Washington State Health Care Authority
Health Technology Assessment

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"

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

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

SEE ATTACHED RWJ STATEMENT

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		X

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 _____ 9/9/13 ROBERT M BERSAK, MD

Signature *Date* *Print Name*

For questions contact: Christine Masters
Health Technology Assessment
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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
Tel: 206-320-4399
Cell: 206-617-9048
Fax: 206-320-4820
Email: robert.bersin@swedish.org

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

EDUCATION

Dates	Institution & Location	Degrees Conferred	Major Subjects
1981	University of California, Los Angeles, School of Medicine	M.D.	Medicine
1981	University of California, Los Angeles, School of Public Health	M.P.H.	Health Services Administration
1976	Stanford University, Stanford, California	B.A., B.S.	Psychology/Biology

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

	San Francisco, CA	
1981 – 1984	Department of Medicine University of California, San Francisco, CA	Internal Medicine Resident
1981	Department of Microbiology and Immunology University of California, Los Angeles, CA	Post-Doctoral Researcher
1978 – 1979	World Health Organization Lausanne, Switzerland	Pre-Doctoral Researcher
1977	Department of Medicine University of New Mexico Albuquerque, New Mexico	Pre-Doctoral Researcher

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)

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 Interventioal 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

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 – 2012 Principal Investigator, Abbott CHOICE Carotid Stent Post-Market Surveillance Study, Swedish Medical Center, Seattle, Washington
2009 – 2010 Co-Investigator, CABANA Carotid Stent Post-Market Surveillance Study, 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, SAPPHIRE WW Carotid Stent Post-Market Surveillance Study, Swedish Medical Center, Seattle, Washington
2007 – 2008 Principal Investigator, Abbott CHOICE Carotid Stent Post-Market Surveillance Study, Overlake Hospital, Bellevue, Washington
2007 – 2008 Principal Investigator, SONOMA 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 Principal 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

1991 – 1992 Co-Investigator, Coronary Angioplasty Versus Excisional Atherectomy Trial CAVEAT, Carolinas Heart Institute, Charlotte, North Carolina

1991 – 1992 Co-Investigator, Lovastatin Restenosis Trial LRT, 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

	Principal Investigator at the Intensive Care Unit, Moffitt Hospital, University of California, San Francisco
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.
1978 – 1979	World Health Organization, Immunology Research and Training Centre, and the Swiss Institute for Experimental Cancer Research, Lausanne, Switzerland. Investigation of cellular and subcellular requirements of cytotoxic T-lymphocyte activation 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

1) Bersin RM, Tubau J. Merz R, Wolf A and Schiller N. Diagnostic yield of echocardiography with routine treadmill testing. Abstr., 58th Scientific Sessions, American Heart Association, November, 1985. Circulation 1985; 72: III-449.

2) Bersin RM, Chatterjee K, Arieff AI. Metabolic and systemic effects of bicarbonate in hypoxic patients with heart failure. Abstr., 18th Annual Scientific Sessions, American Society of Nephrology, December, 1985. Kidney Int 1986; 29:180.

3) Bersin RM, Chatterjee K, Arieff AI. Cardiovascular effects of bicarbonate in patients with hypoxia and cardiac decompensation. Abstr., 35th Annual Scientific Sessions, American College of Cardiology, March, 1986. J Am Coll Cardiol 1986; 7(2):76A.

4) Bersin RM, Horton A, Arieff AI. Hemodynamic Effects of Carbicarb versus NaHCO3 in Dogs with Hypoxic Lactic Acidosis. Abstr., 59th Scientific Sessions, American Heart Association, November, 1986. Circulation 1986; 74: II-240.

5) Bersin RM, Arieff AI. Primary lactic alkalosis: A new syndrome. Abstr., 19tyh Annual Meeting, American Society of Nephrology, December, 1986. Kidney Int 1986; 31:191, 1987.

6) Bersin RM, Arieff AI, Chatterjee K. Importance of 2,3-diphosphoglyceric acid to oxygen transport in congestive heart failure. Abstr., 36th Annual Scientific Sessions, American College of Cardiology, March, 1987. J Am Coll Cardiol 1987; 9: 186A.

7) Bersin RM, Arieff AI. Metobolic effects of carbicarb versus bicarbonate in dogs with hypoxic lactic acidosis. Abstr., Annual Meeting, American Society for Clinical Investigation, May, 1987. Clin Res 35: 634A.

8) Bersin RM, Arieff AI. Metabolic and cardiac effects of carbicard versus sodium bicarbonate in dogs with hypoxic lactic acidosis. Abstr., Xth International Congress of Nephrology, July, 1987. Trans Intl Soc Nephrol 1987; 10: 106.

9) Bersin, RM, Chatterjee K, Arieff AI. Metabolic and hemodynamic effects of sodium bicarbonate in patients with heart disease. Abstr., Xth International Congress of Nephrology, July, 1987. Trans Intl Soc Nephrol 1987; 10: 106.

10) Bersin, RM, Chatterjee K. Impaired coronary vasodilator responsiveness in patients with dilated cardiomyopathy. Abstr., 60th Scientific Sessions, American Heart Association, November, 1987. Circulation 1987; 76: IV-459.

11) Graf H, Mayer G, Cada E, Muller MM, Bersin RM. Is erythropoietin a direct stimulator of 2,3 DPG? Abstr., Annual Meeting, American Society for Clinical Investigation, April, 1988. Clin Res 1988; 36: 482A.

12) Bersin RM, Kwasman M, DeMarco T, Lau D, Klinski C, Wolfe C, Chatterjee K. Improved hemodynamic function in chronic heart failure with the metabolic agent sodium dichloroacetate. Abstr., 39th Annual Scientific Sessions, American College of Cardiology, March, 1990. J Am Coll Cardiol 1990; 15: 157A**.**

13) Bersin RM, Kwasman M, Demarco T, Lau D, Klinski C. Golonka J, Wolfe C, Chatterjee K. Quantitative importance of oxygen-hemoglobin binding to oxygen transport in congestive heart failure. Abstr., 39th Annual Scientific Sessions, American College of Cardiology, March, 1990. J Am Coll Cardiol 1990; 15: 208A.

14) Elliott CM, Bersin RM, Fedor JM, Gallagher JJ, Jordan L, Simonton CA, Svenson RH, Wilson BH, Zimmern SH. Mobile cardiac catheterization: Preliminary report of an ongoing registry. Abstr., 63rd Scientific Sessions, American Heart Association, November, 1990. Circulation 1990; 82: 90.

15) Elliott CM, Bersin RM, Fedor JM, Gallagher JJ, Jordan L, Simonton CA, Svenson RH, Wilson BH, Zimmern SH. Mobile cardiac catheterization: Comparison with outpatient and inpatient catheterization at tertiary facilities. Abstr., 41st Annual Scientific Sessions, American College of Cardiology, April, 1992. J Am Coll Cardiol 1992; 19: 42A.

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

Svenson RH, Wilson BH, Zimmern SH. Mobile cardiac catheterization registry: Report of the first one thousand patients. Abstr., Annual Scientific Sessions, Society for Cardiac Angiography and Interventions, May, 1992. Cath Cardiovasc Diag 1992; 26: 73.

17) Bersin RM, Williams TC. Improved metabolic and hemodynamic function with a new buffering agent for cardiac arrest. Abstr., 42nd Annual Scientific Sessions, American College of Cardiology, March, 1993. J Am Coll Cardiol 1993; 21(2): 254A.

18) Bersin RM, Davis NH, Applegate DS, Williams TC, Goldberg MA, Enny C, Dempsey WH, Matthews E. A New Therapeutic Strategy for the Treatment of Congestive Heart Failure: Facilitation of Oxygen Unloading with Erythropoietin: Preliminary Report of a Pilot Study. Abstr., XVth Congress of the European Society of Cardiology, September, 1993. Eur Heart J 1993; 14(Suppl): 380.

19) Bersin RM, Davis NH, Applegate DS, Williams TC, Goldberg MA, Enny C, Dempsey WH, Matthews E. Direct facilitation of oxygen-hemoglobin dissociation with erythropoietin: Report of a pilot study in congestive heart failure patients. Abstr., 35th Annual Meeting of the American Society of Hematology, December, 1993. (Blood, in press).

20) Bersin RM, Davis NH, Applegate DS, Williams TC, Goldberg MA, Enny C, Dempsey WH, Matthews E. Facilitation of oxygen-hemoglobin dissociation in patients with congestive heart failure with recombinant human erythropoietin (r-HuEPO): A pilot study. Abstr., 1st Annual Meeting of the European Hematology Association, June, 1994. Br J Haematol 1994; 87 (Suppl 1): 153.

