

Selected treatments for varicose veins

Clinical Expert

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BIRTHPLACE: Roswell, New Mexico

DATE OF BIRTH: March 25, 1957

EDUCATION:

University of Colorado School of Medicine 1981-1985
Denver, Colorado
Degree: M.D. (with Honors) 1985

University of Utah 1980-1981
Salt Lake City, Utah
Post B.S. Course work

University of Utah 1975-1980
Salt Lake City, Utah
Major: Biology
Degree: B.S. (magna cum laude) 1980

Dartmouth College 6/77 - 9/77
Hanover, New Hampshire

POST GRADUATE TRAINING:

Interventional Radiology Fellow 6/03-12/03
University of Washington
Seattle, WA
Program Director: R. Torrance Andrews, MD

Vascular Surgery Fellow 1991-1993
University of Washington
Seattle, Washington
Program Director: D. Eugene Strandness, Jr., MD

Chief Surgical Resident 1989-1990
University of Washington Affiliated Hospitals
Seattle, Washington

Residency (General Surgery) 1985-1989
University of Washington Affiliated Hospitals
Seattle, Washington
Chairman: C. James Carrico, MD
Program Director: Clifford M. Herman, MD

FACULTY POSITIONS:

Peter J. Gloviczki Professor of Venous and Lymphatic Disease University of Washington School of Medicine Seattle, Washington	7/14/16-Present
Professor University of Washington School of Medicine Seattle, Washington	7/1/08-Present
Associate Professor University of Washington School of Medicine Seattle, Washington	7/1/00 -6/30/08
Assistant Professor University of Washington School of Medicine Seattle, Washington	7/1/94 – 6/30/00
Acting Assistant Professor University of Washington School of Medicine Seattle, Washington	7/1/93 - 6/30/94
Acting Instructor in Surgery University of Washington School of Medicine Seattle, Washington	7/1/90 - 6/30/91

CLINICAL POSITIONS:

Attending Surgeon Vascular Surgery & Interventional Radiology University of Washington Medical Center Seattle, Washington	9/1/05 – Present
Attending Surgeon General and Vascular Surgery Harborview Medical Center Seattle, Washington	7/1/93 – 9/1/05
Attending Surgeon General and Thoracic Surgery Harborview Medical Center Seattle, Washington	7/1/90 - 6/30/91

HONORS:

	<u>Professional</u>	
Gore Pioneers in Performance		2016
Emeritus Fellow Australasian College of Phlebology		2016
Australasian College of Phlebology Excellence in Research & Scientific Standards		2016
Lifetime Achievement Award in Venous Disease (American Board of Venous & Lymphatic Medicine)		2014
Seattle Top Doctor (Seattle Met Magazine)		2012 - 2016
25 Most Influential Vein Professionals (Vein Magazine)		2008
Argentine Society of Lymphophlebology, Honorary Member		2007
American Venous Forum Sigvaris Fellowship in Venous Disease		1997
	<u>Medical School</u>	
Alpha Omega Alpha Honor Medical Society		1985
George B. Packard Award (Outstanding Performance in Surgery)		1985
Alpert Cardiology Award (Outstanding Senior Cardiology Achievement)		1985

Lange Award (Outstanding Academic Achievement)	1983
Promotions Committee Citation	1982, 1983

Undergraduate

Phi Kappa Phi Senior Honor Society	1980
Mortar Board Honor Society	1979
Nonresident Merit Scholarship	1976
Phi Eta Sigma Freshman Honor Society	1976

BOARD CERTIFICATION:

American Board of Surgery	1991	Certificate Number 36356
Recertified	2000	
General Vascular Surgery	1994	Certificate Number 100500
Recertified	2002	
Recertified	2013	
American Board of Venous & Lymphatic Medicine	2014	Certificate Number 649

MEDICAL LICENSES:

Washington	Number 252-09 0024078	7/1/85 - Present
DEA	Number BM2489246	

PROFESSIONAL ORGANIZATIONS

Fellow American College of Surgeons	
National Ultrasound Faculty	10/99 – Present
Advanced Trauma Life Support Instructor	1992 – 2005
ACS Washington Committee on Trauma	1995 - 1999
Society for Vascular Surgery, Distinguished Fellow	6/01 – Present
Postgraduate Education Committee	6/15 – Present
Program Committee	6/12 – 6/16
Advisory Assembly for Vascular Surgery	2006 – 2008
Practice Guidelines Committee	2006 – 2010
Comparative Effectiveness Committee	2008 – 2012
Document Oversight Committee	2010
American Venous Forum	2/97 – 2/98
President	2007
President Elect	2006
Recorder	2/03 – 2/06
Councilor	2/99 – 2/02
Ad Hoc Committee on Reporting Standards	2/98 – Present
American Venous Forum Foundation	
Board of Directors	2/00 – 2/03
President	2/10 – 2/11
American College of Phlebology	
Secretary	11/16 -
Board of Directors	11/10 -
Chairman, Fellowship Review Committee	11/10 – 6/16
Program Committee	2012

Chairman, UIP Scientific Program committee	2013
American Board of Venous & Lymphatic Medicine Chairman, Fellowship Oversight & Accreditation Committee Curriculum Task Force	6/16 - 10/10 -
International Union of Phlebology Vice President, North America American Venous Forum Representative Scientific Program Chairman	9/13 - Present 9/09 – 9/13 2013
Peripheral Vascular Surgery Society	5/97 – 6/16
Western Vascular Society	10/97 - Present
Pacific Northwest Vascular Society President President Elect Secretary / Treasurer Program Chairman Councilor	11/96 – Present 2007 2006 11/03 – 11/06 2000 11/99 – 11/02
Seattle Surgical Society	1/97 – Present

