2006;44:258-69.

[vi] Non-published. Data presented at ACC 2006.

[vii] MAVErIC I 30 day results presented at TCT 2004 (Gary M. Ansel MD).

[viii] Hill MD, *et al*. Multicenter evaluation of a self-expanding carotid stent system with distal protection in the treatment of carotid stenosis. *Am J Neuroradiol.* 2006; 27:759-65.

[ix] Safian RD, *et al*. Protected carotid stenting in high-risk patients with severe carotid artery stenosis. *JACC*. 2006;47:2384-9.

[x] Xact® Rapid Exchange Carotid Stent System 5.7Fr (1.9mm) Instructions for Use.

[xi] CaRESS Steering Committee: Carotid Revascularization Using Endarterectomy or Stenting Systems (CaRESS) phase I clinical trial: 1-year results. *J Vasc Surg.* 2005; 42:213-9

[xii] Phatouros CC, *et al*. Carotid artery stent placement for atherosclerotic disease: rationale, technique, and current status. *Radiology*. 2000;217:26-41.

[xiii] Brooks WH, *et al*. Carotid angioplasty and stenting versus carotid endarterectomy for treatment of asymptomatic carotid stenosis: A randomized trial in a community hospital. *Neurosurgery*. 2004;54:318-25.

[xiv] Bush RL, *et al*. A comparison of carotid artery stenting with neuroprotection versus carotid endarterectomy under local anesthesia. *Am J Surg*. 2005;190:696-700.

[xv] Yen MH, *et al*. Symptomatic patients have similar outcomes compared with asymptomatic patients after carotid artery stenting with emboli protection. *Am J Cardiol*. 2005;95:297-300.

[xvi] Park B, *et al*. Clinical outcomes and cost comparison of carotid artery angioplasty with stenting versus carotid endarterectomy. *J Vasc Surg*. 2006;44:270-6.

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August 25, 2006

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Title of NCA: Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG – 00085R3)

Dear Dr. Phurrough:

Cordis strongly supports the proposal set forth for comment by CMS to expand coverage for carotid artery stenting with emboli protection.

Further to our earlier correspondence of March 31st 2006, April 3rd 2006 and June 5th 2006 and in response to CMS initiating a period of public comment pertaining to expanding coverage for carotid artery stenting with emboli protection, we are writing to share our rationale for the expansion in coverage. This is based on substantial new and expanded data that were not available at the time the current NCD was issued. We believe these data address the concerns that had previously been expressed with regards to expanding coverage for carotid artery stenting with emboli protection.

Specifically, the new data are: 1) long-term (3 year) follow-up data from the SAPPHIRE study; and 2) preliminary 30-day data from the CASES-PMS study.

The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) study is the only currently available, completed, prospective, randomized, controlled trial of carotid artery stenting with emboli protection vs. carotid endarterectomy in patients at high risk of carotid endarterectomy. The SAPPHIRE study consisted of 774 patients in 29 centers that were evaluated by a panel of physicians comprised of an interventionalist, a surgeon and a neurologist. Both the surgeon and interventionalist determined that they could treat 334 of the 747 patients.

These 334 patients were randomized with 167 receiving carotid artery stenting with emboli protection using the Cordis PRECISE ® Nitinol Stent System and the Cordis ANGIOGUARD® Emboli Capture Guidewire and 167 receiving carotid endarterectomy. Of the remainder, 406 patients were deemed to constitute an unacceptable risk for surgery by a surgeon and were treated in a non-randomized carotid stent arm of the trial; 7 patients were deemed to represent an unacceptable risk for stenting and were treated in a non-randomized carotid endarterectomy arm. Inclusion criteria consisted of one or more high-risk surgical criteria and a carotid artery stenosis $\geq$ 50% in symptomatic patients and a carotid artery stenosis $\geq$ 80% in asymptomatic patients.

The trial had a non-inferiority design with a primary composite endpoint being cumulative incidence of death, stroke or myocardial infarction (MI) within 30 days after the procedure and death or ipsilateral stroke between 31 days and 1 year. Yearly follow-up to 3 years was pre-specified. At 1 year, the SAPPHIRE study was successful in demonstrating the non-inferiority of carotid artery stenting with emboli protection to carotid endarterectomy. Clinical follow-up was available at 3 years on 80.6% (106/131) of the surviving stent patients and 70.8% (75/106) of the surviving endarterectomy patients.

The CASES-Post Market Surveillance (PMS) study, is an FDA required condition of approval study conducted in 73 centers throughout the US that enrolled 1,493 patients. It is worth noting that the CASES-PMS study was also done under an IDE with strict adherence to Good Clinical Practice, with identical inclusion and exclusion criteria to the SAPPHIRE study. As such, it provides very high quality information on patients treated in a more general setting that can readily be compared to the SAPPHIRE trial data.

The main objective of the CASES-PMS study was to assess the safety and efficacy of carotid artery stenting with emboli protection when performed by physicians in different settings, who have various levels of experience with carotid artery stenting and who have received training through the CASES™ (Carotid Artery Stenting Education System) training program. The extent of the training was determined by their level of experience with both carotid artery stenting with emboli protection and specifically the Cordis ANGIOGUARD® Emboli Capture Guidewire.

We seek to address questions raised by CMS with regard to expanding the coverage for carotid artery stenting with emboli protection to a broader group of patients than are currently covered by CMS. Available data from the SAPPHIRE and CASES-PMS trials together strongly support the expansion of coverage to include patients who are at high-risk for carotid endarterectomy and who also have asymptomatic carotid artery stenosis $\geq$ 80% or have symptomatic carotid artery disease with a diameter stenosis $\geq$ 50%.

Broadly speaking we submit that the body of data now available (SAPPHIRE 3 year and CASES PMS 30 day) confirms that carotid artery stenting with emboli protection is at least as effective as carotid endarterectomy at preventing the occurrence of stroke with a somewhat lower rate of repeat revascularization in both symptomatic and asymptomatic

patients at a high-risk for surgery. In the SAPPHIRE randomized trial, carotid stenting also resulted in a 1-day shorter hospital stay than carotid endarterectomy.

Figure 1

At 3 years, the SAPPHIRE study showed no difference in the rate of major adverse events (death, stroke and myocardial infarction) between three groups of patients who were either symptomatic with ≥ 50% diameter stenosis or asymptomatic with ≥ 80% diameter stenosis: 1) Patients randomized to be treated by carotid endarterectomy (30.3%) 2) Patients randomized to be treated by carotid artery stent with emboli protection (26.2%), and 3) Non-randomized patients treated by carotid artery stent with emboli protection (33.3%) **. Therefore, we conclude that at 3 years, carotid artery stenting with emboli protection is effective in preventing major adverse events in asymptomatic patients with a carotid artery stenosis ≥ 80% and symptomatic patients with a carotid artery stenosis ≥50% who are at high risk for surgery.**

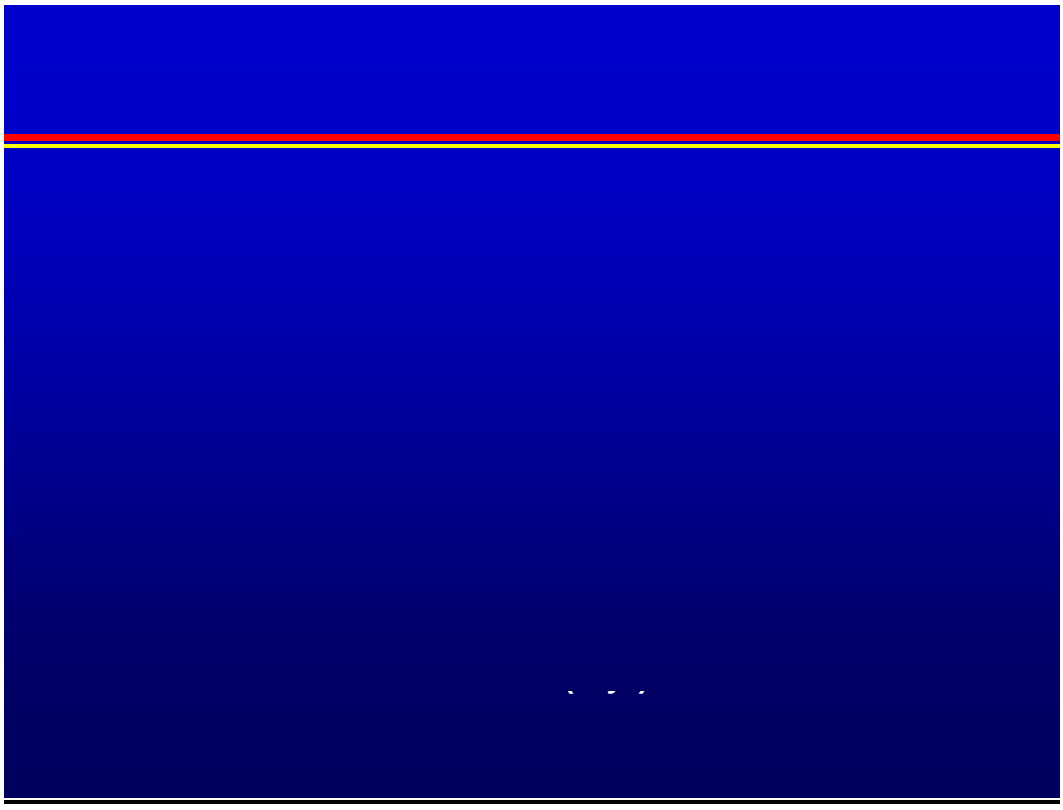


Figure 1: Source document: SAPPHIRE 3-Year data, FDA submission 1/31/06

Figure 2

At 3 years the SAPPHIRE study showed no difference in the cumulative percentage of stroke to 30 days and ipsilateral stroke from 31 days to 3 years in this same patient population between 1) Patients randomized to be treated by carotid endarterectomy (6.7%), 2) Patients randomized to be treated by carotid artery stent with emboli protection (8.0%), and 3) Non-randomized patients treated by carotid artery stent with emboli protection (10.3%). **Therefore, we conclude that at 3 years, carotid artery stenting with emboli protection has a durable effect in preventing stroke in asymptomatic patients with a carotid artery stenosis ≥ 80% and symptomatic patients with a carotid artery stenosis ≥50% who are at high risk for surgery.**