21) Simonton CA, Kuntz RE, Ho KKL, Vetter J, Fitzgerald PJ, Bersin RM, Lewis LT, Conway T, Popma JJ. Intravascular ultrasound and quantitative angiographic correlates of reference vessel diameter after "optimal" directional coronary atherectomy: Clinical implications for balloon selection. Abstr., 67th Scientific Sessions, American Heart Association, November, 1994.

22) Popma JJ, Mintz GS, Kuntz RE, Simonton CA, Vetter J, Bersin RM, Satler LF. Impact of adjunctive balloon angioplasty following ultrasound-guided "optimal" directional atherectomy. Abstr., 67th Scientific Sessions, American Heart Association, Nov, 1994.

23) Mintz GS, Kuntz RE, Popma JJ, Simonton CA, Hinohara T, Bersin RM, Painter JA, Yock PG, Griffin J, Kleiber B, Leon MB. Residual plaque burden in patients undergoing ultrasound-guided "optimal" directional atherectomy. Abstr., 67th Scientific Sessions, American Heart Association, November, 1994.

24) Fitzgerald PJ, Mooney MR, Susuki S, Ohtaki E, Walter PD, Dorros G, Bersin RM, Russo RJ, Wyrens FJ, Yock PG. Lesion composition impacts size and symmetry of stent expansion: Initial report from the STRUT registry. Abstr., 44th Annual Scientific Sessions, American College of Cardiology, March, 1995

25) Leon MB,Kuntz RE, Popma JJ, Simonton CA, Hinohara T, Mintz GS, Bersin RM, Yock PG and Baim DS. Acute Angiographic, Intravascular Ultrasound and Clinical Results of Directional Atherectomy in the Optimal Atherectomy Restenosis Study. Abstr., 44th Annual Scientific Sessions, American College of Cardiology, March, 1995. J Am Coll Cardiol 1995; 25(2)(Supplement 1): 137A.

26) Simonton CA, Leon MB, Kuntz RE, Popma JJ, Hinohara T, Mintz GS, Bersin RM, Yock PG, Wilson BH, Cutlip DE, Baim DE. Acute and late clinical and angiographic results of directional atherectomy in the Optimal Atherectomy Restenosis Study. Abstr., 68th Scientific Sessions, American Heart Association, November, 1995. Circulation 1995; 92(8): I-545.

27) Mintz GS, Fitzgerald PJ, Kuntz RE, Simonton, CA, Bersin RM, Yock PG, Popma JJ, Baim DE for the Oars Investigators. Lesion site and reference vessel remodeling after directional coronary atherectomy: An analysis from the Optimal Atherectomy Restenosis Study. Abstr., 68th Scientific Sessions, American Heart Association, November, 1995. Circulation 1995; 92(8): 1-93.

28) Baim DE, Simonton CA, Popma JJ, Hinohara T, Bersin RM, DeFeo T, Kent KM, Yock PG, Kuntz RE for the OARS investigators. Mechanism of luminal enlargement by optimal atherectomy – IVUS insights from the OARS study. Abstr., 45th Annual Scientific Sessions, American College of Cardiology, March, 1996. J Am Coll Cardiol 1996; 27(2) (Suppl 1): 291A.

29) Sharaf BL, McKendall GR, Love TW, Bersin RM, Talley D, Williams DO for the Intracoronary t-PA Investigators. Treatment of intracoronary thrombus: Successful lysis with intracoronary t-PA. Abstr., 45th Annual Scientific Sessions, American College of Cardiology, March, 1996. J Am Coll Cardiol 1996; 27(2) (Suppl 1): 332A.

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May 6, 2012

Washington State Health Care Authority
Health Technology Assessment

Carotid Artery Stenting

Order of Scheduled Presentations

	Name	Representing
1.	Larry Dean, MD	Society for Cardiovascular Angiography and Interventions/ WA Chapter American College of Cardiology
2.	Louis Kim, MD	American Association of Neurological Surgeons/ College of Neurological Surgeons/ WA State Association of Neurological Surgeons
3.	R. Torrance Andrews, MD, FSIR	Society of Interventional Radiology

Disclosure (WITH RESPECT TO THIS PRESENTATION)

Any unmarked topic will be considered a "Yes"

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

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

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).	X	

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ACC – 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 _____ 8/30/13 LARRY S. OFAN

Signature *Date* *Print Name*

For questions contact: Christine Masters
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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

2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS Guideline on the Management of Patients With Extracranial Carotid and Vertebral Artery Disease

Developed in Collaboration with the American Academy of Neurology and Society of Cardiovascular Computed Tomography

The Society for Cardiovascular Angiography and Interventions Foundation SCAI | Washington CHAPTER

Citation

This slide set was adapted from the:

2011ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS Guideline on the Management of Patients With Extracranial Carotid and Vertebral Artery Disease

The full-text guidelines are available at: (www.scai.org/asset.axd?id=e4450288ae4c-4595-8e02-39e46286d201&t=634320825807300000

The Society for Cardiovascular Angiography and Interventions Foundation SCAI | Washington CHAPTER

Revascularization

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.

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Classification of Recommendations and Levels of Evidence

SIZE OF TREATMENT EFFECT

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* Procedure/ Test / Treatment COR III: No benefit — Not Helpful — No Proven Benefit COR III: Harm — Excess Cost w/o Benefit or Harmful — Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit is not recommended is not indicated should not be done is not useful/ beneficial/ effective COR III: Harm potentially harmful causes harm associated with excess morbidity/mortality should not be done
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

*Data available from clinical trials or registries about the usefulness/efficacy 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

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.

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Recommendations for Selection of Patients for Carotid Revascularization (continued)

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%.

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Recommendations for Selection of Patients for Carotid Revascularization (continued)

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.

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Recommendations for Selection of Patients for Carotid Revascularization (continued)

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.

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Recommendations for Selection of Patients for Carotid Revascularization (continued)

It is reasonable to choose CAS over CEA when revascularization is indicated in patients with neck anatomy unfavorable for arterial surgery. §

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.

§ 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.

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Recommendations for Selection of Patients for Carotid Revascularization (continued)

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.

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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.

Recommendations for Selection of Patients for Carotid Revascularization (continued)

Carotid revascularization is not recommended for patients with severe disability¶ caused by cerebral infarction that precludes preservation of useful function.

¶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

Disc

Any

If

	Potential Conflict Type	Yes	No
1	consulting fees or honoraria in excess of $10,000.		✓
2	stock options or other ownership interests.	✓	
3	board member, trustee, owner.	✓	
4		✓	
5		✓	
6		✓	

If ya ... id for #6, describe other relationship:

2- Spi Surgical Inc 3- Spi Surgical Inc 4 - Spi Surgical Inc
5 - NIH/NINDS, FDA
None of these relations are relevant to my presentation

		Yes	No
7	... organization, include the name and ... commercial products ... comment)		✓

If ye ... sources?

If yo ... are concerned that it may appear that you do, you may **attach** addi ... that you should not be excluded.

I ce ... Conflict of Interest Form and that the info ... complete and correct as of this date.

X 8/30/13 Louri Icim

Print Name

For ... Technology Assessment

Washington HTA

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"

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

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

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7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).	X	

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.

X  **9/3/13** **R. Torrance Andrews, MD**

Signature *Date* *Print Name*

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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

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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)

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Symptomatic Patients

- CREST & the 2011 Guidelines Affirm
  - o CAS should be offered as an option in addition to CEA
  - o 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

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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%

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Costs

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

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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

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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

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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

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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

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Questions?

- SIR thanks the Washington Health Care Authority for the opportunity to present our comments

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Health Technology Assessment

Carotid Artery Stenting

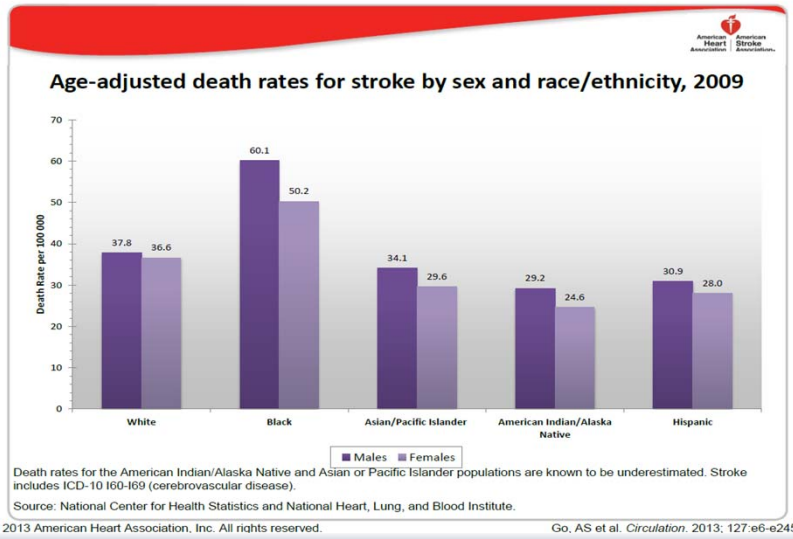
Agency Medical Director Comments

Health Technology Clinical Committee

Gary Franklin, MD, MPH
Medical Director
Washington State Department of Labor & Industries
September 20, 2013

Carotid Artery Stenting:
Background

Stroke is a leading cause of death



Go, AS et al. *Circulation*. 2013; 127:e6-e245.

