Carotid Artery Stenting

Clinical Expert

Robert M. Bersin, MD, MPH
Medical Director, Structural Heart Services
Medical Director, Endovascular Services
Swedish Medical Center
Disclosure

Any unmarked topic will be considered a “Yes”

<table>
<thead>
<tr>
<th>Potential Conflict Type</th>
<th>Yes</th>
<th>No</th>
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<td>1. Salary or payments such as consulting fees or honoraria in excess of $10,000.</td>
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<td>5. Research funding.</td>
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<td>6. Any other relationship, including travel arrangements.</td>
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If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

**SEE ATTACHED RWI STATEMENT**

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<td></td>
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<tr>
<td>grants from industry or government).</td>
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If yes to #7, provide name and funding Sources:

If you believe that you do not have a conflict but are concerned that it may appear that you do, you may attach additional sheets explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.

**X**

*Signature* 9/9/13

*Date*  "SERTAL, N.O*

*Print Name*

For questions contact: Christine Masters
Health Technology Assessment
PO Box 42712
Olympia, WA 98504-2712
360-725-5126
Relationships with Industry Statement for Robert M. Bersin, M.D.:

Abbott Vascular C, P, SB
Boston Scientific AB, C, EI, P, SB
Cook Medical, Inc. C, P
Cordis Endovascular C, EI
Covidien, Inc. C, P
Medtronic Vascular C
Omeros Corp, EI
Sapheon, Inc. EI
Spectranetics, Inc. C, P
St. Jude Medical C
Trireme, Inc. AB, EI
Vatrix Medical EI
W.L. Gore C, P

AB: Advisory Board
C: Consulting Relationship
EI: Equity Interest
GS: Grant Support
P: Proctor or Training Course Sponsorships
SB: Speakers Bureau
SE: Spouse Employee
SO: Stock Options or Positions
CURRICULUM VITAE
ROBERT M. BERSIN, M.D.

CONTACT INFORMATION

Swedish Heart and Vascular
550 17th Avenue, Suite 680
Seattle, Washington 98122 USA
Citizenship: USA

Tel: 206-320-4399
Cell: 206-617-9048
Fax: 206-320-4820
Email: robert.bersin@swedish.org

Marital Status: Married
Wife: Michelle Marie Sailor
Children: Bradford Robert, Brenton Matthew

EDUCATION

<table>
<thead>
<tr>
<th>Dates</th>
<th>Institution &amp; Location</th>
<th>Degrees Conferred</th>
<th>Major Subjects</th>
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<tr>
<td>1981</td>
<td>University of California, Los Angeles, School of Medicine</td>
<td>M.D.</td>
<td>Medicine</td>
</tr>
<tr>
<td>1981</td>
<td>University of California, Los Angeles, School of Public Health</td>
<td>M.P.H.</td>
<td>Health Services, Administration</td>
</tr>
<tr>
<td>1976</td>
<td>Stanford University, Stanford, California</td>
<td>B.A., B.S.</td>
<td>Psychology/Biology</td>
</tr>
</tbody>
</table>

LICENSES AND CERTIFICATES

2005  Licensure, Washington State Board of Medical Examiners, No. 45286
2003  Certified, American Board of Internal Medicine, Interventional Cardiology, No. 098645
1990  Licensure, South Carolina State Board of Medical Examiners, No. 14748
1989  Licensure, North Carolina State Board of Medical Examiners, No. 38298
1987  Certified, American Board of Internal Medicine, Subspecialty of Cardiovascular Diseases, No. 098645
1987  Fluoroscopy Operator Permit, Department of Health Services, State of California, No. 128331
1984  Certified, American Board of Internal Medicine, No. 098645
1982  Licensure, California State Board of Medical Quality Assurance, No. G48862
1982  Diplomate, National Board of Medical Examiners, No. 236333
PRINCIPAL POSITIONS HELD

2011 – Swedish Medical Center  
Seattle, Washington  
Medical Director  
North End Cardiology Operations

2010 – 2011 Seattle Cardiology  
Seattle, Washington  
Management Board Member

2007 – 2010 Society for Cardiac Angiography and Interventions (SCAI)  
Washington, DC  
Member, Board of Trustees

2006 – Swedish Medical Center  
Seattle, Washington  
Medical Director  
Endovascular Services

2006 – 2010 Hope Heart Institute  
Seattle, Washington  
Medical Director  
Endovascular Research

2006 – 2009 Seattle Cardiovascular Center  
Seattle, Washington  
Medical Director

2005 – 2009 Seattle Cardiology, PLLC  
Cardiovascular Consultants of Washington, PLLC  
Senior Partner  
Director of Endovascular Services  
Director of Clinical Research

1989 – 2004 The Sanger Clinic, P.A.  
Carolinas Heart Institute  
Heineman Medical Research Ctr.  
University of North Carolina  
Chapel Hill, North Carolina  
Senior Partner  
Faculty Member  
Senior Clinical Investigator  
Associate Clinical Professor of Medicine

1988 – 1989 Cardiology Division, and Cardiovascular Research Institute,  
University of California  
San Francisco, CA  
Assistant Professor of Medicine  
Assistant Director, Coronary Care Unit, Moffitt Hospital

1986 – 1988 Cardiology Division, and Cardiovascular Research Institute,  
University of California  
San Francisco, CA  
Instructor and Attending Physician Coronary Care Unit, Moffitt Hospital

1984 – 1986 Cardiology Division  
University of California,  
Cardiology Fellow
1981 – 1984 Department of Medicine
Internal Medicine Resident
University of California, San Francisco, CA

1981 Department of Microbiology
and Immunology
Post-Doctoral Researcher
University of California, Los Angeles, CA

1978 – 1979 World Health Organization
Pre-Doctoral Researcher
Lausanne, Switzerland

1977 Department of Medicine
Pre-Doctoral Researcher
University of New Mexico
Albuquerque, New Mexico

HONORS AND AWARDS

2011 America’s Top Physicians, Cardiology, Consumers’ Research Council of America
2011 Best Doctors in America
2010 America’s Top Physicians, Cardiology, Consumers’ Research Council of America
2009 America’s Top Physicians, Cardiology, Consumers’ Research Council of America
2008 Who’s Who Global Directory - Medicine
2007 Best Doctors in America
2007 Biltmore Who’s Who Among Executives and Professional Men
2006 Manchester Who’s Who Among Professionals in Research, Medicine and Healthcare
2006 Biltmore Who’s Who Among Executives and Professional Men
2006 America’s Top Physicians, Cardiology, Consumers’ Research Council of America
2004 America’s Top Physicians, Cardiology, Consumers’ Research Council of America
1988 American Heart Association, National Center Research Award
1987 International Society of Nephrology Travel Award
1985 Physician-Scientist Award, National Heart, Blood and Lung Institute, National Institutes of Health
1980 Visiting Scientist, Chinese Academy of Medical Sciences, Shanghai, Peoples Republic of China
1979 Anna Bing Arnold Fund Scholarship
Medical Faculty Wives of UCLA Scholarship
1978 USPHS Research Service Award
UNESCO International Research Grant
Medical Foundation of North Carolina International Travel Grant
Exchange Student, University of Geneva, Switzerland, and Oxford University Medical School, Oxford, England
1977 Kroc Foundation Award Fellowship in Immunology
1976 Distinction and Departmental Honors, Stanford University
MEMBERSHIPS IN PROFESSIONAL ORGANIZATIONS

American College of Cardiology, Fellow
American College of Physicians, Fellow
American Federation for Clinical Research, Member
American Heart Association, Silver Heart Member and Fellow, Council on Clinical Cardiology
American Society for Cardiac Interventionists, Member
European Society of Cardiology, Fellow
International Andreas Gruentzig Society, Fellow
International Society for Endovascular Specialists, Fellow
Society for Cardiac Angiography and Interventions, Fellow

ADVISORY AND EDITORIAL REVIEW BOARDS

American Journal of Medicine, Ad hoc reviewer
American Journal of Physiology, Ad hoc reviewer
Boston Scientific Corporation, Medical Advisory Board
Catheterization and Cardiovascular Interventions, Ad hoc reviewer
Circulation, Ad hoc reviewer
Clinical Cardiology, Ad hoc reviewer
Cordis Endovascular, Key Opinion Leader Member
Endovascular Today, Editorial Review Board Member
Food and Drug Administration, Orphan Drug Division, Scientific Council Advisor
Genentech, Inc., Scientific Advisory Board
Journal of the American College of Cardiology, Editorial Review Board Member
ReVascular Therapeutics, Medical Advisory Board
Vascular Solutions, Inc., Medical Advisory Board

CLINICAL ACTIVITIES AND SPECIAL PROCEDURAL SKILLS

Diagnostic Coronary Angiography
Flowwire and Pressurewire Lesion Characterization
Intravascular Ultrasound
Optical Coherence Tomography
Percutaneous Transluminal Coronary Angioplasty and Stenting
Coronary Laser and Rotational Atherectomy, Thrombectomy and Thrombolysis
Transfemoral Aortic Valve Replacement (TAVR)
Peripheral Angiography and Interventions (all circulations)
Percutaneous Transluminal Peripheral Angioplasty and Stenting
Peripheral Atherectomy (Excisional, Extractional, Rotational, Orbital and Laser)
Peripheral Thrombectomy and Thrombolysis
Brachiocephalic, Carotid and Vertebral Interventions
Endoluminal Stent Grafting (EVAR, TEVAR and Endovascular)
Embolization (all circulations except intracranial)
IVC Filter placement and retrieval
INSTITUTIONAL COMMITTEES

2007 – 2010  Member, Board of Trustees
Society for Cardiac Angiography and Interventions

2006 –  Member, Board of Medical Directors, Swedish Heart and Vascular Institute

2006 – 2009  Member, Endovascular Quality Review Committee, Swedish Medical Center

2006 – 2009  Co-Chairman, Endovascular Committee
Society for Cardiac Angiography and Interventions

2005 –  Member, Vascular Program Council, Swedish Medical Center

2005 – 2007  Member, SCAI Carotid Stent Registry Working Group
eSCAI Committee, Society for Cardiac Angiography and Interventions

2004 – 2005  Member, Interventional Cardiology Task Force, American College of Cardiology

1993 – 2004  Director, Peripheral Invasive Laboratories, Carolinas Heart Institute
Carolinas Medical Center

1992 –  Interventional Cardiology Committee
Society for Cardiac Angiography and Interventions

1990 - 2004  Cardiac Cath Lab Committee
Critical Care Committee
Clinical Research Committee
Thrombolysis Committee, Chairman
Carolinas Medical Center, Charlotte, North Carolina

1988 – 1989  Coronary Care Committee
UCSF Moffitt Hospital, San Francisco, CA

SPECIAL PROFESSIONAL EDUCATIONAL ACTIVITIES

2012 –  Faculty Member, Endovascular & Coronary Revascularization (ENCORE), Seoul, Korea

2012 –  Faculty Member, Taiwan Society for Vascular Surgery (TSVS), Taipei, Taiwan

2011 –  Faculty Member, Paris Course on Revascularization (EuroPCR) Paris

2011 –  Faculty Member, Endo-Vascular Challenges and Solutions (E-VACS) Venice

2010  Faculty Member, Venice Extreme Intervention Meeting (EVIVENICE)

2010 –  Faculty Member, Joint Interventional Meeting (JIM)

2010 –  Faculty Member, International Symposium on Endovascular Therapy (ISET)
BERSIN, Robert M., M.D.
Curriculum Vitae
Page 6 of 17

2008 – 2010  Course Director, SCAI Meeting of the Americas-Cabo Interventional Summit
2008 – 2010  Course Co-Director, Science Innovation Synergy (SIS) Meeting
2008 –       Faculty Member, TransValve Therapeutics (TVT)
2008 –       Faculty Member, Global Endovascular Complications Seminar
2008 –       Live Case Operator and Faculty Member, TransCatheter Therapeutics (TCT)
2007 – 2011  Faculty Member, Latin American Society of Interventional Cardiology (SOLACI)
2007 –       Faculty Member, Complex Interventional Cardiovascular Therapy (CICT)
2007 – 2010  Faculty Member, Society for Cardiovascular Angiography and Interventions (SCAI) Acute Stroke Intervention Conference
2007 – 2010  Faculty Member, Society for Cardiovascular Angiography and Interventions (SCAI) Fellows Course
2005 – 2009  Course Co-Director, SCAI Annual Cardiovascular Conference at Snowmass
2000 – 2004  Faculty Member, ACC Annual Cardiovascular Conference at Snowmass
2005 –       Faculty Member, TransCatheter Therapeutics (TCT)
2003 – 2004  Live Case Operator and Faculty Member, TransCatheter Therapeutics (TCT)
2003 – 2004  Course Co-Director, Advanced Cardiovascular Interventions, Hilton Head, SC
1993 – 2002  Faculty Member, Advanced Cardiovascular Interventions, Hilton Head, SC
2000 – 2009  Faculty Member, SCAI/ACC Cardiovascular Conference in Hawaii
2000 –       Faculty Member, ACC National Meeting Interventions/I2 Summit
2003 –       Faculty Member, Vascular Interventional Advances (VIVA)
1999 – 2006  Faculty Member, New Devices Seminar, Orlando, Florida
2002 –       Faculty Member, Emory Practical Intervention Course (EPIC)
2002 – 2005  Faculty Member, Interventions Course (ACRI)
2007 – 2010  Faculty Member, All That Jazz Course Oschner Clinic
2000 – 2003  Faculty Member, All That Jazz Course Oschner Clinic
2006 –       Faculty Member, Japan Circulation Society Meeting, Nagoya, Japan
2005 –       Faculty Member, 22nd Annual Kokura Live Case Demonstration Course, Fukuoka, Japan
2005 –       Faculty Member, Tokyo Percutaneous Coronary Intervention Conference (TOPIC), Tokyo, Japan
2005 – 2008  Faculty Member, Society for Cardiovascular Angiography and Interventions (SCAI) Core Curriculum on Carotid Stenting
2005 –       Faculty Member, Society for Cardiovascular Angiography and Interventions (SCAI) Annual Meeting
2000 –       Co-Chairman, Society for Cardiovascular Angiography and Interventions (SCAI) Annual Meeting
2000 –       Faculty Member, International Congress on Endovascular Interventions, Arizona Heart Institute

**DEVICE CERTIFICATION DIRECTORSHIPS AND PROCTORSHIPS**

2006 –       Proctor, Abbott XACT Carotid Stent Device Certification
2005 –       Proctor, Coronary BSC Rotablator Device Certification
2004 – 2005  Course Director, CASES Cordis Carotid Stent Device Certification
2004 –       Proctor, Guidant Acculink Carotid Stent Device Certification
2002 – 2004  Proctor, Guidant Ancure Device Certification
BERSIN, Robert M., M.D.
Curriculum Vitae
Page 7 of 17
2002 – 2004 Faculty Member, BSC IVUS Advanced Technology Training Program
2002 – 2006 Faculty Member, LuMend Frontrunner Device Certification
1999 – 2006 Proctor, AneuRx Endoluminal Stent Graft Device Certification
1992 – 1994 Course Director, Peripheral Rotablator Device Certification

RESEARCH ACTIVITIES

2012 – Principal Investigator, Cordis INSPIRATION Trial, Swedish Medical Center, Seattle, Washington
2012 – Principal Investigator, Abbott CANOPY Carotid Stent Post-Market Surveillance Study, Swedish Medical Center, Seattle, Washington
2010 – Co-Investigator, ev3 DEFINITIVE LE Trial, Swedish Medical Center, Seattle, Washington
2010 – Co-Investigator, ev3 DURABILITY SFA Stent Trial, Swedish Medical Center, Seattle, Washington
2009 – 2010 Co-Investigator, BSC ORION Iliac IDE Trial, Swedish Medical Center, Seattle, Washington
2009 – 2011 Principal Investigator, CardioMems PRICELESS AAA Endograft Pressure Sensor Monitoring Study, Swedish Medical Center, Seattle, Washington
2009 – 2009 Co-Investigator, BSC PLATINUM DES IDE Trial, Swedish Medical Center, Seattle, Washington
2008 – 2010 US Principal Investigator, Cook REFORM Renal Stent IDE Trial, Swedish Medical Center, Seattle, Washington
2008 – 2008 Principal Investigator, ARMOUR Carotid Embolic Protection IDE Trial, Swedish Medical Center, Seattle, Washington
2008 – 2009 Principal Investigator, VIVA SALVAGE Trial, Swedish Medical Center, Seattle, Washington
2008 – 2009 Principal Investigator, VIVA EXCEL Trial, Swedish Medical Center, Seattle, Washington
2007 – Principal Investigator, SAPHIRE WW Carotid Stent Post-Market Surveillance Study, Swedish Medical Center, Seattle, Washington
2006 – 2007 Principal Investigator, Abbott XACT Carotid Stent Post-Market Surveillance Study, Overlake Hospital, Bellevue, Washington
2005 – 2008 Co-Investigator, CREST Trial, Swedish Medical Center, Seattle, Washington
2004 – 2004 Principal Investigator, VALOR Talent Thoracic Endograft Trial, Carolinas Medical Center, Charlotte, North Carolina
2004 – 2004 Principal Investigator, CAPTURE I Carotid Stent Post-Market Surveillance Study, Carolinas Medical Center, Charlotte, North Carolina
2004 – 2004 Principal Investigator, CASES Carotid Stent Post-Market Surveillance Study, Carolinas Medical Center, Charlotte, North Carolina
2003 – 2004 Co-Investigator, CREST Carotid Stent Trial, Carolinas Medical Center, Charlotte, North Carolina
2002 – 2004 Principal Investigator, EndoTex CABERNET Carotid Stent Trial, Carolinas Medical Center, Charlotte, North Carolina
2002 – 2004 Co-Investigator, COMBAT Trial, Carolinas Medical Center, Charlotte, North Carolina
2002 – 2004 Co-Investigator, CROSS Registry, Carolinas Medical Center, Charlotte, North Carolina
2002 – 2004 Co-Investigator, ENLIGHTEN-II Protocol, Carolinas Medical Center, Charlotte, North Carolina
2002 – 2003 Co-Investigator, TAXUS IV Protocol, Carolinas Medical Center, Charlotte, North Carolina
2002 – 2004 Principal Investigator, TALENT Enhanced Endograft Protocol, Carolinas Medical Center, Charlotte, North Carolina
2002 – 2004 US Principal Investigator, Teramed QUANTUM LP Endograft Study, Carolinas Medical Center, Charlotte, North Carolina
2002 – 2004 Co-Investigator, FilterWire BLAZE Registry, Carolinas Medical Center
2001 – 2002 Co-Investigator, REPLACE-2 Trial, Carolinas Medical Center, Charlotte, North Carolina
2001 – 2002 Co-Investigator, FilterWire FIRE Trial, Carolinas Medical Center, Charlotte, North Carolina
2001 – 2004 Principal Investigator, Intertherapeutics Iliac Stent Trial, Carolinas Medical Center, Charlotte, North Carolina
2001 – 2004 Principal Investigator, Jo Stent SVG BARRICADE Trial, Carolinas Medical Center, Charlotte, North Carolina
2001 – 2002 Co-Investigator, SWING Trial, Carolinas Medical Center, Charlotte, North Carolina
2001 – 2002 Co-Investigator, Antrin Injection and Far Light, Carolinas Medical Center, Charlotte, North Carolina
2001 – 2002 Principal Investigator, Entire TIMI 23, Carolinas Medical Center, Charlotte, North Carolina
2001 – 2002 Co-Investigator, Gamma V Trial, Carolinas Medical Center, Charlotte, North Carolina
2001 – 2003 Co-Investigator, GUARD Trial, Carolinas Medical Center, Charlotte, North Carolina
2001 – 2002 Co-Investigator, SIRIUS Trial, Carolinas Medical Center, Charlotte, North Carolina
2001 – 2002 Co-Investigator, VICTORY Trial, Carolinas Medical Center, Charlotte, North Carolina
1999 – 2001 Principal Investigator, TALENT LPS Endograft Study, Carolinas Medical Center, Charlotte, North Carolina
1999 – 2000  Principal Investigator, WALLGRAFT Aneurysm/Trauma Study, Carolinas Medical Center, Charlotte, North Carolina
1998 – 2000  National Co-Principal Investigator, AMIGO Atherectomy Trial, Carolinas Medical Center, Charlotte, North Carolina
1998 – 2004  Principal Investigator, TALENT Emergency Use Endograft Protocol, Carolinas Medical Center, Charlotte, North Carolina
1998 – 2004  Principal Investigator, TALENT Low Risk Endograft Protocol, Carolinas Medical Center, Charlotte, North Carolina
1997 – 2004  Principal Investigator, AneuRx III Study, Carolinas Medical Center, Charlotte, North Carolina
1996 – 2004  Principal Investigator, AneuRx II Study, Carolinas Medical Center, Charlotte, North Carolina
1996 – 1998  Principal Investigator, NIRVANA NIR Stent Trial, Carolinas Medical Center, Charlotte, North Carolina
1996 – 1998  Co-Investigator, WIN/WINS Wallstent Trials, Carolinas Medical Center, Charlotte, North Carolina
1995 – 1996  Co-Investigator, PRESTO Trial, Carolinas Medical Center, Charlotte, North Carolina
1995 – 1996  Principal Investigator, STRATAS Rotablator Trial, Carolinas Medical Center, Charlotte, North Carolina
1995 – 1996  Co-Principal Investigator, Stent Anticoagulation Regimen Study STARS Trial, Carolinas Medical Center, Charlotte, North Carolina
1993 – 1995  Principal Investigator, Optimal Atherectomy Restenosis Study OARS, Carolinas Medical Center, Charlotte, North Carolina
1992 – 1993  Principal Investigator, Genentech Intracoronary rt-PA Trial, Carolinas Heart Institute, Charlotte, North Carolina
1992        Principal Investigator, Erythropoietin in Congestive Heart Failure Pilot Study, Carolinas Heart Institute, Charlotte, North Carolina
1991 – 1993  Principal Investigator, CHAMPS Trial, Charlotte Heart Attack Medic-Prehospital Study, Carolinas Heart Institute, Charlotte, North Carolina
1990 – 1991  Co-Investigator, PATENT Trail, rt-PA and SCU-PA multicenter pro-urokinase patency trial, Carolinas Heart Institute, Charlotte, North Carolina
1990 – 1991  Co-Investigator, ACS Streak, alpha-14 and RX Perfusion catheter clinical trials, Carolinas Heart Institute, Charlotte, North Carolina
1989 – 1990  Co-Investigator, Thrombolysis and Angioplasty in Myocardial Infarction TAMI RESCUE Angioplasty Trial, Carolinas Heart Institute, Charlotte, North Carolina
1989 – 1990  Co-Investigator, Abbott Urokinase/rt-PA randomized trial, Carolinas Heart Institute, Charlotte, North Carolina
1989 – 1990  Co-Investigator, UCSI autoperfusion catheter (APC) and Probe 3 clinical trials, Carolinas Heart Institute, Charlotte, North Carolina
1987 – 1989  Co-Investigator, DCA Lactic Acidosis Multicenter International Trial, and
1986 – 1989  Cardiology Division, University of California, San Francisco.  Cardiovascular and metabolic effects of sodium bicarbonate, Carbicarb and sodium dichloroacetate (DCA) therapy in patients with lactic acidosis, congestive heart failure and ischemia.