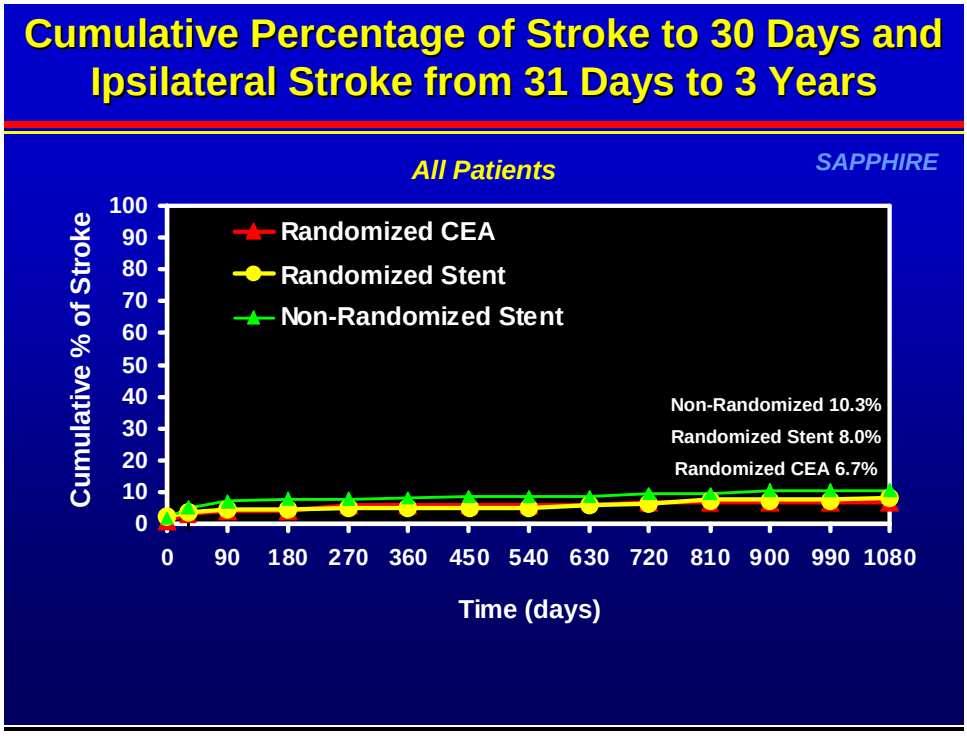


Figure 2: Source document: SAPPHIRE 3-Year data, FDA submission 1/31/06

Figure 3

In the SAPPHIRE study at 3 years, both carotid artery stenting with emboli protection and carotid endarterectomy demonstrated the same rate of stroke (9.0 %, 15 / 167). Even though the total rates of stroke are the same for both carotid endarterectomy and carotid artery stenting with emboli protection, there was a somewhat higher rate of major ipsilateral stroke (3.0% versus 1.2%) and major non-ipsilateral stroke (3.0% versus 0.6%) with carotid endarterectomy versus stenting. Conversely, there was a somewhat higher rate of minor ipsilateral stroke with stenting than with carotid endarterectomy (5.4% versus 2.4%). It is worth noting that about 2/3 of the minor strokes resolved within a few months of the procedure while the major strokes did not. **Therefore, while carotid artery stenting with emboli protection and carotid endarterectomy both show the same, relatively low, overall rate of stroke, the type of stroke seen in patients who received carotid artery stenting with emboli protection were more often of a less severe nature compared to patients who underwent carotid endarterectomy.**

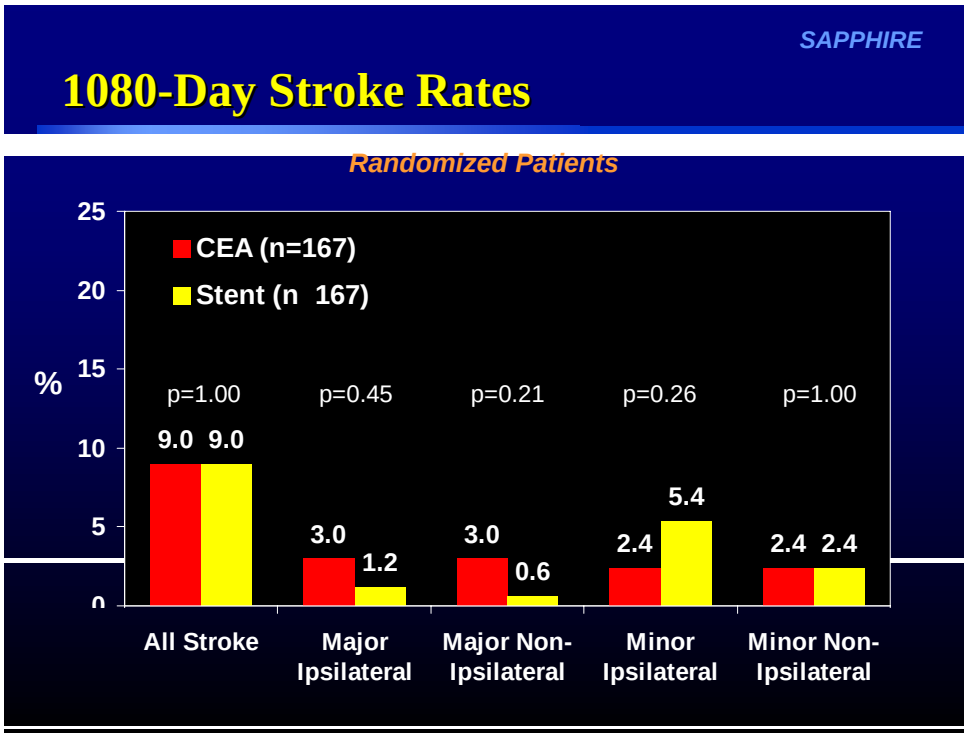


Figure 3. Source Document: SAPPHIRE 3-Year data, Cordis data on file

Figure 4

In the SAPPHIRE randomized study at 1 year, the rate of major adverse events in asymptomatic patients with ≥ 80% diameter stenosis treated with stenting was not different from carotid endarterectomy (10.3% versus 19.2%; p=0.07). Similarly, at 1,080 days carotid artery stenting was no worse than carotid endarterectomy in terms of major adverse events (22.7% versus 33.6% respectively; p=0.063) in this patient population. **Therefore we conclude that carotid artery stenting with emboli protection is not different to carotid endarterectomy in terms of major adverse events in asymptomatic patients at high risk for surgery with ≥ 80% diameter stenosis to three years:**

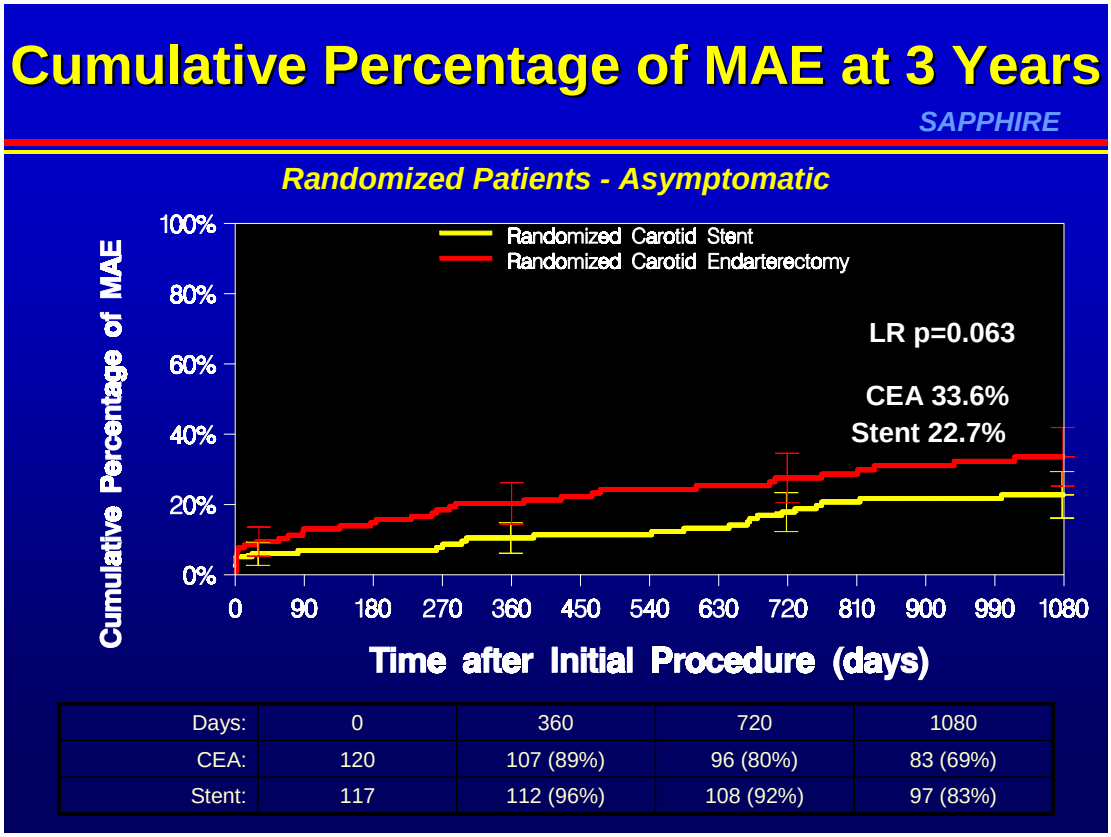


Figure 4: Source document: SAPPHIRE 3-Year data, FDA submission 1/31/06

Figure 5

In the SAPPHIRE study at 1 year, both randomized (7.7%) and non-randomized stent arms (8.2%) were not different from the randomized carotid endarterectomy arm (7.5%) in the stroke rate in asymptomatic patients with a ≥ 80% diameter stenosis. Similarly at 1,080 days the stroke rate in the randomized and non-randomized stent arms of the trial were similar to that seen in the carotid endarterectomy arm (8.0%, 8.4% and 7.3%, respectively). **Therefore, we conclude that carotid artery stenting with emboli protection has a durable effect in preventing stroke in high surgical risk asymptomatic patients with a carotid artery stenosis ≥ 80%:**

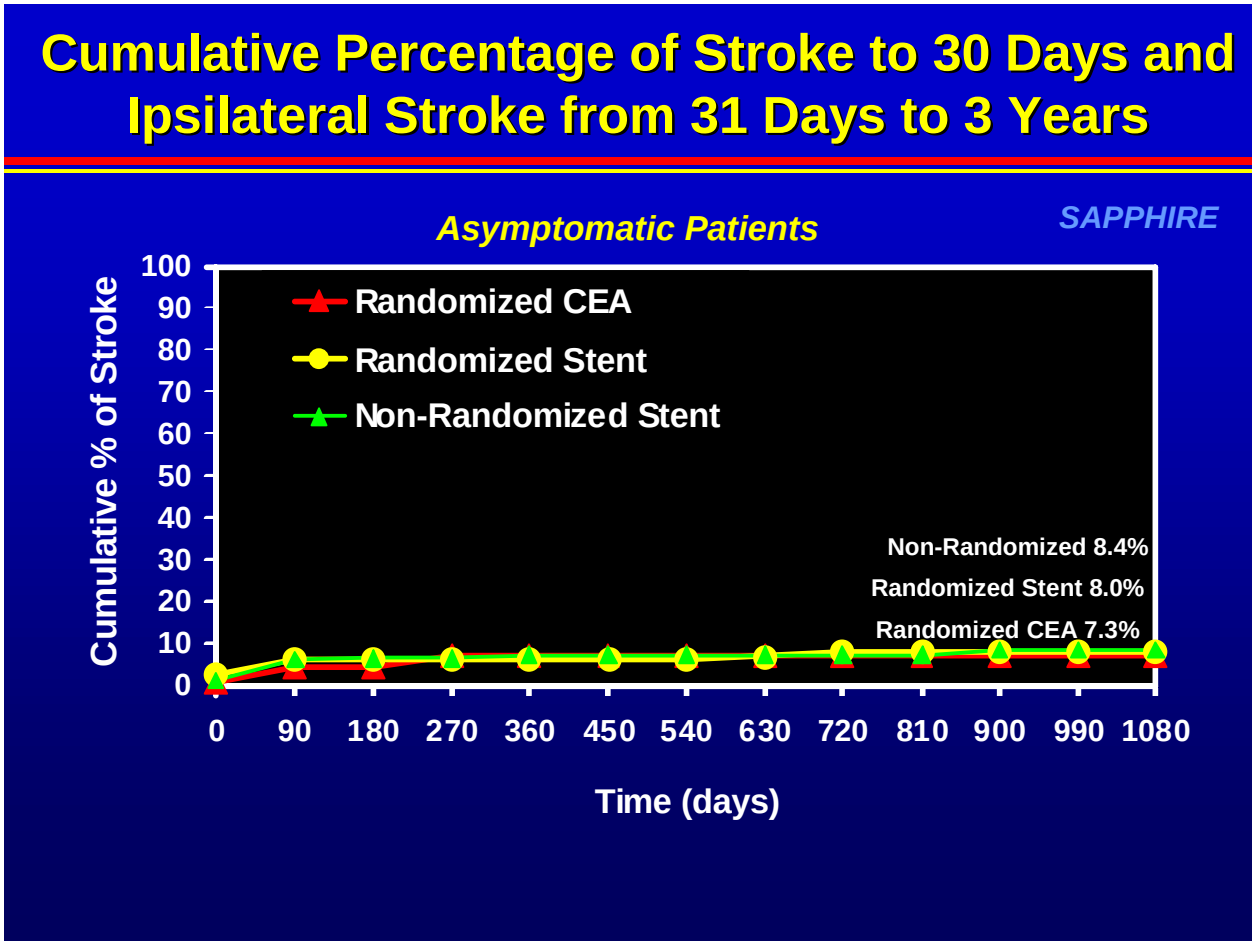


Figure 5. Source Document: SAPPHIRE 3-Year data, FDA submission 1/31/06

Figure 6 – Figure 9

We also submit that carotid artery stenting is a safe and effective mode of treating carotid artery stenosis in order to prevent stroke in a geographically diverse, representative sample of hospitals of various sizes and in users with varying levels of experience with respect to carotid artery stenting. **The CASES Post Market Surveillance Study has demonstrated that carotid artery stenting with emboli protection is safe and effective in a broad representation of patients, hospitals and physicians:**