TEACHING RESPONSIBILITIES

Medical Students – Vascular surgery faculty for junior clerkship (Surgery 665) and surgery subinternship (Surgery 688) 12 months / year
Resident Education Surgery – Teaching faculty on UWMC Surgery B service 12 months / year Interventional Radiology – Adjunct Interventional Radiology teaching faculty 1 day per week 12 months / year
Mentored Resident Research Projects

Brant Oelschlager, MD	Delayed abdominal closure in the management of ruptured abdominal aortic aneurysms	1996
Yvonne Carter, MD	The relationship between blood group and deep venous thrombosis in trauma patients	2001
Shyamili Mallick, MD	Mesenteric venous thrombosis	2002
Shyam Krishnan, MD	Retrievable inferior vena cava filters	2004
Arjun Jayaraj, MD	Novel venous aneurysm repair	2011
	Post-thrombotic scoring systems	2012
Daiva Nevidomskyye	Iliocaval venous recanalization	2013
	Gender disparities in AAA	2014
April Rodriguez, MD	Hybrid Management of Venous Malformations	2014
Derek Nathans, MD	Management of Pelvic Congestion Syndrome	2014

EDITORIAL RESPONSIBILITIES

Editorial Board – Phlebology	2008 - Present
Distinguished Reviewer – Journal of Vascular Surgery	2001

NATIONAL RESPONSIBILITIES

Ad Hoc Reviewer National Institutes of Health	2006, 2007
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UNIVERSITY / HOSPITAL COMMITTEES

Medical Quality Assurance Committee University of Washington Medical Center	6/2014 - present
Associate Director, Endovascular Center University of Washington School of Medicine	1/1/04 - 2006
Ambulatory Care Committee Harborview Medical Center	1/01 – 9/1/05
Imaging Council Harborview Medical Center	1/1/00 – 9/1/05
Trauma Council Harborview Medical Center	7/1/93 – 9/1/05
Transfusion Practices Committee Harborview Medical Center	10/1/97 – 1/02
Housestaff Committee University of Washington School of Medicine Seattle, Washington	7/1/96 – 7/00
Resource Use Committee Harborview Medical Center Seattle, Washington	7/1/95 – 7/1/00

FUNDED RESEARCH**Active***Vitrus Iliac Stent Trial*

Principal Investigator
Ventii Corp
12/15 – present

Quality of Life in Venous Malformations

Principal Investigator
BTG Pharmaceuticals
12/15 – present

Inactive*Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis: The ATTRACT Trial*

Data Safety and Monitoring Board
National Institutes of Health
12/08 – 12/10

Compression Stockings in the Prevention of Post-Thrombotic Syndrome

\$347,499
Principal Investigator
Beiersdorf-Jobst, Inc
8/99 - Present

The Natural History of Asymptomatic Calf Vein Thrombosis in High-Risk Trauma Patients

\$10,000
Co-Investigator
Principal Investigator: Brenda Zierler, PhD
Suzanne E. VanHouser Endowed Fund
2/03 – 2/10

Venous Thromboembolism in Trauma

Principal Investigator
Centers for Disease Control Project Grant R49/CC011706-01
12/95 – 6/00

Non-Invasive Study of Venous Flow and Thrombosis

\$442,813
National Institutes of Health
Co-Investigator
9/1/97 - 8/31/00

Inactive Industry Sponsored Trials*A double-blind, efficacy and safety study of the oral thrombin inhibitor, H376/95 versus standard therapy (enoxaparin and warfarin) in patients with acute, symptomatic deep venous thrombosis with or without pulmonary embolism (Thrive 5)*

\$52,837
Principal Investigator
AstraZeneca, L.P.
2/1/01-8/31/03

Unrestricted Grant for Investigation of Cardiovascular Disease;

\$12,000
Principal Investigator
Abbott Laboratories
7/1/1997-12/31/01

A Prospective, Multicenter, Open-label study to Evaluate the Safety and Efficacy of Appligraf™ in the Treatment of Venous Leg Ulcers

\$23, 924
Principal Investigator
Novartis Pharmaceuticals
5/1/98 – 12/31/01

Lovenox in MICU

\$16,103
Principal Investigator
Aventis Pharmaceuticals
3/1/97-12/31/99

Randomized trial of compression devices in the treatment of lower extremity edema after infra-inguinal bypass

\$23, 504
Principal Investigator
Kendall Healthcare
6/1/95 – 6/30/98

A Prospective, Multicenter, Randomized trial of Ifetroban in the Treatment of Venous Leg Ulcers

\$105, 149
Principal Investigator
Bristol Myers Squibb
6/1/95 – 7/31/98

INVITED LECTURES:

1. Keynote Address. Current Status of the Insufficient Perforator System. XVI Argentine Congress of Cardiovascular and Endovascular Surgery. Buenos Aires, Argentina. October 1, 2007.
2. Presidential Address. “I enjoyed your talk, but”...Evidence –based medicine and the scientific foundation of the American Venous Forum. 20th Annual Meeting of the American Venous Forum. Charlotte, SC. February 22, 2008.
3. Keynote Address. Reporting results and outcomes in the treatment of vascular disease. International Symposium on Vascular Diseases. Ferrara, Italy. September 13, 2008.
4. The Inaugural Royal Society of Medicine Press Lecture. Outcomes and evidence in venous disease. Royal Society of Medicine. London, UK. April 29, 2009.
5. Keynote Address. Endovenous ablation: Reporting standards, how it compares with other techniques, is it here to stay? Seventh International Vein Congress. Miami, FL. May 8, 2009.
6. Invited Presidential Speaker. Japanese Society of Phlebology. Miyazaki City, Japan. June 17 – 18, 2010.
7. Jobst Lecturer. University of Michigan. Toledo, OH. October 21, 2010.
8. Surgery Grand Rounds, “Comparative Effectiveness and Vascular Surgery”. Stony Brook University, Long Island, NY, April 8, 2012.
9. 4th Annual William H. Baker, MD Visiting Professor, Loyola University, Chicago. April 10, 2013.
10. Keynote Lecture, “Venous Valves”. The VEINS, Chicago, IL. September 21, 2013.
11. Keynote Lecture. “The Future of Phlebology: Where Are We Going?”. 29th Annual Congress of the American College of Phlebology. Orlando, Fl. November 13, 2015.
12. Keynote lecture. Management of Pelvic Congestion Syndrome: Sense & Nonsense. Australasian College of Phlebology. Ayers Rock, AU July 6, 2016.
13. Keynote Lecture. Contemporary Management of Acute DVT. Tuscon Cardiovascular Conference. Tuscon, AZ. October 29, 2016.