1984 – 1986  Cardiology Division, University of California, San Francisco.  Application of 2-D echocardiography to the detection and quantitation of ischemia during exercise treadmill testing.

1981  Department of Microbiology and Immunology, University of California, Los Angeles.  Cytolytic mechanisms of, and effects of interferon and anti-interferon antibody on, human antibody dependent cell mediated cytotoxicity (ADDCC) in vitro.

1980  Visiting Scientist, Department of Diagnosis and Immunology, Institute for Parasitic Diseases, Chinese Academy of Medical Sciences, Shanghai, Peoples Republic of China.  Collaboration on experiments to develop hybridomas to Schistosomula antigens in vitro.


1977  Kroc Foundation Fellowship in Immunology, Department of Medicine, University of New Mexico, Albuquerque, New Mexico.  Immunogenetic Analysis of families afflicted with Huntington’s Chorea.

PUBLICATIONS/ABSTRACTS


16) Bersin RM, Elliott CM, Elliott AV, Fedor JM, Gallagher JJ, Jordan L, Simonton CA,


ORIGINAL ARTICLES


66) Bersin, RM. Percutaneous femoral access for TAVR. Cardiac Interventions Today 2012; 6(5): 38-44.

BOOK CHAPTERS


72) Bersin RM. Complications of Peripheral Procedures. In: “King S: The Interventional Cardiologist,” (Part VI, Ch. 60), 2006

May 6, 2012
**Carotid Artery Stenting**

**Order of Scheduled Presentations**

<table>
<thead>
<tr>
<th></th>
<th>Name</th>
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<tbody>
<tr>
<td>1</td>
<td>Larry Dean, MD</td>
<td>Society for Cardiovascular Angiography and Interventions/</td>
</tr>
<tr>
<td></td>
<td></td>
<td>WA Chapter American College of Cardiology</td>
</tr>
<tr>
<td>2</td>
<td>Louis Kim, MD</td>
<td>American Association of Neurological Surgeons/</td>
</tr>
<tr>
<td></td>
<td></td>
<td>College of Neurological Surgeons/</td>
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<tr>
<td></td>
<td></td>
<td>WA State Association of Neurological Surgeons</td>
</tr>
<tr>
<td>3</td>
<td>R. Torrance Andrews, MD, FSIR</td>
<td>Society of Interventional Radiology</td>
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Disclosure (WITH RESPECT TO THIS PRESENTATION)

Any unmarked topic will be considered a "Yes"

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<td>X</td>
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<tr>
<td>funding sources (e.g. member dues, governmental/taxes, commercial products or</td>
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<td></td>
</tr>
<tr>
<td>services, grants from industry or government).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If yes to #7, provide name and funding Sources: SAGE - MEMBER DUES

All - MEMBER DUES

__________________________________________________________________________
__________________________________________________________________________

If you believe that you do not have a conflict but are concerned that it may appear that you do, you may attach additional sheets explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.

X

Signature                                   Date                  Print Name

8/30/13

For questions contact: Christine Masters
Health Technology Assessment
PO Box 42712
Olympia, WA 98504-2712
360-725-5126
ACC Washington State Chapter & Society for Cardiovascular Angiography and Interventions

Presentation to the Washington State Health Technology Assessment Program’s Clinical Committee on Carotid Stenting

September 20, 2013

By Larry Dean, MD, FSCAI, FACC
Past President of SCAI
Chair of Community Relations with Washington Chapter of ACC
Professor of Medicine and Surgery
University of Washington School of Medicine
Director, UW Medicine Regional Heart Center

Goals:

• Review existing multi-society guideline recommendations for carotid stenting

• Consideration of upcoming NIH study in this field

• Consideration of possible changes in Medicare Coverage
Recommendations for Selection of Patients for Carotid Revascularization*

*Recommendations for revascularization in this section assume that operators are experienced, having successfully performed the procedures in 20 cases with proper technique and a low complication rate based on independent neurological evaluation before and after each procedure.

Classification of Recommendations and Levels of Evidence

<table>
<thead>
<tr>
<th>CLASS</th>
<th>Recommendation</th>
<th>Levels of Evidence</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Recommendation that procedure or treatment is useful/effective</td>
<td>A or B</td>
<td>Sufficient evidence from multiple randomized trials or meta-analyses</td>
</tr>
<tr>
<td>IIa</td>
<td>Recommendation that procedure or treatment is probably useful/effective</td>
<td>A or B</td>
<td>Sufficient evidence from single randomized trials or nonrandomized studies</td>
</tr>
<tr>
<td>IIb</td>
<td>Recommendation that procedure or treatment is possibly useful/effective</td>
<td>A or B</td>
<td>Sufficient evidence from single randomized trials or nonrandomized studies</td>
</tr>
<tr>
<td>III</td>
<td>Recommendation that procedure or treatment is probably not useful/effective</td>
<td>A or B</td>
<td>No evidence or evidence from uncontrolled studies</td>
</tr>
<tr>
<td>IIIa</td>
<td>Recommendation that procedure or treatment is probably not useful/effective</td>
<td>A or B</td>
<td>No evidence or evidence from uncontrolled studies</td>
</tr>
</tbody>
</table>

Suggested actions for setting recommendations:
- To achieve level of evidence A, randomized controlled trials with a large number of participants are required.
- To achieve level of evidence B, nonrandomized controlled trials or meta-analyses are required.

*Data available from clinical trials or registries about the usefulness/effectiveness in different subpopulations, such as gender, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

For comparative effectiveness recommendations (Class I and IIa, Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.
**Recommendations for Selection of Patients for Carotid Revascularization**

**A**

Patients at average or low surgical risk who experience nondisabling ischemic stroke† or transient cerebral ischemic symptoms, including hemispheric events or amaurosis fugax, within 6 months (symptomatic patients) should undergo CEA if the diameter of the lumen of the ipsilateral internal carotid artery is reduced more than 70%‡ as documented by noninvasive imaging...

or more than 50% as documented by catheter angiography and the anticipated rate of perioperative stroke or mortality is less than 6%.

†Nondisabling stroke is defined by a residual deficit associated with a score ≤2 according to the Modified Rankin Scale.

‡The degree of stenosis is based on catheter-based or noninvasive vascular imaging compared with the distal arterial lumen or velocity measurements by duplex ultrasonography.

---

**Recommendations for Selection of Patients for Carotid Revascularization (continued)**

**B**

CAS is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery is reduced by more than 70% as documented by noninvasive imaging or more than 50% as documented by catheter angiography and the anticipated rate of periprocedural stroke or mortality is less than 6%.
Selection of asymptomatic patients for carotid revascularization should be guided by an assessment of comorbid conditions, life expectancy, and other individual factors and should include a thorough discussion of the risks and benefits of the procedure with an understanding of patient preferences.

It is reasonable to perform CEA in asymptomatic patients who have more than 70% stenosis of the internal carotid artery if the risk of perioperative stroke, MI, and death is low.

It is reasonable to choose CEA over CAS when revascularization is indicated in older patients, particularly when arterial pathoanatomy is unfavorable for endovascular intervention.
It is reasonable to choose CAS over CEA when revascularization is indicated in patients with neck anatomy unfavorable for arterial surgery.\(^5\)

When revascularization is indicated for patients with TIA or stroke and there are no contraindications to early revascularization, intervention within 2 weeks of the index event is reasonable rather than delaying surgery.

\(^5\) Conditions that produce unfavorable neck anatomy include but are not limited to arterial stenosis distal to the second cervical vertebra or proximal (intrathoracic) arterial stenosis, previous ipsilateral CEA, contralateral vocal cord paralysis, open tracheostomy, radical surgery, and irradiation.

Prophylactic CAS might be considered in highly selected patients with asymptomatic carotid stenosis (minimum 60% by angiography, 70% by validated Doppler ultrasound), but its effectiveness compared with medical therapy alone in this situation is not well established.

In symptomatic or asymptomatic patients at high risk of complications for carotid revascularization by either CEA or CAS because of comorbidities, the effectiveness of revascularization versus medical therapy alone is not well established.
Recommendations for Selection of Patients for Carotid Revascularization (continued)

Except in extraordinary circumstances, carotid revascularization by either CEA or CAS is **not recommended** when atherosclerosis narrows the lumen by less than 50%.

Carotid revascularization is **not recommended** for patients with chronic total occlusion of the targeted carotid artery.

Carotid revascularization is **not recommended** for patients with severe disability\(^\text{¶}\) caused by cerebral infarction that precludes preservation of useful function.

\(^\text{¶}\)In this context, severe disability refers generally to a Modified Rankin Scale score of 3, but individual assessment is required, and intervention may be appropriate in selected patients with considerable disability when a worse outcome is projected with continued medical therapy alone.
Upcoming NIH Research on Treatment of Carotid Stenosis

- CREST-2 (best medical therapy vs. revascularization in asymptomatic patients) was recommended for funding by NINDS Council May 23, 2013
- FDA approved the protocol August 14, 2013
- IDE application hoped to be in by mid-September, and
- Should have the official award in October. Site selection is underway.

-per Dr. Thomas G. Brott, Principal Investigator

Ongoing Efforts to Update Medicare Coverage Policy: Coverage with Evidence Development

- Center for Medical Technology Policy is coordinating a multi-stakeholder effort to carefully expand coverage of carotid stenting
  - Individuals from CMS, FDA, NIH, AHRQ and relevant clinical disciplines are participating
- Coverage would be for patients in CREST II, and clearly defined patients not enrolled in the trial
- Policy includes robust data collection requirements (including long term outcomes) on all patients
- Also includes provider credentialing and facility accreditation
- A primary goal is to ensure successful enrollment of CREST II
Summary

• CAS in symptomatic patients is supported by the multi-society document with a class 1 (LOE B) recommendation
• CAS is reasonable vs. CEA in symptomatic patients with unfavorable neck anatomy, class II, LOE A
• The appropriate approach to asymptomatic patients is less clear

Summary

• CREST 2 and the CMS CED will examine best medical therapy vs. revascularization in this population
• We believe the people of the State of Washington should have access to this technology based on the current evidence and have the opportunity to expand the evidence base by participating in clinical trials, e.g. CREST II
### Disclosure

Any applicant who answers "Yes" to the following must provide written response to the following question: "Describe any other potential conflicts of interest.

<table>
<thead>
<tr>
<th>Potential Conflict Type</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Payment or compensation for consulting, lecturing, writing, or editorial work</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Payment or compensation for travel or other expenses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Payment or compensation for stock options or other ownership interests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Payment or compensation for employment or ownership of patents, trademarks, licenses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Payment or compensation for other financial interests</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If you answer "Yes" to any of the above, please describe the relationship:

2. **Spi Surgical Inc**
3. **Spi Surgical Inc**
4. **Spi Surgical Inc**
5. **NIH/NINDS, FDA**

None of these relationships are relevant to my presentation.

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If you answer "Yes" to any of the above, please describe the relationship:

If you answer "Yes" to any of the above, you may attach additional information that will not be excluded.

I certify that I have completed this Conflict of Interest Form and that the information provided is complete and correct as of this date.

X [Signature] 8/30/13  [Print Name] Louis Kim

For

[Health Technology Assessment]

[Date: 8/30/13]
Key Question 1

- There are no studies comparing extracranial CAS vs. medical therapy alone
- Numerous clinical trials have evaluated CEA compared to medical therapy in both symptomatic and asymptomatic populations
- All of the trials NASCET, ECST, ACAS and ACST have demonstrated that endarterectomy definitively prevents strokes in these populations compared to medical therapy
- CREST has demonstrated that the rates of short and long term comparative efficacy are similar for CEA and CAS in both populations
- There is ample evidence in particular for symptomatic patients that both treatments provide short and long term efficacy
Key Question 2

- SAMMPRIS is the definitive trial that demonstrated aggressive medical therapy is favorable to angioplasty and stenting
- For patients who are refractory to aggressive medical therapy angioplasty and stenting should remain an option for this population

Key Question 3

- There is ample evidence on the periprocedural complication rates for CEA and CAS
- Over the course of time the complication rates of both procedures has decreased in particular for CAS
- CREST demonstrated lower complication rates for both CEA and CAS compared to historical trials
- Even within the CREST trial alone the complication rates for CAS decreased in the latter half of the study
- Currently in qualified US centers both procedures likely meet the AHA criteria of <3% and <6% for asymptomatic and symptomatic patients
Key Question 4

- Age is the primary subpopulation where there is evidence of differential efficacy
- Numerous studies have demonstrated the increasing risk of adverse outcomes for CAS with increasing age likely secondary to increasing difficulty with access
- CREST has confirmed a superiority of CEA compared to CAS with a crossover around 70

Key Question 5

- There is no data comparing the cost effectiveness of CAS to medical therapy
- The best data comparing cost effectiveness of CAS to CEA comes from CREST which demonstrate minimal difference in the hospitalization cost and the one year cumulative cost in both asymptomatic and symptomatic patients
- The cost effectiveness data from SAPPHIRE suggests CAS may be superior
- Overall cost effectiveness of CAS to CEA is likely a minor consideration compared to the medical factors addressed in the prior questions
Conclusion

- In light of the recent publication of the CREST trial, the FDA expansion of indication for the Abbott Vascular CAS system, published recommendations from multiple specialties and the MEDCAC meeting in Jan 2012, CAS is a reasonable alternative to the gold standard treatment of CEA for younger, symptomatic patients with standard surgical risk
- Coverage should be expanded to include this population
- Although current rates of stroke and death for CEA and CAS are below the AHA guideline of 3% for the asymptomatic population, a randomized trial with modern medical therapy is warranted prior to expansion of coverage
Disclosure

Any unmarked topic will be considered a “Yes”

<table>
<thead>
<tr>
<th>Potential Conflict Type</th>
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<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Salary or payments such as consulting fees or honoraria in excess of $10,000.</td>
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<td>2. Equity interests such as stocks, stock options or other ownership interests.</td>
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<tr>
<td>3. Status or position as an officer, board member, trustee, owner.</td>
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<td>X</td>
</tr>
<tr>
<td>4. Loan or intellectual property rights.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Research funding.</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>6. Any other relationship, including travel arrangements.</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

If yes to #7, provide name and funding Sources: My attendance is on behalf of the Society of Interventional Radiology. The SIR is a professional medical specialty association of approximately 5,000 members, funded primarily by membership dues.

If you believe that you do not have a conflict but are concerned that it may appear that you do, you may attach additional sheets explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.

9/3/13

R. Torrance Andrews, MD

For questions contact: Christine Masters
Health Technology Assessment
PO Box 42712
Olympia, WA 98504-2712
360-725-5126
Carotid Artery Stenting
Final Evidence Report
WA State Health Care Authority
Health Technology Assessment

September 20, 2013
Seattle, WA

• Commenter
  – R. Torrance Andrews, MD, FSIR
  – Vascular & Interventional Radiology
    Swedish Medical Center, First Hill
  – Seattle Radiologists, PC

SIR’s Key Points

• The Final Evidence Report is a comprehensive review of the literature
• CAS is an appropriate option for select patients
• Symptomatic and Asymptomatic Patients: Differing Recommendations
• CREST Data/CREST II
• 2011 Multi-Society Guidelines
• Reimbursement must be contingent on Accreditation: (i.e., ICACSF or ACE)
Symptomatic Patients

- CREST & the 2011 Guidelines Affirm
  - CAS should be offered as an option in addition to CEA
  - Individualized decision as to CEA or CAS: Both should be considered
- Good CAS outcomes (3% S/D for asx, 6% for sx) requires skilled providers
- Stroke rate for CAS about = or better to CEA

Appropriate Patients

- Value of CAS depends on treating appropriate pts with low complication rates
- 30-day stroke/death rates for sx/asx pts <6%/3%
Costs

- Data show CEA and CAS have minor cost differences
- LOS appears to be shorter with CAS
  - (1.9 days vs. 2.9)

Accreditation Will Help Ensure Optimal Patient Care

- Intersocietal Commission for the Accreditation of Carotid Stenting Facilities (ICASF)
- Accreditation for Cardiovascular Excellence (ACE)
- Currently, few facilities meet ICASF or ACE accreditation
- SIR’s Position: CAS should only be performed/reimbursed in accredited facilities
Achieving Best Outcomes

• CMS current accreditation – not based on outcomes
• Current ICASF experience:
  – Assessment of pre CAS sx status not always accurate
  – Stenosis severity frequently significantly overestimated
  – Inconsistent pt follow up to determine outcomes
• Accreditation Requires:
  – Pts treated for appropriate indications based on sx and % stenosis
  – Pts accurately assessed for complications and success
  – Outcomes meet national benchmarks

Why Accreditation is Key

• Accreditation is necessary to ensure that the good outcomes from CAS documented in the HTA report are achieved in routine clinical practice
Unresolved Questions

- CREST II: SIR supports reimbursement for pts enrolled in CREST II
- BMT vs CEA/CAS
- Ongoing trials need to be powered to evaluate CAS therapy for both sx and asx pts

Questions?