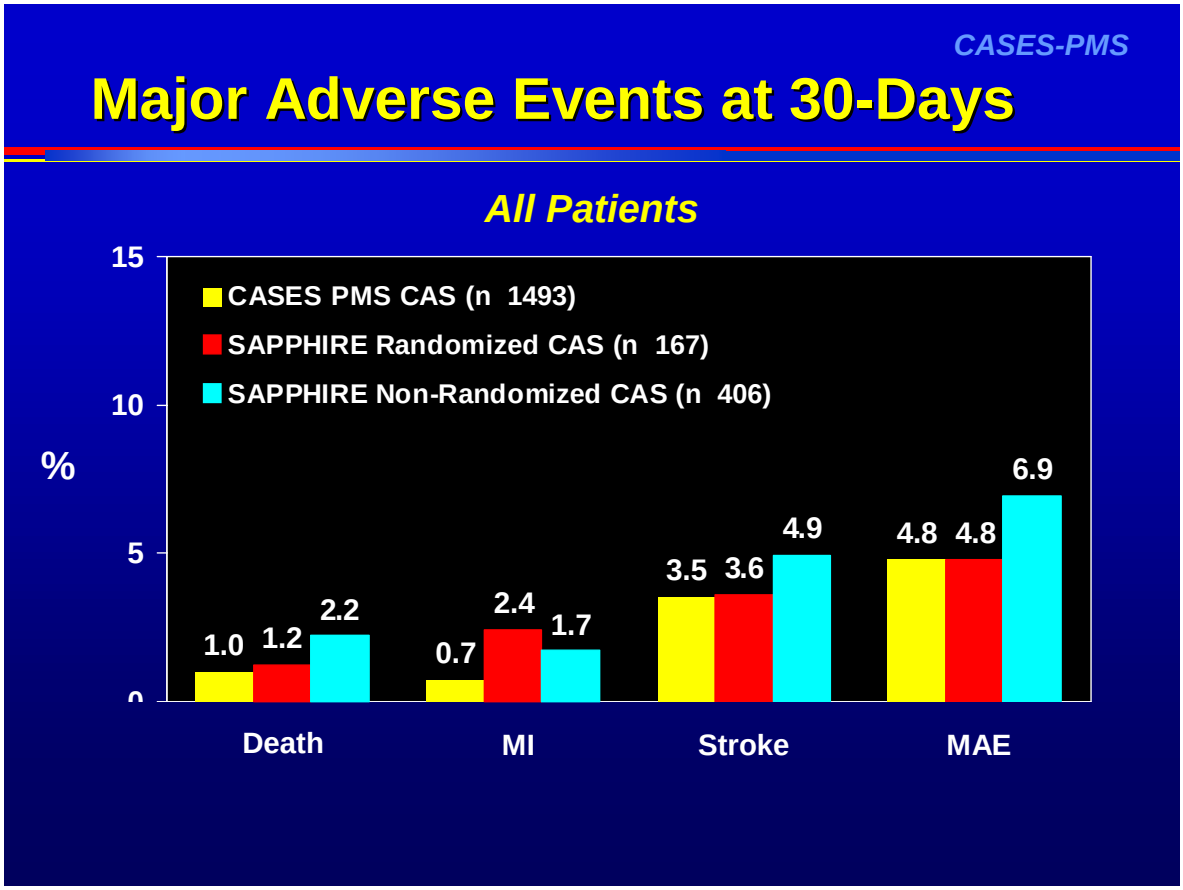


Figure 6: Source document:

1) **CASES-PMS CMS data submission 3/31/2006**
2) **SAPPHIRE 3-Year data, FDA submission 1/31/06**

Figure 7

The CASES PMS study demonstrated no difference in the rate of major adverse events following carotid artery stenting with emboli protection between academic sites (n=801) and non-academic sites (n=692). **Therefore, we conclude that carotid artery stenting with emboli protection is safe and effective in both academic and non-academic institutions:**

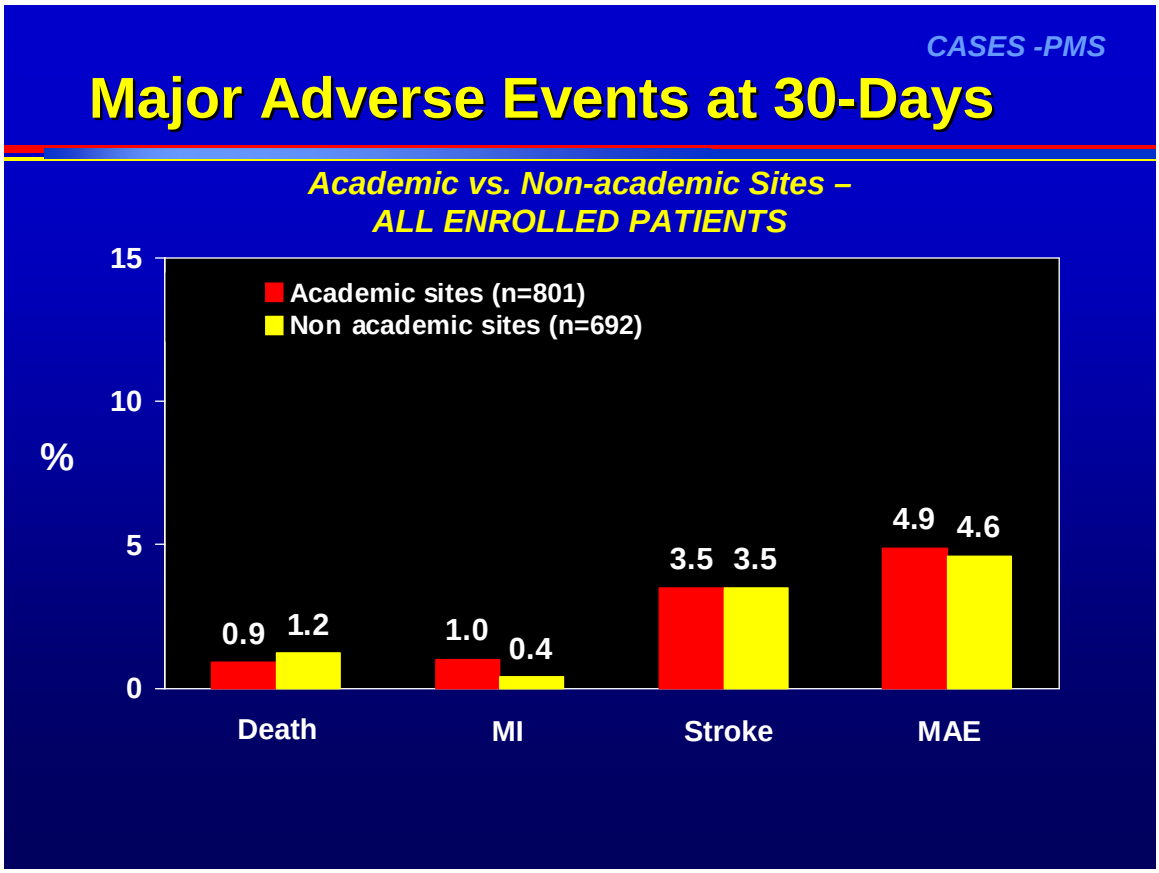


Figure 7: Source document: CASES-PMS CMS data submission 3/31/2006

Figure 8

In the CASES PMS study, there was no difference in the rate of adverse events at 30 days following carotid artery stenting with emboli protection when comparing physicians with varying levels of familiarity and training with Cordis devices, specifically the Cordis PRECISE® Nitinol Stent System and the Cordis ANGIOGUARD® Emboli Capture Guidewire.

The distribution of experience was classified as follows: Level 1 represented physicians who were already experienced with carotid artery stenting procedures and Cordis devices and hence received no additional training. Level 2 represented physicians who had some experience performing carotid artery stenting procedures and little to no experience with Cordis devices and hence received an intermediate level of additional training. Level 3 represented physicians who had little to no experience performing carotid artery stenting procedures with any devices and hence received the full Cordis CASES™ (Carotid Artery Stenting Education System) training program. These results also suggest the effectiveness of the Cordis CASES™ training program. **Therefore, carotid artery stenting with emboli protection is safe and effective when performed by appropriately trained physicians with varying levels of prior experience:**

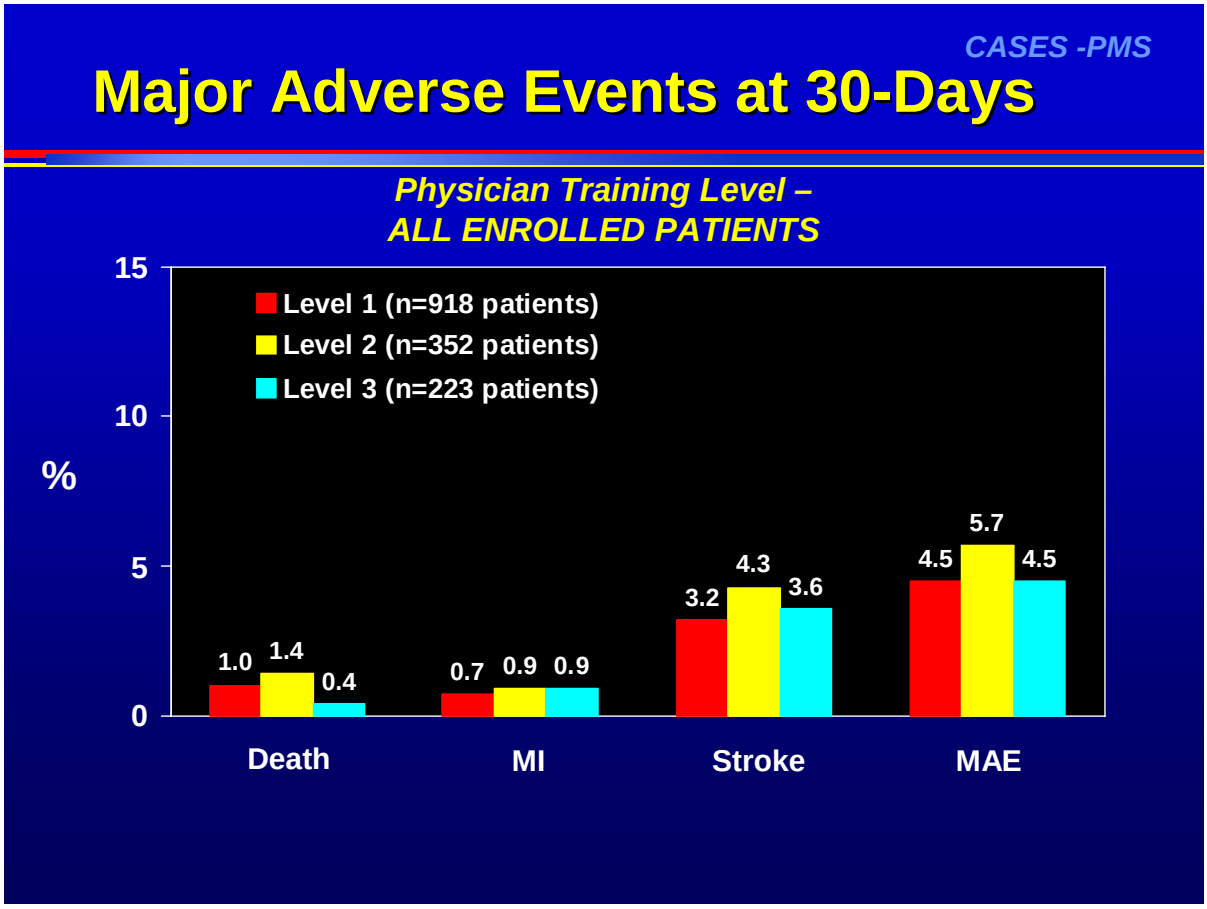


Figure 8: Source document: CASES-PMS CMS data submission 3/31/2006

Figure 9

In addition there was no difference in the rate of adverse events at 30 days between physicians with varying rates of annual procedural volume.