BIBLIOGRAPHY:**Peer Reviewed Journal Articles**

1. Meissner M, Paun M, Johansen K. Duplex scanning for arterial trauma. *Am. J. Surg*, 1991; 161:552-555.
2. Meissner MH, Johansen K. Colon infarction after ruptured abdominal aortic aneurysm. *Arch Surg*. 1992; 127 (8): 979-985.
3. Langdale LA, Meissner M, Nolan C, Ashbaugh DG. Tuberculosis and the surgeon. *Am J Surg*, 1992; 163: 505-509.
4. Meissner MH, Manzo RA, Berglin RO, Strandness DE. Deep venous insufficiency: The relationship between lysis and subsequent reflux. *J Vasc Surg*, 1993; 18: 596-608.
5. Markel A, Meissner MH, Manzo RA, Bergelin RO, Strandness DE. A comparison of the cuff deflation method with the Valsalva maneuver and limb compression in detecting venous valvular reflux. *Arch Surg*; 1994; 129: 701-705 .
6. Meissner MH, Manzo RA, Bergelin RO, Strandness DE. Venous diameter and compliance after deep venous thrombosis. *Thrombosis & Haemostasis*, 1994; 72: 372-376.
7. Cogbill TH, Moore EE, Meissner, MH et al . The spectrum of blunt injury to the carotid artery: a multicenter perspective. *J Trauma*, 1994; 37: 473-479.
8. Meissner, MH. Venous thromboembolism following trauma. *Vascular Forum*, 1994; 2: 224-226.
9. Meissner, MH. The effect of recanalization of venous thrombi on valve function. *Vascular Medicine Review*, 1995; 6: 143-152.
10. Meissner MH, Caps MC, Bergelin RO, Manzo RA, Strandness DE. Propagation, rethrombosis, and new thrombus formation after acute deep venous thrombosis. *J Vasc Surg*, 1995; 22: 558-567.
11. Caps MC, Bergelin RO, Manzo R, Meissner MH, Strandness DE. Venous valvular reflux in veins not involved at the time of acute deep vein thrombosis. *J Vasc Surg*, 1995; 22: 524-531.
12. Patel N, Bradshaw B, Meissner MH, Townsend M. Post-traumatic Budd-Chiari syndrome treated with thrombolytic therapy and angioplasty. *J Trauma*, 1996; 40: 294-298.
13. Bonk RT, Harrison SD, Meissner MH. Intravascular bullet localization by sonography. *AJR Am J Roentgenol*, 1996; 167: 152.
14. Tullis MJ, Meissner MH, Bergelin RO, Manzo RA, Strandness DE. The relationship of venous diameter to reflux, cephalad thrombus, and cephalad reflux following deep venous thrombosis. *Thromb Haemost*, 1997; 77: 462-465.
15. Oelschlager BK, Boyle EM, Johansen KJ, Meissner MH. Delayed abdominal closure in the management of ruptured abdominal aortic aneurysms. *Am J Surg*, 1997; 172: 411-415.
16. Meissner MH, Caps MC, Bergelin RO, Manzo RA, Strandness DE. Early outcome after isolated tibial vein thrombosis. *J Vasc Surg*, 1997; 26: 749-756.
17. Meissner MH, Chandler WC, Nicholls, SC. Coagulopathy after ruptured abdominal aortic aneurysm. *Vascular Surgery* , 1997; 31: 727-736.