- SIR thanks the Washington Health Care Authority for the opportunity to present our comments
Stroke is a leading cause of death

Age-adjusted death rates for stroke by sex and race/ethnicity, 2009

- White Males: 67.6
c - White Females: 56.6
- Black Males: 85.2
c - Black Females: 63.2
- Asian/Pacific Islander Males: 34.1
c - Asian/Pacific Islander Females: 27.5
- American Indian/Alaska Native Males: 74.2
c - American Indian/Alaska Native Females: 54.6
- Hispanic Males: 36.5
c - Hispanic Females: 26.0

Source: National Center for Health Statistics and National Heart, Lung, and Blood Institute.

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Stroke in Washington State

- **Stroke is the third leading cause of death**
  - Stroke caused 3,167 deaths in 2005
  - In 2004, 26,612 hospitalizations included a diagnosis of stroke at discharge
  - These hospitalizations cost $600 million

- **Stroke is a leading cause of serious long-term disability**


Site of Stenosis

The most common site of plaque formation and stenosis in the carotid artery is near the bifurcation into the internal and external carotid arteries.
**Carotid Artery Stenting:**

**Background**

**Therapeutic Options for Atherosclerotic Stenosis**

**Medical therapy alone (MT)**
- Medical therapy has changed significantly in the past decade. Modern medical therapy includes rigorous and compliant use of statins and antiplatelet agents, along with treatment of hypertension, cigarette smoking, and diabetes.

**Carotid endarterectomy plus medical therapy (CEA)**
- CEA has been the gold-standard to restore vascular patency in the surgical management of carotid artery stenosis.

**Carotid angioplasty with or without stenting plus medical therapy (CAS)**
- CAS has become an alternative to CEA, especially in persons who are at high risk for surgically-related morbidity and mortality, because of lower degree of invasiveness. However, less invasive may not equal safer.

---

**Patient Populations (Extracranial Stents)**

**Symptomatic patients**
- Have neurological evidence of an ipsilateral stroke, TIA or transient monocular blindness
- Much of the evidence available from RCTs in this population
- Target population for CAS: moderate (50%-69) or severe (70%-99%) stenosis at risk of stroke

**Asymptomatic patients**
- Less is known about the efficacy of medical treatment, CEA and CAS in this patient population
- The management of the disease in this population is still evolving
- Target population for CAS: current FDA labeling requires ≥70% stenosis, not able to tolerate general anesthesia for CEA; ref vessel diameter 4-9 mm at target lesion, prior ipsilateral neck surgery, restenosis after prior CEA
Intracranial Stents

The primary therapeutic approach for intracranial atherosclerotic disease is medical therapy.
- Angioplasty with or without stenting has been reported
- Surgical options are limited

The FDA approved the intracranial stents through the humanitarian device exemption (HDE)* process.
- For use in patients with ≥ 70% stenosis of an intracranial vessel experiencing recurrent intracranial stroke secondary to atherosclerotic disease that is refractory to medical therapy.

*An application of marketing an Humanitarian Use Device (HUD), which is similar to a premarket approval (PMA) application, but is exempt from the effectiveness requirements of sections 514 and 515 of the Food, Drug, and Cosmetic Act (the Act). An annual distribution number (ADN) is assigned for each HUD by the FDA.

Agency Medical Directors’ Concerns

Primary Criteria Ranking
- Safety = High
- Efficacy = High
- Cost = Medium
### Carotid Artery Stenting: Current State Agency Policy

<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
<th>Medicaid</th>
<th>UMP</th>
<th>DOC</th>
<th>LNI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0075T</td>
<td>Extracranial stenting</td>
<td>C</td>
<td>PA</td>
<td>PA</td>
<td>C</td>
</tr>
<tr>
<td>0076T</td>
<td>Extracranial stenting (additional vessel)</td>
<td>C</td>
<td>PA</td>
<td>PA</td>
<td>C</td>
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<tr>
<td>37215</td>
<td>Cervical carotid artery stenting without distal embolic protection device (EPD)</td>
<td>C</td>
<td>PA</td>
<td>PA</td>
<td>PA</td>
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<tr>
<td>37216</td>
<td>Cervical carotid artery stenting with distal EPD</td>
<td>C</td>
<td>PA</td>
<td>PA</td>
<td>PA</td>
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<tr>
<td>61635</td>
<td>Intracranial</td>
<td>NC</td>
<td>PA</td>
<td>PA</td>
<td>NC</td>
</tr>
</tbody>
</table>

C: Covered  
NC: Not covered  
PA: Prior authorization required

---

### Carotid Artery Stenting: Other Centers, Agencies & HTAs

**Centers for Medicare & Medicaid Services (NCD 20.7, last update 2008)**

For treatment purpose, Medicare covers percutaneous transluminal angioplasty (PTA) with carotid stent and embolic protection only for patients with symptomatic carotid artery stenosis:

- Patients for whom surgical risk of CEA is high and have **symptomatic** carotid artery stenosis ≥70% (measured by duplex Doppler ultrasound and confirmed by carotid artery angiography)

*For participation in research only,* Medicare covers angioplasty and stenting in the following conditions:

- Patients for whom surgical risk of CEA is high and have **symptomatic** carotid artery stenosis between **50% and 70%**
- Patients for whom surgical risk of CEA is high and have **asymptomatic** carotid artery stenosis ≥80%
- (Intracranial) Cerebral artery stenosis ≥50% in patients with intracranial atherosclerotic disease
### Carotid Artery Stenting: State Agency Utilization

<table>
<thead>
<tr>
<th>Agency/Year</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>4 Year Overall</th>
<th>Avg % Chng*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PEBB Carotid Artery Stenting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAS Procedures</td>
<td>19</td>
<td>12</td>
<td>10</td>
<td>12</td>
<td>53</td>
<td>-11.4%</td>
</tr>
<tr>
<td>Total Paid</td>
<td>$501,687</td>
<td>$188,391</td>
<td>$211,519</td>
<td>$66,304</td>
<td>$967,901</td>
<td>-39.6%</td>
</tr>
<tr>
<td>Average Per Procedure**</td>
<td>$33,066</td>
<td>$26,011</td>
<td>$26,598</td>
<td>$29,261</td>
<td>$33,672</td>
<td>-3.0%</td>
</tr>
<tr>
<td><strong>Medicaid Carotid Artery Stenting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAS Procedures</td>
<td>21</td>
<td>25</td>
<td>26</td>
<td>11</td>
<td>82</td>
<td>-12.0%</td>
</tr>
<tr>
<td>Total Paid</td>
<td>$170,064</td>
<td>$228,546</td>
<td>$183,868</td>
<td>$132,089</td>
<td>$714,567</td>
<td>-5.0%</td>
</tr>
<tr>
<td>Average Per Procedure**</td>
<td>$9,149</td>
<td>$11,358</td>
<td>$10,948</td>
<td>$7,468</td>
<td>$10,229</td>
<td>-3.7%</td>
</tr>
<tr>
<td><strong>All Agency Carotid Artery Stenting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAS Procedures</td>
<td>40</td>
<td>37</td>
<td>36</td>
<td>23</td>
<td>135</td>
<td></td>
</tr>
<tr>
<td>Total Paid</td>
<td>$671,751</td>
<td>$316,937</td>
<td>$385,387</td>
<td>$198,393</td>
<td>$1.78M</td>
<td></td>
</tr>
</tbody>
</table>

*Average change for procedure counts and total paid is adjusted for population growth

** Only procedures where PEBB or Medicaid were primary are included in the average

---

### Carotid Artery Stenting: State Agency Utilization

<table>
<thead>
<tr>
<th>Agency/Year</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>4 Year Overall</th>
<th>Avg % Chng</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PEBB Endarterectomy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endarterectomy Procedures</td>
<td>57</td>
<td>65</td>
<td>59</td>
<td>61</td>
<td>242</td>
<td>2.3%</td>
</tr>
<tr>
<td>Total Paid, Endarterectomy</td>
<td>$249,225</td>
<td>$276,084</td>
<td>$258,463</td>
<td>$288,503</td>
<td>$1.072M</td>
<td>4.9%</td>
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<tr>
<td>Avg Paid, Endarterectomy</td>
<td>$16,781</td>
<td>$15,281</td>
<td>$19,313</td>
<td>$15,864</td>
<td>$17,284</td>
<td>-0.4%</td>
</tr>
<tr>
<td><strong>Medicaid Endarterectomy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endarterectomy Procedures</td>
<td>68</td>
<td>54</td>
<td>64</td>
<td>52</td>
<td>235</td>
<td>-7.7%</td>
</tr>
<tr>
<td>Total Paid, Endarterectomy</td>
<td>$411,449</td>
<td>$288,334</td>
<td>$509,735</td>
<td>$547,618</td>
<td>$1.76M</td>
<td>17.4%</td>
</tr>
<tr>
<td>Avg Paid, Endarterectomy</td>
<td>$7,958</td>
<td>$7,434</td>
<td>$12,437</td>
<td>$14,200</td>
<td>$10,554</td>
<td>25.0%</td>
</tr>
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</table>
Extracranial includes procedures on the intrathoracic and cervical carotid arteries - they make up almost 90% of PEBB and 95% of Medicaid procedures.
## Carotid Artery Stenting: State Agency Utilization

### Breakdown 1

<table>
<thead>
<tr>
<th></th>
<th>PEBB Primary (n=23)</th>
<th>PEBB Medicare (n=30)</th>
<th>Medicaid (n=62)</th>
<th>Medicaid Medicare (n=20)</th>
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<tbody>
<tr>
<td><strong>Professional Services</strong></td>
<td>$3,500</td>
<td>$1,815</td>
<td>$1,391</td>
<td>$1,516</td>
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<tr>
<td><strong>Facility/Other</strong></td>
<td>$38,110</td>
<td>$30,657</td>
<td>$11,360</td>
<td>$7,662</td>
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### Breakdown 2

<table>
<thead>
<tr>
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<th>PEBB Primary (n=23)</th>
<th>PEBB Medicare (n=30)</th>
<th>Medicaid (n=62)</th>
<th>Medicaid Medicare (n=20)</th>
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<tr>
<td><strong>Stent Placement</strong></td>
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<td>$1,685</td>
<td>$1,071</td>
<td>$1,431</td>
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<td><strong>Study</strong></td>
<td>$126</td>
<td>$65</td>
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<td><strong>Facility/DRG</strong></td>
<td>$32,588</td>
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<td>$10,825</td>
<td>$5,683</td>
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<td><strong>Anesthesia</strong></td>
<td>$481</td>
<td>$149</td>
<td>$213</td>
<td>$199</td>
</tr>
<tr>
<td><strong>Imaging</strong></td>
<td>$1,516</td>
<td>$589</td>
<td>$387</td>
<td>$399</td>
</tr>
<tr>
<td><strong>Patient Care</strong></td>
<td>$521</td>
<td>$924</td>
<td>$243</td>
<td>$1,463</td>
</tr>
<tr>
<td><strong>Avg Allowed/Procedure</strong> (95% upper limit)</td>
<td>$41,610 ($128,502)</td>
<td>$32,472 ($116,983)</td>
<td>$12,750 ($43,174)</td>
<td>$9,178 ($33,328)</td>
</tr>
</tbody>
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## Carotid Artery Stenting: State Agency Utilization

### Inpatient

<table>
<thead>
<tr>
<th></th>
<th>PEBB Primary (n=23)</th>
<th>PEBB Medicare (n=30)</th>
<th>Medicaid (n=62)</th>
<th>Medicaid Medicare (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Professional Services</strong></td>
<td>$3,587</td>
<td>$1,365</td>
<td>$1,502</td>
<td>$1,937</td>
</tr>
<tr>
<td><strong>Facility</strong></td>
<td>$39,456</td>
<td>$45,569</td>
<td>$15,811</td>
<td>$25,296</td>
</tr>
<tr>
<td><strong>Avg Allowed/Procedure</strong></td>
<td>$43,043</td>
<td>$46,934</td>
<td>$17,313</td>
<td>$27,233</td>
</tr>
</tbody>
</table>

### Outpatient

<table>
<thead>
<tr>
<th></th>
<th>PEBB Primary (n=23)</th>
<th>PEBB Medicare (n=30)</th>
<th>Medicaid (n=62)</th>
<th>Medicaid Medicare (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Professional Services</strong></td>
<td>$3,088</td>
<td>$2,593</td>
<td>$478</td>
<td>$105</td>
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<tr>
<td><strong>Facility</strong></td>
<td>$31,718</td>
<td>$4,900</td>
<td>$1,118</td>
<td>$1,336</td>
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<tr>
<td><strong>Avg Allowed/Procedure</strong></td>
<td>$34,806</td>
<td>$7,492</td>
<td>$1,596</td>
<td>$1,441</td>
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Carotid Artery Stenting:
State Agency Utilization

<table>
<thead>
<tr>
<th>PEBB Diagnosis Description</th>
<th>Patient Ct n=53</th>
<th>Medicaid Diagnosis Description</th>
<th>Patient Ct n=82</th>
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<tr>
<td>OCL CRTD ART WO INFRCT</td>
<td>31</td>
<td>OCL CRTD ART WO INFRCT</td>
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<td>OCL CRTD ART W INFRCT</td>
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<tr>
<td>OCL MLT BI ART WO INFRCT</td>
<td>3</td>
<td>CRBL ART OCL NOS W INFRC</td>
<td>3</td>
</tr>
<tr>
<td>OCL VRTB ART W INFRCT</td>
<td>3</td>
<td>OCL BSLR ART W INFRCT</td>
<td>2</td>
</tr>
<tr>
<td>CRBL ART OCL NOS W INFRC</td>
<td>2</td>
<td>OCL MLT BI ART W INFRCT</td>
<td>2</td>
</tr>
<tr>
<td>NONRUPT CEREBRAL ANEURYM</td>
<td>2</td>
<td>OCL VRTB ART W INFRCT</td>
<td>2</td>
</tr>
<tr>
<td>CRBL ART OC NOS WO INFRC</td>
<td>1</td>
<td>OCL VRTB ART WO INFRCT</td>
<td>2</td>
</tr>
<tr>
<td>CRNRY ATHRSCL NATVE VSSL</td>
<td>1</td>
<td>COR ATH UNSP VSL NTV/GFT</td>
<td>1</td>
</tr>
<tr>
<td>CVA</td>
<td>1</td>
<td>CVA</td>
<td>1</td>
</tr>
<tr>
<td>DISSECT CAROTID ARTERY</td>
<td>1</td>
<td>DISSECT CAROTID ARTERY</td>
<td>1</td>
</tr>
<tr>
<td>OCL BSLR ART WO INFRCT</td>
<td>1</td>
<td>NONRUPT CEREBRAL ANEURYM</td>
<td>1</td>
</tr>
<tr>
<td>OCL VRTB ART WO INFRCT</td>
<td>1</td>
<td>OCL BSLR ART WO INFRCT</td>
<td>1</td>
</tr>
<tr>
<td>PERIPH VASCULAR DIS NOS</td>
<td>1</td>
<td>OCL MLT BI ART W INFRCT</td>
<td>1</td>
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<tr>
<td>STRicture OF ARTERy</td>
<td>1</td>
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</tr>
</tbody>
</table>

Evidence- Extracranial Stenting

**Symptomatic patients**
- Equivalent effectiveness, evidence moderate
- Worse safety profile
- Less cost-effective

**Asymptomatic patients**
- Overall, weak studies that appear underpowered to detect differences in relatively rare events (eg, death):
  - No difference in effectiveness
  - Nearly doubled morbidity (NS) for CAS; any stroke or death 2.5% vs 1.4%
  - More costly
Efficacy and Safety - Intracranial Stenting

Symptomatic patients (SAMMPRIS)
- The efficacy data was limited. Nevertheless, MT is superior to CAS+MT, especially in terms of any stroke, stroke or death and any major hemorrhage (1 RCT)
- Safety: superiority of MT compared to CAS+MT

Asymptomatic patients
- No data

State Agency Recommendations:

Cover (With Conditions)
(Consistent with Medicare NCD 20.7 - last update 2008)
- Extracranial carotid artery stenting with embolic protection device
  - For symptomatic patients, ≥ 70% stenosis, and anatomic contraindications for CEA or at high surgical risk.

Define high surgical risk, anatomic contraindications
State Agency Recommendations:
Due to poor adverse event profile, low cost/benefit considerations and potential for poor quality registry studies, we recommend the following policy which deviates from NCD 20.7:

Cover with conditions:
At agency discretion, only in FDA-approved Category B IDE clinical trials:

**Extracranial carotid stenting**
- Patients for whom surgical risk of CEA is high and have *symptomatic* carotid artery stenosis between 50% and 70%
- Patients for whom surgical risk of CEA is high and have *asymptomatic* carotid artery stenosis ≥80%

**Intracranial carotid stenting**
- Cerebral artery stenosis ≥50% in patients with intracranial atherosclerotic disease

Questions?