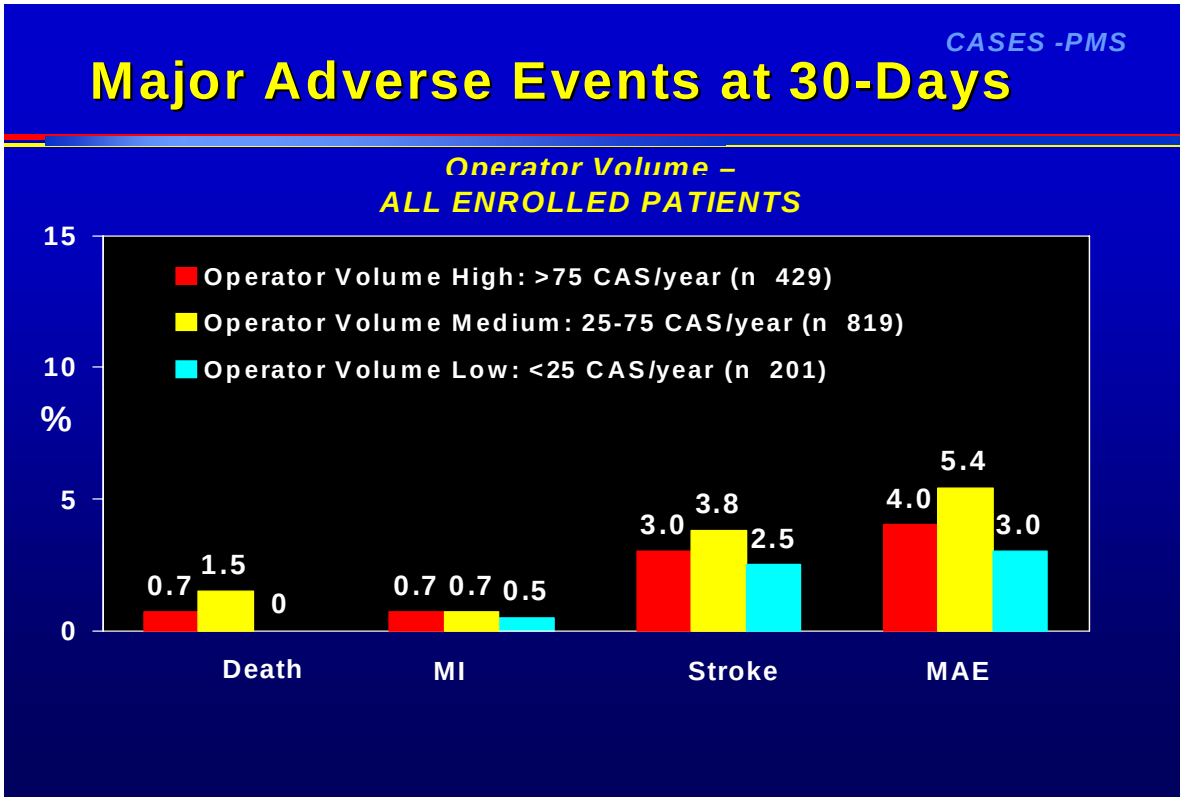


Figure 9: Source document: CASES-PMS CMS data submission 3/31/2006

Figure 10

Across a distribution of 1,493 patients, the CASES PMS study demonstrated no difference in the rates of MAE between symptomatic (5.9%) and asymptomatic (4.5%) patients. The study demonstrated no difference between symptomatic and asymptomatic patients for the rates of death (0.9% versus 1.0%), MI (1.2% versus 0.6%) and stroke (4.7% versus 3.1 %). **Therefore, we submit that CASES-PMS demonstrates that carotid artery stenting with emboli protection is safe and effective in both symptomatic patients with a diameter stenosis ≥50% and asymptomatic patients with a diameter stenosis ≥80% at high risk for surgery:**

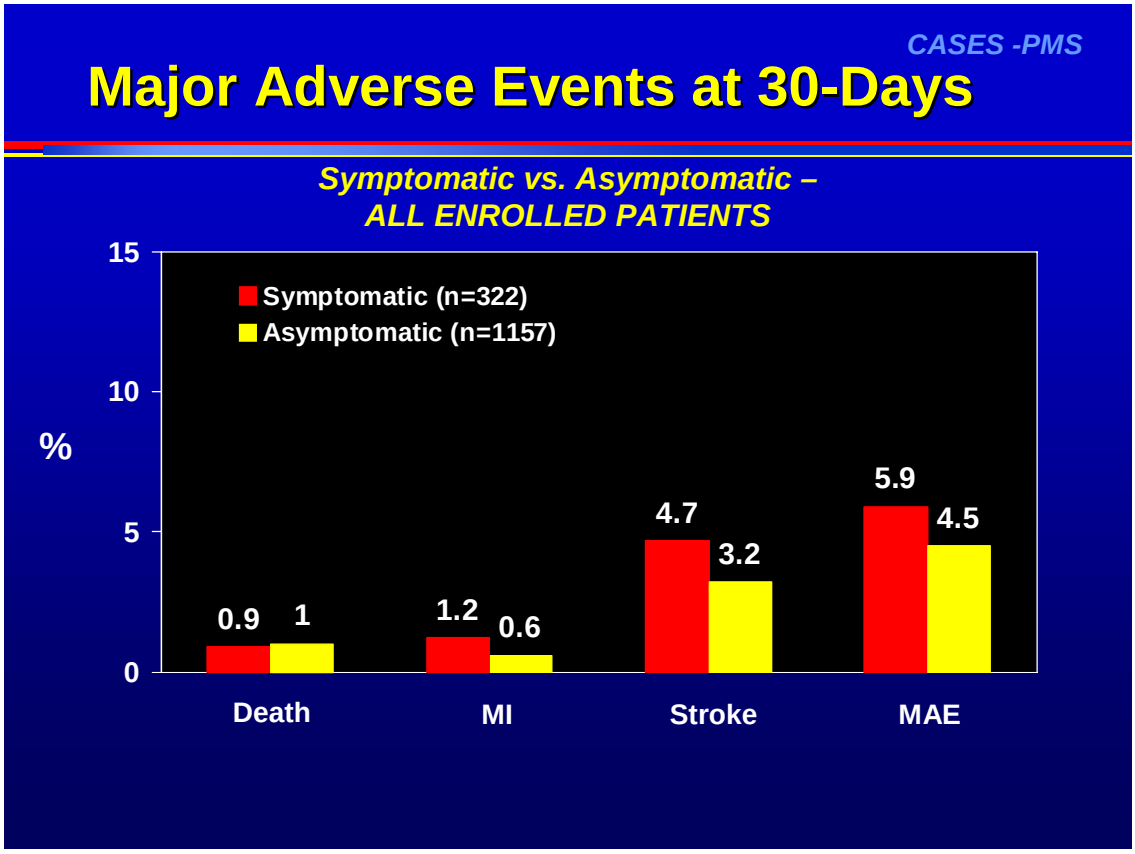


Figure 10: Source document: CASES-PMS CMS data submission 3/31/2006

Figure 11

It is instructive to compare the rates of major adverse events seen in asymptomatic patients in the CASES PMS study and the SAPPHIRE study, both performed under an IDE with the same inclusion and exclusion criteria. The CASES-PMS study represents a much larger number of centers, with a broader distribution of geographical locations, physician experience and academic versus non-academic centers. Importantly, this comparison, across a total combined distribution of some 1,555 patients, demonstrates no difference in the rates of MAE between both randomized and non-randomized asymptomatic patients in the SAPPHIRE study and the CASES-PMS study.

Specifically, the rates of stroke observed in asymptomatic patients treated by carotid artery stenting with emboli protection in these studies are not different. **Therefore we conclude that carotid artery stenting in asymptomatic patients with ≥ 80% diameter stenosis at high risk for carotid endarterectomy has been shown to be safe and effective in both a controlled, randomized study and a broader patient registry:**

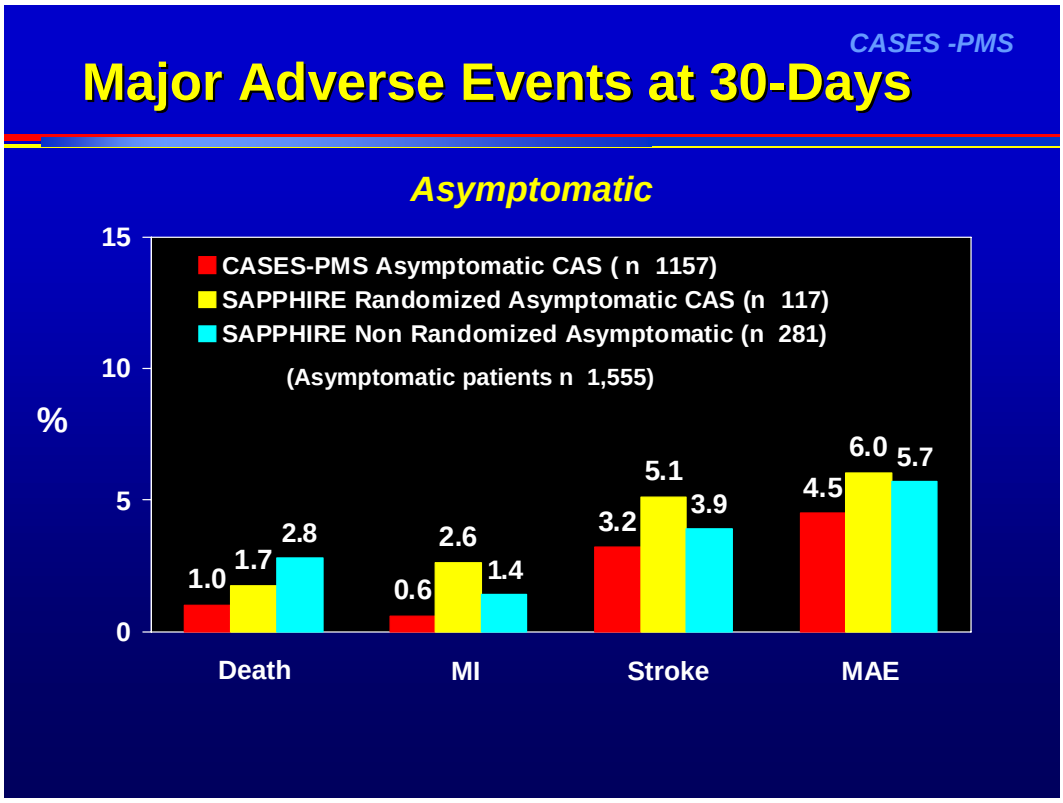


Figure 11: Source document:

1. CASES-PMS CMS data submission 3/31/2006
2. SAPPHIRE – 1 YEAR data contained in the FDA submission dated 10/7/2003

Figure 12

As we look in greater detail at the incidence of stroke rates observed within the CASES PMS study, no difference was seen between symptomatic and asymptomatic patients for major ipsilateral stroke (2.5% versus 0.9%), major non-ipsilateral stroke (0% versus 0.1%), or minor ipsilateral stroke (1.2% versus 1.8%). **Therefore we conclude that carotid artery stenting with emboli protection has been shown to be no less effective in preventing stroke in asymptomatic patients versus symptomatic patients at high-risk for carotid endarterectomy:**