Carotid Artery Stenting:
Background

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**

http://www.doh.wa.gov/Portals/1/Documents/5500/CD-STR2007.pdf

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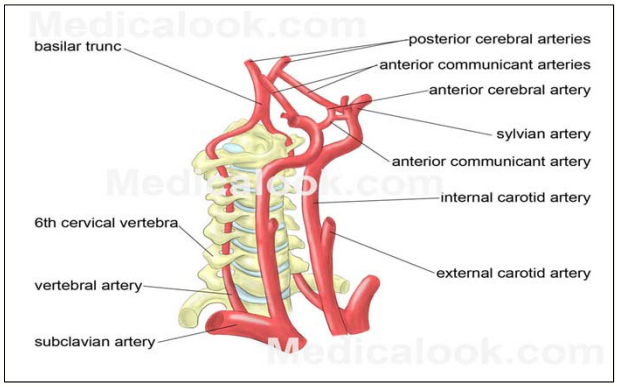
Carotid Artery Stenting:
Background

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.



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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.

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Carotid Artery Stenting:
Background

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

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Carotid Artery Stenting:
Background

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.

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Carotid Artery Stenting:
State Agency Utilization

Agency Medical Directors' Concerns

Primary Criteria Ranking

Safety = **High**

Efficacy = **High**

Cost = **Medium**

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Carotid Artery Stenting:
Current State Agency Policy

CPT	Description	Medicaid	UMP	DOC	LNI
0075T	Extracranial stenting	C	PA	PA	C
0076T	Extracranial stenting (additional vessel)	C	PA	PA	C
37215	Cervical carotid artery stenting without distal embolic protection device (EPD)	C	PA	PA	PA
37216	Cervical carotid artery stenting with distal EPD	C	PA	PA	PA
61635	Intracranial	NC	PA	PA	NC

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

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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

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Carotid Artery Stenting:
State Agency Utilization

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

*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

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Carotid Artery Stenting:
State Agency Utilization

Agency/Year	2009	2010	2011	2012	4 Year Overall	Avg % Chnge
PEBB Endarterectomy						
Endarterectomy Procedures	57	65	59	61	242	**2.3%**
Total Paid, Endarterectomy	**$249,225**	**$276,084**	**$258,463**	**$288,503**	**$1.072M**	**4.9%**
Avg Paid, Endarterectomy	$16,781	$15,281	$19,313	$15,864	$17,284	-0.4%
Medicaid Endarterectomy						
Endarterectomy Procedures	68	54	64	52	235	**-7.7%**
Total Paid, Endarterectomy	**$411,449**	**$288,334**	**$509,735**	**$547,618**	**$1.76M**	**17.4%**
Avg Paid, Endarterectomy	$7,958	$7,434	$12,437	$14,200	$10,554	25.0%

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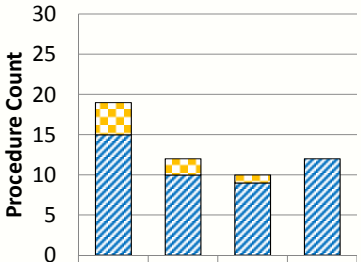
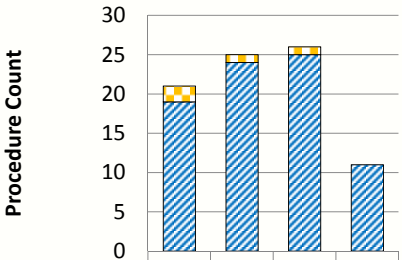
Carotid Artery Stenting:
State Agency Utilization

PEBB Carotid Artery Stenting
By Procedure Type, 2009-2012



	2009	2010	2011	2012
Intracranial	4	2	1	0
Extracranial	15	10	9	12

Medicaid Carotid Artery Stenting
By Procedure Type, 2009-2012



	2009	2010	2011	2012
Intracranial	2	1	1	0
Extracranial	19	24	25	11

Extracranial includes procedures on the intrathoracic and cervical carotid arteries - they make up almost 90% of PEBB and 95% of Medicaid procedures.

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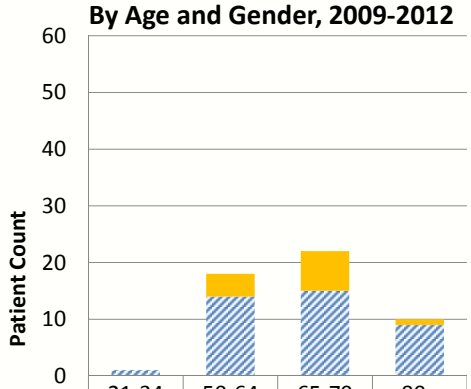
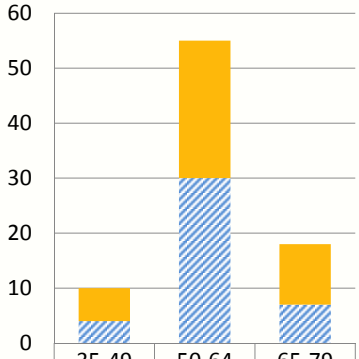
Carotid Artery Stenting:
State Agency Utilization

PEBB
Carotid Artery Stenting
By Age and Gender, 2009-2012



	21-34	50-64	65-79	80+
Female	0	4	7	1
Male	1	14	15	9

Medicaid
Carotid Artery Stenting
By Age and Gender, 2009-2012



	35-49	50-64	65-79
Female	6	25	11
Male	4	30	7

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Carotid Artery Stenting:
State Agency Utilization

Per Procedure Avg Allowed Charges By Agency and Payer	PEBB Primary (n=23)	PEBB Medicare (n=30)	Medicaid (n=62)	Medicaid Medicare (n=20)
Breakdown 1				
Professional Services	$3,500	$1,815	$1,391	$1,516
Facility/Other	$38,110	$30,657	$11,360	$7,662
Breakdown 2				
Stent Placement	$6,378	$1,685	$1,071	$1,431
Study	$126	$65	$12	$3
Facility/DRG	$32,588	$29,059	$10,825	$5,683
Anesthesia	$481	$149	$213	$199
Imaging	$1,516	$589	$387	$399
Patient Care	$521	$924	$243	$1,463
Avg Allowed/Procedure (95% upper limit)	**$41,610 ($128,502)**	**$32,472 ($116,983)**	**$12,750 ($43,174)**	**$9,178 ($33,328)**

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Carotid Artery Stenting:
State Agency Utilization

Per Procedure Avg Allowed Charges By Agency, Payer & Setting	PEBB Primary (n=23)	PEBB Medicare (n=30)	Medicaid (n=62)	Medicaid Medicare (n=20)
Inpatient	**83%**	**63%**	**71%**	**30%**
Professional Services	$3,587	$1,365	$1,502	$1,937
Facility	$39,456	$45,569	$15,811	$25,296
Avg Allowed/Procedure	**$43,043**	**$46,934**	**$17,313**	**$27,233**
Outpatient	**17%**	**37%**	**29%**	**70%**
Professional Services	$3,088	$2,593	$478	$105
Facility	$31,718	$4,900	$1,118	$1,336
Avg Allowed/Procedure	**$34,806**	**$7,492**	**$1,596**	**$1,441**

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Carotid Artery Stenting:
State Agency Utilization

PEBB Diagnosis Description	Patient Ct n=53
OCL CRTD ART WO INFRCT	31
OCL CRTD ART W INFRCT	7
OCL MLT BI ART WO INFRCT	3
OCL VRTB ART W INFRCT	3
CRBL ART OCL NOS W INFRC	2
NONRUPT CEREBRAL ANEURYM	2
CRBL ART OC NOS WO INFRC	1
CRNRY ATHRSCL NATVE VSSL	1
CVA	1
DISSECT CAROTID ARTERY	1
OCL BSLR ART WO INFRCT	1
OCL VRTB ART WO INFRCT	1
PERIPH VASCULAR DIS NOS	1
STRICTURE OF ARTERY	1

Medicaid Diagnosis Description	Patient Ct n=82
OCL CRTD ART WO INFRCT	47
OCL CRTD ART W INFRCT	17
CRBL ART OCL NOS W INFRC	3
OCL BSLR ART W INFRCT	2
OCL MLT BI ART WO INFRCT	2
OCL VRTB ART W INFRCT	2
OCL VRTB ART WO INFRCT	2
COR ATH UNSP VSL NTV/GFT	1
CVA	1
DISSECT CAROTID ARTERY	1
NONRUPT CEREBRAL ANEURYM	1
OCL BSLR ART WO INFRCT	1
OCL MLT BI ART W INFRCT	1

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Carotid Artery Stenting:
Risks, Benefits, & Costs

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

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Carotid Artery Stenting:
Risks, Benefits, & Costs

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

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Carotid Artery Stenting:

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

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Carotid Artery Stenting:

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

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Questions?