More Information:
http://www.hta.hca.wa.gov/degenerative-disc_disease.html

Gary Franklin, MD, MPH
Medical Director
Washington State Department of Labor & Industries
FRAL235@LNI.WA.GOV
### Carotid Artery Stenting: Billing Codes

<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
<th>Main Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>0075T</td>
<td>Transcatheter placement of extracranial vertebral or intrathoracic carotid artery stent(s), including radiologic supervision / interpretation, percutaneous; initial vessel</td>
<td>- extracranial (may include some vertebral stents)</td>
</tr>
<tr>
<td>0076T</td>
<td>Transcatheter placement of extracranial vertebral or intrathoracic carotid artery stent(s), including radiologic supervision and interpretation, percutaneous; each additional vessel</td>
<td>- extracranial (may include some vertebral stents)</td>
</tr>
<tr>
<td>37215</td>
<td>Transcatheter placement of Intravascular Stent(s), Cervical carotid artery, percutaneous; without distal embolic protection</td>
<td>- extracranial</td>
</tr>
<tr>
<td>37216</td>
<td>Transcatheter placement of Intravascular Stent(s), Cervical carotid artery, percutaneous; with distal embolic protection</td>
<td>- extracranial</td>
</tr>
<tr>
<td>61635</td>
<td>Transcatheter placement of intravascular stent(s), intracranial (eg, atherosclerotic stenosis), including balloon angioplasty, if performed</td>
<td>- intracranial</td>
</tr>
</tbody>
</table>
Stenting for Treatment of Atherosclerotic Stenosis of the Extracranial Carotid Arteries or Intracranial Arteries

Presentation to
Washington State Health Care Authority
Health Technology Clinical Committee
Andrea C. Skelly, PhD, MPH
September 20, 2013

Report prepared by:
Andrea C. Skelly, PhD, MPH
Erika D. Brodt, BS
Robin E. Hashimoto, PhD
Jeannette M. Schenk-Kisser, PhD
Mark Junge, BS
Haley Holmer, MPH

Scope of Report

Critically summarize research on the efficacy, effectiveness and safety of stenting for the treatment of atherosclerotic disease of the external carotid arteries and intracranial arteries

The report focuses on the highest quality evidence available based on systematic review of the literature
Background
Cardiovascular disease: leading cause of morbidity and mortality in the U.S. (>1 in 3); leading cause of long-term disability; 2030 projected prevalence of 40.5%

Stroke is the 4th leading cause of death
- ~87% of strokes are ischemic, primarily from thromboembolic events (various origins e.g. heart);
- 20%-25% due to atherosclerotic stenosis of carotid arteries
- Intracranial atherosclerotic disease (ICAD): 8% -10% of stroke in U.S.; 30%-50% in Asian countries; more common in persons of Asian, African or Hispanic origin
- Public health and economic burdens are high

Background: Anatomy
Carotid arteries
- Anatomic variation
- Typical bifurcation of the distal common carotid at level of thyroid cartilage
- Bifurcation – most common site for atherosclerotic plaque
- External carotid - face, scalp, tongue, neck
- Internal carotid – front part of the brain, eye, branches to forehead and nose
Background: Anatomy

**Intracranial arteries**
- Begin at base of skull
- Vertebral arteries join to form the basilar artery
- Vertebrobasilar gives rise to posterior communicating
- Internal carotid bifurcates into anterior and middle cerebral arteries
- Circle of Willis – highly variable; complete in <50%
- Tortuosity, collaterals, calcification – induce variability

Background: Pathophysiology

**Carotid arteries (extracranial)**
- Plaque (cholesterol, calcium, fibrous tissue) deposition – vessel narrowing, ↓ blood flow
- Bifurcation most common – turbulence and shear stress
- Plaque disruption and clot formation contribute to narrowing and clinical events
- Mechanisms:
  - Thrombus on plaque embolizes
  - Atheroembolism of atheromatous debris
  - Plaque rupture leading to acute thrombotic occlusion
  - Structural – dissection or subintimal hematoma
  - Occlusion leading to ↓ blood flow

**Intracranial (ICAD)**
- Two primary mechanisms (not mutually exclusive)
  - Thrombus at stenosis site, embolization distally
  - Occlusion reducing blood flow to areas w/o sufficient collateral flow
- Intracranial ICA, MCA, VA and BA most frequently involved
- Traditional risk factors; DM and metabolic syndrome in particular
- True prevalence and impact unknown; annual risk estimate as high as 24%
- WASID trial – stenosis of 70%-99% had greatest stroke risk
- Not all stenoses symptomatic
Background: Imaging

**Duplex Ultrasound (DUS)**
- Peak systolic velocity and/or end diastolic velocity; PSV of ICA \(\geq 125\) cm/s for predicting >50% angiographic stenosis \(\geq 230\) cm/s predicting >70% stenosis;
- Sensitivity/specificity for \(\geq 70\)% stenosis vs. angio: 85%-90%; most accurate for >70% stenosis
- Categories: 50% - 69% (moderate); 70% -99% (severe);

**Conventional Digital Angiography**
- NASCET dominant method for determining %; used in most modern trials; greater reliance on non-invasive methods

**Magnetic Resonance Angiography**
- Sensitivity 97%-100%; specificity 82%-96% vs. angio

**Computed Tomography Angiography**
- Sensitivity up to 100%; specificity 63% vs. angio

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**Treatment Options – Carotid (Extracranial)**

**Best Medical Therapy – has evolved**
- Pharmacotherapy and lifestyle modification
- Hypertension, hyperlipidemia, smoking, DM
- DM, obesity, hyperhomocysteinemia

**Carotid Endarterectomy (CEA)**
- No contemporary trials vs. best medical therapy

**Carotid Stenting (CAS)**
- Expertise (Appendix I)
- Embolic protection
Treatment Options: Intracranial

Aggressive Medical Therapy – Primary option

PTA with or without stenting;
Stenting: Wingspan (FDA, HDE approval)

Surgical options: External to internal carotid bypass in patients with poor hemodynamic proposed, not widely recommended

Carotid Stenting: FDA (devices)

- Labeling stipulates use of embolic protection device; Vessel diameter: 4.0 mm - 9.0 mm at target lesion
- Asymptomatic: ≥80% stenosis (most devices)
  - RX Acculink: High surgical risk ≥ 80% by DUS or angio;
  - Standard surgical risk ≥ 70% by DUS, ≥ 60% by angio
- Symptomatic: ≥ 50% stenosis
  - RX Acculink: High surgical risk ≥ 70% by DUS or angio;
  - Standard surgical risk ≥ 70% by DUS, ≥ 50% by angio

FDA Indications
- Inability to tolerate general anesthesia for CEA
- Prior damage to contralateral vocal cord
- Previous neck surgery on ipsilateral side
- Restenosis after CEA

FDA Contraindications
- Unfavorable anatomy
- Unstable plaque(carotid, aortic arch)
- Allergy to nickel-titanium
- Anticoagulant or antiplatelet medication is contraindicated.
- Uncorrected bleeding disorder.
- Lesions at the opening of the common carotid artery.
Intracranial artery stenting: FDA

- FDA approval: humanitarian device exemption (HDE) process
- NEUROLINK® (no longer available) and Wingspan™ Stent System with Gateway™ PTA Balloon Catheter
- March 2012 – FDA safety communication limiting use of Wingspan™ and requiring IRB approval

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>(all criteria must be met)</td>
<td></td>
</tr>
<tr>
<td>- Age between 22 and 80 years</td>
<td>- Unfavorable anatomy</td>
</tr>
<tr>
<td>- Two or more strokes despite aggressive medical management</td>
<td>- Treatment of acute strokes (i.e. onset of symptoms within 7 days or less of treatment)</td>
</tr>
<tr>
<td>- Most recent stroke occurred &gt; 7 days prior to planned treatment with Wingspan</td>
<td>- Treatment of transient ischemic attacks (TIAs)</td>
</tr>
<tr>
<td>- 70%-99% stenosis due to atherosclerosis of the intracranial artery related to the recurrent strokes</td>
<td>- Highly calcified lesions that could prevent access or appropriate expansion of stent.</td>
</tr>
<tr>
<td>- Good recovery from previous stroke and have a modified Rankin score of 3 or less prior to Wingspan treatment.</td>
<td>- Antiplatelet or anticoagulation therapy is contraindicated.</td>
</tr>
</tbody>
</table>

Key Questions

1. In symptomatic or asymptomatic persons with atherosclerotic carotid artery stenosis what is the evidence of short- and long-term comparative efficacy and effectiveness of:
   a) Extracranial carotid artery stenting (CAS) and medical therapy compared with medical therapy alone?
   b) Extracranial carotid artery stenting (CAS) and medical therapy compared with carotid endarterectomy (CEA) and medical therapy?

2. In asymptomatic or symptomatic persons with atherosclerotic stenosis of the intracranial arteries, what is the evidence of short- and long-term comparative efficacy and effectiveness of intracranial artery stenting and medical therapy compared with medical therapy alone? n.b. information on intracranial stenting safety included here
Key Questions (continued)

3. What is the evidence regarding adverse events and complications, particularly during the periprocedural period and longer term, for stenting compared with alternative treatments? In persons with extracranial carotid artery stenosis, are rates of periprocedural death or stroke <3% for asymptomatic patients and <6% for symptomatic patients?

4. Is there evidence of differential efficacy or safety for special populations, (including consideration of age, gender, race, diabetes, atrial fibrillation or other comorbidities, ethnicity, or disability)?

5. What is the evidence of cost-effectiveness of CAS compared with other treatment options (medical therapy, CEA) in the short-term and the long term?

Scope: Inclusion Criteria

Population
- Adults with extracranial carotid artery stenosis undergoing primary treatment for symptomatic or asymptomatic atherosclerotic carotid artery stenosis who have not had previous revascularization.
- Adults with atherosclerotic stenosis of intracranial arteries

Intervention
- Stenting of carotid arteries (with or without use of embolic protection devices or strategies) or stenting of intracranial arteries, using FDA approved devices

Comparator
- Medical therapy or surgical alternatives including carotid endarterectomy (CEA)

Study design
- Randomized controlled trials (RCTs), comparative studies with concurrent controls, full economic studies sought

Publication
- Full-length studies published in English in peer-reviewed journals, FDA reports (no meeting abstracts, proceedings)
Methods: Primary Outcomes

**Efficacy and Effectiveness**
- Short term (>30 periprocedural – 12 months) and longer term (< 12 months) outcomes
  - Stroke (any, ipsilateral)
  - Death
  - Composite of death or stroke

**Safety**: 30 day peri-procedural
- Stroke (any, ipsilateral)
- Death
- Composite – death or stroke
- MI
- Others – Major bleeding, persistent cranial nerve palsy

**Economic**
- ICER or similar

Literature search and overall quality

- Electronic databases, HTA sites were searched using a systematic approach; bibliographic review was done
- Literature search: 1043 unique potentially relevant citations; 260 full text reviewed; 71 citations included
- Primary evidence base summarized here (some studies used for multiple questions)
  - Key Questions 1, 3: 9 RCTs (15 reports), 27 nonrandomized
  - Key Question 2 (intracranial): 1 RCT, 5 prospective case series
  - Key Question 4: 1 meta-analysis, 5 RCTs (8 reports), 9 nonrandomized
  - Key Question 5: 5 full economic studies
Format and Overall Evidence Strength

Presentation Format:
- Asymptomatic, Symptomatic, Intracranial

Overall Strength (quality) of evidence interpretation (AHRQ)
- **High** – Very confident that effect size estimates lie close to the true effect for outcome; few or no deficiencies in body of evidence; believe the findings are stable.
- **Moderate** – Moderately confident that effect size estimates lie close to the true effect; some deficiencies in the body of evidence; findings are likely to be stable but some doubt remains.
- **Low** – Limited confidence that effect size estimates lie close to the true effect; major or numerous deficiencies in the body of evidence; additional evidence needed before concluding that findings are stable or the estimate is close to the true effect.
- **Insufficient** – We have no evidence, are unable to estimate an effect or have no confidence in the effect estimate; No available evidence or the body of evidence has unacceptable deficiencies precluding judgment.

Additional study information

- Six of the included RCT of extracranial carotid stenting and the 1 RCT of intracranial stenting were terminated early:
  - The EVA, SPACE, Leicester stopped secondary to concerns over the safety of stenting and/or based on interim futility analysis.
  - SAPPHIRE terminated early due to slowed recruitment
  - BACASS and Regensburg-ICSS and SPACE trials respectively were being initiated
  - SAMMPRIS (intracranial) terminated due to safety concerns (versus aggressive med)
- Embolic protection use (extracranial): 6 of 10 RCTs (CREST, SAPPHIRE, EVA-3S, ICSS, SPACE, BACASS); 12/17 nonrandomized studies
Clinical guideline overview: Extracranial

Brott, et. al. 2011 Guideline on the Management of Patients with Extracranial and Vertebral Artery Disease
ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS

Summary of recommendations regarding revascularization

<table>
<thead>
<tr>
<th>Asymptomatic Patients</th>
<th>Symptomatic Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>70%-99% Stenosis</td>
<td>50%-69% Stenosis</td>
</tr>
<tr>
<td>CEA</td>
<td>Class IIa</td>
</tr>
<tr>
<td>LoE A</td>
<td>LoE B</td>
</tr>
<tr>
<td>CAS</td>
<td>Class IIb</td>
</tr>
<tr>
<td>LoE B</td>
<td>LoE B</td>
</tr>
</tbody>
</table>

Stenosis based on angiographic criteria by the method used in NASCET; generally corresponds to assessment by DUS, other accepted methods; LoE = level of evidence

Clinical guideline overview: Extracranial

Summary of acceptable periprocedural risk*

<table>
<thead>
<tr>
<th>Stenosis (%)</th>
<th>Acceptable Periprocedural Death/Stroke Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td></td>
</tr>
<tr>
<td>60-99%</td>
<td>&lt;3% (Level A); 5 year life expectancy</td>
</tr>
<tr>
<td>Symptomatic</td>
<td></td>
</tr>
<tr>
<td>50-69%</td>
<td>&lt;6% (Level A); 5 year life expectancy</td>
</tr>
<tr>
<td>70-99%</td>
<td>&lt;6% (Level A); 2 - 5 year life expectancy</td>
</tr>
</tbody>
</table>

*Summary based on AAN (Chaturvedi et al. 2005) and BCBS Tec Report
Chaturvedi et al. (2005) recommend a 5-year life expectancy; however, NASCET (1991a) demonstrated benefit by 2 years.
### Payer Policies

**Aetna**

*Extracranial*
- Considers PTA with or without stenting with embolic protection medically necessary in symptomatic patients with ≥ 50% stenosis of the internal carotid artery

*Intracranial*
- Considered experimental and investigational for both prophylaxis or treatment of atherosclerotic stenosis of the intracranial arteries

**Cigna**

*Extracranial*
- CAS considered medically necessary when conducted with a FDA-approved carotid stent system in patients at high risk for CEA and:
  - neurological symptoms and ≥50% stenosis of the common or internal carotid artery,
  - or with no neurological symptoms and ≥80% stenosis

*Intracranial*
- None

**Priority Health**

*Extracranial*
- Covered when FDA approved device for indications of use; reference vessel diameter 4.0-9.0 mm
- Asymptomatic patients: >70% stenosis by ultrasound or > 60% by angiogram
- Symptomatic patients: >70% stenosis by ultrasound or > 50% by angiogram

*Intracranial*
- Angioplasty with or without stenting considered investigational; not a covered benefit
Asymptomatic

Clinical Guidelines ASYMPTOMATIC

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Patient selection guided by: comorbidities, life expectancy, individual factors</td>
</tr>
</tbody>
</table>
| Class IIA | CEA reasonable: >70% stenosis, risk of perioperative stroke, MI or death low (LoE A)  
Reasonable to choose CEA over CAS: Older patients; unfavorable anatomy (LoE B)  
Reasonable to choose CAS over CEA: neck anatomy unfavorable for surgery (LoE B) |
| Class IIB | Prophylactic CAS may be considered: highly selected patients; ≥ 60% stenosis by angio or ≥70% by DUS; Effectiveness vs. medical therapy not well established (LoE B)  
Effectiveness of CEA or CAS (vs. medical therapy) not well established in patients at high risk of complications (LoE B) |
| Class III (no benefit) | CEA or CAS not recommended in <50% stenosis (LoE A); for total occlusion (LoE C) or in patients with severe disability by cerebral infarction precluding preservation of useful function (LoE B) |
KQ 1: Efficacy in Asymptomatic Persons

Short term (>30 days – 12 months) and long term (>12 months)
- No RCTs of CAS plus medical therapy versus medical therapy
- CAS vs. CEA - Two RCTs (Kentucky 2004, n = 85, CREST, n = 1181)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Treatment groups</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Studies* N range</td>
<td>Overall quality of evidence</td>
</tr>
<tr>
<td>Any stroke</td>
<td>4 years</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>1 RCT N = 85</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 RCTs N = 1181, N = 85</td>
<td>Low</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any peri-procedural stroke or death or post-procedural ipsilateral stroke</td>
<td>4 years</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>1 RCT N = 1181</td>
<td></td>
</tr>
</tbody>
</table>

KQ 1: Effectiveness in Asymptomatic Persons

CAS versus medical therapy alone: 1 retrospective, single-center cohort (2005)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Treatment groups</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Studies Follow-up (median)</td>
<td>Overall quality</td>
</tr>
<tr>
<td>Any stroke</td>
<td>1 retrospective registry N = 946</td>
<td>Low</td>
</tr>
<tr>
<td>Death</td>
<td>2.1 years</td>
<td>Low</td>
</tr>
<tr>
<td>Any stroke or death</td>
<td></td>
<td>Low</td>
</tr>
</tbody>
</table>

†Kaplan-Meier estimates for projected 5 years of follow-up.
**KQ 1: Effectiveness in Asymptomatic Persons (nonrandomized studies)**

**CAS versus CEA**: three nonrandomized comparative studies (2 clinical cohorts and one registry)

- No statistical differences at any time point (1.5 – 4 years)
  - Primary outcomes: stroke, death, composite of any stroke or death, myocardial infarction or composite of any periprocedural stroke, death or post-procedural ipsilateral stroke
  - Cognitive function, ADLs or depression - Exception was 1 small study reported improvement in working memory after CAS (compared with CEA) and in processing speed following CEA (compared with CAS).

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**KQ 3: Safety in Asymptomatic Persons – 30 day/periprocedural**

**CAS vs. Medical therapy**: Insufficient evidence from 1 cohort (N = 75) of no difference in 30 day stroke or death.

**CAS vs. CEA**: 2 RCTs (Kentucky, N = 85, CREST, N = 1191)

<table>
<thead>
<tr>
<th></th>
<th>Studies*</th>
<th>Overall quality of evidence</th>
<th>CAS (% range)</th>
<th>CEA (% range)</th>
<th>RD range, % (95% CI)†</th>
<th>RR range, % (95% CI)</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any stroke</strong></td>
<td>2 RCTs</td>
<td>Moderate</td>
<td>2.5% (15/594)</td>
<td>1.4% (8/597)</td>
<td>RD = 1.2 (-0.4, 2.7)</td>
<td>RR = 1.9 (0.8, 4.4)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>N = 1191</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>N = 85</td>
<td></td>
<td>0.0% (0/43)</td>
<td>0.0% (0/42)</td>
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</tr>
<tr>
<td><strong>Death</strong></td>
<td>1 RCT</td>
<td>Low</td>
<td>0.0% (0/43)</td>
<td>0.0% (0/42)</td>
<td>Not estimable</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>N = 85</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Any stroke or death</strong></td>
<td>2 RCTs</td>
<td>Moderate</td>
<td>2.5% (15/594)</td>
<td>1.4% (8/597)</td>
<td>RD = 1.2 (-0.4, 2.7)</td>
<td>RR = 1.9 (0.8, 4.4)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>N = 1191</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>N = 85</td>
<td></td>
<td>0.0% (0/43)</td>
<td>0.0% (0/42)</td>
<td>Not estimable</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MI</strong></td>
<td>1 RCT</td>
<td>Moderate</td>
<td>1.2% (7/594)</td>
<td>2.2% (13/597)</td>
<td>RD = -1.0 (-2.5, 0.4)</td>
<td>RR = 0.6 (0.2, 1.4)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>N = 1191</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
KQ 3: Safety in Asymptomatic Persons (non randomized studies)

Low to insufficient evidence: 5 cohorts, 2 registry studies

• Mixed results across studies
  o No statistical differences were seen in the cohort studies (possibly due to sample size) for any outcome.
  o 1 prospective registry reported significantly higher risk of any stroke, death, and composite of stroke or death within 30 days for CAS; the other registry, no difference in these for the in-hospital time period.

KQ 4: Differential efficacy or safety-Asymptomatic Persons

CAS vs. Medical therapy – Insufficient evidence

• No RCT data, 1 Retrospective cohort – no modification based on severity of ipsilateral stenosis

CAS vs. CEA

Age. No RCT data were available. Data from one registry study were available (insufficient evidence)
  o Safety: Age (< 65 versus ≥ 65) did not modify the treatment effect for the following outcomes:
    • Periprocedural death
    • Periprocedural stroke
    • Periprocedural MI
    • Periprocedural death, stroke, or MI (composite)
KQ 4: Differential efficacy or safety - Asymptomatic Persons

CAS vs. CEA

- **Sex**: Moderate evidence, one RCT (CREST):
  - **Safety**: Did not modify the treatment effect for the following outcomes:
    - Periprocedural stroke
    - Periprocedural stroke or death (composite)
    - Periprocedural MI
    - Periprocedural death, stroke, or MI (composite)
  - **Efficacy**: Did not modify the treatment effect for the following outcomes:
    - Ipsilateral stroke (4 years) (Low evidence)
    - Ipsilateral stroke or death (composite) (4 years).