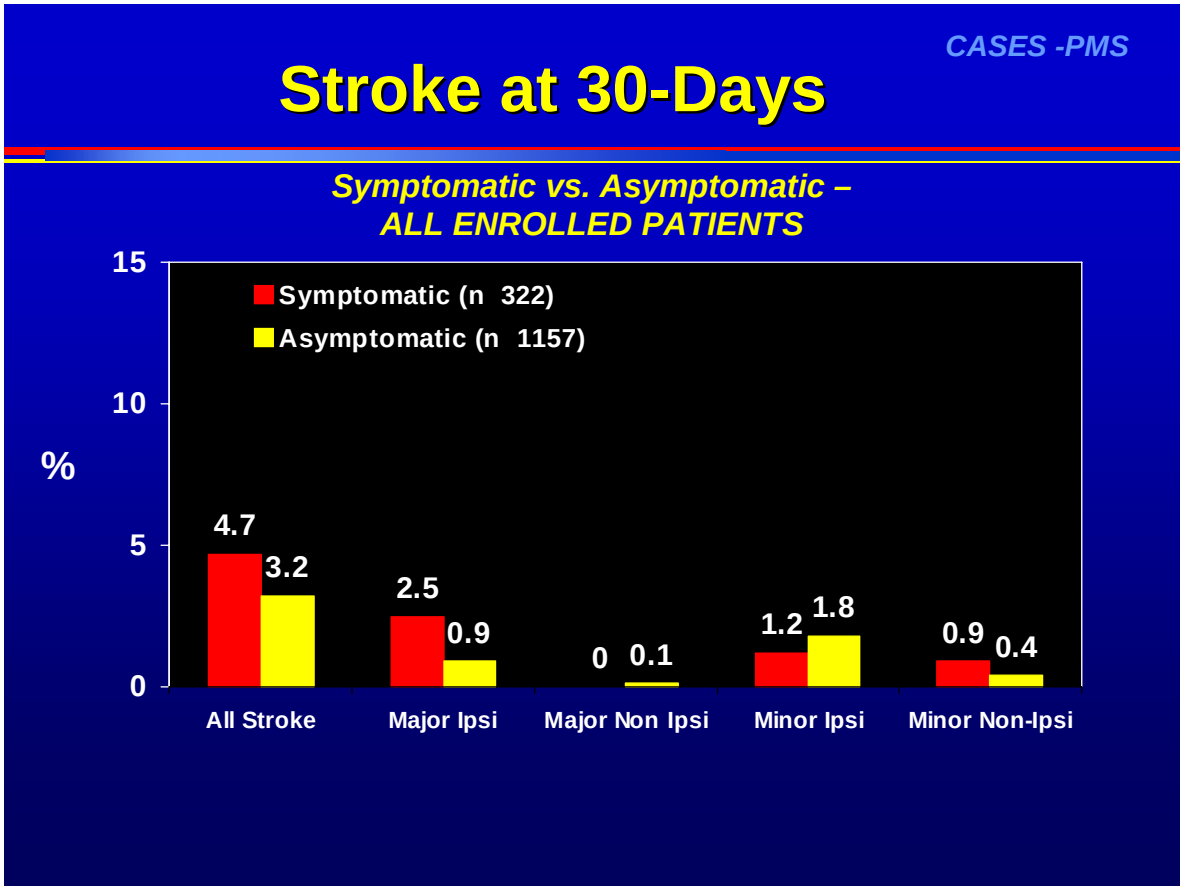


Figure12: Source document: CASES-PMS CMS data submission 3/31/2006

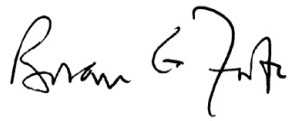
Conclusion

We submit that carotid artery stenting with emboli protection is a safe and effective mode of treatment for asymptomatic patients with carotid artery stenosis ≥80% and symptomatic patients with carotid artery stenosis ≥50%, at a high-risk for carotid endarterectomy, based on summary data provided in this letter. It therefore seems appropriate for CMS to provide the same coverage for this patient population when they are treated by carotid artery stenting with emboli protection or by carotid endarterectomy. We encourage CMS to expand coverage to include asymptomatic patients at a high-risk for surgery and with carotid artery stenosis ≥ 80% and symptomatic patients at a high risk for surgery with carotid artery stenosis ≥ 50%.

We plan to provide you with additional information related to the SAPPHIRE trial 3-year follow-up. We will also provide final 30 day data on all patients as well as 1-year follow-up data on approximately half of the patients in the CASES-PMS study at the same time, and will be happy to respond to any additional questions you may have concerning this important topic.

If you have any questions about this submission, please contact Dr. Brian Firth (908) 412-3099 or Dr Liesl Cooper (908) 412-3000.

Sincerely,



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October 1, 2004

Joseph Chin, MD, MS,
Medical Officer, Division of Medical and Surgical Services
Centers for Medicare and Medicaid Services
7500 Security Blvd
Baltimore, MD 21244

RE: Draft Decision Memo for Carotid Artery Stenting in Post-Approval Studies (CAG-00259N)

Dear Dr. Chin,

The American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS), representing organized neurosurgery in the United States, appreciate the opportunity to comment on the above referenced draft coverage decision memo.

While we are pleased to see that the Centers for Medicare and Medicaid Services (CMS) has recognized "the importance of carotid artery stenosis as a risk factor for stroke and the importance of making available new FDA approved technologies to Medicare beneficiaries," we are nevertheless concerned with the scope of the proposed coverage decision and urge you to revise your coverage memorandum per our recommendations below. The AANS and CNS, along with seven other national medical specialty societies, previously outlined these proposed criteria in a letter to Sean Tunis, MD, on February 3, 2004 (see attached letter), and we believe that notwithstanding the recent FDA decision, nothing has changed to merit expanding the scope of Medicare coverage for carotid stenting to asymptomatic patients, as your proposal would do.

Food and Drug Administration Action

As the draft CMS memo states, the Food and Drug Administration has approved the premarket application (PMA) for one company's carotid stent system with a requirement that it conduct a post-approval study. The approval is limited for the treatment of patients at high-risk of adverse events from carotid endarterectomy and is subject to two additional criteria:

- Patients with neurological symptoms and ≥50% stenosis of the common or internal carotid artery ***by ultrasound*** or angiogram ***OR patients without neurological symptoms and ≥80% stenosis of the common or internal carotid artery by ultrasound or angiogram*** (emphasis added), AND

- Patients must have a reference vessel diameter within the range of 3.6 mm and 9.1 mm at the target lesion.

The FDA has agreed with the sponsor's proposal to conduct a multicenter post-approval study in the practices of physicians at both academic and private hospitals, who will have a mixture of high, medium and low annual carotid stent implant volumes. The post-approval study will gather data on patient outcomes including stroke and rare adverse events.

CMS Proposed Coverage Criteria

CMS coverage regulations make a distinction between the criteria necessary for FDA approval of a device versus Medicare's criteria for coverage. The FDA determines if a product is safe and effective, while CMS must determine if the product is reasonable and necessary for the diagnosis and treatment of illness or injury. These determinations involve two different sets of standards, and FDA approval and/or clearance alone does not automatically entitle a device to coverage.

CMS has determined that percutaneous transluminal angioplasty (PTA) with carotid stent placement is reasonable and necessary when performed consistent with FDA approval of the carotid stent device and in a FDA required post-approval study. In reaching this conclusion, CMS acknowledges that this is a promising new treatment for carotid artery stenosis, but that it also has considerable patient risks. Furthermore, CMS notes that additional data needs to be collected to ascertain which patients are most appropriate for carotid artery stenting.

Ischemic stroke is a major cause of death and disability to Medicare beneficiaries. Carotid endarterectomy has been conclusively demonstrated to be a safe and effective treatment for the prevention of stroke in both symptomatic and asymptomatic patients suffering from carotid stenosis. Any proposed new treatment for stroke prevention in this patient population should be measured against this well proven treatment. However, as with any medical treatment, carotid endarterectomy is not without risk. Certain anatomic considerations or medical comorbidities may place some patients at a higher risk from endarterectomy lessening the overall benefit form this procedure. The FDA in its approval of a PMA for a carotid stent device, considered evidence that showed the *noninferiority* of carotid stenting compared to endarterectomy in patients that were considered high risk for surgical intervention.

Clearly, if Medicare reimburses hospitals and physicians for this procedure, it will enhance our ability to provide a new and valuable medical treatment for our Nation's elderly patients who are not candidates for carotid endarterectomy, but are at considerable risk of suffering a stroke. It will also expand our ability to collect patient outcomes data to better determine which patients will best benefit from this procedure. At present, however, there are insufficient data to support Medicare coverage for those patients who are asymptomatic. In fact, the available data would suggest that carotid angioplasty and stenting may be inferior to medical treatment for the prevention of stroke in asymptomatic patients.

The AANS and CNS therefore believe that CMS should not completely adopt the FDA's criteria as the basis of the proposed coverage decision, as we believe:

1. **That carotid stenting for asymptomatic patients is not yet proven to be "reasonable and necessary" and coverage should be limited to symptomatic "high-risk" patients (as defined below).**
2. **That ultrasound alone is not acceptable for defining the degree of stenosis necessary to consider treatment of symptomatic "high risk" patients (as defined below).**

AANS and CNS Recommended Coverage Criteria

As noted above, nine national medical specialty societies, representing all physicians who treat carotid artery disease, previously proposed detailed criteria for Medicare coverage of carotid stenting. Based on the evidence gathered through the SAPPHIRE and CREST trials (comparing the efficacy of carotid endarterectomy – CEA – to carotid stenting), the medical societies informed CMS that "it is appropriate to expand coverage for carotid artery stenting to certain "high-risk" patients." In our letter, we noted that:

> As data continue to accrue, and while the technology of carotid stenting and cerebral protection devices, as well as the skill of those performing this therapy, continues to evolve, we believe that a most challenging task will be defining "high-risk". This decision is crucial since withholding stent treatment from those who would benefit is as undesirable as allowing it for subsets in whom equivalence to CEA has not yet been shown.

We went on to recommend that Medicare coverage policy should be based on the inclusion criteria from the SAPPHIRE trial, to wit:

> Our societies have examined the available SAPPHIRE data and suggest that the inclusion criteria from that study may be parsed into two groups. The first of those includes anatomic criteria that have been established in large studies to increase surgical risk. For these we suggest immediate expansion of Medicare coverage to include carotid artery angioplasty with stenting. The indications include symptomatic carotid stenosis >50% in patients with:
>
> " contralateral carotid occlusion
> " contralateral laryngeal nerve palsy
> " radiation therapy to neck
> " previous CEA with recurrent stenosis
>
> For the remaining inclusion criteria in SAPPHIRE, we believe that another layer of consideration should be added to the decision-making process to reflect local surgical expertise. In the following patient subsets we believe the degree of risk from CEA faced by the patient is significantly influenced by the outcomes of the surgery/anesthesiology team performing the operation, and that will impact which patients should be offered carotid stenting. We believe it will be important for the interventionalists to collaborate with surgeons who perform carotid endarterectomy at their center to reach agreement on high-risk. If there is concurrence that a particular patient, or patient subset, would be considered "high-risk" for CEA in the hands of the team providing that service, then carotid stenting should be offered as an alternative. As local carotid stenting outcomes data accrue at individual centers we recommend objective review by local peer review processes as a means of certifying the clinical benefit derived from these procedures.
>
> Taken from the SAPPHIRE inclusion criteria set, we suggest the following patients would require a collaborative decision making process including multiple physicians and a surgeon who performs carotid endarterectomy to establish risk level for CEA prior to offering carotid stenting. These would include symptomatic patients with carotid stenosis >50% plus:

- severe pulmonary disease (FEV1 <30%)
- high cervical ICA lesions or CCA lesions below the clavicle
- severe tandem lesions
- age greater than 80 years
- congestive heart failure (class III/IV) and/or known severe LVEF<30%
- open heart surgery needed within six weeks
- recent MI (>24 hours and <4 weeks)
- unstable angina (CCS class III/IV)

Since potential carotid stent patients will be undergoing arteriography, for purposes of inclusion under this coverage policy, we recommend that the final determination of 50% or greater stenosis must be calculated from the angiographic images using the methodology defined in NASCET.