18. Patel N, Plorde JJ, Meissner MH. Catheter directed thrombolysis in the treatment of phlegmasia cerulea dolens. *Ann Vasc Surg* 1998; 12: 471-475.
19. Earls JP, Patel NH, DeSena S, Meissner MH. Gadolinium-enhanced three-dimensional MR angiography of the aorta and peripheral arteries: Evaluation of a multistation examination using two gadopentetate dimeglumine infusions. *AJR Am J Roentgenol* 1998; 171: 599-604.
20. Dawson DW, Cutler BS, Meissner MH, Strandness DE. Cilastazol has beneficial effects in treatment of intermittent claudication. Results from a multicenter, randomized, prospective double-blind trial. *Circulation* 1998; 98: 678-686.
21. Meissner MH, Caps MT, Zierler BK, Polissar N, Bergelin RO, Manzo RA, Strandness DE. Determinants of chronic venous disease after acute deep venous thrombosis. *J Vasc Surg* 1998; 28: 826-833.
22. Nicholls SC, Gardner JB, Meissner MH, Johansen KH. Rupture in small abdominal aortic aneurysms. *J Vasc Surg* 1998; 28: 884-888.
23. Meissner MH, Beach KW, Johansen KH, Nicholls SC. Circadian variation in the rupture of abdominal aortic aneurysms. *Vascular Surgery* 1998; 32: 577-586.
22. Meissner, MH. Deep venous thrombosis in the trauma patient. *Semin Vasc Surg* 1998; 11: 274-282.
23. Caps MT, Meissner MH, Tullis MJ, Pollisar NL, Manzo RA, Zierler BK, Chandler WL, Strandness DE Jr. Venous Thrombus Stability During Acute Phase of Therapy. *Vascular Medicine* 1999; 4: 9-14.
24. Mewissen MW, Seabrook GR, Meissner MH, Cynamon J, Labrapoulos N, Haughton SH. Catheter-directed thrombolysis for lower extremity deep vein thrombosis: Report of a national multi-center registry. *Radiology* 1999; 211: 39-49.
25. Eddy VA and the Zone I Penetrating Neck Injury Study Group. Is routine arteriography mandatory for penetrating injuries to zone 1 of the neck? *J Trauma* 2000; 48: 208-214.
26. Paun M, Beach K, Ahmad S, Hickman R, Meissner M, Plett C, Strandness DE. New ultrasound approaches to dialysis access monitoring. *Am J Kidney Dis* 2000; 35: 477-481.
27. Karmy-Jones R, Wilson M, Cornejo C, Gibson K, Meissner M. Surgical management of cardiac arrest caused by massive pulmonary embolism in trauma patients. *J Trauma* 2000; 48: 519-520.
28. Rutherford RB, Padberg FT, Comerota AJ, Kistner RL, Meissner MH, Moneta GL. Venous severity scoring: An adjunct to venous outcome assessment. *J Vasc Surg* 2000; 31: 1307-1312.
29. Meissner MH, Caps MT, Zierler BK, Bergelin RO, Manzo RA, Strandness DE. Deep venous thrombosis and superficial venous reflux. *J Vasc Surg*; 2000; 32: 48-56.
30. Meissner MH, Zierler BK, Bergelin RO, Chandler, WC, Manzo RA, Strandness DE. Markers of plasma coagulation and fibrinolysis after acute deep venous thrombosis. *J Vasc Surg*; 2000; 32: 870-880.
31. Karmy Jones R, Carter YM, Nathans A, Brundage S, Meissner MH, Borsa J, Demirer S, Jukovich G. Impact of presenting physiology and associated injuries on outcome following traumatic rupture of the thoracic aorta. *Am Surg* 2001; 67: 61-66.
32. Karmy-Jones R, Carter Y, Meissner M, Mulligan MS. Choice of venous cannulation for bypass during repair of traumatic rupture of the aorta. *Ann Thorac Surg* 2001; 71: 39 – 41.
33. Meissner MH. The natural history of acute deep venous thrombosis. *Seminars in Interventional Radiology* 2001; 18: 83-97.

34. Meissner MH. Duplex follow-up of patients with DVT: Does it have clinical significance? *Semin Vasc Surg* 2001; 14: 215-221.
35. Carter Y, Meissner M, Bulger E, Demirer S, Brundage S, Jurkovich G, Borsa J, Mulligan MS, Karmy-Jones R. Anatomical considerations in the surgical management of blunt thoracic aortic injury. *J Vasc Surg* 2001; 34: 628-633.
36. Carter YC, Caps MT, Meissner MH. Deep venous thrombosis and ABO blood group are unrelated in trauma patients. *J Trauma* 2002; 52: 112-116.
37. Meissner MH, Zierler BZ, Chandler WL, Bergelin RO, Strandness DE. Coagulation, fibrinolysis, and recanalization after acute deep venous thrombosis. *J Vasc Surg* 2002; 35: 278-285.
38. Meissner MH. Overview: The management of lower extremity venous problems. *Semin Vasc Surg* 2002; 15: 1-4.
39. Tran N, Meissner MH. The epidemiology, pathophysiology, and natural history of chronic venous disease. *Semin Vasc Surg* 2002; 15: 5-12.
40. Borsa J, Hoffer EK, Karmy-Jones R, Fontaine AB, Bloch RD, Yoon JK, So CR, Meissner MH, Demirer S. Angiographic description of blunt traumatic injuries to the thoracic aorta with specific relevance to endografts repair. *J Endovasc Ther* 2002; 9: II84-II91.
41. Zierler BK, Meissner MH, Cain K, Strandness DE. A survey of physician's knowledge and management of venous thromboembolism. *Vasc Endovascular Surgery* 2002; 36: 367-375.
42. Guerrco A, Gibson K, Kralovich KA, Pipinos I, Agnostopolous P, Carter Y, Bulger E, Meissner M, Karmy-Jones R. Limb loss following lower extremity arterial trauma: what can be done proactively. *Injury* 2002; 33: 765-769.
43. Hoffer EK, Karmy-Jones R, Bloch FD, Meissner MH, Borsa JJ, Nicholls SC, So CR. Treatment of acute thoracic aortic injury with commercially available abdominal aortic stent-grafts. *J Vasc Interv Radiol* 2002; 13: 1037-1041.
44. Meissner MH, Natiello C, Nicholls, SC. Performance characteristics of the Venous Clinical Severity (VCS) score. *J Vasc Surg* 2002; 36: 889-895.
45. Meissner MH, Chandler WL, Elliott JS. Venous thromboembolism in trauma: A local manifestation of systemic hypercoagulability. *J Trauma* 2003; 54: 224-231.
46. Meissner MH. Thrombolytic therapy for acute DVT and the venous registry. *Rev Cardiovasc Med* 2002; 3 (suppl 2): S53-S60.
47. Axillary-subclavian venous thrombosis. *Rev Cardiovasc Med* 2002; 3 (suppl 2): S76-S83.
48. Meissner MH. Diagnosis of venous thromboembolic disease in cancer patients. (editorial) *Oncology* 2003; 17: 142-144.
49. Karmy-Jones R, Hoffer E, Meissner MH, Nicholls S, Mattos. Endovascular stent grafts and aortic rupture: A case series. *J Trauma* 2003; 55: 805-810.
50. Karmy-Jones R, Hoffer E, Meissner M, Bloch RD. Management of traumatic rupture of the thoracic aorta in pediatric patients. *Ann Thorac Surg* 2003; 75: 1513 – 1517..