---

KQ 4: Differential efficacy or safety - Asymptomatic Persons

**High surgical risk**: SAPPHIRE (high surgical risk patients)  
(Insufficient for differential effectiveness/safety; Moderate for efficacy and safety)

- **Efficacy**

<table>
<thead>
<tr>
<th></th>
<th>CAS % (n/N)</th>
<th>CEA % (n/N)</th>
<th>RD (95% CI)</th>
<th>RR (95% CI)</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-year Ipsilateral stroke or Death</td>
<td>9.9% (12/117)</td>
<td>21.5% (26/120)</td>
<td>-11% (-21%, -2%)</td>
<td>0.47 (0.25, 0.89)</td>
<td>CAS</td>
</tr>
<tr>
<td>3-year Stroke</td>
<td>10.3% (12/117)</td>
<td>9.2% (11/120)</td>
<td>-2% (-9%, 4%)</td>
<td>0.74 (0.34, 1.62)</td>
<td>NS</td>
</tr>
<tr>
<td>3-year Ipsilateral stroke or Death</td>
<td>21.4% (25/117)</td>
<td>29.2% (35/120)</td>
<td>-8% (-19%, 3%)</td>
<td>0.73 (0.47, 1.14)</td>
<td>NS</td>
</tr>
</tbody>
</table>

- **Safety**

<table>
<thead>
<tr>
<th></th>
<th>CAS % (n/N)</th>
<th>CEA % (n/N)</th>
<th>RD (95% CI)</th>
<th>RR (95% CI)</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periprocedural Death, Stroke, or MI</td>
<td>5.4% (6/117)</td>
<td>10.2% (12/120)</td>
<td>-5% (-12%, 2%)</td>
<td>0.51 (0.20, 1.32)</td>
<td>NS</td>
</tr>
</tbody>
</table>
KQ 5: Cost-effectiveness in Asymptomatic Persons

Three cost-utility studies: Overall low evidence

- 2 based on SAPPHIRE (high surgical risk patients)
  - ICERs: $49,514 and $67,891 for 1-year time horizon (plausible, not verifiably superior)
  - 1 study: CAS may be cost-effective over life-time; concerns regarding methods, extrapolation

- 1 study (standard surgical risk)
  - CEA was the preferred treatment given commonly assumed cost-effectiveness thresholds

Symptomatic

* * *
**Clinical Guidelines: SYMPTOMATIC**

(from Brott 2011 except where noted)

<table>
<thead>
<tr>
<th>Class I</th>
<th>&gt;70% stenosis (noninvasive) or &gt;50% stenosis (angiography) when anticipated rate of periprocedural stroke or mortality is &lt;6%:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Patients with low or average surgical risk, symptoms within 6 months; should undergo CEA</td>
</tr>
<tr>
<td></td>
<td>• CAS alternative to CEA (LoE B) in patients with average or low risk for endovascular intervention.</td>
</tr>
</tbody>
</table>

| Class IIa | Reasonable to choose CEA over CAS: Older patients; unfavorable anatomy (LoE B) |
|           | Reasonable to choose CAS over CEA: neck anatomy unfavorable for arterial surgery (LoE B) |
|           | CAS may be considered in patients with >70% stenosis if: difficult surgical access, increased surgical risk or other specific circumstances -radiation-induced stenosis, restenosis after CEA -(LoE B, Furie 2011 AHA/ASA guideline –Stroke Prevention) |

| Class IIb | Effectiveness of CEA or CAS (vs. medical therapy) not well established in patients at high risk of complications (LoE B) |

| Class III | CEA or CAS not recommended in <50% stenosis (LoE A); for total occlusion (LoE C) or in patients with severe disability by cerebral infarction precluding preservation of useful function |

---

**KQ 1: Efficacy in Symptomatic Persons**

**CAS vs. medical therapy:** No RCTs found

**CAS vs. CEA:** 10 reports from 7 RCTS

- 2 reported short term, 7 longer-term; 2 had N ≤ 20

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies* N range Follow-up</th>
<th>Overall quality of evidence</th>
<th>CAS (%)</th>
<th>CEA (%)</th>
<th>RD % (95% CI)†</th>
<th>RR (95% CI)</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any stroke (excluding periprocedural)</td>
<td>4 months 1 RCT N = 1710</td>
<td>Moderate</td>
<td>0.8% (7/853)</td>
<td>0.9% (8/857)</td>
<td>RD = -0.11 (-0.99, 0.77)</td>
<td>RR = 0.88 (0.32, 2.42)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>2-4 years 2 RCTs N = 1712</td>
<td>Moderate</td>
<td>3.5% (30/866)</td>
<td>3.5% (30/846)</td>
<td>RD‡ = -0.08 (-1.82, 1.66)</td>
<td>RR‡ = 0.98 (0.59, 1.61)</td>
<td>NS</td>
</tr>
<tr>
<td>Ipsilateral stroke (excluding periprocedural)</td>
<td>4 months 1 RCT N = 1710</td>
<td>Moderate</td>
<td>0.7% (6/853)</td>
<td>0.5% (5/857)</td>
<td>RD = 0.12 (-0.63, 0.87)</td>
<td>RR = 1.20 (0.37, 3.93)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>2-5.4 years 4 RCTs N = 3120</td>
<td>Moderate</td>
<td>2.0% (31/1577)</td>
<td>1.9% (30/1543)</td>
<td>RD‡ = -0.01 (-1.36, 1.34)</td>
<td>RR‡ = 0.97 (0.55, 1.73)</td>
<td>NS</td>
</tr>
</tbody>
</table>
### KQ 1: Efficacy in Symptomatic Persons

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies* N range Follow-up</th>
<th>Overall quality of evidence</th>
<th>CAS (%)</th>
<th>CEA (%)</th>
<th>RD % (95% CI)†</th>
<th>RR (95% CI)</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>4 months 1 RCT N = 1710</td>
<td>Moderate</td>
<td>2.3% (19/853)</td>
<td>0.8% (7/857)</td>
<td>RD = 1.37 (0.23, 2.51)</td>
<td>RR = 2.69 (1.14, 6.36)</td>
<td>CEA</td>
</tr>
<tr>
<td></td>
<td>2-5.4 years 5 RCTs (including peri-procedural) N = 1934</td>
<td>Moderate</td>
<td>7.9% (77/975)</td>
<td>8.2% (79/959)</td>
<td>RD‡ = -0.10 (-2.17, 1.96)</td>
<td>RR‡ = 0.97 (0.72, 1.30)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>2-5.4 years 2 RCTs (excluding peri-procedural) N = 1308</td>
<td>Moderate</td>
<td>4.1% (27/664)</td>
<td>3.7% (24/644)</td>
<td>RR‡ = 0.38 (-1.87, 2.64)</td>
<td>RR‡ = 1.09 (0.64, 1.87)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Effect size estimates from pooled meta-analysis with weighting based on sample size; data for n/N are numbers of total events/total number of patients

### KQ 1: Efficacy in Symptomatic Persons

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies* N range Follow-up</th>
<th>Overall quality of evidence</th>
<th>CAS (%)</th>
<th>CEA (%)</th>
<th>RD % (95% CI)†</th>
<th>RR (95% CI)</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any stroke or death (including peri-procedural)</td>
<td>4-6 months 2 RCTs N = 1277</td>
<td>Moderate</td>
<td>11.8% (31/262)</td>
<td>9.8% (26/265)</td>
<td>RD = 1.65 (-3.17, 6.46)</td>
<td>RR = 1.18 (0.72, 1.94)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>2-4 years 2 RCTs N = 124</td>
<td>Low</td>
<td>8.5% (72/853)</td>
<td>4.7% (40/857)</td>
<td>RD = 3.32 (1.13, 5.52)</td>
<td>RR = 1.75 (1.20, 2.54)</td>
<td>CEA</td>
</tr>
<tr>
<td>Any peri-procedural stroke or death or post-procedural ipsilateral stroke</td>
<td>6 months 1 RCT N = 527</td>
<td>Moderate</td>
<td>10.2% (27/262)</td>
<td>4.2% (11/265)</td>
<td>RD = 5.36 (1.28, 9.43)</td>
<td>RR = 2.34 (1.19, 4.63)</td>
<td>CEA</td>
</tr>
<tr>
<td></td>
<td>2-5.4 years 5 RCTs N = 2728</td>
<td>Low</td>
<td>8.1% (12/138)</td>
<td>6.6% (89/1347)</td>
<td>RD‡ = 1.28 (-1.64, 4.19)</td>
<td>RR‡ = 1.20 (0.89, 1.62)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Effect size estimates from pooled meta-analysis with weighting based on sample size; data for n/N are numbers of total events/total number of patients
**KQ 1: Effectiveness in Symptomatic Persons (nonrandomized studies)**

- Insufficient evidence (1 study, N = 128) at 4 years of no difference in stroke or death, but composite of stroke or death favored CAS: Risk were CAS 12.4%, CEA 33.5%
- Low evidence: No statistical difference reported in 1 cohort study (n = 684) at 2.8 years for any periprocedural stroke or death or post-procedural ipsilateral stroke

**KQ 3: Safety in Symptomatic Persons (30-day periprocedural outcomes)**

Any periprocedural stroke – based on sensitivity analysis

<table>
<thead>
<tr>
<th>Studies</th>
<th>Overall Quality</th>
<th>CAS (% range)</th>
<th>CEA (% range)</th>
<th>RD, % (95% CI)</th>
<th>RR, (95% CI)</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 RCTs§</td>
<td>Moderate</td>
<td>6.8% (163/2393)</td>
<td>4.0% (94/2361)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N = 4754</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CAS</td>
</tr>
</tbody>
</table>

**Studies Overall Quality**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>CAS</th>
<th>CEA</th>
<th>Risk Difference</th>
<th>Risk Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>CREST (Silver)</td>
<td>37</td>
<td>21</td>
<td>668</td>
<td>21</td>
</tr>
<tr>
<td>EVA-3S (Mas 2008)</td>
<td>24</td>
<td>9</td>
<td>285</td>
<td>9</td>
</tr>
<tr>
<td>ICSS (2010)</td>
<td>58</td>
<td>27</td>
<td>853</td>
<td>27</td>
</tr>
<tr>
<td>SPACE (Eckstein 2008)</td>
<td>44</td>
<td>37</td>
<td>607</td>
<td>37</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>2393</td>
<td>2361</td>
<td>100.0%</td>
<td>0.0288 [0.0133, 0.0444]</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>163</td>
<td>94</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 4.24, df = 3 (P = 0.24); I² = 29%

Test for overall effect: Z = 3.64 (P = 0.0003)
## KQ 3: Safety in Symptomatic Persons (30-day periprocedural outcomes)

### Death – based on sensitivity analysis

<table>
<thead>
<tr>
<th>Studies</th>
<th>Overall Quality</th>
<th>CAS† (% range)</th>
<th>CEA† (% range)</th>
<th>RD range, % (95% CI)‡</th>
<th>RR range (95% CI)</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 RCTs</td>
<td>Low</td>
<td>1.1% (19/1774)</td>
<td>0.7% (13/1756)</td>
<td>RD = 0.4 (-0.3, 1.0)</td>
<td>RR = 1.4 (0.7, 2.9)</td>
<td>NS</td>
</tr>
</tbody>
</table>

#### Study or Subgroup

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Difference M-H, Random, 95% CI</th>
<th>Risk Difference CEA</th>
<th>Favors CAS Favors CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVA-3S (Mas 2008)</td>
<td>2</td>
<td>261</td>
<td>3 259</td>
<td>-0.009 [-0.0207, 0.0128]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICSS (2010)</td>
<td>11</td>
<td>853</td>
<td>4 657</td>
<td>0.0082 [0.0008, 0.0171]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPACE (Eckstein 2008)</td>
<td>6</td>
<td>607</td>
<td>5 589</td>
<td>0.0014 [-0.0094, 0.0122]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 1721 1705 100.0% 0.0041 [-0.0002, 0.0105]

Test for overall effect: Z = 1.28 (P = 0.20)

### Any Stroke or Death – based on sensitivity analysis

<table>
<thead>
<tr>
<th>Studies</th>
<th>Overall Quality</th>
<th>CAS† (% range)</th>
<th>CEA† (% range)</th>
<th>RD, % (95% CI)</th>
<th>NNH (95% CI)</th>
<th>RR, (95% CI)</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 RCTs§</td>
<td>Moderate</td>
<td>7.1% (171/2393)</td>
<td>4.1% (98/2361)</td>
<td>RD = 3.1 (1.4, 4.7)</td>
<td>NNH = 33 (2.70)</td>
<td>RR = 1.8 (1.2, 2.6)</td>
<td>CEA</td>
</tr>
</tbody>
</table>

#### Study or Subgroup

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Difference M-H, Random, 95% CI</th>
<th>Risk Difference CEA</th>
<th>Favors CAS Favors CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>CREST (Silver)</td>
<td>40</td>
<td>668</td>
<td>21 653</td>
<td>31.2% 0.0277 [0.0552, 0.0502]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVA-3S (Mas 2008)</td>
<td>25</td>
<td>265</td>
<td>10 262</td>
<td>12.6% 0.0092 [0.0043, 0.0693]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICSS (2010)</td>
<td>61</td>
<td>853</td>
<td>28 857</td>
<td>33.8% 0.0388 [0.0178, 0.0588]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPACE (Eckstein 2008)</td>
<td>45</td>
<td>607</td>
<td>39 589</td>
<td>22.5% 0.0070 [0.0210, 0.0369]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 2393 2361 100.0% 0.0306 [0.0143, 0.0469]

Test for overall effect: Z = 3.08 (P = 0.0022)
KQ 3: Safety in Symptomatic Persons (30-day periprocedural)

Ipsilateral stroke —

<table>
<thead>
<tr>
<th>Studies</th>
<th>Overall Quality</th>
<th>CAS (% range)</th>
<th>CEA (% range)</th>
<th>RD range, % (95% CI)</th>
<th>NNH range (95% CI)</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 RCTs N = 2906</td>
<td>Moderate</td>
<td>6.2% (91/1460)</td>
<td>3.9% (56/1446)</td>
<td>RD = 2.4 (0.42, 4.3)</td>
<td>NNH = 42 (23, 238)</td>
<td>CEA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>CAS</th>
<th>CEA</th>
<th>Risk Difference</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICSS (2010)</td>
<td>52</td>
<td>853</td>
<td>25  497 49.3%</td>
<td>0.0018 [0.0122, 0.0514]</td>
</tr>
<tr>
<td>SPACE (Eckstein 2008)</td>
<td>39</td>
<td>607</td>
<td>31  589 47.5%</td>
<td>0.0116 [-0.0149, 0.0302]</td>
</tr>
<tr>
<td>Leicester (Naylor 1998)</td>
<td>5</td>
<td>7</td>
<td>0   10  3.3%</td>
<td>0.7143 [0.3703, 1.0583]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1467</td>
<td>1406</td>
<td>100.0%</td>
<td>0.0447 [-0.0199, 0.0199]</td>
</tr>
<tr>
<td>Total events</td>
<td>56</td>
<td>56</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 1.45, df = 1 (P = 0.23); I² = 31%
Test for overall effect: Z = 2.39 (P = 0.02)

Sensitivity analysis – 2 studies

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>CAS</th>
<th>CEA</th>
<th>Risk Difference</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICSS (2010)</td>
<td>52</td>
<td>853</td>
<td>25  497 49.3%</td>
<td>0.0018 [0.0122, 0.0514]</td>
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<td>SPACE (Eckstein 2008)</td>
<td>39</td>
<td>607</td>
<td>31  589 47.5%</td>
<td>0.0116 [-0.0149, 0.0302]</td>
</tr>
<tr>
<td>Leicester (Naylor 1998)</td>
<td>5</td>
<td>7</td>
<td>0   10  3.3%</td>
<td>0.7143 [0.3703, 1.0583]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1467</td>
<td>1406</td>
<td>100.0%</td>
<td>0.0447 [-0.0199, 0.0199]</td>
</tr>
<tr>
<td>Total events</td>
<td>56</td>
<td>56</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 16.87, df = 2 (P = 0.0002); I² = 88%
Test for overall effect: Z = 1.36 (P = 0.17)

KQ 3: Safety in Symptomatic Persons (30-day periprocedural)

Fatal, major or disabling stroke

<table>
<thead>
<tr>
<th>Studies</th>
<th>Overall Quality</th>
<th>CAS (% range)</th>
<th>CEA (% range)</th>
<th>RD % (95% CI)</th>
<th>RR (95% CI)</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 RCTs N = 4764</td>
<td>Moderate</td>
<td>3.0% (73/2396)</td>
<td>2.1% (49/2368)</td>
<td>RD = 0.9 (-0.4, 2.2)</td>
<td>RR = 1.5 (1.0, 2.1)</td>
<td>NS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>CAS</th>
<th>CEA</th>
<th>Risk Difference</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>CREST (Silver)</td>
<td>8</td>
<td>666</td>
<td>6  653 56.6%</td>
<td>0.0028 [-0.0062, 0.0138]</td>
</tr>
<tr>
<td>EVA-3S (Mas 2008)</td>
<td>9</td>
<td>261</td>
<td>4  259 15.4%</td>
<td>0.0160 [-0.0077, 0.0488]</td>
</tr>
<tr>
<td>ICSS (2010)</td>
<td>22</td>
<td>853</td>
<td>17  857 30.3%</td>
<td>0.0060 [-0.0082, 0.0201]</td>
</tr>
<tr>
<td>SPACE (Eckstein 2008)</td>
<td>31</td>
<td>607</td>
<td>22  589 19.5%</td>
<td>0.0137 [-0.0065, 0.0370]</td>
</tr>
<tr>
<td>Leicester (Naylor 1998)</td>
<td>3</td>
<td>7</td>
<td>0   10  0.1%</td>
<td>0.4286 [0.0634, 0.7937]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>2306</td>
<td>2306</td>
<td>100.0%</td>
<td>0.0086 [-0.0039, 0.0219]</td>
</tr>
<tr>
<td>Total events</td>
<td>73</td>
<td>49</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 7.51, df = 4 (P = 0.11); I² = 47%
Test for overall effect: Z = 1.36 (P = 0.18)
### KQ 3: Safety in Symptomatic Persons (30-day periprocedural)

#### Myocardial infarction

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Overall Quality</th>
<th>CAS (%) Range</th>
<th>CEA (%) Range</th>
<th>RD % (95% CI)</th>
<th>RR (95% CI)</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>Moderate</td>
<td>0.6% (11/1813)</td>
<td>1.3% (23/1787)</td>
<td>RD = -0.4 (-1.0, 0.1)</td>
<td>RR = 0.5 (0.2, 1.0)</td>
<td>NS</td>
</tr>
</tbody>
</table>

#### KQ 3: Safety in Symptomatic Persons – Other

- Cranial nerve injury/palsy (various definitions)
  - Lower for CAS compared with CEA (RD: -5.19%, 95%CI: -6.24, -4.14% and RR: 0.07, 95%CI: 0.02, 0.24) across 7 RCTs
- Bleeding – variable reporting

<table>
<thead>
<tr>
<th>Study</th>
<th>CAS</th>
<th>CEA</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any Hematoma</strong></td>
<td>(n/N)</td>
<td>%</td>
<td>(n/N)</td>
</tr>
<tr>
<td>CREST (2011)</td>
<td>(0/668)</td>
<td>0%</td>
<td>(8/653)</td>
</tr>
<tr>
<td>ICSS (2010)</td>
<td>(30/853)</td>
<td>3.5%</td>
<td>50/857</td>
</tr>
<tr>
<td>BACASS (2008)</td>
<td>(0/10)</td>
<td>0%</td>
<td>(0/10)</td>
</tr>
<tr>
<td>Regensburg (2008)</td>
<td>(1/43)</td>
<td>2.3%</td>
<td>(6/44)</td>
</tr>
<tr>
<td><strong>Pooled estimates</strong></td>
<td>-2.13 (-4.57, 0.31)</td>
<td>0.30 (0.08, 1.15)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>CAS</th>
<th>CEA</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severe Hematoma requiring treatment</strong></td>
<td>(n/N)</td>
<td>%</td>
<td>(n/N)</td>
</tr>
<tr>
<td>EVA-3S (2006)</td>
<td>(1/226)</td>
<td>0.4%</td>
<td>(2/2159)</td>
</tr>
<tr>
<td>ICSS (2010)</td>
<td>(8/853)</td>
<td>0.9%</td>
<td>(28/857)</td>
</tr>
<tr>
<td>Kentucky (2008)</td>
<td>(3/53)</td>
<td>5.7%</td>
<td>(1/51)</td>
</tr>
<tr>
<td>BACASS (2008)</td>
<td>(0/10)</td>
<td>0%</td>
<td>(0/10)</td>
</tr>
<tr>
<td><strong>Pooled estimates</strong></td>
<td>-0.99 (-3.08, 1.10)</td>
<td>0.56 (0.15, 2.13)</td>
<td></td>
</tr>
</tbody>
</table>
KQ 3: Safety in Symptomatic Persons (non randomized studies)