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

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Carotid Artery Stenting: **Billing Codes**

CPT	0075T	Transcatheter placement of extracranial vertebral or intrathoracic carotid artery stent(s), including radiologic supervision / interpretation, percutaneous; initial vessel	Main Procedure - extracranial (may include some vertebral stents)
CPT	0076T	Transcatheter placement of extracranial vertebral or intrathoracic carotid artery stent(s), including radiologic supervision and interpretation, percutaneous; each additional vessel	Main Procedure - extracranial (may include some vertebral stents)
CPT	37215	Transcatheter placement of Intravascular Stent(s), Cervical carotid artery, percutaneous; without distal embolic protection	Main Procedure - extracranial
CPT	37216	Transcatheter placement of Intravascular Stent(s), Cervical carotid artery, percutaneous; with distal embolic protection	Main Procedure - extracranial
CPT	61635	Transcatheter placement of intravascular stent(s), intracranial (eg, atherosclerotic stenosis), including balloon angioplasty, if performed	Main Procedure - intracranial

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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:
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1

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

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2

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 heath and economic burdens are high

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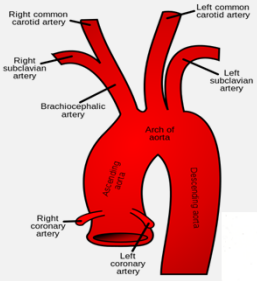
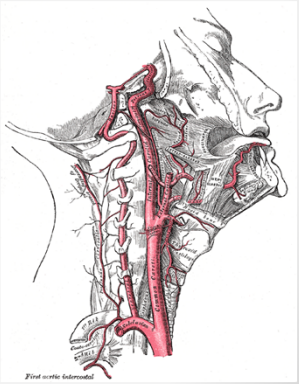
Background: Anatomy

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





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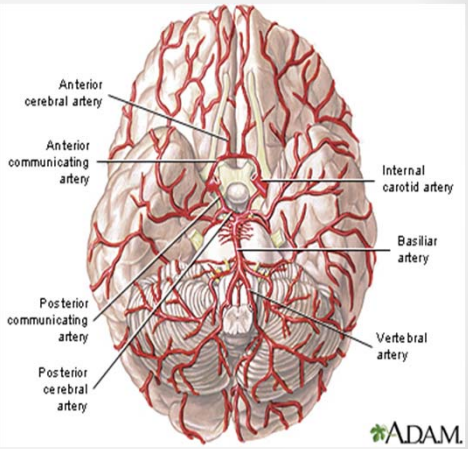
Background: Anatomy

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



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Background: Pathophysiology

Carotid arteries (extracranial)

- Plaque (cholesterol, calcium, fibrous tissue) deposition – vessel narrowing, ↓ blood flow
- Bifurcation most common – turbulence and sheer 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

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Background: Imaging

Duplex Ultrasound (DUS)

- Peak systolic velocity and/or end diastolic velocity; PSV of ICA ≥ 125 cm/s for predicating >50% angiographic stenosis ≥ 230 cm/s predicting >70% stenosis;
- Sensitivity/specificity for ≥ 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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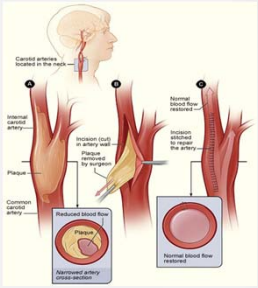
Treatment Options – Carotid (Extracranial)

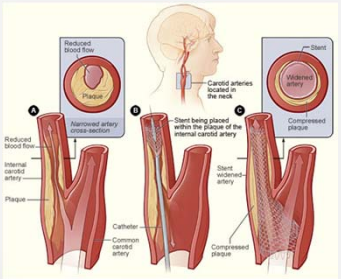
Best Medical Therapy – has evolved

- 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

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Images: http://www.nhlbi.nih.gov/health/health-topics/topics/catd/

8

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

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

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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

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

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

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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?

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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)

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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

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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

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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.

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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

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Clinical guideline overview: Extracranial

Brott, et. al. 2011Guideline 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

	Asymptomatic Patients	Symptomatic Patients	
	70%-99% Stenosis	50%-69% Stenosis	70%-99% Stenosis
CEA	Class IIa LoE A	Class I LoE B	Class I LoE A
CAS	Class IIb LoE B	Class I LoE B	Class I LoE B

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

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Clinical guideline overview: Extracranial

Summary of acceptable periprocedural risk*

	Stenosis (%)	Acceptable Periprocedural Death/Stroke Rate
Asymptomatic	60-99%	<3% (Level A); 5 year life expectancy
Symptomatic	50-69%	<6% (Level A); 5 year life expectancy
	70-99%	<6% (Level A); 2 - 5 year life expectancy

*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

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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

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Payer Policies

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

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Asymptomatic

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Clinical Guidelines ASYMPTOMATIC

	Brott, 2011:ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS
Class I	• Patient selection guided by: comorbidities, life expectancy, individual factors
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)

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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)

KQ1: Asymptomatic CAS vs. CEA			Treatment groups		Effect size	
Outcome	Studies* N range Follow-up	Overall quality of evidence	CAS (%)	CEA (%)	RD % (95% CI)† RR (95% CI)	Favors
Any stroke	4 years 1 RCT N = 85	Low	0.0% (0/43)	0/0% (0/42)	Not estimable	NA
Ipsilateral stroke	4 years 2 RCTs N = 1181 N = 85	Low	1.5% (9/584) 0.0% (0/43)	0.9% (5/582) 0.0% (0/43)	RD = 0.7 (-0.57, 1.9) RR = 1.78 (0.60, 5.28) Not estimable	NS NA
Any peri-procedural stroke or death or post-procedural ipsilateral stroke	4 years 1 RCT N = 1181	Low	4.5% (24/594)	2.7% (13/587)	RD = 1.9 (-0.5, 4.3) HR = 1.9 (0.95, 3.7)	NS

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KQ 1: Effectiveness in Asymptomatic Persons

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

KQ1:Asymptomatic CAS vs. medical therapy only			Treatment groups		Effect size	
Outcome	Studies Follow-up (median)	Overall quality	CAS (%)†	Medical (%)†	Adjusted HR (95% CI)†	Favors
Any stroke	1 retrospective registry N = 946 2.1 years	Low	9	11	0.5 (0.2, 0.9)	CAS
Death		Low	20	32	0.7 (0.5, 0.9)	CAS
Any stroke or death		Low	29	38	0.7 (0.5, 0.9)	CAS

†Kaplan-Meier estimates for projected 5 years of follow-up.

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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)

	Studies* N range	Overall quality of evidence	CAS (% range)	CEA (% range)	RD range, % (95% CI)† RR range (95% CI)	Favors
Any stroke	2 RCTs N = 1191 N = 85	Moderate	2.5% (15/594) 0.0% (0/43)	1.4% (8/597) 0.0% (0.42)	RD = 1.2 (-0.4,2.7) RR = 1.9 (0.8, 4.4) Not estimable	NS
Death	1 RCT N = 85	Low	0.0% (0/43)	0.0% (0/42)	Not estimable	NA
Any stroke or death	2 RCTs N = 1191 N = 85	Moderate	2.5% (15/594) 0.0% (0/43)	1.4% (8/597) 0.0% (0/42)	RD = 1.2 (-0.4,2.7) RR = 1.9 (0.8, 4.4) Not estimable	NS NA
MI	1 RCT N = 1191	Moderate	1.2% (7/594)	2.2% (13/597)	RD = -1.0 (-2.5, 0.4) RR = 0.6 (0.2, 1.4)	NS

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.