The SAPPHIRE inclusion criteria did include asymptomatic patients with greater than 80% stenosis of the internal carotid artery. The SAPPHIRE data would suggest that carotid angioplasty and stenting is *not inferior to* endarterectomy in this subset of patients at high risk for a surgical procedure. However, the SAPPHIRE trial did not have a medical treatment arm and could not evaluate the safety or efficacy compared to medical treatment. In fact, if the major adverse event rates from the SAPPHIRE trial are extrapolated and compared to data from the major asymptomatic carotid surgery trials (Asymptomatic Carotid Atherosclerosis Study [ACAS]; Asymptomatic Carotid Surgery Trial [ACST]), no benefit can be demonstrated for carotid angioplasty and stenting beyond medical treatment in these patients.

The AANS and CNS believe that the above outlined criteria provide a more reasonable basis for Medicare's coverage policy for carotid stenting, and we urge you to adopt these limitations as opposed to the more expansive FDA guidelines.

Thank you for considering our recommendations. Please contact us if you have any questions or need additional information.

Sincerely,

Robert A. Ratcheson, MD, President
American Association of Neurological Surgeons

Vincent C. Traynelis, MD, President
Congress of Neurological Surgeons

Attachments:
February 3, 2004 Letter to Sean Tunis, MD

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February 3, 2004

Sean Tunis, MD, MSc.
Chief Medical Officer & Director of the Office of Clinical Standards
Centers for Medicare and Medicaid Services
7500 Security Blvd
Baltimore, MD 21244

RE: Medicare Coverage for Carotid Angioplasty and Stenting

Dear Dr. Tunis;

The undersigned medical, surgical and radiologic specialty societies, representing over 50,000 physicians in the United States, offer the following comments regarding reconsideration of the Medicare National Coverage Policy for percutaneous transluminal angioplasty of the carotid artery concurrent with stenting (CAG-00085A, dated March 19, 2001). We acknowledge that the 2001 policy contains a thorough timeline of medical scientific and regulatory events plus an in-depth analysis of the data available at that time, and we agree with the appropriateness of subsequent coverage limited to devices placed in clinical trials receiving Category B IDE designation from the FDA.

At this time, however, our societies believe that data collected over the last three years under auspices of the SAPPHIRE and CREST trials provide sufficiently convincing safety and efficacy information on carotid angioplasty and stenting to allow expansion of coverage to the Medicare beneficiaries considered to be at high-risk for carotid endarterectomy.

We know that CMS will undertake a major review of all available scientific data prior to any decision that would expand the current coverage policy, so only a brief summary of the information that was most convincing to us will be provided herein.

The SAPPHIRE trial recently presented one-year follow-up data on 310 "per protocol" high-risk patients randomized to carotid endarterectomy (CEA) or carotid stenting with cerebral protection (Stent). In SAPPHIRE, the definition of "high-risk" was based on anatomic factors that increase risk due to surgical considerations, and physiologic factors that increase the likelihood of postoperative cardiopulmonary complications. Examples of the former include radiation therapy to the neck or previous CEA with recurrent stenosis, while examples of the latter include advanced congestive heart failure or a recent myocardial infarction. At one-year follow-up, there were no major ipsilateral strokes in the Stent group and 5 major ipsilateral strokes in the CEA group (3.3%, P=0.03). At one-year, a total of 9 strokes (major plus minor, ipsilateral and contralateral) had occurred in the Stent group (5.7%), while 11 strokes (7.3%) occurred in the CEA group (P=0.65). There were 4 MIs (2.5%) in the Stent group and 12 (7.9%) in the CEA group (P=0.04). Finally, at one year there were 11 deaths (6.9%) in the Stent group, and 19 (12.6%) in the CEA group, a statistically similar incidence (P=0.12). Many of these deaths at one-year, however, were unrelated to the carotid treatment, such that the cumulative major

adverse event rate excluding non-neurological deaths occurring after 30-days was 5.7% in the Stent group and 12.6% in the CEA group ($P<0.05$). Although many questions regarding carotid stenting remain to be answered, we believe these data support the SAPPHIRE investigators hypothesis of "non-inferiority" of stenting compared to CEA in this high-risk cohort.

The CREST Lead-In data has also been presented recently. This multicenter NINDS, NIH sponsored trial is designed to compare efficacy of CEA to carotid stenting in all symptomatic patients. The lead-in data for interventionalists was obtained from symptomatic patients with >50% stenosis and asymptomatic patients with >70% stenosis. Stroke, MI, death and other adverse events within 30 days of stenting were ascertained by an independent clinical events committee. As of April 30, 2003, 57 interventionalists from 41 sites had implanted stents in 465 patients. Combined 30-day stroke/death rate for all patients was 3.4% (95% CI: 1.7, 5.0). MIs occurred in only 4 patients (<1%). For symptomatic patients, the 30-day stroke/death rate was 5.6% while the analogous incidence in asymptomatic patients was 2.4%. Although no prospective randomized comparison of Stent to CEA is available yet from CREST, these 30-day stroke/death rates for carotid stenting are remarkably similar to published values from the large prospective NASCET and ACAS CEA trials.

Based on this evidence, our societies now believe it is appropriate to expand coverage for carotid artery stenting to certain "high-risk" patients. As data continue to accrue, and while the technology of carotid stenting and cerebral protection devices, as well as the skill of those performing this therapy, continues to evolve, we believe that a most challenging task will be defining "high-risk". This decision is crucial since withholding stent treatment from those who would benefit is as undesirable as allowing it for subsets in whom equivalence to CEA has not yet been shown. We also acknowledge that this is a moving playing-field, a decision that will need reconsideration several more times in future years.

Our societies have examined the available SAPPHIRE data and suggest that the inclusion criteria from that study may be parsed into two groups. The first of those includes anatomic criteria that have been established in large studies to increase surgical risk. For these we suggest immediate expansion of Medicare coverage to include carotid artery angioplasty with stenting. The indications include symptomatic carotid stenosis >50% in patients with:

" contralateral carotid occlusion
" contralateral laryngeal nerve palsy
" radiation therapy to neck
" previous CEA with recurrent stenosis

For the remaining inclusion criteria in SAPPHIRE, we believe that another layer of consideration should be added to the decision-making process to reflect local surgical expertise. In the following patient subsets we believe the degree of risk from CEA faced by the patient is significantly influenced by the outcomes of the surgery / anesthesiology team performing the

operation, and that will impact which patients should be offered carotid stenting. We believe it will be important for the interventionalists to collaborate with surgeons who perform carotid endarterectomy at their center to reach agreement on high-risk. If there is concurrence that a particular patient, or patient subset, would be considered "high-risk" for CEA in the hands of the team providing that service, then carotid stenting should be offered as an alternative. As local carotid stenting outcomes data accrue at individual centers we recommend objective review by local peer review processes as a means of certifying the clinical benefit derived from these procedures.

Taken from the SAPPHIRE inclusion criteria set, we suggest the following patients would require a collaborative decision making process including multiple physicians and a surgeon who performs carotid endarterectomy to establish risk level for CEA prior to offering carotid stenting. These would include symptomatic patients with carotid stenosis >50% plus:

" severe pulmonary disease (FEV1 <30%)
" high cervical ICA lesions or CCA lesions below the clavicle
" severe tandem lesions
" age greater than 80 years
" congestive heart failure (class III/IV) and/or known severe LVEF<30%
" open heart surgery needed within six weeks
" recent MI (>24 hours and <4 weeks)
" unstable angina (CCS class III/IV)

Since potential carotid stent patients will be undergoing arteriography, for purposes of inclusion under this coverage policy, we recommend that the final determination of 50% or greater stenosis must be calculated from the angiographic images using the methodology defined in NASCET.

We do not believe that coverage of "high risk" patients will adversely impact completion of the CREST trial, which will provide invaluable data about treatment of "normal risk" patients with stenting vs. carotid endarterectomy.

The undersigned societies realize the magnitude of the decision facing CMS regarding expansion of the carotid angioplasty and stenting coverage policy, and we offer our services in whatever means possible. We hope the coverage algorithm offered above will be found acceptable because we believe it offers each patient the optimal choice of treatments, based on a combination of national prospective study data, and the experience and outcomes of interventionalists and surgeons at the patient's chosen medical center. Our societies represent physicians with the greatest surgical and interventional skills available in the United States, and our foremost goal is to provide the best coverage policy for Medicare beneficiaries. We emphasize that this decision will require reconsideration as more scientific data becomes available, and finally, we thank you for the opportunity to comment.

For any further information or discussion, we encourage you to contact any of the listed individuals on the following page. Communications to the entire group may be directed individually or you may contact Anne Marie Bicha, American College of Cardiology, at 301-492-2384 or abicha@acc.org, who would be pleased to distribute any communications to all of the listed contacts.

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September 1, 2006

Steve E. Phurrough, MD, MPA
Director, Coverage Analysis Group
Centers for Medicare & Medicaid Services
Room C1-13-18
7500 Security Boulevard
Baltimore, Maryland 21244

RE: PTA of the Carotid Artery Concurrent with Stenting (CAG-00085R3)

Dear Dr. Phurrough:

On behalf of the AANS/CNS Joint Section on Cerebrovascular Surgery, the American Association of Neurological Surgeons (AANS), the American Society of Interventional & Therapeutic Neuroradiology (ASITN), the American Society of Neuroradiology (ASNR), and the Congress of Neurological Surgeons (CNS), we would like to thank the Centers for Medicare and Medicaid for their thoughtful consideration of PTA of the carotid artery concurrent with stenting. We feel that this is a valuable procedure that can reduce the risk of stroke in the appropriate setting.

We continue to agree with the CMS in their recommendations, and also believe that additional data to support expanded indications beyond the ≥70% symptomatic high surgical risk group is necessary. We also thank the CMS for continuing the policy for coverage for patients in ongoing trials. This will enable physicians to determine other groups of patients who will also benefit from this procedure.

We also believe that the definitions for a symptomatic patient are appropriate, that the medical conditions qualifying as comorbidities as defined by CMS were clearly reasoned, and that the procedure should be based on angiographic confirmation of the degree of stenosis.

We do not feel that the data exists yet to expand coverage of this procedure to the asymptomatic patient outside of the current ruling of stenosis ≥80% within a Category B IDE clinical trial.

We completely agree that the opinion of a surgeon continues to be necessary to determine if a patient is a poor candidate for carotid endarterectomy and urge CMS to retain that language in the coverage policy.

We look forward to ongoing dialogue with the CMS to further clarify any issues or concerns that the agency may have.

Sincerely,

B. Gregory Thompson, MD
Chairman
AANS/CNS Joint Section on Cerebrovascular Surgery

Donald O. Quest, MD
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Gary M. Nesbit, MD
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September 1, 2006

Steve Phurrough, MD, MPA
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RE: Reconsideration of Carotid Artery Stenting Coverage Guidance CAG-00085R3

Dear Dr. Phurrough;

The Society for Vascular Surgery represents over 2,300 physicians in the United States. SVS offers the following comments regarding reconsideration of the Medicare National Coverage Policy for percutaneous transluminal angioplasty of the carotid artery with stenting, CAG-00085R3. SVS appreciates the thorough and ongoing effort expended by the CAG to allow responsible introduction of this exciting technology.

SVS is in a unique position to comment on this topic given the fact that ours is the only specialty involved in treatment of carotid disease using all three modalities; 1) best medical therapy, 2) carotid endarterectomy (CEA), and 3) carotid stenting (CAS). We are particularly excited about the emergence of carotid stenting, a technology that was readily embraced by our specialty.