Low to insufficient evidence: 5 cohorts, 2 registry studies

- Mixed results across studies
  - 2 large prospective registry studies (Low evidence)
    - Significantly higher risk of any stroke and death with CAS; neither differences in MI risk
    - 1 of the registries (in-hospital) reported significantly higher risk of any stroke or death and higher risk of ipsilateral stroke with CAS
  - No statistical differences were seen in the cohort studies (possibly due to sample size) for any outcome. (Insufficient evidence)

KQ 4: Differential efficacy or safety - Symptomatic Persons

CAS vs. Medical therapy – no studies

CAS vs. CEA

Efficacy - Age (moderate evidence)

- Age (< 68 versus ≥ 68 years) did not modify the treatment effect for the outcome ipsilateral stroke (4 years, SPACE) but did modify for composite of ipsilateral stroke or death (2 years): those ≥ 68 had better outcomes with CEA (EVA-3S)

- Age (< 70 versus ≥ 70) did not modify treatment for the outcomes of 120 day composite death, stroke or MI (ICSS) or for ipsilateral stroke at 4 years (EVA-3S)
KQ 4: Differential efficacy or safety- Symptomatic Persons

Safety – Age (recent studies with EPD) Moderate evidence for modification: Periprocedural death or stroke

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>CAS Events Total</th>
<th>CEA Events Total</th>
<th>Risk Difference</th>
<th>Risk Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>M-H, Weight</td>
<td>M-H, Weight</td>
</tr>
<tr>
<td>7.1.1 Age &lt; 70</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVA-3S (2006)</td>
<td>10 127 6 106</td>
<td>11.5%</td>
<td>0.0221 [0.0421, 0.0864]</td>
<td>0.0221 [0.0421, 0.0864]</td>
</tr>
<tr>
<td>SPACE (Stingelen)</td>
<td>17 347 22 333 19.4%</td>
<td>-0.0171 [-0.0521, 0.0180]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICSS (2010)</td>
<td>20 395 14 494 21.7%</td>
<td>0.0160 [0.0120, 0.0440]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>869 943 52.6%</td>
<td>0.0047 [0.0189, 0.0283]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>47 42</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.091 [0.0297, 0.1525]</td>
<td>0.0413 [0.0072, 0.0898]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.0541 [0.0208, 0.0873]</td>
<td>0.0568 [0.0318, 0.0810]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.1.2 Age ≥ 70</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVA-3S (2006)</td>
<td>17 138 5 156 12.1%</td>
<td>0.091 [0.0297, 0.1525]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPACE (Stingelen)</td>
<td>28 260 17 256 10.3%</td>
<td>0.0413 [0.0072, 0.0898]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICSS (2010)</td>
<td>45 458 20 453 20.0%</td>
<td>0.0541 [0.0208, 0.0873]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>856 965 47.4%</td>
<td>0.0568 [0.0318, 0.0810]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>90 42</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.091 [0.0297, 0.1525]</td>
<td>0.0413 [0.0072, 0.0898]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.0541 [0.0208, 0.0873]</td>
<td>0.0568 [0.0318, 0.0810]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1725 1708 100%</td>
<td>0.0308 [0.0024, 0.0593]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.12 (P = 0.03)</td>
<td>0.0072 [0.0034, 0.0110]</td>
<td>0.0072 [0.0034, 0.0110]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

KQ 4: Differential efficacy or safety- Symptomatic Persons

Efficacy- Sex (moderate evidence)
- No modification: Death, stroke or MI composite at 120 days, ipsilateral stroke or death (2 years), stroke or death (4 years);
- Ipsilateral stroke (4 years): Modification suggested in one RCT (EVA) but not in another (CREST)

Safety- no modification (moderate evidence, EPD used) periprocedural stroke or death

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>CAS Events Total</th>
<th>CEA Events Total</th>
<th>Risk Difference</th>
<th>Risk Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>M-H, Weight</td>
<td>M-H, Weight</td>
</tr>
<tr>
<td>7.3.1 Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVA-3S (2006)</td>
<td>21 193 7 204 8.0%</td>
<td>0.0745 [0.0245, 0.1250]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPACE (Stingelen)</td>
<td>31 436 29 422 15.4%</td>
<td>0.0624 [0.0171, 0.0308]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICSS (2010)</td>
<td>46 601 18 466 22.2%</td>
<td>0.0468 [0.0216, 0.0720]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CREST (2010)</td>
<td>25 338 15 237 22.3%</td>
<td>0.0363 [0.0101, 0.0643]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>103 1169 44 1548 44.4%</td>
<td>0.0517 [0.0046, 0.0584]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>137 84</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.091 [0.0297, 0.1525]</td>
<td>0.0413 [0.0072, 0.0898]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.0541 [0.0208, 0.0873]</td>
<td>0.0568 [0.0318, 0.0810]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1725 1708 100%</td>
<td>0.0308 [0.0024, 0.0593]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.32 (P = 0.02)</td>
<td>0.0072 [0.0034, 0.0110]</td>
<td>0.0072 [0.0034, 0.0110]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

7.3.2 Female

EVA-3S (2006) 6 72 4 58 3.0% 0.0114 [0.0079, 0.0156] 0.0114 [0.0079, 0.0156]
SPACE (Stingelen) 14 171 10 167 7.5% 0.0230 [0.0028, 0.0186] 0.0230 [0.0028, 0.0186]
ICSS (2010) 19 202 15 251 10.7% 0.0186 [0.0093, 0.0646] 0.0186 [0.0093, 0.0646]
CREST (2010) 18 240 6 236 13.0% 0.0480 [0.0081, 0.0878] 0.0480 [0.0081, 0.0878]
Subtotal (95% CI) 735 792 33.6% 0.0298 [0.0051, 0.0548] 0.0298 [0.0051, 0.0548]
Total events 57 35
Heterogeneity: Tau² = 0.00, Chisq = 8.18, df = 3 (P = 0.04); I² = 63%
Test for overall effect: Z = 2.32 (P = 0.02)
KQ 4: Differential efficacy or safety- Symptomatic Persons

Safety- Sex:
- no modification-periprocedural stroke or periprocedural MI
- modified treatment for composite of any periprocedural death, stroke or MI (moderate evidence, CREST Trial):

<table>
<thead>
<tr>
<th></th>
<th>CAS % (n/N)</th>
<th>CEA % (n/N)</th>
<th>HR (95% CI)</th>
<th>Favors</th>
<th>Interaction p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>NR</td>
<td>NR</td>
<td>2.33 (1.07, 5.07)</td>
<td>CEA</td>
<td>P = 0.04</td>
</tr>
<tr>
<td>Male</td>
<td>NR</td>
<td>NR</td>
<td>0.88 (0.50, 1.55)</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

Other Factors: No modification for the following
- Moderate evidence: severity of ipsilateral stenosis
- Low evidence: Diabetes, smoking status, severity of contralateral stenosis
- Insufficient evidence: Hypertension, surgical risk, type of qualifying event, time to treatment

KQ 5: Cost-effectiveness in Symptomatic Persons

Four cost-utility studies: Overall low evidence

- Across studies, CEA more cost effective
  - 2 studies found insufficient evidence to favor one or the other treatment

- Subanalysis from SAPPHIRE (high risk patients)
  - CAS more expensive with negligible QALY improvement, thus extremely high ICERs
Clinical Guidelines: Intracranial artery stenosis

AHA/ASA guidelines
- Asymptomatic: None made
- Symptomatic (Stroke or TIA): Class IIb
  - 50% to 99% stenosis of a major intracranial artery, the usefulness of angioplasty and/or stent placement is unknown and is considered investigational (Furie 2011; LoE C).
  - The usefulness of emergent/acute (i.e. within the first 48 hours from stroke onset) intracranial angioplasty and/or stenting is not well established; should be used in the setting of clinical trials (Jauch 2013; LoE C).

ASINT/SIR/ASN guidelines (Higashida 2005; Grade: NR; LoE: NR)
- Asymptomatic: Insufficient evidence for recommendation on endovascular therapy for severe stenosis; counsel, monitor, optimal prophylactic medical therapy
- Symptomatic: Patients with >50% intracranial stenosis who have failed medical therapy, balloon angioplasty with or without stenting should be considered

KQ 2: Intracranial Atherosclerosis

- No studies in asymptomatic patients
- 1 RCT (SAMMPRIS) –terminated early due to safety
- No studies on differential efficacy/safety or economics
- Efficacy (primary end point): Stroke or death within 30 days or ischemic stroke in the territory of the qualifying artery beyond 30 days;

<table>
<thead>
<tr>
<th>Study Follow-up</th>
<th>Overall quality</th>
<th>CAS Probability (%) 1 year (95% CI)</th>
<th>Medical Patient Events (n/N)</th>
<th>Treatment groups</th>
<th>Effect size*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 RCT N = 451</td>
<td>Low 20.0 (15.2–26.0) (46/224)</td>
<td>12.2 (8.4–17.6) (26/227)</td>
<td>.009 Medical</td>
<td>*Authors do not report effect size; probabilities and p-values are provided.</td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td></td>
<td></td>
<td></td>
<td>Medical</td>
<td>RD 7.8% NNH 13</td>
</tr>
</tbody>
</table>
### KQ 2: Intracranial Atherosclerosis

#### Safety – 30 day periprocedural outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies</th>
<th>Overall quality</th>
<th>CAS</th>
<th>Medical</th>
<th>P-value</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any stroke</td>
<td>1 RCT</td>
<td>Low</td>
<td>14.7 (10.7–20.1) (33/224)</td>
<td>5.3 (3.1–9.2) (12/227)</td>
<td>.03</td>
<td>Medical RD 9.4% NNH 11</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td>Low</td>
<td>2.2 (0.9–5.3) (5/224)</td>
<td>0.4 (0.1–3.1) (1/227)</td>
<td>.95</td>
<td>NS</td>
</tr>
<tr>
<td>Any stroke or death</td>
<td>1 RCT</td>
<td>Low</td>
<td>14.7 (10.7–20.1) (33/224)</td>
<td>5.8 (3.4–9.7) (13/227)</td>
<td>.009</td>
<td>Medical RD 8.9% NNH 11</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td>Low</td>
<td>0.5 (0.1–3.2) (NR)</td>
<td>1.3 (0.4–4.1) (NR)</td>
<td>.60</td>
<td>NS</td>
</tr>
<tr>
<td>Any major hemorrhage</td>
<td></td>
<td>Low</td>
<td>8.0 (5.1–12.5) (NR)</td>
<td>0.9 (0.2–3.5) (NR)</td>
<td>&lt;.001</td>
<td>Medical RD 7.9% NNH 13</td>
</tr>
</tbody>
</table>

*Authors do not report effect size; probabilities and p-values are provided.

#### Efficacy – 1 year probabilities reported

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies</th>
<th>Overall quality</th>
<th>CAS</th>
<th>Medical</th>
<th>P-value</th>
<th>Favors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any stroke</td>
<td>1 RCT</td>
<td>Low</td>
<td>22.3 (17.2–28.7) (50/224)</td>
<td>14.9 (10.6–20.7) (32/227)</td>
<td>.03</td>
<td>Medical RD 7.4% NNH 13</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td>Low</td>
<td>3.4 (1.6–7.2) (7/224)</td>
<td>4.1 (2.0–8.5) (7/227)</td>
<td>.95</td>
<td>NS</td>
</tr>
<tr>
<td>Any stroke or death</td>
<td>1 RCT</td>
<td>Low</td>
<td>23.4 (18.1–29.8) (52/224)</td>
<td>17.5 (12.8–23.6) (37/227)</td>
<td>.06</td>
<td>NS</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td>Low</td>
<td>2.2 (0.8–5.8) (5/224)</td>
<td>4.0 (1.9–8.4) (7/227)</td>
<td>.60</td>
<td>NS</td>
</tr>
<tr>
<td>Any major hemorrhage</td>
<td></td>
<td>Low</td>
<td>9.0 (5.9–13.5) (22/224)</td>
<td>1.8 (0.7–4.8) (5/227)</td>
<td>&lt;.001</td>
<td>Medical RD 7.2% NNH 14</td>
</tr>
</tbody>
</table>

*Authors do not report effect size; probabilities and p-values are provided.
Summary

OVERALL SUMMARY: Asymptomatic Patients

CAS vs. medical therapy: No RCTs. Insufficient evidence from 1 registry that CAS favored

CAS vs. CEA: 2 RCTs

- **Efficacy:** Low evidence for
  - Similar risk for stroke, ipsilateral stroke and vessel patency up to 4 years;
  - Differences in any peri-procedural stroke or death or post-procedural ipsilateral stroke (4.5% for CAS, 2.7% for CEA) failed to reach significance

- **Safety:** Moderate evidence for
  - No statistical differences for safety outcomes (30-day peri-procedural period) based on CREST
  - Risk of stroke and composite of death or stroke: 2.5% for CAS, 1.4% for CEA, failed to reach significance
OVERALL SUMMARY: Asymptomatic Patients

- **Differential efficacy or safety:**
  - Insufficient: CAS vs. medical therapy that there is no modification by percent of ipsilateral stenosis
  - Insufficient: CAS vs. CEA that age, surgical risk do not modify treatment
  - Insufficient: Surgical risk; No RCT comparison
  - Moderate evidence: sex does not modify

- **Economic: Low evidence**
  - In high risk patients, cost-effectiveness of CAS may be plausible but not it is not verifiably superior at 1 year; may be cost-effective over life time (methodological concerns)
  - In standard risk patients, CEA preferred

OVERALL SUMMARY: Symptomatic Patients

**CAS vs. medical therapy:** No studies found

**CAS vs. CEA: Efficacy:**

- **Short term (>30 days – 12 months)- Moderate**
  - At 4 months: Similar risk for stroke, ipsilateral stroke at when periprocedural stroke excluded; Risk of death higher following CAS
  - 4 – 6 months: significantly higher risk with CAS for composites of any stroke or death (including periprocedural) and any periprocedural stroke or death or postprocedural ipsilateral stroke

- **Longer Term (>12 months): across 5 RCTs at up to 5.4 years**
  - Moderate evidence: risk of death similar between treatment whether or not periprocedural death was included
  - Low evidence of no difference death or stroke(including periprocedural) and any periprocedural stroke or death or postprocedural ipsilateral stroke
SUMMARY: Symptomatic Patients

- **Safety**: Moderate Evidence
  - Risk of stroke and the composite of any stroke or death are significantly higher in symptomatic persons who received CAS; (4 RCTs with EPD)
  - Risk of any stroke or death was 7.1% for CAS and 4.1% for CEA, RD 3.1% (1.4%, 4.7%), NNH = 35.

- **Differential efficacy or safety**: Moderate evidence
  - **Age**:
    - Efficacy: Modification by age for composite of ipsilateral stroke or death (2 years): those ≥ 68 had better outcomes with CEA; No modification for other outcomes
    - Safety: Risk of periprocedural death or stroke, CEA favored in ≥ 70 years old while those under 70 years of age had similar results regardless of treatment. (3 RCTs with EPD)

- **Sex**: Moderate evidence of no modification

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SUMMARY: Symptomatic Patients

- **Differential efficacy or safety**:
  - Surgical risk: Insufficient evidence from RCTs (no comparison with average surgical risk patients)
  - Moderate evidence: Severity of ipsilateral stenosis does not modify
  - Insufficient to low evidence for no modification by: diabetes, type of symptomatic qualifying event, severity of contralateral stenosis, time to treatment, hypertension or smoking

- **Economic**: Low evidence
  - Four cost-utility studies: CEA tended to be cost effective than CAS
  - SAPPIRE trial: CAS more expensive with negligible improvement in QALY.
SUMMARY: Intracranial stenting

No studies in asymptomatic patients

1 RCT (symptomatic); terminated for safety concerns

- **Efficacy**: Low evidence
  - Significantly higher probability of stroke or death within 30 days or ischemic stroke in the territory of the qualifying artery beyond 30 days for stenting (20.0%) compared with medical therapy (12.2%).

- **Safety**: Low evidence
  - Significantly higher probability of stroke, stroke or death or hemorrhage with stenting compared with medical therapy

- **Differential efficacy/safety**: No studies found

- **Economic**: No studies found

Evidence limitations, remaining questions

- No high quality data comparing stenting with current best medical practices in asymptomatic patients and limited data from randomized controlled trials in asymptomatic, low-risk patients; trials lacked a medical treatment comparator.

- Limited information on long-term (>5 years) benefits of CAS and whether these would outweigh risks associated with periprocedural events.

- Impact of better medical therapy, enhanced surgical techniques and improvements in stent technology requires further study.

- The extent to which there is differential efficacy and safety in some special populations (including those at high surgical risk) is not clear. Overall, studies were underpowered to detect modification of treatment.

- There is a need for high quality full economic studies.
HTA’s goal is to achieve better health care outcomes for enrollees and beneficiaries of state programs by paying for proven health technologies that work.

To find best outcomes and value for the state and the patient, the HTA program focuses on three questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

**Principle One: Determinations are Evidence-Based**

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective\(^1\) as expressed by the following standards\(^2\):

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

**Principle Two: Determinations Result in Health Benefit**

- The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms\(^3\):
- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.

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\(^1\) Based on Legislative mandate: See RCW 70.14.100(2).
\(^2\) The principles and standards are based on USPSTF Principles at: [http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm](http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm)
\(^3\) The principles and standards are based on USPSTF Principles at: [http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm](http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm)
• Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.

• The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.

• In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.

The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

Using Evidence as the Basis For a Coverage Decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. **Availability of Evidence:**

   Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

2. **Sufficiency of the Evidence:**

   Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence using characteristics such as:

   • Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
   • The amount of evidence (sparse to many number of evidence or events or individuals studied);
   • Consistency of evidence (results vary or largely similar);
   • Recency (timeliness of information);
   • Directness of evidence (link between technology and outcome);
   • Relevance of evidence (applicability to agency program and clients);
   • Bias (likelihood of conflict of interest or lack of safeguards).

   Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

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4 Based on GRADE recommendation:  [http://www.gradeworkinggroup.org/FAQ/index.htm](http://www.gradeworkinggroup.org/FAQ/index.htm)
<table>
<thead>
<tr>
<th>Not Confident</th>
<th>Confident</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.</td>
<td>Very certain of evidentiary support. Further information is unlikely to change confidence.</td>
</tr>
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</table>

3. **Factors for Consideration - Importance**

At the end of discussion a vote is taken on whether sufficient evidence exists regarding the technology’s safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:

- Risk of event occurring;
- The degree of harm associated with risk;
- The number of risks; the burden of the condition;
- Burden untreated or treated with alternatives;
- The importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- The degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- Value variation based on patient preference.

**Medicare Coverage and Guidelines**

**Medicare (National Coverage Determination)**

The Centers for Medicare and Medicaid Services (CMS) will cover PTA both with and without the placement of a stent (CAS) when used in accordance with FDA-approved protocols for carotid artery dilation for patients who are at high risk for the likely alternative treatment carotid endarterectomy (CEA) or in FDA-approved Category B Investigational Device Exemption (IDE) clinical trials and Post-Approval studies. Coverage for all other devices is at the discretion of local CMS contractors.