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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)*

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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).*

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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**

	CAS % (n/N)	CEA % (n/N)	RD (95% CI) RR (95% CI)	Favors
1-year Ipsilateral stroke or Death	9.9% (12/117)	21.5% (26/120)	-11% (-21%, -2%) 0.47 (0.25, 0.89) NNH 9 (5, 50)	CAS
3-year Stroke	10.3% (12/117)	9.2% (11/120)	-2% (-9%, 4%) 0.74 (0.34, 1.62)	NS
3-year Ipsilateral stroke or Death	21.4% (25/117)	29.2% (35/120)	-8% (-19%, 3%) 0.73 (0.47, 1.14)	NS

- **Safety**

	CAS % (n/N)	CEA % (n/N)	RD (95% CI) RR (95% CI)	Favors
Periprocedural Death, Stroke, or MI	5.4% (6/117)	10.2% (12/120)	-5% (-12%, 2%) 0.51 (0.20, 1.32)	NS

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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

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Symptomatic

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Clinical Guidelines: *SYMPTOMATIC*

	(from Brott 2011 except where noted)
Class I	>70 stenosis (noninvasive) or > 50% stenosis (angio) when anticipated rate of periprocedural stroke or mortality is <6%: • Patients with low or average surgical risk, symptoms w/in 6 months; should undergo CEA • CAS alternative to CEA (LoE B) in patients with average or low risk for endovascular intervention.
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

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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

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

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KQ 1: Efficacy in *Symptomatic* Persons

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

‡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

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KQ 1: Efficacy in *Symptomatic* Persons

Outcome	Studies* N range Follow-up	Overall quality of evidence	CAS (%)	CEA (%)	RD % (95% CI)† RR (95% CI)	Favors
Any stroke or death (including peri-procedural)	4-6 months 2 RCTs N = 527 N =1710	Moderate	11.8% (31/262) 8.5% (72/853)	9.8% (26/265) 4.7% (40/857)	RD = 1.65 (-3.17, 6.46) RR = 1.18 (0.72, 1.94) RD = 3.32 (1.13, 5.52) RR = 1.75 (1.20, 2.54)	NS CEA
	2-4 years 2 RCTs N = 124	Low	1.6% (1/63)	4.9% (3/61)	RD‡= -2.18 (-7.33, 2.96) RR‡ = 0.43 (0.07, 2.69)	NS
Any peri-procedural stroke or death or post-procedural ipsilateral stroke	6 months 1 RCT N = 527	Moderate	10.2% (27//262)	4.2% (11/265)	RD = 5.36 (1.28, 9.43) RR = 2.34 (1.19, 4.63)	CEA
	2-5.4 years 5 RCTs N = 2728	Low	8.1% (112/1381)	6.6% (89/1347)	RD‡ = 1.28 (-1.64, 4.19) RR‡ = 1.20 (0.89, 1.62)	NS

‡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

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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

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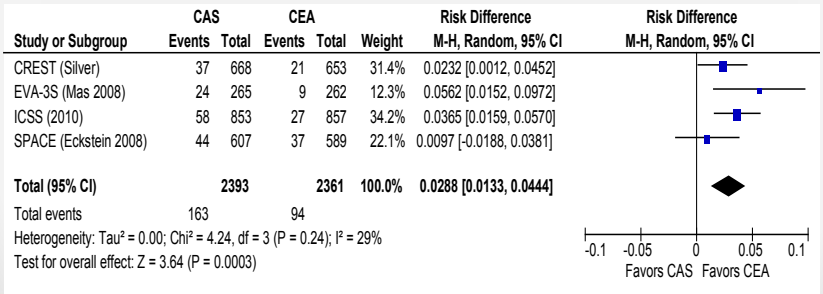
KQ 3: Safety in *Symptomatic* Persons (30-day periprocedural outcomes

Any periprocedural stroke – based on sensitivity analysis

Studies	Overall Quality	CAS (% range)	CEA (% range)	RD, % (95% CI) RR, (95% CI)	Favors
4 RCTs§ N = 4754	Moderate	6.8% (163/2393)	4.0% (94/2361)	RD = 2.9 (1.3, 4.4) NNH = 35 (22, 75) RR = 1.7 (1.2, 2.5)	CEA



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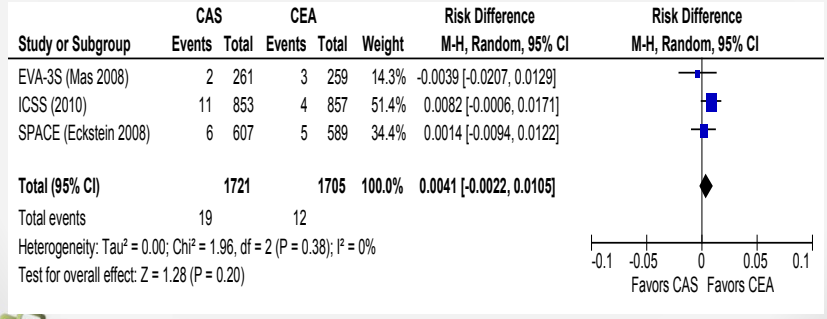
KQ 3: Safety in *Symptomatic* Persons (30-day periprocedural outcomes

Death – based on sensitivity analysis

Studies	Overall Quality	CAS† (% range)	CEA† (% range)	RD range, % (95% CI)‡ RR range (95% CI)	Favors
4 RCTs N = 3530	Low	1.1% (19/1774)	0.7% (13/1756)	RD = 0.4 (-0.3, 1.0) RR = 1.4 (0.7, 2.9)	NS



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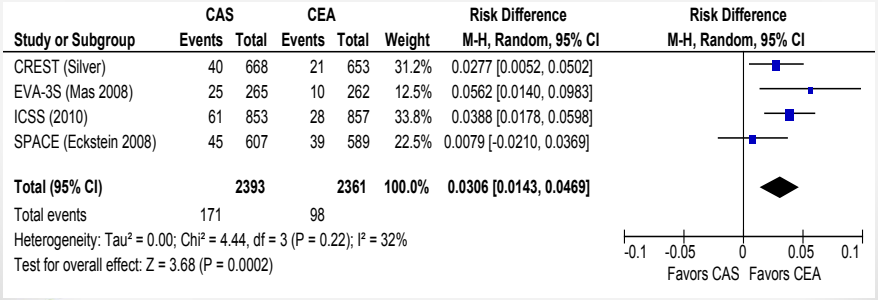
KQ 3: Safety in *Symptomatic* Persons (30-day periprocedural outcomes

Any Stroke or Death – based on sensitivity analysis

Studies	Overall Quality	CAS (% range)	CEA (% range)	RD, % (95% CI) NNH (95% CI) RR, (95% CI)	Favors
4 RCTs§ N = 4754	Moderate	7.1% (171/2393)	4.1% (98/2361)	RD = 3.1 (1.4, 4.7) NNH = 33 (2, 70) RR = 1.8 (1.2, 2.6)	CEA



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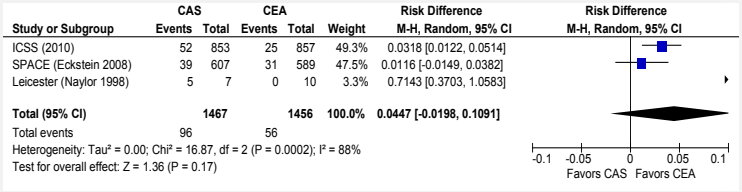
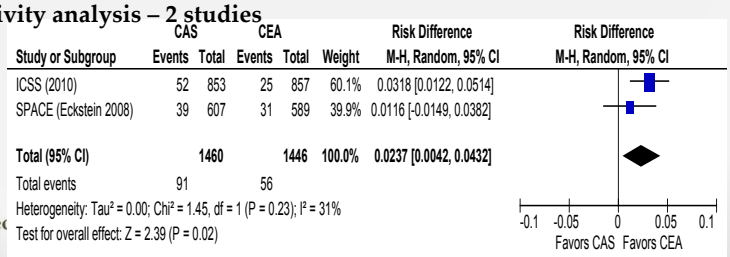
KQ 3: Safety in *Symptomatic* Persons (30-day periprocedural)

Ipsilateral stroke –

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



Sensitivity analysis – 2 studies



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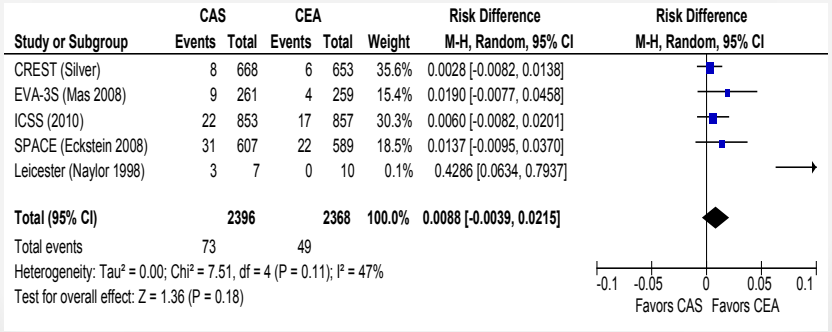
KQ 3: Safety in *Symptomatic* Persons (30-day periprocedural)