Vascular surgeons have performed extensive research on endovascular therapies in a variety of anatomic locations, and we continue to do so with publication of many peer-reviewed articles on CAS. Indeed, 22% of the operators in the recently presented CAPTURE trial were vascular surgeons. Thus, we have no vested interest in a specific procedure, rather a global perspective on an evidence based approach to the treatment of carotid atherosclerosis and the prevention of stroke.

This comment provides CMS with our interpretation of the current evidence surrounding safety, efficacy, and durability of CAS in light of the existing alternatives, medical therapy and CEA. In preparing the comment, SVS has also reviewed in detail the "Summary of New Clinical Evidence" document submitted to CMS as part of this reconsideration request.[1]

SVS supports evidence-based diffusion of CAS. Our specific recommendations are listed here. Details and justification are provided in subsequent sections of our letter. SVS recommends:

1. Medicare coverage for CAS with embolic protection should be expanded to include clinical situations when the lesion is surgically inaccessible or when fundamental surgical considerations increase the risk of CEA. We call these "anatomic high risk factors". Specifically, SVS recommends Medicare CAS coverage for asymptomatic patients with ≥80% angiographic stenosis, when and only when the patients harbor anatomic factors that place them high risk for CEA. This is justified primarily by the surgical literature that indicates higher complication rates for CEA under these anatomic circumstances. These are the patients who would typically be considered "at high risk" for CEA in the opinion of an experienced CEA surgeon.

2. Medicare coverage for CAS with embolic protection should not be expanded to include symptomatic patients with 50-70% angiographic stenosis or asymptomatic "physiologic high-risk" patients with ≥80% angiographic stenosis. This recommendation is based on lack of convincing evidence that CAS is superior to best medical therapy, or that CAS is equivalent to CEA, in these subsets. Furthermore, objective determination of physiologic high risk criteria is lacking on a global perspective, and highly dependent on individual surgeon outcomes on a local level.

3. Medicare coverage for CAS should be suspended in patients >80 years of age based on extensive literature demonstrating an unacceptably high stroke/death rate for these patients. Further investigation of CAS in the very elderly is critically important and should be promoted by the Agency in an effort to determine why the complication rate is so high in octogenarians, if there is some means to distinguish the extremely high risk CAS octogenarian from a safer subset, and whether early and late outcomes justify CAS in any subset of patients older than 80. Until such new information is attained, this very elderly subset should remain "noncovered".

4. Medicare coverage for CAS without embolic protection should be implemented for the very small subset of beneficiaries who meet all existing clinical coverage criteria, but for whom the experienced CAS operator deems the use of embolic protection devices more hazardous than protective (e.g. extremely tortuous distal vessel).

5. CMS and other governmental agencies should support to the maximum possible extent, prospective randomized controlled trials and other objective scientific examinations of CAS vs. CEA, and CAS vs. best medical therapy to determine the optimal means to reduce stroke in specific subsets of symptomatic and asymptomatic Medicare beneficiaries (e.g. CREST trial and other high quality scientific investigations).

6. SVS applauds the Agency's initiative to involve national professional societies in development of more formal CAS facility accreditation and recertification processes.

History

In March 2005, CMS published a Decision Memo for Carotid Artery Stenting (CAG-00085R).[2] That document laid out Medicare coverage conditions to include patients who meet three

conditions: 1) are at high risk for carotid endarterectomy (CEA) from an anatomic or physiologic perspective, plus 2) have lateralizing neurological symptoms due to carotid artery stenosis, and 3) have an angiographically proven cervical carotid artery stenosis ≥ 70%. In addition, coverage is limited to procedures performed using FDA approved carotid artery stenting systems and embolic protection devices. That policy has been in place for just over one year.

Issue

CMS received a coverage request to revise a current policy on CAS to cover symptomatic high surgical risk patients with greater than a 50% carotid stenosis, and high-risk asymptomatic patients with greater than an 80% carotid stenosis. The request also proposed deleting language from the current policy that states the patient should be determined to be a poor candidate for CEA "in the opinion of a surgeon".[1]

CMS also plans to use this NCD to explore the possibility of establishing more formal accreditation and recertification processes for CAS facilities, including those developed by national professional societies.[1]

SVS has reviewed the accompanying 'Summary of New Clinical Evidence' document that summarizes recently published and unpublished data and purports to make the case that significant numbers of beneficiaries at risk for stroke are underserved or denied appropriate therapy as a consequence of the current CMS reimbursement policy. We have considered the recently completed and ongoing CAS trials to determine if, in our opinion, sufficient scientific evidence exists to broaden CAS coverage to include the requested populations. The trials and registries we reviewed include:

ARCHER[3]
CAPTURE[1, 10]
CREST lead-in data[5]
CAVATAS[12,13]
EVA 3S[14]
SPACE[8]

Criteria for defining patients at high risk for CEA

SVS begins this review by stating that the criteria for "high risk for CEA" have never been tightly defined by CMS, and in at least one circumstance (octogenarians), high risk for CEA as defined by CAS investigators would appear to be even higher risk for CAS. The following includes our assessment and specific recommendations.

While it is intuitively logical to argue that complications of any intervention will increase with increasing risk profile of the patients considered for treatment, the definition of the subgroup of patients deemed to be "high-risk" for CEA has been elusive. Most would agree that there are two general categories of consideration including 1) anatomic high-risk indicators, i.e. circumstances of the lesion itself or fundamental surgical considerations of the neck, and 2) physiologic high-risk comorbidities including cardiac, pulmonary, or renal dysfunction. It is

important to note that the anatomic high-risk markers are discreet and clearly definable, while several of the generally considered physiologic high-risk criteria are less clearly defined. In addition, individual high-risk CEA markers may have variable effects on CAS outcomes. For instance, in the SAPPHIRE trial, nearly one third of the patients were considered high-risk on the basis of a prior ipsilateral CEA. While prior CEA is an anatomic high risk criterion for CEA, this subgroup is generally considered a low risk marker for CAS. In contrast, in the CAPTURE study (discussed in detail below) less than 10% of the patients were high-risk based on anatomic considerations, while 90% had "physiologic" high-risk markers.

It is important to note that nearly 25% of the CAPTURE patients were high-risk based on their status as octogenarians.[1] This is an excellent example of how the catch-all "high-risk" basket has failed, and we urge CMS to focus on refining high-risk criteria in the upcoming decision. Age >80 has universally been considered a high-risk indicator for CEA in CAS studies and registries, and therefore a positive indicator for CAS. However, the bulk of available evidence clearly demonstrates that CAS in octogenarians is attended by a significantly elevated, in fact, an unacceptably high risk of stroke. In the CREST Lead-In data, octogenarians had a 12% stroke/death rate.[5] In SPACE, symptomatic patients >75 years had an 30-day stroke/death rate of 11%.[8] In CAPTURE, patients >80 years (90% asymptomatic/10% symptomatic) had a 30-day stroke/death rate of 7.4%.[10] For comparison, Goldstein et al identified a stroke/death rate of 7.8% after CEA in those older than 75 in a review published back in 1998.[15] Teso et al published a review of >14,000 CEAs performed in Connecticut between 1990 and 2002, and found a 1.8% stroke death rate in octogenarians.[16] Miller et all reviewed a single center 12-year experience that included 334 patients older than 80 years. The combined stroke/death rate was 3.1%, based on a 6.0% rate in symptomatic patients vs. 0.9% in asymptomatics.[17] While we remain very optimistic about the CAS modality overall, SVS recommends that CMS exclude individuals ≥80 years in age due to an excessive risk of peri-procedural stroke until further research clarifies the best clinical recommendation for these patients.

We recommend that conditions that constitute "high risk for CEA" be more precisely defined to allow more specific analysis. This is especially important if the coverage language referring to opinion by a surgeon is deleted. These are the anatomic high risk criteria that we recommend:

Anatomic High-Risk Criteria for CEA

1. contralateral carotid occlusion
2. previous CEA with recurrent stenosis
3. prior radiation therapy to neck with ablative neck surgery, e.g. radical neck dissection
4. surgically inaccessible cervical lesion, above C2
5. CCA lesion below the clavicle
6. Contralateral vocal cord palsy
7. Presence of tracheostomy stoma

REVIEW OF RECENT LITERATURE AND AVAILABLE DATA

Observation: Study results are oftentimes not parsed between symptomatic and asymptomatic patients, rendering meaningful interpretation impossible.

Observation: Study results that fail to independently analyze lower risk subsets (e.g. recurrent carotid stenosis after CEA) are difficult to interpret.

Observation: The only new Level 1 CAS evidence we are aware of includes the recently published SPACE trial and the soon-to-be-published EVA 3S trial.

Observation: Several of the trials providing "new data" are yet to be published in peer-reviewed journals.

Observation: The CAPTURE and ARCHeR Registries are uncontrolled datasets. They attempt to draw conclusions regarding CAS from comparisons with conglomerated historical datasets, or from comparison to CEA vs. medical therapy studies (e.g. NASCET, ACAS, ACST).

Observation: Status of Level 1 evidence:

- CAVATAS II RCT CEA vs. CAS in normal surgical risk pts. No data available
- CREST RCT CEA vs. CAS in normal surgical risk pts. Currently enrolling
- EVA-3S recently completed RCT CEA vs. CAS in normal-risk pts
- SAPPHIRE, published in 2004 prior to CMS CAG 00085R.
- SPACE, published in Lancet, 2006
- TACIT no funding source identified yet.

New Information

CAPTURE trial[1,10]

Sponsor: Guidant. FDA required post approval study
Peer-reviewed data not available. Data extracted from Guidant publications
Study Design: Prospective, multi-center, non-randomized, 140 centers, 341 physicians
>2500 “primarily” high-risk patients

	30 Day Stroke/ Death/ MI	**30 Day Stroke/ Death**
CAPTURE[1] Asymptomatic n=2656	5.1%	4.6%
CAPTURE[1] Symptomatic n=284	12.3%	10.6%

Narrative: Detailed data from the capture trial were presented in March 2006 at the ACC meeting. These data raise considerable concern about the safety of angioplasty and stenting, although the presenters concluded that in asymptomatic, so-called high-risk patients less than 80 years of age, the combined stroke and death rate of 3.6% "approaches" that same complication rate in, for example, the ACST CEA trial.

SVS observation: 30-day SDMI rate of 5.1% in asymptomatic patients is unacceptable, at least double that achieved in many large series of CEA (see Table of CEA results). For example, in a recently reported multicenter study containing nearly 2000 patients treated in 6 New York state hospitals in 1997 and 1998 by 64 surgeons, the overall stroke/death rates at 30 days was 2.3% in asymptomatic patients, 2.9% in those with TIAs, and 7.1% in patients who had suffered a recent stroke.[4] Similarly, in the massive national surgical quality improvement database (NSQIP), in private practice hospitals, a recent report of over 13,000 CEA operations performed between 2000 and 2003 in 137 facilities noted a 30-day stroke/death rate of 3.4%.[7] In the ACST trial, the figure was 3.4%.[18] The surgical series contain considerable overlap of patients who might well be considered "high-risk for CEA". Indeed, the NSQIP database study reported that 25% of its patients would be considered at "high-risk" by SAPPHIRE study criteria.[7] Furthermore, subgroup analysis of results in the CAPTURE study provides cause for concern. The 30-day stroke and death rate in asymptomatic individuals was 4.4%. This exceeds the 3% complication threshold long-established by an American Heart Association consensus panel and generally used in the surgical literature as a maximum acceptable rate for these complications and the treatment of asymptomatic patients.

The data from CAPTURE are also genuinely worrisome and consideration of treatment of patients with symptomatic carotid lesions, with a 30-day stroke and death rate of 12.3%. Depending on the degree of stenosis present in symptomatic patients, the 12.3% 30-day SDMI rate may not represent an improvement over natural history, especially if many of these were 50-70% rather than >70% stenoses.