51. Markel M, Meissner MH, Manzo, RA, Bergelin RO, Strandness DE. Deep venous thrombosis. Rate of spontaneous lysis and thrombus extension. *Int Angiol* 2003; 22: 376 - 382.
52. Eklof B, Rutherford RB, Bergan JJ, Carpentier PH, Gloviczki P, Kistner RL, Meissner MH, Moneta G, Myers K, Padberg FT, Perrin M, Ruckley CV, Smith PC, Wakefield TW. Revision of the CEAP classification for chronic venous disorders. A consensus statement. *J Vasc Surg* 2004; 40: 1248 – 1252.
53. Meissner MH, Karmy-Jones R. Management of the anticoagulated patient. *Thorac Surg Clin* 2005; 15: 243-262.
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55. Vendantham S, Rundback JH, Khilnani NM, Gloviczki P, Andrews RT, Saddick NS, Fan CM, Meissner MH, Comerota AJ, Hume KM, Chrisman HB, Pavcnik D, Kaufman JA, Min RJ. Development of a research agenda for endovenous treatment of lower extremity venous reflux: proceedings of a multidisciplinary consensus panel. *J Vasc Interv Radiol* 2005; 16: 1567-1573.
56. Meissner MH. Lower extremity venous anatomy. *Semin Intervent Radiol* 2005; 22: 147-156.
57. Cook J, Salerno C, Krishnadasan B, Nicholls S, Meissner M. The effect of changing presentation and management on the outcome of blunt rupture of the thoracic aorta. *J Thorac Cardiovasc Surg* 2006; 131: 594-600.
58. Karmy-Jones R, Cook J, Burdick T, Meissner M. Traumatic thoracic aortic pseudocoarctation treated with a n endograft. *J Trauma* 2007; 62: 1036 – 1038.
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71. Starnes BW, Quiroga E, Hutter C, Tran NT, Hatsukami T, Meissner M, Tang G, Kohler K. Management of ruptured abdominal aortic aneurysm in the endovascular era. *J Vasc Surg* 2010; 51: 9-17.
72. Labropoulos N, Spentzouris G, Gasparis AP, Meissner M. Impact and clinical significance of recurrent venous thromboembolism. *Br J Surg*, 2010; 97; 989-999.
73. Vasquez MA, Rabe E, McLafferty RB, Shortell CK, Marston WA, Gillespie D, Meissner MH, Rutherford RB. Revision of the venous clinical severity score: venous outcomes consensus statement: special communication of the American Venous Forum Ad Hoc Outcomes Working Group. *J Vasc Surg* 2010; 52; 1387-1396.
74. Meissner MH. Conventional anticoagulant therapy remains the standard of care for the treatment of iliofemoral deep venous thrombosis. *Dis Mon* 2010; 56: 642-652.
75. Henke P, Vandy F, Comerota A, Kahn SR, Lal BK, Lohr J, Meissner M, Caprini J, McLafferty R, Bender D, Jarvis G, Meyer P, Wu D, Wakefield T. Prevention and treatment of the post-thrombotic syndrome. *J Vasc Surg* 2010; 52 (Supple 5): 21S-28S.
76. Meissner MH. The effectiveness of deep vein thrombosis prevention. *J Vasc Surg* 2010; 52 (Supple 5): 65S-67S.
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Agency medical director comments

Selected treatments for varicose veins

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May 19, 2017



Background: Varicose Veins

- Definition: Enlargement (≥ 3 mm) and tortuosity of veins, typically associated with venous reflux
- Estimates of prevalence range from 5 to 40%, may be more common in women, increases with age
- CEAP (Clinical, Etiologic, Anatomic, Pathophysiologic) grading score for venous disease:
 - C1: Telangectasias
 - C2: **Varicose veins**
 - C3: Edema, no skin changes
 - C4: Skin changes (pigmentation etc)
 - C5: Healed ulceration
 - C6: Active ulceration
 - A: Asymptomatic
 - S: Symptomatic (Pain, tightness, etc)

2



Indications for treatment

- Therapeutic management of:
 - Pain, tightness, burning sensation
 - Edema
 - Skin changes (stasis dermatitis, discoloration)
 - Ulceration
 - Variceal hemorrhage
 - Recurrent thrombophlebitis
- Cosmetic

3



Goals and risks of treatment

- Goals:
 - Reduced pain
 - Reduced swelling
 - Improvement in function including mobility
 - Reduction in complications (ulceration, etc)
- Risks:
 - Peri-procedural pain, scarring, hematoma, thrombophlebitis, nerve damage, skin burns
 - Serious adverse effects: DVT/PE, infection

4



Modalities of treatment

- Surgical ligation and stripping
- Endovenous Laser Ablation (EVLA): removal or destruction of vein or vein segment by laser light
- Radiofrequency Ablation (RFA): removal or destruction of vein or vein segment by radiofrequency energy
- Sclerotherapy: Obliteration of a vein/vein segment by chemical injection (liquid [LS] or foam [FS])
- Phlebectomy: removal of a vein segment through small incisions (1-3mm)

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Modality uses/limitations

- EVLA and RFA: ineffective with aneurysm or vein over 12 mm (RFA) or 20 mm (EVLA), or very tortuous veins
- Foam sclerotherapy: preferred for very large veins
- Liquid sclerotherapy: often used for smaller veins
- Phlebectomy: Often adjuvant for tributary veins during another procedure