Fatal, major or disabling stroke

	Overall Quality	CAS (% range)	CEA (% range)	RD % (95% CI) RR (95% CI)	Favors
5 RCTs N = 4764	Moderate	3.0% (73/2396)	2.1% (49/2368)	RD = 0.9 (-0.4, 2.2) RR = 1.5 (1.0, 2.1)	NS



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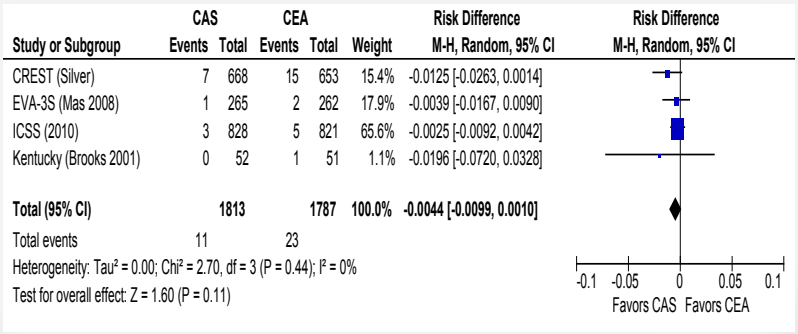
KQ 3: Safety in *Symptomatic* Persons (30-day periprocedural)

Myocardial infarction

	Overall Quality	CAS (% range)	CEA (% range)	RD % (95% CI) RR (95% CI)	Favors
4 RCTs N = 3600	Moderate	0.6% (11/1813)	1.3% (23/1787)	RD = -0.4 (-1.0, 0.1) RR = 0.5 (0.2, 1.0)	NS



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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

Study	CAS		CEA		Effect Size	
Any Hematoma	(n/N)	%	(n/N)	%	**RD%* (95% CI)**	**RR (95% CI)**
CREST (2011)	(0/668)	0%	(8/653)	1.2%	-0.01 (-0.02, -0.00)	0.06 (0.00, 0.99)
ICSS (2010)	(30/853)	3.5%	50/857)	5.8%	-0.02 (-0.04, -0.00)	0.60 (0.39, 0.94)
BACASS (2008)	(0/10)	0%	(0/10)	0%	NE	NE
Regensburg (2008)	(1/43)	2.3%	(6/44)	13.6%	-0.11 (-0.22, -0.00)	0.17 (0.02, 1.36)
Pooled estimates					**-2.13 (-4.57, 0.31)**	**0.30 (0.08, 1.15)**
Severe Hematoma requiring treatment	(n/N)	%	(n/N)	%	**RD%* (95% CI)**	**RR (95% CI)**
EVA- 3S (2006)†	(1/261)†	0.4%	(2/259)†	0.8%	-0.00 (-0.02, 0.01)	0.50 (0.05, 5.44)
ICSS (2010)	(8/853)	0.9%	(28/857)	3.3%	-0.02 (-0.04, -0.01)	0.29 (0.13, 0.63)
Kentucky (2001)	(3/53)	5.7%	(1/51)	2.0%	0.04 (-0.04, 0.11)	2.89 (0.31, 26.85)
BACASS (2008)	(0/10)‡	0%	(0/10)‡	0%	NE	NE
Pooled estimates					**-0.99 (-3.08, 1.10)**	**0.56 (0.15, 2.13)**

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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)

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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 <u>not</u> modify the treatment effect for the outcome ipsilateral stroke (4 years, SPACE) but <u>did</u> 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)

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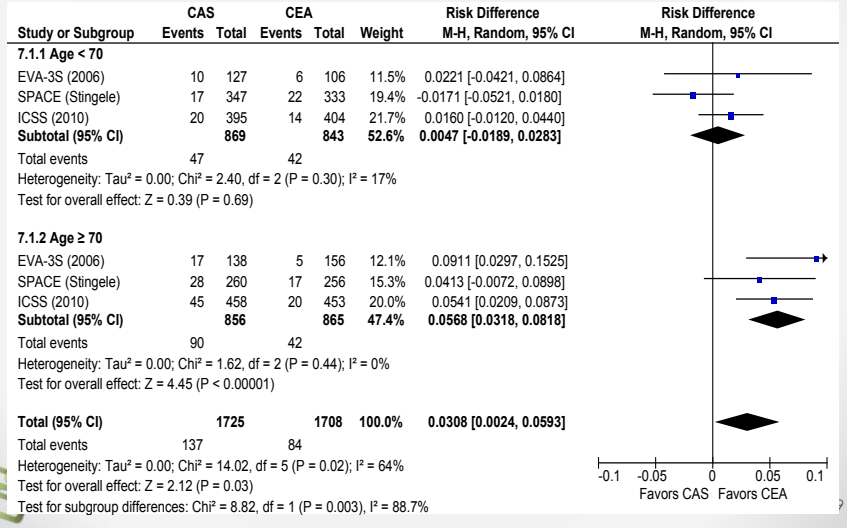
KQ 4: Differential efficacy or safety- *Symptomatic* Persons

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



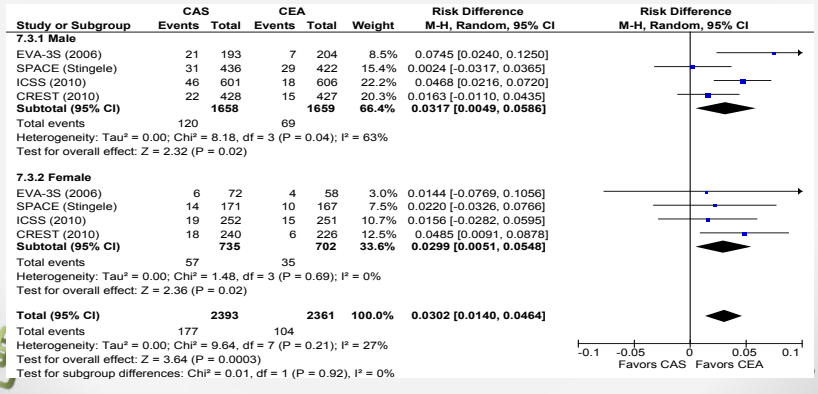
Study or Subgroup	CAS Events	CAS Total	CEA Events	CEA Total	Weight	Risk Difference M-H, Random, 95% CI
7.1.1 Age < 70						
EVA-3S (2006)	10	127	6	106	11.5%	0.0221 [-0.0421, 0.0864]
SPACE (Stingele)	17	347	22	333	19.4%	-0.0171 [-0.0521, 0.0180]
ICSS (2010)	20	395	14	404	21.7%	0.0160 [-0.0120, 0.0440]
Subtotal (95% CI)		**869**		**843**	**52.6%**	**0.0047 [-0.0189, 0.0283]**
Total events	47		42			
Heterogeneity: Tau² = 0.00; Chi² = 2.40, df = 2 (P = 0.30); I² = 17%						
Test for overall effect: Z = 0.39 (P = 0.69)						
7.1.2 Age ≥ 70						
EVA-3S (2006)	17	138	5	156	12.1%	0.0911 [0.0297, 0.1525]
SPACE (Stingele)	28	260	17	256	15.3%	0.0413 [-0.0072, 0.0898]
ICSS (2010)	45	458	20	453	20.0%	0.0541 [0.0209, 0.0873]
Subtotal (95% CI)		**856**		**865**	**47.4%**	**0.0568 [0.0318, 0.0818]**
Total events	90		42			
Heterogeneity: Tau² = 0.00; Chi² = 1.62, df = 2 (P = 0.44); I² = 0%						
Test for overall effect: Z = 4.45 (P < 0.00001)						
Total (95% CI)		**1725**		**1708**	**100.0%**	**0.0308 [0.0024, 0.0593]**
Total events	137		84			
Heterogeneity: Tau² = 0.00; Chi² = 14.02, df = 5 (P = 0.02); I² = 64%						
Test for overall effect: Z = 2.12 (P = 0.03)						
Test for subgroup differences: Chi² = 8.82, df = 1 (P = 0.003), I² = 88.7%						