CAPTURE also emphasizes a fact that has been repetitively demonstrated in the recent literature, namely an unacceptably high periprocedural complication rate in octogenarians. In CAPTURE, the composite end point of death, stroke, and MI, or stroke considered individually, or death considered individually, were all statistically increased in octogenarians.

ARCHeR trial[3]

Sponsor: Guidant
Study design: prospective non-randomized registry, three phases
Published: JVS 2006

	30 Day Stroke/ Death/ MI	**30 Day Stroke/ Death**	**One-year major ipsilateral stroke rate**	**One-year target lesion revascularization**
ARCHeR Asymptomatic	6.8%	5.4%	1.6% combined	2.2%

ARCHeR Symptomatic	13%	11.6%		

SVS observation: Uncontrolled data appears to have unacceptably high 30-day SDMI rate for asymptomatic patients. See comments on CAPTURE above.

SVS observation: Uncontrolled data. Depending on the degree of stenosis present in symptomatic patients, these results may not represent an improvement over natural history. See comments on CAPTURE above.

EVA-3S[14] Endarterectomy versus Angioplasty in Severe Symptomatic carotid Stenosis
Sponsor: French Government
Study design: RCT of CEA vs. CAS in normal-risk patients
Arm with CAS without DEP terminated by DSMC due to high stroke incidence

This was a multicenter, randomized, non-inferiority trial comparing stenting to endarterectomy in patients with a symptomatic carotid stenosis of at least 60 percent. The primary end point was the incidence of stroke or death within 30 days of treatment. It is our understanding that the trial was stopped prematurely after the inclusion of 527 patients for safety issues. The rates of death and stroke at 1 and 6 months were reportedly lower with endarterectomy than with stenting. We believe the manuscript has been accepted for publication in a first-line peer-reviewed journal.

SECuRITY trial[1]

Whitlow PL. Multicenter registry in high-risk Symptomatic and Asymptomatic Carotid Disease with the Abbott Xact stent and MedNova Filter. The results of this trial were presented at TCT 2004.

	30 Day Stroke/Death/MI
SECuRITY Asymptomatic	7.5% combined
SECuRITY Symptomatic	

SVS conclusion: Cannot interpret results until parsed between asymptomatic and symptomatic.

SPACE trial[8]
Sponsor: German Research Foundation
Study Design: Prospective, multicenter, randomized CAS vs. CEA, 1183 symptomatic "normal-risk patients, non-inferiority design

Results: SPACE failed to prove non-inferiority of CAS compared to CEA for the periprocedural complication rate.

	30 Day Stroke/ Death
SPACE CAS	6.84%
SPACE CEA	6.34%

SVS conclusion: Excellent study, but not exactly relevant to CMS question at hand regarding coverage for "high-risk" patients.

Contemporary results of CEA

Carotid endarterectomy is a mature procedure, but refinements in technique and periprocedural care continue. A frequent criticism is that favorable results reported in large series from academic medical centers are not representative of the broad spectrum of practice. Multiple single center series can be cited with combined stroke/death rates less than 2%. However, a variety of recent studies representing a spectrum of surgical practice are now available in the literature, and these manuscripts indicate that procedural safety of CEA is generally well-established (see Table). Processes of care in the practice of CEA have been refined to make a good treatment even safer. For example, two large studies recently documented the benefit of regional anesthesia in decreasing perioperative complications. As difficult as it is to complete a randomized controlled trial or a concurrent controlled trial, evolution of the safety of CEA must be considered whenever CAS results require a basis for comparison. Historical CEA results may not suffice.

Author	Reference	Comment	# Patients	Stroke/Death
Matsen et al[11]	J Vasc Surg In press	Administrative database from Maryland	23,237	Stroke rate 0.29-0.65% in asymptomatic patients annually from 1996 to 2003. Stroke rate 0.90-2.29% in symptomatic patients annually from 1996-2003. Death rate 0.33%-0.58% annually. Data at hospital discharge
Stoner et al[7]	J Vasc Surg 2006	NSQIP	13,622	3.4% stroke/death @ 30-days
Halm et al[4]	J Vasc Surg 2005	6 NY State hospitals	1,972	2.3% stroke/death @ 30-days in asymptomatic patients, 2.9% in TIA patients, 7.1% in patients who had prior stroke

Several groups have stratified patients treated by carotid endarterectomy into low and high risk cohorts (as defined by Sapphire) and have been unable to demonstrate a statistically significant difference in outcome.[19,20]

It is likely that there does exist a small cohort of patients that are indeed physiologically high risk for carotid endarterectomy. It is not, however, clear whether these patients are best treated with angioplasty and stent or alternatively medical therapy. Moreover, the precise makeup and size of this cohort of patients needs to be further defined.

Comments on Facility Accreditation and Recertification

Due in large part to our commitment to the management of carotid artery disease, SVS appointed an Outcomes Committee that worked diligently to put together an on-line registry that would not only include CAS but also CEA cases. This registry is HIPAA-compliant, auditable, and has the capacity of providing to authorized individuals risk-adjusted results of their center anonymously compared to all other centers contributing data to the registry. This registry is consistent with the "Registries for Evaluating Patient Outcomes" Task Order set forth by the Agency for Healthcare Research and Quality (AHRQ). Participating centers will be capable of providing CMS with their results on a 6 monthly-basis as required by the current facility accreditation rules set forth by CMS. The objectives of the audits are to ensure that all cases are entered into the Vascular Registry and that the data entered are accurate and avoid selection bias. We are in the process of scheduling audits of the participating Medical Centers contributing data to the registry. As of August 1, 2006 we have 1387 procedures entered into the registry divided almost equally between CEA and CAS. SVS hopes that it can obtain CMS support of this registry as part of the agency's effort to create appropriate CAS facility accreditation and recertification.

CAS Without Embolic Protection

Regarding requirement for distal embolic protection, SVS agrees that current scientific data supports the efficacy of distal embolic protection during CAS. Nevertheless, there are individualized clinical situations when the operator determines use of embolic protection to carry more risk than benefit. In other cases the operator will have undertaken appropriate attempts to deploy embolic protection but found it technically impossible to do so. We therefore recommend coverage for CAS without embolic protection: 1) when the operator documents the rationale that risks of embolic protection exceed potential benefits, or 2) when the operator documents reasonable attempts to deploy embolic protection and sites the technical reasons why this was not possible.

SVS Conclusions Regarding CAS Coverage

There is no new level 1 evidence to justify expansion of CAS with embolic protection to patient subgroups beyond those already approved by CMS for coverage.

Data from ARCHeR and CAPTURE for CAS with embolic protection in patients at high risk for carotid endarterectomy reveal discouraging 30 Day rates of death, stroke, and MI. It is impossible to be convinced that these data provide a sufficient evidence base to expand CAS coverage. Parenthetically, the complication rates and these trials far exceed that which would be accepted by typically applied surgical thresholds.

SVS encourages CMS CAG to withdraw routine coverage for CAS in octogenarians. Until further investigative data become available, carotid endarterectomy or medical therapy would appear to be safer routes of intervention. CMS should strongly support well-designed research trials to further examine the issue of CAS in the very elderly.

SVS encourages our governmental agencies to support randomized controlled trials and concurrent controlled trials to help determine the populations that will truly benefit from CAS with distal embolic protection.

SVS encourages all CAS providers to participate in randomized controlled trials such as CREST

The Society for Vascular Surgery thanks CMS and the CAG for their objective assessment of the carotid stent issue. We would like to end by emphasizing our commitment to the complete management of carotid disease to include medical, surgical, and endovascular therapy. We are committed to the advancement of all these therapies in general and carotid stenting in particular. Although some of our members would like to see this new technology liberalized, we do feel that strong evidence is not yet available to make this recommendation at this time. However, we will be ready to reconsider this position as soon as level 1 evidence becomes available to support expanding coverage. We are available at any time for telephone or in-person discussions regarding our comments.

K. Craig Kent, M.D.
President
and the Executive Council of
The Society for Vascular Surgery

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To whom it concerns:

I am an Interventional Radiologist who has performed approximately 100 CAS. I have had only 1 complication- a small reperfusion bleed- in a severely ill patient. This procedure is the future and the future is yesterday. We, the medical field, have done all we can do to drag our feet on this issue, essentiallly due to hard lobbying from a strong surgical society. I firmly believe in this procedure and I ask you to put yourselves in the position of my carotid patients- many of whom were not high risk. Would you rather have a minimally invasive procedure with a 36 hour average hospital stay or would you prefer to have your neck and artery cut open, often under general anesthesia, with an extended hospital stay with greater risk of stroke? What are we waiting for, support from the old school surgeons? I will be retired by then and I am not even forty. Look no further than the newly tained vascular surgeons who are very excited about CAS. Unfortunately, they are younger and less influential than their older collegues. WE NEED TO DUE WHAT IS IN THE BEST INTEREST OF THE PATIENT. Do not kid yourself, the answer is already obvious to the patients, why is the government taking so long ?

Michael Rogoff, MD

As a physician who performs CAS both within and IDE(CAPTURE) study and outside the study, I believethe criteria for medicare patients should beincreased to assymptomatic patients > 80y andSymptomatic> 50%.Carotid stenting has been shown to be safe andeffective and will, in fact, become the first linetreatment of carotid stenosis.

Kenneth E. Najarian MDProfessor of RadiologyDirector, Vascular and Interventional Radiology802-847-3663 Angio Suite802-847-3592 Executive Assistant 802-847-4822 FAX 802-847-2700 Provider Access

I am in strong favor of the revision of the guidelines under consideration. R Freedman MD

I am writing to state my feelings that coverage for carotid stenting should be extended to 50% lesions that are symptomatic and 70% lesions that are asymptomatic. These are the proven criteria in NASCET that support treating such lesions to reduce the incidence of stroke and TIA. To set different criteria for CEA and stenting flies in the face of all rationale and shows a bias towards CEA that can no longer be accepted.
While the need for the patient to be high risk is one approach to the issue I believe this too biases towards CEA and will slow down the adoption of the least invasive and intrusive therapy.

Michael Horowitz, M.D. Associate Professor of Neurosurgery and Radiology Director, Neuroendovascular Surgery Co-Director, Cerebrovascular Surgery Academic Director, Center for Cranial Nerve Disorders University of Pittsburgh Medical Center

I strongly support the proposal to extend Medicare coverage of carotid stenting to high-risk patients (high risk for CEA) with symptomatic carotid disease >50% or asymptomatic patients with >80% disease. The registry trials evaluating carotid stenting in such patients have consistently shown good outcomes with acceptable complication rates, especially the Guidant CAPTURE trial (results reported 10/05 at TCT 2005). I would also strongly support the proposal that physicians implanting carotid stents should not be required to have a vascular surgeon confirm high surgical risk. There are both anatomic and co-morbid circumstances that create "high risk" for endarterectomy. In the case of co-morbid medical conditions such as CAD, CHF, or COPD, cardiologists are better suited to make the risk assessment vice a vascular surgeon who is not familiar with the patients conditions and treatments. In fact, vascular surgeons routinely have cardiologists consult on their patients prior to surgery to evaluated their cardiopulmonary status.

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I am commenting to express my support for expanding Medicare coverage for carotid stenting for high risk patients. Specifically, I feel that asymptomatic patients with > 80% stenos is should be included.
I base my comments on my eight years experience with carotid stenting, having performed several hundred procedures. We have participated in Archer, Beach, and Capture trials, and we are currently enrolling in Exact, Capture II, and Act I trials. The results of Sapphire clearly show that carotid stenting is superior to CEA in high risk patients, even if they are asymptomatic. The post market studies show that carotid stenting can be safely performed. The majority of patients in these studies were asymptomatic. To exclude these patients from coverage would subject them to a higher risk procedure.
The conditions that make patients high risk have been well established in the clinical trials. The opinion of a surgeon is not necessary to make the determination of high risk. I feel that age > 80 should also be considered high risk.
Thank you for allowing me to express my concerns.
Charles Zacharias Medical Director, St Mary’s Cardiac Cath Lab Richmond, Virginia