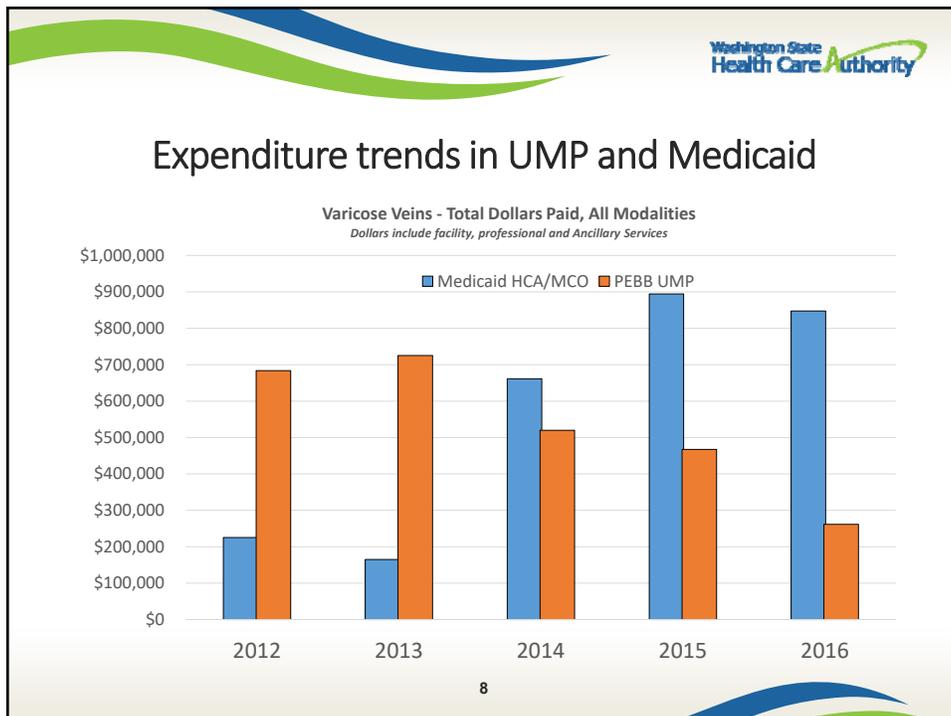
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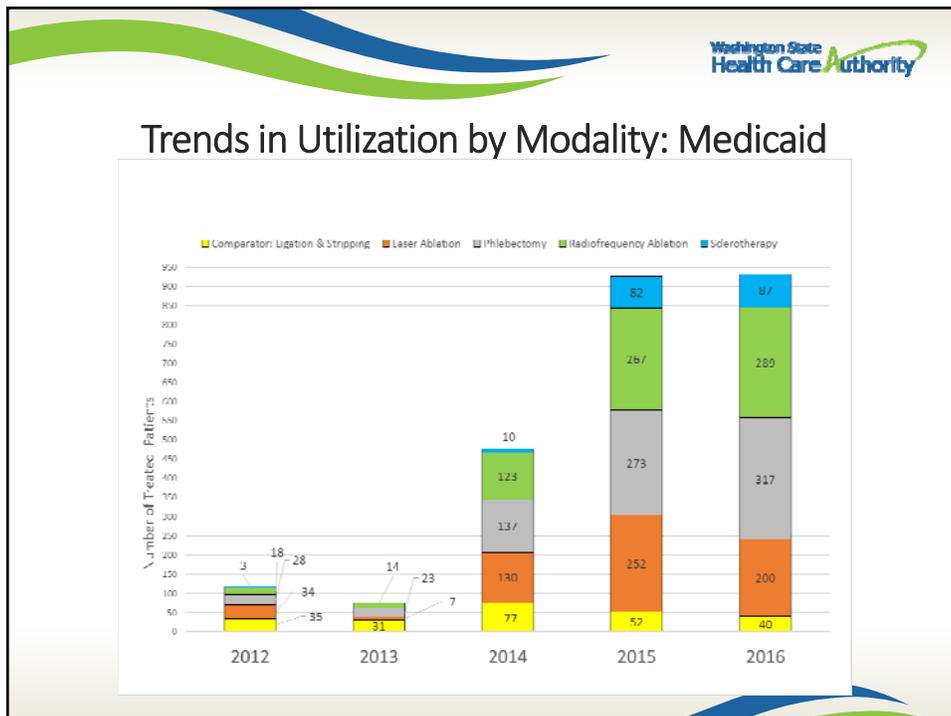
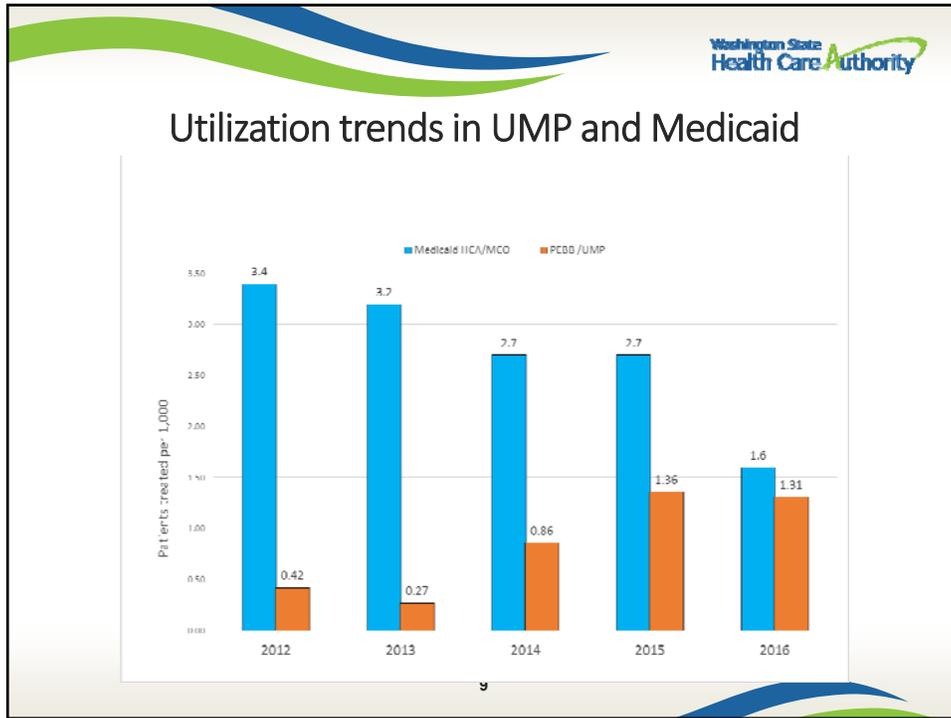