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



Study or Subgroup	CAS Events	CAS Total	CEA Events	CEA Total	Weight	Risk Difference M-H, Random, 95% CI
7.3.1 Male						
EVA-3S (2006)	21	193	7	204	8.5%	0.0745 [0.0240, 0.1250]
SPACE (Stingele)	31	436	29	422	15.4%	0.0024 [-0.0317, 0.0365]
ICSS (2010)	46	601	18	606	22.2%	0.0468 [0.0216, 0.0720]
CREST (2010)	22	428	15	427	20.3%	0.0163 [-0.0110, 0.0435]
Subtotal (95% CI)		**1658**		**1659**	**66.4%**	**0.0317 [0.0049, 0.0586]**
Total events	120		69			
Heterogeneity: Tau² = 0.00; Chi² = 8.18, df = 3 (P = 0.04); I² = 63%						
Test for overall effect: Z = 2.32 (P = 0.02)						
7.3.2 Female						
EVA-3S (2006)	6	72	4	58	3.0%	0.0144 [-0.0769, 0.1056]
SPACE (Stingele)	14	171	10	167	7.5%	0.0220 [-0.0326, 0.0766]
ICSS (2010)	19	252	15	251	10.7%	0.0156 [-0.0282, 0.0595]
CREST (2010)	18	240	6	226	12.5%	0.0485 [0.0091, 0.0878]
Subtotal (95% CI)		**735**		**702**	**33.6%**	**0.0299 [0.0051, 0.0548]**
Total events	57		35			
Heterogeneity: Tau² = 0.00; Chi² = 1.48, df = 3 (P = 0.69); I² = 0%						
Test for overall effect: Z = 2.36 (P = 0.02)						
Total (95% CI)		**2393**		**2361**	**100.0%**	**0.0302 [0.0140, 0.0464]**
Total events	177		104			
Heterogeneity: Tau² = 0.00; Chi² = 9.64, df = 7 (P = 0.21); I² = 27%						
Test for overall effect: Z = 3.64 (P = 0.0003)						
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.92), I² = 0%						

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):

	CAS % (n/N)	CEA % (n/N)	HR (95% CI)	Favors	Interaction p-values
Female	NR	NR	2.33 (1.07, 5.07)	CEA	$P = 0.04$
Male	NR	NR	0.88 (0.50, 1.55)	NS	

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

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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

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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

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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;

		Treatment groups Probability (%) 1 year (95% CI) Patient Events (n/N)		Effect size*	
Study Follow-up	**Overall quality**	**CAS**	**Medical**	***P*-value***	**Favors**
1 RCT N = 451 1 year	Low	20.0 (15.2–26.0) (46/224)	12.2 (8.4–17.6) (26/227)	.009	Medical RD 7.8% NNH 13

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

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KQ 2: Intracranial Atherosclerosis

Safety – 30 day periprocedural outcomes			Treatment groups Probability (%) 1 year (95% CI) Patient Events (n/N)		Effect size*	
Outcome	**Studies N**	**Overall quality**	**CAS**	**Medical**	***P*-value**	**Favors**
Any stroke	1 RCT N = 451	Low	14.7 (10.7–20.1) (33/224)	5.3 (3.1–9.2) (12/227)	.03	Medical RD 9.4% NNH 11
Death		Low	2.2 (0.9–5.3) (5/224)	0.4 (0.1–3.1) (1/227)	.95	NS
Any stroke or death		Low	14.7 (10.7–20.1) (33/224)	5.8 (3.4–9.7) (13/227)	.009	Medical RD 8.9% NNH 11
Myocardial infarction		Low	0.5 (0.1–3.2) (NR)	1.3 (0.4–4.1) (NR)	.60	NS
Any major hemorrhage		Low	8.0 (5.1–12.5) (NR)	0.9 (0.2–3.5) (NR)	< .001	Medical RD 7.9% NNH 13

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

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KQ 2: Intracranial Atherosclerosis

Efficacy – 1 year probabilities reported

Outcome	Studies† N Follow-up	Overall quality of evidence	CAS	Medical	*P*-value	Favors
Any stroke	1 RCT N = 451 1 year	Low	22.3 (17.2–28.7) (50/224)	14.9 (10.6–20.7) (32/227)	.03	Medical RD 7.4% NNH 13
Death		Low	3.4 (1.6–7.2) (7/224)	4.1 (2.0–8.5) (7/227)	.95	NS
Any stroke or death		Low	23.4 (18.1–29.8) (52/224)	17.5 (12.8–23.6) (37/227)	.06	NS
Myocardial infarction		Low	2.2 (0.8–5.8) (5/224)	4.0 (1.9–8.4) (7/227)	.60	NS
Any major hemorrhage		Low	9.0 (5.9–13.5) (22/224)	1.8 (0.7–4.8) (5/227)	< .001	Medical RD 7.2% NNH 14

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

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Summary

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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 periprocedural 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

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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

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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

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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.

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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

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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.

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HTCC Coverage and Reimbursement Determination
Analytic Tool

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.

[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

[3] The principles and standards are based on USPSTF Principles at: 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[4] 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.

[4] Based on GRADE recommendation: http://www.gradeworkinggroup.org/FAQ/index.htm

Not Confident	Confident
Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.	Very certain of evidentiary support. Further information is unlikely to change confidence

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.
Link to NCD: http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=201&ncdver=9&bc=BAABAAAAAAAA&

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 patientfs 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

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

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
National Guideline Clearinghouse						
Canadian Stroke Strategy Canadian Best Practice Recommendations for Stroke Care (2010)	Through 6/30/10	CAS for symptomatic and asymptomatic carotid artery stenosis	4 RCTs (CREST, EVA-3S, SPACE, ICSS)	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%.	NR	A
				CEA is more appropriate than CAS for patients >70 who are otherwise fit for surgery because stenting carries a higher short-term risk of stroke and death.	NR	A
				CAS may be considered in asymptomatic or remotely symptomatic patients (60-99% carotid stenosis, >3 months) who are not operative candidates for technical, anatomic or medical reasons provided there is a <3 percent risk of peri-procedural morbidity and mortality.	NR	A
National Stroke Foundation Clinical	Through 2/19/10	CAS for carotid artery stenosis	1 Cochrane review; 1 RCT (SPACE)	CAS should NOT routinely be undertaken for patients with carotid stenosis.	A	NR

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
Guidelines for Stroke Management (2010)				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 >80y).	NR	NR
Singapore Ministry of Health Stroke and Transient Ischaemic Attacks. Assessment, Investigation, Immediate Management and Secondary Prevention (2009)	NR	CAS for symptomatic and asymptomatic extracranial carotid artery stenosis	1 RCT (SAPPHIRE);	Carotid artery stenting may be considered in patients who are not suitable for carotid endarterectomy.	A	1++
Scottish Intercollegiate Guidelines Network Management of Patients with Stroke or TIA: Assessment, Investigation, Immediate Management and Secondary	2000 to 2007	Carotid angioplasty and CAS and endovascular stenting for carotid artery stenosis and extracranial cervical arterial dissection	1 Cochrane review; 2 case series	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)	A	NR

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
Prevention. A National Clinical Guideline (2008)				Endovascular stenting is not routinely recommended for extracranial cervical arterial dissection or cervical artery pseudo-aneurysms. Stenting may be considered if recurrent ischaemic events occur despite medical therapy or where traumatic dissection has occurred with a high risk of stroke.	D	NR
Catalan Agency for Health Information, Assessment and Quality Clinical Practice Guideline for Primary and Secondary Prevention of Stroke (2008)	Through 9/07	CAS for symptomatic or asymptomatic carotid artery stenosis	1 systematic review of RCTs	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.	B	1+
National Institute for Healthcare and Excellence (NICE)						
National Institute for Health and Clinical Excellence Diagnosis and Initial Management of Acute Stroke and Transient Ischaemic Attack (TIA) (2008)	NR	CAS for symptomatic carotid artery stenosis	NR	No basis was found for CAS.	NR	NR

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
National Institute for Health and Clinical Excellence Carotid artery stent placement for symptomatic extracranial carotid stenosis (2011)	8/28/10 to 1/06/11	CAS for symptomatic carotid artery stenosis	NR	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.	NR	NR
National Institute for Health and Clinical Excellence Carotid artery stent placement for asymptomatic extracranial carotid stenosis (2011)	8/28/10 to 1/06/11	CAS for asymptomatic carotid artery stenosis	NR	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.	NR	NR
Other sources						
American Heart Association/ American Stroke Association Guidelines for the Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack (2011)	Through 7/09	CAS for symptomatic carotid artery stenosis	5 RCTs (CAVATAS, SAPPHIRE, EVA-3S, SPACE, CREST)	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 >70% by noninvasive imaging or >50% by catheter angiography.	I	B

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
				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.	IIa	B
				Among patients with symptomatic severe stenosis (>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.	IIb	B
				When the degree of stenosis is <50%, there is no indication for carotid revascularization by either CEA or CAS.	III	A
American Heart Association/ American Stroke Association Guidelines for the Primary Prevention of Stroke (2011)	12/06 to 4/09	CAS for asymptomatic carotid stenosis	2 RCTs (SAPPHIRE, CREST) 1 non-randomized trial (CaRESS), Registries (NR)	Prophylactic carotid artery stenting might be considered in highly selected patients with an asymptomatic carotid stenosis (>60% on angiography, >70% on validated Doppler ultrasonography, or >80% on computed tomographic angiography or MRA if the stenosis on ultrasonography was 50%	IIb	B