**Complete text of NCD:**

**Benefit Category**

**Inpatient Hospital Services**

**Physicians’ Services**

*Note: This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.*
**Item/Service Description**

A. General

This procedure involves inserting a balloon catheter into a narrow or occluded blood vessel to recanalize and dilate the vessel by inflating the balloon. The objective of PTA is to improve the blood flow through the diseased segment of a vessel so that vessel patency is increased and embolization is decreased. With the development and use of balloon angioplasty for treatment of atherosclerotic and other vascular stenoses, PTA (with and without the placement of a stent) is a widely used technique for dilating lesions of peripheral, renal, and coronary arteries.

**Indications and Limitations of Coverage**

B. Nationally Covered Indications

The PTA is covered when used under the following conditions:

1. Treatment of Atherosclerotic Obstructive Lesions
   – In the lower extremities, i.e., the iliac, femoral, and popliteal arteries, or in the upper extremities, i.e., the innominate, subclavian, axillary, and brachial arteries. The upper extremities do not include head or neck vessels.
   – Of a single coronary artery for patients for whom the likely alternative treatment is coronary bypass surgery and who exhibit the following characteristics:
     - Angina refractory to optimal medical management;
     - Objective evidence of myocardial ischemia; and
     - Lesions amenable to angioplasty.
   – Of the renal arteries for patients in whom there is an inadequate response to a thorough medical management of symptoms and for whom surgery is the likely alternative. PTA for this group of patients is an alternative to surgery, not simply an addition to medical management.
   – Of arteriovenous dialysis fistulas and grafts when performed through either a venous or arterial approach.

2. Concurrent with Carotid Stent Placement in Food and Drug Administration (FDA)-Approved Category B Investigational Device Exemption (IDE) Clinical Trials

Effective July 1, 2001, Medicare covers PTA of the carotid artery concurrent with carotid stent placement when furnished in accordance with the FDA-approved protocols governing Category B IDE clinical trials. PTA of the carotid artery, when provided solely for the purpose of carotid artery dilation concurrent with carotid stent placement, is considered to be a reasonable and necessary service when provided in the context of such a clinical trial.

3. Concurrent with Carotid Stent Placement in FDA-Approved Post Approval Studies

Effective October 12, 2004, Medicare covers PTA of the carotid artery concurrent with the placement of an FDA-approved carotid stent and an FDA-approved or -cleared embolic protection device (effective December 9, 2009) for an FDA-approved indication when furnished in accordance with FDA-approved protocols governing post-approval studies. CMS determines that coverage of PTA of the carotid artery is reasonable and necessary in these circumstances.
4. Concurrent with Carotid Stent Placement in Patients at High Risk for Carotid Endarterectomy (CEA)

Effective March 17, 2005, Medicare covers PTA of the carotid artery concurrent with the placement of an FDA-approved carotid stent with embolic protection for the following:

- Patients who are at high risk for CEA and who also have symptomatic carotid artery stenosis ≥70%. Coverage is limited to procedures performed using FDA-approved carotid artery stenting systems and FDA-approved or -cleared (effective December 9, 2009) embolic protection devices. If deployment of the embolic protection device is not technically possible, and not performed, then the procedure is not covered by Medicare (effective December 9, 2009);
- Patients who are at high risk for CEA and have symptomatic carotid artery stenosis between 50% and 70%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on carotid artery stenting (CAS) post-approval studies (Medicare NCD Manual 20.7);
- Patients who are at high risk for CEA and have asymptomatic carotid artery stenosis ≥80%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on CAS post-approval studies (Medicare NCD Manual 20.7).

Coverage is limited to procedures performed using FDA-approved carotid artery stents and FDA-approved or -cleared embolic protection devices.

The use of an FDA-approved or cleared embolic protection device is required. If deployment of the embolic protection device is not technically possible, and not performed, then the procedure is not covered by Medicare.

Patients at high risk for CEA are defined as having significant comorbidities and/or anatomic risk factors (i.e., recurrent stenosis and/or previous radical neck dissection), and would be poor candidates for CEA. Significant comorbid conditions include but are not limited to:

- Congestive heart failure (CHF) class III/IV;
- Left ventricular ejection fraction (LVEF) < 30 %;
- Unstable angina;
- Contralateral carotid occlusion;
- Recent myocardial infarction (MI);
- Previous CEA with recurrent stenosis;
- Prior radiation treatment to the neck; and
- Other conditions that were used to determine patients at high risk for CEA in the prior carotid artery stenting trials and studies, such as ARCHER, CABERNET, SAPPHIRE, BEACH, and MAVERIC II.

Symptoms of carotid artery stenosis include carotid transient ischemic attack (distinct focal neurological dysfunction persisting less than 24 hours), focal cerebral ischemia producing a nondisabling stroke (modified Rankin scale < 3 with symptoms for 24 hours or more), and transient monocular blindness (amaurosis fugax). Patients who have had a disabling stroke (modified Rankin scale ≥ 3) shall be excluded from coverage.
The determination that a patient is at high risk for CEA and the patient's symptoms of carotid artery stenosis shall be available in the patient medical records prior to performing any procedure.

The degree of carotid artery stenosis shall be measured by duplex Doppler ultrasound or carotid artery angiography and recorded in the patient’s medical records. If the stenosis is measured by ultrasound prior to the procedure, then the degree of stenosis must be confirmed by angiography at the start of the procedure. If the stenosis is determined to be <70% by angiography, then CAS should not proceed.

In addition, CMS has determined that CAS with embolic protection is reasonable and necessary only if performed in facilities that have been determined to be competent in performing the evaluation, procedure and follow-up necessary to ensure optimal patient outcomes. Standards to determine competency include specific physician training standards, facility support requirements and data collection to evaluate outcomes during a required reevaluation.

The CMS has created a list of minimum standards modeled in part on professional society statements on competency. All facilities must at least meet CMS’s standards in order to receive coverage for carotid artery stenting for high risk patients.

- Facilities must have necessary imaging equipment, device inventory, staffing, and infrastructure to support a dedicated carotid stent program. Specifically, high-quality x-ray imaging equipment is a critical component of any carotid interventional suite, such as high resolution digital imaging systems with the capability of subtraction, magnification, road mapping, and orthogonal angulation.
- Advanced physiologic monitoring must be available in the interventional suite. This includes real time and archived physiologic, hemodynamic, and cardiac rhythm monitoring equipment, as well as support staff who are capable of interpreting the findings and responding appropriately.
- Emergency management equipment and systems must be readily available in the interventional suite such as resuscitation equipment, a defibrillator, vasoactive and antiarrhythmic drugs, endotracheal intubation capability, and anesthesia support.
- Each institution shall have a clearly delineated program for granting carotid stent privileges and for monitoring the quality of the individual interventionalists and the program as a whole. The oversight committee for this program shall be empowered to identify the minimum case volume for an operator to maintain privileges, as well as the (risk-adjusted) threshold for complications that the institution will allow before suspending privileges or instituting measures for remediation. Committees are encouraged to apply published standards from national specialty societies recognized by the American Board of Medical Specialties to determine appropriate physician qualifications. Examples of standards and clinical competence guidelines include those published in the December 2004 edition of the American Journal of Neuroradiology, and those published in the August 18, 2004 Journal of the American College of Cardiology.
- To continue to receive Medicare payment for CAS under this decision, the facility or a contractor to the facility must collect data on all CAS procedures done at that particular facility. This data must be analyzed routinely to ensure patient safety. This data must be made available to CMS upon request. The interval for data analysis will be determined by the facility but shall not be less frequent than every 6 months.

Since there currently is no recognized entity that evaluates CAS facilities, CMS has established a mechanism for evaluating facilities. Facilities must provide written documentation to CMS that the facility meets one of the following:
1. The facility was an FDA-approved site that enrolled patients in prior CAS IDE trials, such as SAPPHIRE, and ARCHER;
2. The facility is an FDA-approved site that is participating and enrolling patients in ongoing CAS IDE trials, such as CREST;
3. The facility is an FDA-approved site for one or more FDA post approval studies; or
4. The facility has provided a written affidavit to CMS attesting that the facility has met the minimum facility standards. This should be sent to:

   **Director, Coverage and Analysis Group**  
   **7500 Security Boulevard, Mailstop S3-02-01**  
   **Baltimore, MD 21244**

The letter must include the following information:
- Facility's name and complete address;
- Facility's national provider identifier (formerly referred to as the Medicare provider number);
- Point-of-contact for questions with telephone number;
- Discussion of how each standard has been met by the hospital;
- Mechanism of data collection of CAS procedures; and
- Signature of a senior facility administrative official.

A list of certified facilities will be made available and viewable at:  
http://www.cms.gov/coverage/carotid-stent-facilities.asp. In addition, CMS will publish a list of approved facilities in the Federal Register.

Facilities must recertify every two (2) years in order to maintain Medicare coverage of CAS procedures. Recertification will occur when the facility documents that and describes how it continues to meet the CMS standards.

The process for recertification is as follows:

1. **At 23 months after initial certification:**
   - Submission of a letter to CMS stating how the facility continues to meet the minimum facility standards as listed above.
2. **At 27 months after initial certification:**
   - Submission of required data elements for all CAS procedures performed on patients during the previous two (2) years of certification.
   - Data elements:
     a. Patients’ Medicare identification number if a Medicare beneficiary;
     b. Patients’ date of birth;
     c. Date of procedure;
     d. Does the patient meet high surgical risk criteria (defined below)?
       - Age ≥80;
       - Recent (< 30 days) Myocardial Infarction (MI);
       - Left Ventricle Ejection Fraction (LVEF) <30%;
       - Contralateral carotid occlusion;
       - New York Heart Association (NYHA) Class III or IV congestive heart failure;
       - Unstable angina: Canadian Cardiovascular Society (CCS) Class III/IV;
- Renal failure: end stage renal disease on dialysis;
- Common Carotid Artery (CCA) lesion(s) below clavicle;
- Severe chronic lung disease;
- Previous neck radiation;
- High cervical Internal Carotid Artery (ICA) lesion(s);
- Restenosis of prior carotid endarterectomy (CEA);
- Tracheostomy;
- Contralateral laryngeal nerve palsy.

e. Is the patient symptomatic (defined below)?
   - Carotid Transient Ischemic Attack (TIA) persisting less than 24 hours;
   - Non-disabling stroke: Modified Rankin Scale
   - Transient monocular blindness: amaurosis fugax.

f. Modified Rankin Scale score if the patient experienced a stroke.
g. Percent of stenosis of stented lesion(s) by angiography.
h. Was embolic protection used?
i. Were there any complications during hospitalization (defined below)?
   - All stroke: an ischemic neurologic deficit that persisted more than 24 hours;
   - MI;
   - All death.

Recertification is effective for two (2) additional years during which facilities will be required to submit the requested data every April 1 and October 1.

The CMS will consider the approval of national CAS registries that provide CMS with a comprehensive overview of the registry and its capabilities, and the manner in which the registry meets CMS data collection and evaluation requirements. Specific standards for CMS approval are listed below. Facilities enrolled in a CMS-approved national CAS registry will automatically meet the data collection standards required for initial and continued facility certification. Hospitals' contracts with an approved registry may include authority for the registry to submit required data to CMS for the hospital. A list of approved registries will be available on the CMS coverage Web site.

National Registries

As noted above, CMS will approve national registries developed by professional societies and other organizations and allow these entities to collect and submit data to CMS on behalf of participating facilities to meet facility certification and recertification requirements. To be eligible to perform these functions and become a CMS-approved registry, the national registry, at a minimum, must be able to:

1. Enroll facilities in every US state and territory;
2. Assure data confidentiality and compliance with HIPPA;
3. Collect the required CMS data elements as listed in the above section;
4. Assure data quality and data completeness;
5. Address deficiencies in the facility data collection, quality, and submission;
6. Validate the data submitted by facilities as needed;
7. Track long term outcomes such as stroke and death;
8. Conduct data analyses and produce facility specific data reports and summaries;
9. Submit data to CMS on behalf of the individual facilities; and

8
10. Provide quarterly reports to CMS on facilities that do not meet or no longer meet the CMS facility certification and recertification requirements pertaining to data collection and analysis.

Registries wishing to receive this designation from CMS must submit evidence that they meet or exceed our standards. Though the registry requirements pertain to CAS, CMS strongly encourages all national registries to establish a similar mechanism to collect comparable data on CEA. Having both CAS and CEA data will help answer questions about carotid revascularization, in general, in the Medicare population. The CAS for patients who are not at high risk for CEA remains covered only in FDA-approved Category B IDE clinical trials under 42 CFR 405.201.

The CMS has determined that PTA of the carotid artery concurrent with the placement of an FDA-approved carotid stent and an FDA-approved or cleared embolic protection device is not reasonable and necessary for all other patients.

5. Concurrent with Intracranial Stent Placement in FDA-Approved Category B IDE Clinical Trials

Effective November 6, 2006, Medicare covers PTA and stenting of intracranial arteries for the treatment of cerebral artery stenosis ≥50% in patients with intracranial atherosclerotic disease when furnished in accordance with the FDA-approved protocols governing Category B IDE clinical trials. CMS determines that coverage of intracranial PTA and stenting is reasonable and necessary under these circumstances.

C. Nationally Non-Covered Indications

All other indications for PTA with or without stenting to treat obstructive lesions of the vertebral and cerebral arteries remain noncovered. The safety and efficacy of these procedures are not established. All other indications for PTA without stenting for which CMS has not specifically indicated coverage remain noncovered.

D. Other

Coverage of PTA with stenting not specifically addressed or discussed in this NCD is at local Medicare contractor discretion.

(This NCD last reviewed December 2009.)
### Table 1. Clinical Practice Guidelines for Extracranial Carotid Artery Stenosis