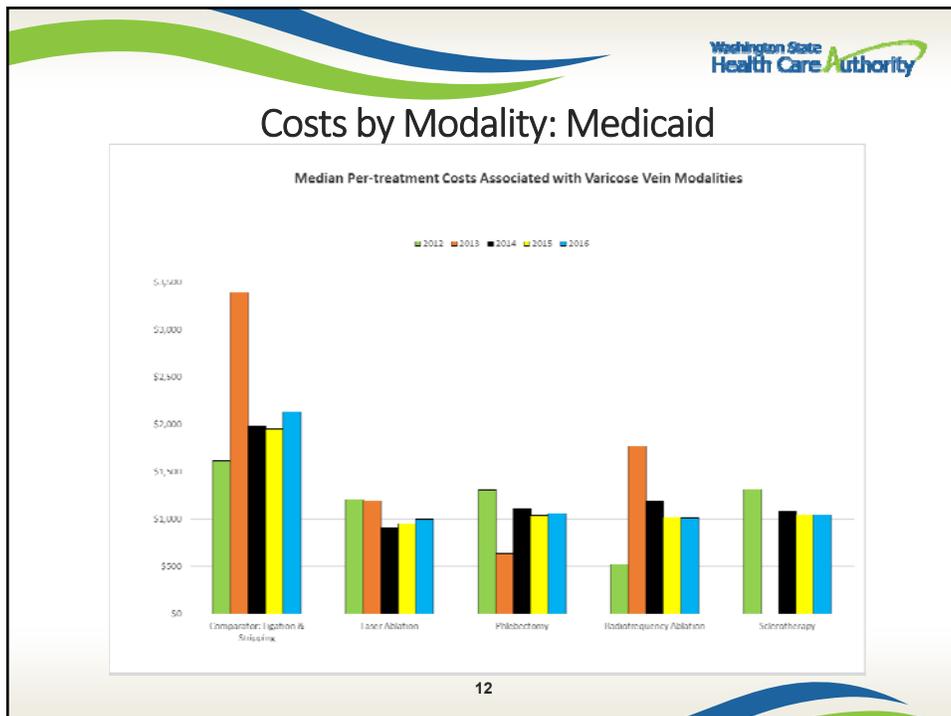
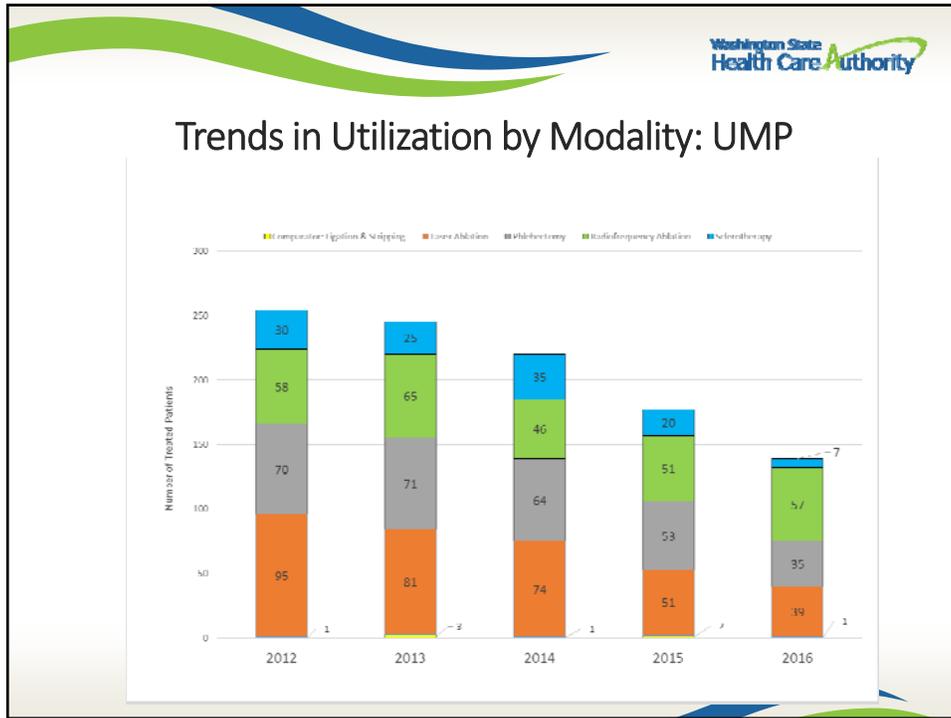
Key Questions

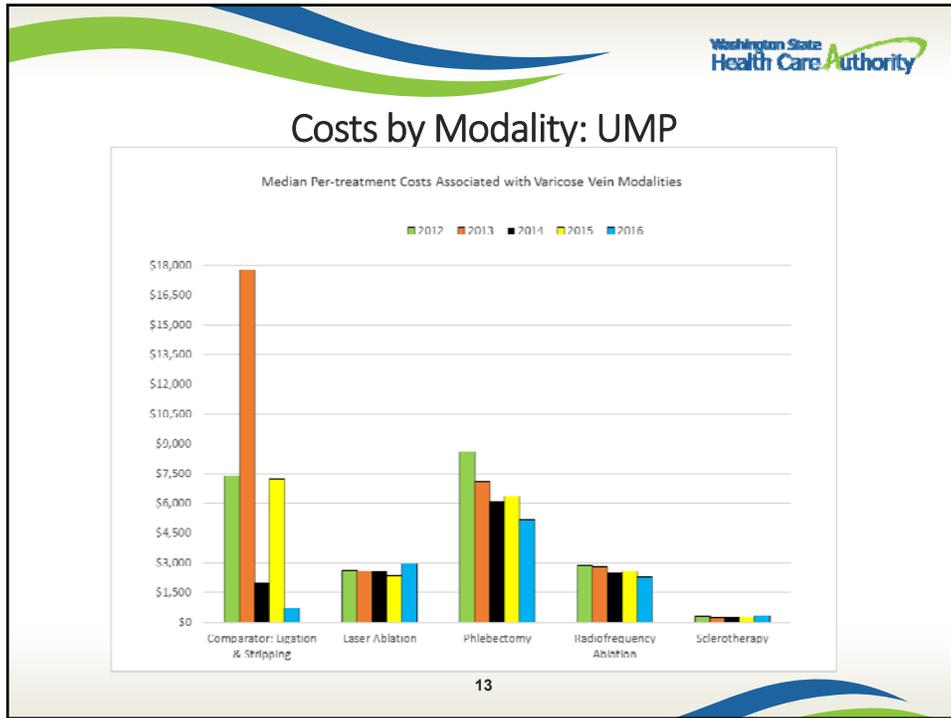
- Effectiveness
- Safety
- Varying effectiveness and safety for subgroups
- Cost implications