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
				to 69%). The advantage of revascularization over current medical therapy alone is not well established.		
				The usefulness of CAS as an alternative to CEA in asymptomatic patients at high risk for the surgical procedure is uncertain	IIb	C
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)	NR	Emergent angioplasty and/or stenting of the extracranial carotid or vertebral arteries	8 retrospective case-series	The usefulness of emergent angioplasty and/or stenting of the extracranial carotid or vertebral arteries in unselected patients is not well established	IIb	C
				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.	IIb	C

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
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)	Through 05/10	Carotid artery balloon angioplasty and CAS for symptomatic extracranial carotid disease	5 RCTs (CREST, SAPPHIRE, EVA-3S, SPACE, ICSS)	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 >70% as documented by noninvasive imaging or >50% as documented by catheter angiography and anticipated rate of peri-procedural stroke or mortality is <6%.	I	B
				It is reasonable to choose CEA over CAS when revascularization is indicated in older patients, particularly when arterial pathoanatomy is unfavorable for endovascular intervention.	IIa	B
				It is reasonable to choose CAS over CEA when revascularization is indicated in patients with neck anatomy unfavorable for arterial surgery.	IIa	B
				Prophylactic CAS might be considered in highly selected patients with asymptomatic carotid stenosis (minimum 60% by angiography, 70% by validated Doppler ultrasound), but its	IIb	B

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
				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, effectiveness of revascularization versus medical therapy alone is not well established.	IIb	B
				Except in extraordinary circumstances, carotid revascularization by either CEA or CAS is not recommended when atherosclerosis narrows lumen by <50%.	III	A
				Carotid revascularization is not recommended for patients with chronic total occlusion of targeted carotid artery.	III	C
				Carotid revascularization is not recommended for patients with severe disability caused by cerebral infarction that precludes preservation of useful function.	III	C

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
Society for Vascular Surgery Updated Society for Vascular Surgery Guidelines for Management of Extracranial Carotid Disease (2011)	NR	Carotid artery balloon angioplasty and CAS for symptomatic extracranial carotid disease	4 RCTs (CREST, SAPPHIRE, EVA-3S, SPACE1); 2 non-randomized trials (CaRESS, ICSS)	For neurologically symptomatic patients with stenosis <50% or asymptomatic patients with stenosis <60% diameter reduction, optimal medical therapy is indicated. There are no data to support CAS or CEA in this patient group.	I	B
				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 <70 years may be better treated by CAS, but these data need further confirmation.	I	B
				CEA is preferred over CAS in patients aged >70 years of age, with long (>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.	I	A
				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	I	B

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
				perioperative morbidity and mortality is <3%. CAS should not be performed in these patients except as part of an ongoing clinical trial.		
				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.	II	B
				CAS is preferred over CEA in symptomatic patients with ≥50% stenosis and severe uncorrectable CAD, congestive heart failure, or chronic obstructive pulmonary disease.	II	C

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
				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 <3% to ensure benefit for the patient.	II	B
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	NR	CAS for carotid artery stenosis and intracranial artery stenosis	6 RCTs (CREST, SAPPHIRE, CAVATAS, SPACE, ICSS, EVA-3S); 3 registry studies (ARCHeR, EXACT, CAPTURE)	Carotid percutaneous transluminal angioplasty and stenting (CAS) is recommended in selected patients.	I	A
				For patients with hemodynamically significant intracranial stenosis that have symptoms despite medical therapies (antithrombotics, statins, and other treatments for risk factors), the usefulness of	II	C

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
Recommendations for the Management of Patients with Carotid Stenosis (2010)				endovascular therapy (angioplasty and/or stent placement) is uncertain and is considered investigational.		
				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.	IV	GCP
				Carotid angioplasty, with or without stenting, is not recommended for patients with asymptomatic carotid stenosis.	IV	GCP
European Society for Vascular Surgery Invasive Treatments for Carotid Stenosis: Indications, Techniques (2009)	NR	CAS for symptomatic and asymptomatic carotid artery stenosis	11 RCTs (CAVATAS, Kentucky, Leicester, Wallstent, SAPPHIRE, EVA-3S, SPACE, BACASS, ARCHeR, NASCET, ACAS)	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.	C	NR
				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.	C	NR

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
				CAS should not be offered to asymptomatic 'high-risk' patients if the peri-interventional complication rate is >3%.	C	NR
				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.	C	NR
				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.	C	NR
American Society of Interventional and Therapeutic Neuroradiology/ American Society of Neuroradiology/ Society of Interventional Radiology Quality Improvement Guidelines for the Performance of	NR	Cervical carotid angioplasty and CAS for carotid artery stenosis	3 RCTs (CAVATAS, WALLSTENT, SAPPHIRE); 1 other randomized trial	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:	NR	NR

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
Cervical Carotid Angioplasty and Stent Placement (2003)				a. Significant tandem lesion that may require endovascular therapy b. Radiation-induced stenosis c. Restenosis after CEA d. Refusal to undergo CEA after proper informed consent e. Stenosis secondary to arterial dissection f. Stenosis secondary to fibromuscular dysplasia g. Stenosis secondary to Takayasu arteritis • Severe stenosis associated with contralateral carotid artery occlusion requiring treatment before undergoing cardiac surgery. • 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. • Pseudoaneurysm. • Asymptomatic preocclusive lesion in a patient otherwise meeting first three criteria.		

Organization(s) Title (Year)	Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Recmndtn	Level of Evidence
				Relative Contraindications: • Asymptomatic stenosis of any degree, except in particular circumstances, as described above. • Symptomatic stenosis associated with an intracranial vascular malformation. • Symptomatic stenosis in a patient with a subacute cerebral infarction. • Symptomatic stenosis in a patient with a significant contraindication to angiography.	NR	NR
				Absolute Contraindications: • Carotid stenosis with angiographically visible intraluminal thrombus. • A stenosis that cannot be safely reached or crossed by an endovascular approach.	NR	NR

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 2. Clinical Practice Guidelines for Intracranial Carotid Artery Stenosis

Organization(s)	Literature Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Rcmndtn	Level of Evidence
National Guideline Clearinghouse						
American Society of Interventional and Therapeutic Neuroradiology/ Society of Interventional Radiology/ American Society of Neuroradiology Intracranial Angioplasty & Stenting for Cerebral Atherosclerosis (2005)	NR	Intracranial CAS and angioplasty for asymptomatic and symptomatic intracranial artery stenosis	1 non-randomized, multicenter trial (SSYLVIA); 1 prospective, multicenter single-arm trial (WINGSPAN)	For symptomatic patients with a >50% intracranial stenosis who have failed medical therapy, balloon angioplasty with or without stenting should be considered.	NR	NR
				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.	NR	NR

Organization(s)	Literature Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Rcmndtn	Level of Evidence
				Continued evaluation and improvements in both pharmacological and catheter-based therapies are needed to reduce the stroke burden from intracranial atherosclerosis.	NR	NR
Singapore Ministry of Health Stroke and Transient Ischaemic Attacks. Assessment, Investigation, Immediate Management and Secondary Prevention (2009)	NR	Intracranial angioplasty with or without stenting	1 non-randomized multicenter trial (SSYLVIA); 1 prospective multicenter single-arm trial (WINGSPAN)	Intracranial angioplasty with or without stenting may be considered as a treatment option for symptomatic patients who have >50% stenosis and who have failed medical therapy.	C	2+
Other Sources						
American Heart Association/ American Stroke Association Guidelines for the Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack (2011)	Through 7/2009	Intracranial angioplasty with or without stenting	NIH Wingspan Registry; 10 case series	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.	IIb	C
American Heart Association/ American Stroke Association Guidelines for	NR	Emergent intracranial angioplasty with or without stenting	3 case-series (including 1 non-randomized single-center trial, the	The usefulness of emergent intracranial angioplasty and/or stenting is not well established. These procedures should be	IIb	C

Organization(s)	Literature Search Dates	Procedure(s) Evaluated	Evidence Base Available	Recommendations	Class/ Grade of Rcmndtn	Level of Evidence
the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/ American Stroke Association (2013)			SARIS study)	used in the setting of clinical trials		

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

HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

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

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

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:

	Unproven (no)	**Equivalent** (yes)	**Less** (yes)	**More** (yes)
Effective				
Safe				
Cost-effective				

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 _____ Covered Unconditionally _____ Covered 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?
    - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
    - 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?