<table>
<thead>
<tr>
<th>Organization(s)</th>
<th>Search Dates</th>
<th>Procedure(s) Evaluated</th>
<th>Evidence Base Available</th>
<th>Recommendations</th>
<th>Class/ Grade of Recmndtn</th>
<th>Level of Evidence</th>
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<tbody>
<tr>
<td><strong>National Guideline Clearinghouse</strong></td>
<td></td>
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<tr>
<td>Canadian Stroke Strategy</td>
<td>Through 6/30/10</td>
<td>CAS for symptomatic and asymptomatic carotid artery stenosis</td>
<td>4 RCTs (CREST, EVA-3S, SPACE, ICSS)</td>
<td>CAS may be considered for patients who are not operative candidates for technical, anatomic or medical reasons. Interventionalists should have expertise in carotid procedures and an expected risk of peri-procedural morbidity and mortality rate of less than 5%.</td>
<td>NR</td>
<td>A</td>
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<tr>
<td>Canadian Best Practice Recommendations for Stroke Care (2010)</td>
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<tr>
<td>National Stroke Foundation Clinical</td>
<td>Through 2/19/10</td>
<td>CAS for carotid artery stenosis</td>
<td>1 Cochrane review; 1 RCT (SPACE)</td>
<td>CAS should NOT routinely be undertaken for patients with carotid stenosis.</td>
<td>A</td>
<td>NR</td>
</tr>
<tr>
<td>Organization(s)</td>
<td>Search Dates</td>
<td>Procedure(s) Evaluated</td>
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<tr>
<td>Guidelines for Stroke Management (2010)</td>
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<td>While stenting is not routinely recommended it may be considered as an alternative in certain circumstances, that is in patients who meet criteria for CEA but are deemed unsuitable due to conditions that make them technically unsuitable for open surgery (e.g. high carotid bifurcation, symptomatic carotid restenosis, previous neck radiotherapy, possible medical co-morbidities, or age &gt;80y).</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Singapore Ministry of Health Stroke and Transient Ischaemic Attacks. Assessment, Investigation, Immediate Management and Secondary Prevention (2009)</td>
<td>NR</td>
<td>CAS for symptomatic and asymptomatic extracranial carotid artery stenosis</td>
<td>1 RCT (SAPPHIRE); Carotid artery stenting may be considered in patients who are not suitable for carotid endarterectomy.</td>
<td>A</td>
<td>1++</td>
<td></td>
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<tr>
<td>Scottish Intercollegiate Guidelines Network Management of Patients with Stroke or TIA: Assessment, Investigation, Immediate Management and Secondary</td>
<td>2000 to 2007</td>
<td>Carotid angioplasty and CAS and endovascular stenting for carotid artery stenosis and extracranial cervical arterial dissection</td>
<td>1 Cochrane review; 2 case series</td>
<td>Carotid angioplasty and stenting is not recommended without ongoing randomized controlled trials. Angioplasty and stenting may be considered for patients with high risk of stroke recurrence and a “hostile surgical neck” (for example, previous radical neck dissection or radiotherapy)</td>
<td>A</td>
<td>NR</td>
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<tr>
<td>Organization(s)</td>
<td>Search Dates</td>
<td>Procedure(s) Evaluated</td>
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<tr>
<td>Prevention. A National Clinical Guideline (2008)</td>
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<td>Endovascular stenting is not routinely recommended for extracranial cervical arterial dissection or cervical artery pseudoaneurysms. Stenting may be considered if recurrent ischaemic events occur despite medical therapy or where traumatic dissection has occurred with a high risk of stroke.</td>
<td>D</td>
<td>NR</td>
</tr>
<tr>
<td>Catalan Agency for Health Information, Assessment and Quality Clinical Practice Guideline for Primary and Secondary Prevention of Stroke (2008)</td>
<td>Through 9/07</td>
<td>CAS for symptomatic or asymptomatic carotid artery stenosis</td>
<td>1 systematic review of RCTs</td>
<td>Asymptomatic and symptomatic patients: The use of endovascular techniques with stent implantation should be individualized in patients with high surgical risk, in cases where there are technical difficulties for the performance of a CEA or within the context of a clinical trial.</td>
<td>B</td>
<td>1+</td>
</tr>
<tr>
<td>National Institute for Healthcare and Excellence (NICE)</td>
<td></td>
<td></td>
<td></td>
<td>No basis was found for CAS.</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>National Institute for Health and Clinical Excellence Diagnosis and Initial Management of Acute Stroke and Transient Ischaemic Attack (TIA) (2008)</td>
<td>NR</td>
<td>CAS for symptomatic carotid artery stenosis</td>
<td>NR</td>
<td>No basis was found for CAS.</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Organization(s)</td>
<td>Title (Year)</td>
<td>Search Dates</td>
<td>Procedure(s) Evaluated</td>
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<tr>
<td>National Institute for Health and Clinical Excellence</td>
<td>Carotid artery stent placement for symptomatic extracranial carotid stenosis (2011)</td>
<td>8/28/10 to 1/06/11</td>
<td>CAS for symptomatic carotid artery stenosis</td>
<td>NR</td>
<td>Current evidence on the safety and efficacy of carotid artery stent placement for symptomatic extracranial carotid stenosis is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance and audit or research.</td>
<td>NR</td>
</tr>
<tr>
<td>National Institute for Health and Clinical Excellence</td>
<td>Carotid artery stent placement for asymptomatic extracranial carotid stenosis (2011)</td>
<td>8/28/10 to 1/06/11</td>
<td>CAS for asymptomatic carotid artery stenosis</td>
<td>NR</td>
<td>Current evidence on the safety of carotid artery stent placement for asymptomatic extracranial carotid stenosis shows well documented risks, in particular the risk of stroke. The evidence on efficacy is inadequate in quantity. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research.</td>
<td>NR</td>
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<td>Other sources</td>
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<tr>
<td>American Heart Association/ American Stroke Association</td>
<td>Guidelines for the Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack (2011)</td>
<td>Through 7/09</td>
<td>CAS for symptomatic carotid artery stenosis</td>
<td>5 RCTs (CAVATAS, SAPHIRE, EVA-3S, SPACE, CREST)</td>
<td>CAS is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery is reduced by &gt;70% by noninvasive imaging or &gt;50% by catheter angiography.</td>
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<td>Organization(s)</td>
<td>Search Dates</td>
<td>Procedure(s) Evaluated</td>
<td>Evidence Base Available</td>
<td>Recommendations</td>
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<tr>
<td>American Heart Association/ American Stroke Association Guidelines for the Primary Prevention of Stroke (2011)</td>
<td>12/06 to 4/09</td>
<td>CAS for asymptomatic carotid stenosis</td>
<td>2 RCTs (SAPPHIRE, CREST) 1 non-randomized trial (CaRESS), Registries (NR)</td>
<td>CAS in the below setting (see Class IIb Recommendations) is reasonable when performed by operators with established peri-procedural morbidity and mortality rates of 4% to 6%, similar to those observed in trials of CEA and CAS. Among patients with symptomatic severe stenosis (&gt;70%) in whom the stenosis is difficult to access surgically, medical conditions are present that greatly increase the risk for surgery, or when other specific circumstances exist, such as radiation induced stenosis or restenosis after CEA, CAS may be considered. When the degree of stenosis is &lt;50%, there is no indication for carotid revascularization by either CEA or CAS. Prophylactic carotid artery stenting might be considered in highly selected patients with an asymptomatic carotid stenosis (&gt;60% on angiography, &gt;70% on validated Doppler ultrasonography, or &gt;80% on computed tomographic angiography or MRA if the stenosis on ultrasonography was 50%</td>
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<td>IIb</td>
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<td>Organization(s) Title (Year)</td>
<td>Search Dates</td>
<td>Procedure(s) Evaluated</td>
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<tr>
<td>American Heart Association/ American Stroke Association Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/ American Stroke Association (2013)</td>
<td>NR</td>
<td>Emergent angioplasty and/or stenting of the extracranial carotid or vertebral arteries</td>
<td>8 retrospective case-series</td>
<td>To 69%). The advantage of revascularization over current medical therapy alone is not well established.</td>
<td>IIb</td>
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<td>The usefulness of CAS as an alternative to CEA in asymptomatic patients at high risk for the surgical procedure is uncertain</td>
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<td>Use of these techniques may be considered in certain circumstances, such as in the treatment of acute ischemic stroke resulting from cervical atherosclerosis or dissection. Additional randomized trial data are needed.</td>
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<td>Organization(s)</td>
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<td>American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines, and the American Stroke Association, American Association of Neuroscience Nurses, American Association of Neurological Surgeons, American College of Radiology, American Society of Neuroradiology, Congress of Neurological Surgeons, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Neuro-Interventional Surgery, Society for Vascular Medicine, and Society for Vascular Surgery (2011)</td>
<td>Through 05/10</td>
<td>Carotid artery balloon angioplasty and CAS for symptomatic extracranial carotid disease</td>
<td>5 RCTs (CREST, SAPPHIRE, EVA-3S, SPACE, ICSS)</td>
<td>CAS is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention when diameter of lumen of internal carotid artery is reduced by &gt;70% as documented by noninvasive imaging or &gt;50% as documented by catheter angiography and anticipated rate of peri-procedural stroke or mortality is &lt;6%.</td>
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<td>It is reasonable to choose CEA over CAS when revascularization is indicated in older patients, particularly when arterial pathoanatomy is unfavorable for endovascular intervention.</td>
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<td>It is reasonable to choose CAS over CEA when revascularization is indicated in patients with neck anatomy unfavorable for arterial surgery.</td>
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<td>Prophylactic CAS might be considered in highly selected patients with asymptomatic carotid stenosis (minimum 60% by angiography, 70% by validated Doppler ultrasound), but its</td>
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<td>Organization(s) Title (Year)</td>
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<td>Effectiveness compared with medical therapy alone in this situation is not well established.</td>
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<td>In symptomatic or asymptomatic patients at high risk of complications for carotid revascularization by either CEA or CAS because of comorbidities, effectiveness of revascularization versus medical therapy alone is not well established.</td>
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<td>Except in extraordinary circumstances, carotid revascularization by either CEA or CAS is not recommended when atherosclerosis narrows lumen by &lt;50%.</td>
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<td>Carotid revascularization is not recommended for patients with chronic total occlusion of targeted carotid artery.</td>
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<td>Carotid revascularization is not recommended for patients with severe disability caused by cerebral infarction that precludes preservation of useful function.</td>
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<td>Organization(s)</td>
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<td>Society for Vascular Surgery</td>
<td>NR</td>
<td>Carotid artery balloon angioplasty and CAS for symptomatic extracranial carotid disease</td>
<td>4 RCTs (CREST, SAPHIRE, EVA-3S, SPACE1); 2 non-randomized trials (CaRESS, ICSS)</td>
<td>For neurologically symptomatic patients with stenosis &lt;50% or asymptomatic patients with stenosis &lt;60% diameter reduction, optimal medical therapy is indicated. There are no data to support CAS or CEA in this patient group.</td>
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<td>Updated Society for Vascular Surgery Guidelines for Management of Extracranial Carotid Disease (2011)</td>
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<td>In most patients with carotid stenosis who are candidates for intervention, CEA is preferred to CAS for reduction of all-cause stroke and peri-procedural death. Data from CREST suggest that patients aged &lt;70 years may be better treated by CAS, but these data need further confirmation.</td>
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<td>CEA is preferred over CAS in patients aged &gt;70 years of age, with long (&gt;15-mm) lesions, preocclusive stenosis, or lipid-rich plaques that can be completely removed safely by a cervical incision in patients who have a virgin, nonradiated neck.</td>
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<td>Neurologically asymptomatic patients deemed “high risk” for CEA should be considered for primary medical management. CEA can be considered in these patients only with evidence that</td>
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<td>Organization(s)</td>
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<td>perioperative morbidity and mortality is &lt;3%. CAS should not be performed in these patients except as part of an ongoing clinical trial.</td>
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<td>CAS is preferred over CEA in symptomatic patients with ≥50% stenosis and tracheal stoma, situations where local tissues are scarred and fibrotic from prior ipsilateral surgery or external beam radiotherapy, prior cranial nerve injury, and lesions that extend proximal to the clavicle or distal to the C2 vertebral body. CEA may be preferable in situations where ipsilateral tissue planes remain relatively intact.</td>
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<td>Organization(s)</td>
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<td>Croatian Society of Neurovascular Disorders/ Croatian Society of Neurology/ Croatian Society of Ultrasound in Medicine and Biology/Croatian Society for Radiology/ Croatian Society of Vascular Surgery/Croatian Society of Neurosurgery</td>
<td>NR</td>
<td>CAS for carotid artery stenosis and intracranial artery stenosis</td>
<td>6 RCTs (CREST, SAPPHIRE, CAVATAS, SPACE, ICSS, EVA-3S); 3 registry studies (ARCHeR, EXACT, CAPTURE)</td>
<td>There are insufficient data to recommend CAS as primary therapy for neurologically asymptomatic patients with 70% to 99% diameter stenosis. Data from CREST suggest that in properly selected asymptomatic patients, CAS is equivalent to CEA in the hands of experienced interventionalists. Operators and institutions performing CAS must exhibit expertise sufficient to meet the previously established AHA guidelines for treatment of patients with asymptomatic carotid stenosis. Specifically, combined stroke and death rate must be &lt;3% to ensure benefit for the patient.</td>
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<td>Carotid percutaneous transluminal angioplasty and stenting (CAS) is recommended in selected patients.</td>
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<td>For patients with hemodynamically significant intracranial stenosis that have symptoms despite medical therapies (antithrombotics, statins, and other treatments for risk factors), the usefulness of</td>
<td>II</td>
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<tr>
<td>Organization(s) Title (Year)</td>
<td>Search Dates</td>
<td>Procedure(s) Evaluated</td>
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<td>Recommendations for the Management of Patients with Carotid Stenosis (2010)</td>
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<td>endovascular therapy (angioplasty and/or stent placement) is uncertain and is considered investigational.</td>
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<td>CAS should be restricted to the following subgroups of patients with severe symptomatic carotid artery stenosis: those with contraindications for CEA, stenosis at a surgically inaccessible site, restenosis after earlier CEA, and post-radiation stenosis.</td>
<td>IV</td>
<td>GCP</td>
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<td>Carotid angioplasty, with or without stenting, is not recommended for patients with asymptomatic carotid stenosis.</td>
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<td>European Society for Vascular Surgery Invasive Treatments for Carotid Stenosis: Indications, Techniques (2009)</td>
<td>NR</td>
<td>CAS for symptomatic and asymptomatic carotid artery stenosis</td>
<td>11 RCTs (CAVATAS, Kentucky, Leicester, Wallstent, SAPPHIRE, EVA-3S, SPACE, BACASS, ARChEr, NASCET, ACAS)</td>
<td>CAS should be offered to symptomatic patients, if they are at high risk for CEA, in high-volume centers with documented low peri-procedural stroke and death rates or inside an RCT.</td>
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<td>It is advisable to offer CAS in asymptomatic patients only in high-volume centers with documented low peri-procedural stroke and death rates or within well-conducted clinical trials.</td>
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<td>Organization(s)</td>
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<td>Procedure(s) Evaluated</td>
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<td>American Society of Interventional and Therapeutic Neuroradiology/ American Society of Neuroradiology/ Society of Interventional Radiology Quality Improvement Guidelines for the Performance of Cervical carotid angioplasty and CAS for carotid artery stenosis</td>
<td>NR</td>
<td>3 RCTs (CAVATAS, WALLSTENT, SAPPHIRE); 1 other randomized trial</td>
<td>Indications for CAS:  • Symptomatic, severe stenosis surgically difficult to access (e.g., high bifurcation requiring mandibular dislocation).  • Symptomatic, severe stenosis in a patient with significant medical disease that would make the patient high risk for surgery.  • Symptomatic severe stenosis and one of the following conditions:</td>
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<td>CAS should not be offered to asymptomatic ‘high-risk’ patients if the peri-interventional complication rate is &gt;3%.</td>
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<td>CAS is indicated in case of contralateral laryngeal nerve palsy, previous radical neck dissection, cervical irradiation, with prior CEA (restenosis), with high bifurcation or intracranial extension of a carotid lesion, provided that the peri-interventional stroke or death rate is higher than that accepted for CEA.</td>
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<td>CAS is not advisable in patients with extensive aortic and supra-aortic vessel plaques, calcification and tortuosity, unless performed in high-volume centers with documented low peri-procedural stroke and death rate.</td>
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3 RCTs (CAVATAS, WALLSTENT, SAPPHIRE); 1 other randomized trial
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<tr>
<th>Organization(s)</th>
<th>Title (Year)</th>
<th>Search Dates</th>
<th>Procedure(s) Evaluated</th>
<th>Evidence Base Available</th>
<th>Recommendations</th>
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<tbody>
<tr>
<td></td>
<td>Cervical Carotid Angioplasty and Stent Placement (2003)</td>
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<td>a. Significant tandem lesion that may require endovascular therapy</td>
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<td>b. Radiation-induced stenosis</td>
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<td>c. Restenosis after CEA</td>
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<td>d. Refusal to undergo CEA after proper informed consent</td>
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<td>e. Stenosis secondary to arterial dissection</td>
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<td>f. Stenosis secondary to fibromuscular dysplasia</td>
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<td>g. Stenosis secondary to Takayasu arteritis</td>
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<td>• Severe stenosis associated with contralateral carotid artery occlusion requiring treatment before undergoing cardiac surgery.</td>
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<td>• Severe underlying carotid artery stenosis revealed after recanalization of carotid occlusion after thrombolysis for acute stroke (presumed to be the etiology of the treated occlusion) or to enable thrombolysis for acute stroke.</td>
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<td>• Pseudoaneurysm.</td>
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<td>• Asymptomatic preocclusive lesion in a patient otherwise meeting first three criteria.</td>
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<td>Organization(s)</td>
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<td>Relative Contraindications:</td>
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<td>• Asymptomatic stenosis of any degree, except in particular circumstances, as described above.</td>
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<td>• Symptomatic stenosis associated with an intracranial vascular malformation.</td>
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<td>• Symptomatic stenosis in a patient with a subacute cerebral infarction.</td>
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<td>• Symptomatic stenosis in a patient with a significant contraindication to angiography.</td>
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<td>• Carotid stenosis with angiographically visible intraluminal thrombus.</td>
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<td>• A stenosis that cannot be safely reached or crossed by an endovascular approach.</td>
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**Abbreviations:** ARChER: ACCULINK for Revascularization of Carotids in High Risk Patients; ACAS: Asymptomatic Carotid Atherosclerosis Study; BACASS: Basel Carotid Artery Stenting Study; CAPTURE: Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Unanticipated or Rare Events; CaRESS: Carotid Revascularization Using Endarterectomy or Stenting Systems CAS: carotid artery stenting; CAVATAS: Carotid And Vertebral Artery Transluminal Angioplasty Study; CEA: carotid endarterectomy; CREST: Carotid Revascularization Endarterectomy versus Stenting Trial; EVA-3S: Endarterectomy versus Angioplasty in patients with Severe carotid Stenosis Study; EXACT: Emboshield and Xact Post Approval Carotid Stent Trial; ICSS: International Carotid Stenting Study; NASCET: North American Symptomatic Carotid Endarterectomy Trial; NR: not reported; RCT: randomized controlled trial; SAPPHIRE: Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy; SPACE: Stent-Protected Angioplasty versus Carotid Endarterectomy; SSYLVIA: Stenting of symptomatic atherosclerotic lesions in the vertebral or intracranial arteries
<table>
<thead>
<tr>
<th>Organization(s)</th>
<th>Literature Search Dates</th>
<th>Procedure(s) Evaluated</th>
<th>Evidence Base Available</th>
<th>Recommendations</th>
<th>Class/ Grade of Rcmndtn</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Society of Interventional and Therapeutic Neuroradiology/ Society of Interventional Radiology/ American Society of Neuroradiology Intracranial Angioplasty &amp; Stenting for Cerebral Atherosclerosis (2005)</td>
<td>NR</td>
<td>Intracranial CAS and angioplasty for asymptomatic and symptomatic intracranial artery stenosis</td>
<td>1 non-randomized, multicenter trial (SSYLVIA); 1 prospective, multicenter single-arm trial (WINGSPAN)</td>
<td>For symptomatic patients with a &gt;50% intracranial stenosis who have failed medical therapy, balloon angioplasty with or without stenting should be considered.</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>National Guideline Clearinghouse</td>
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<td>Patients who have an asymptomatic intracranial arterial stenosis should first be counseled regarding optimizing medical therapy. There is insufficient evidence to make definitive recommendations regarding endovascular therapy in asymptomatic patients with severe intracranial atherosclerosis. They should be counseled regarding the nature and extent of their disease, monitored for new neurological symptoms, and have periodic non-invasive imaging at regular intervals of 6–12 months (magnetic resonance angiography or computed tomographic angiography) initially, and then by cerebral angiography if warranted. At a minimum, optimal prophylactic medical therapy should be instituted, which might include antiplatelet and/or statin therapy.</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Singapore Ministry of Health Stroke and Transient Ischaemic Attacks. Assessment, Investigation, Immediate Management and Secondary Prevention (2009)</td>
<td>NR</td>
<td>Intracranial angioplasty with or without stenting</td>
<td>1 non-randomized multicenter trial (SSYLVIA); 1 prospective multicenter single-arm trial (WINGSPAN)</td>
<td>Continued evaluation and improvements in both pharmacological and catheter-based therapies are needed to reduce the stroke burden from intracranial atherosclerosis.</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>American Heart Association/ American Stroke Association Guidelines for the Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack (2011)</td>
<td>Through 7/2009</td>
<td>Intracranial angioplasty with or without stenting</td>
<td>NIH Wingspan Registry; 10 case series</td>
<td>Intracranial angioplasty with or without stenting may be considered as a treatment option for symptomatic patients who have &gt;50% stenosis and who have failed medical therapy.</td>
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<td>2+</td>
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<tr>
<td>American Heart Association/ American Stroke Association Guidelines for</td>
<td>NR</td>
<td>Emergent intracranial angioplasty with or without stenting</td>
<td>3 case-series (including 1 non-randomized single-center trial, the</td>
<td>For patients with stroke or TIA due to 50% to 99% stenosis of a major intracranial artery, the usefulness of angioplasty and/or stent placement is unknown and is considered investigational.</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Organization(s)</th>
<th>Literature Search Dates</th>
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<tr>
<td>the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/ American Stroke Association (2013)</td>
<td>SARIS study)</td>
<td>used in the setting of clinical trials</td>
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</table>

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## HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

Discussion Document: What are the key factors and health outcomes and what evidence is there?

<table>
<thead>
<tr>
<th>Safety Outcomes</th>
<th>Safety Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td></td>
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<tr>
<td>Death</td>
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<tr>
<td>Myocardial infarction (MI)</td>
<td></td>
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<tr>
<td>Nerve injury</td>
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<td>Bleeding</td>
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<thead>
<tr>
<th>Efficacy – Effectiveness Outcomes</th>
<th>Efficacy / Effectiveness Evidence</th>
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<tbody>
<tr>
<td>Stroke</td>
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<tr>
<td>Ipsilateral stroke</td>
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<tr>
<td>Death</td>
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<tr>
<td>Periprocedural stroke or death</td>
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<tr>
<td>MI</td>
<td></td>
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<tr>
<td>Activities of daily living (ADLs)</td>
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<tr>
<td>Cognitive function</td>
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<td>Depression</td>
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<thead>
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<th>Special Population / Considerations Outcomes</th>
<th>Special Population Evidence</th>
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<tbody>
<tr>
<td>Age</td>
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<tr>
<td>Sex</td>
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<td>Surgical risk</td>
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<td>Diabetes</td>
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<td>Smoking status</td>
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<td>Severity of contralateral stenosis</td>
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<td>Hypertension</td>
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<td>Time to treatment</td>
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<td>Qualifying event</td>
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<th>Cost</th>
<th>Cost Evidence</th>
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<td>Cost</td>
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<td>Cost-effectiveness</td>
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<td>Cost-utility</td>
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Clinical Committee Evidence Votes

First Voting Question
The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Is there sufficient evidence under some or all situations that the technology is:

<table>
<thead>
<tr>
<th></th>
<th>Unproven (no)</th>
<th>Equivalent (yes)</th>
<th>Less (yes)</th>
<th>More (yes)</th>
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<tbody>
<tr>
<td>Effective</td>
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<tr>
<td>Safe</td>
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<tr>
<td>Cost-effective</td>
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Discussion
Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second Vote
Based on the evidence about the technologies’ safety, efficacy, and cost-effectiveness, it is

_______ Not Covered  ______ Cover Unconditionally  ______ Cover Under Certain Conditions

Discussion Item
Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.
Clinical Committee Findings and Decisions

Next Step: Cover or No Cover
If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

Next Step: Cover with Conditions
If covered with conditions, the Committee will continue discussion.

1) Does the committee have enough information to identify conditions or criteria?
   - Refer to evidence identification document and discussion.
   - Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
   - Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.

2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:
   - What are the known conditions/criteria and evidence state
   - What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

Efficacy Considerations:
- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
  - Direct outcome or surrogate measure
  - Short term or long term effect
  - Magnitude of effect
  - Impact on pain, functional restoration, quality of life
  - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value
- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests’ accuracy
  - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
• Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
• Does use of the test change treatment choices

Safety
• What is the evidence of the effect of using the technology on significant morbidity?
  o Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
  o Adverse effect on health that can result in lasting harm or can be life-threatening.
• Other morbidity concerns
• Short term or direct complication versus long term complications
• What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

Cost Impact
• Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

Overall
• What is the evidence about alternatives and comparisons to the alternatives
• Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?