7









- Washington State Health Care Authority
- ### Current state agency policy
- UMP – Prior Authorization
 - HCA MEDICAID – Prior Authorization
 - LABOR AND INDUSTRIES – PRIOR AUTHORIZATION
 - DEPT. OF CORRECTIONS – PRIOR AUTHORIZATION
- 14



Limitations of literature

- Techniques preclude effective blinding
- Lack of standardized assessment measures for efficacy or safety
- Lack of functional assessments
- Poor correlation between physiologic assessments and symptom/quality of life scores

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Limitations of literature (con't)

- Lack of information on inclusion criteria
- Lack of subgroup analyses
- Costs difficult to calculate (inclusion of facility costs, frequent use of more than one modality, some can be done either in office or in the operating room)
- Very limited information on phlebectomy, likely because it is rarely a stand-alone procedure

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Data: Efficacy (Relative, with quality of evidence)*

	Primary occlusion	Symptom recurrence	CEAP improved	Quality of Life	Reintervention
Ligation/Stripping	Comparator	Comparator	Comparator	Comparator	Comparator
EVLA (Laser)	= or better (Mod)	= (Mod)	= (Low)	= (Mod)	= (Low)
RFA	= (Low)	= (Low)	= (Low)	Conflicting (Very low)	= (Very low)
ScleroRx	= (Low)	Conflicting (Very low)	Conflicting (Very low)	= (Low)	Worse (Very low)
Phlebectomy	No data	No data	No data	No data	No data

*Based on Hayes review

Green: Better than Ligation/stripping
 Yellow: Same as Ligation/stripping
 Red: Worse than Ligation/stripping

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Data: Efficacy (Example, Absolute): Venermo 2016

	1 yr full GSV* occlusion	1 yr full or partial GSV* occlusion	AVSS** score Improvement	Retreatment
Ligation/Stripping	97%	100%	8	7%
EVLA (Laser)	97%	97%	9.5	1%
Foam ScleroRx	51%	81%	8	15%

*GSV: Greater saphenous vein

**AVSS: Aberdeen Varicose Vein Symptom Score

Green: Better than Ligation/stripping
 Yellow: Same as Ligation/stripping
 Red: Worse than Ligation/stripping

18



Data: Safety*

(Relative, with quality of evidence if available)

	DVT/PE	Nerve damage	Infection	Post op pain	Delayed return to work	Other
Ligation/Stripping	Comparator					
EVLA (Laser)	Better	Better	Better	Conflicting (Very low)	Better (Very low)	Better
RFA	= or slightly worse	Conflicting	=	Better (Mod)	Better (Low)	Lower bruising, higher thrombosis/phlebitis
ScleroRx	Conflicting	Better	Mixed	= (Very low)	Better (Low)	Lower bruising, higher thrombosis/phlebitis
Phlebectomy	No data	No data	No data	No data	No data	No data

*Based on Hayes review

Green: Better than Ligation/stripping
 Yellow: Same as Ligation/stripping
 Red: Worse than Ligation/stripping

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Data: Safety

(Example, Absolute; Venermo 2016)

	DVT/PE	Infection (minor)	Pain score at discharge	Sick leave	Hematoma at 1 mo.	Skin pigmentation	Paresthesia
Ligation/Stripping	0	3%	2.2	12 days	62%	4%	2%
EVLA (Laser)	0	4%	0.98	8 days	42%	5%	3%
Foam ScleroRx	0	0	0.3	1 day	20%	67%	1%

Green: Better than Ligation/stripping
 Yellow: Same as Ligation/stripping
 Red: Worse than Ligation/stripping

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Data: Cost Example (Lin, 2014; 2011 costs)

Procedure/Location	Cost
Ligation/Stripping (tertiary center, operating room)	\$6652
Ligation/Stripping (community hospital, operating room)	\$5626
RFA (office)	\$1464
RFA (operating room)	\$6267
EVLA (office)	\$1402
Phlebectomy (office)	\$2463
Phlebectomy (operating room)	\$5910

All office numbers are from a tertiary (referral) center; operating room numbers are from a community hospital unless otherwise stated

21



Data: Subgroups

- No data available

22



Data: Eligibility Criteria

- Data not available on differential eligibility for surgery and minimally invasive procedures
- Typical inclusion criteria:
 - Varicose veins ≥ 3 mm
 - “Referred for surgical treatment”
 - Presence of symptoms: Pain, swelling, heaviness, cramping, etc.
 - Sometimes: Symptoms severe enough to interfere with mobility or ADLs
 - Exclusions: pregnancy, active infection, DVT, severe distal arterial disease

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Comparison guidelines

- Medicare: No NCD; LCD covered if:
 - Symptoms including impaired mobility, ulceration, refractory edema, bleeding, dermatitis, phlebitis
 - Failed 3 months of conservative therapy (compression hose, elevation)
- Regence: Covered if
 - 1 or more of: Functional impairment limiting instrumental ADLs, recurrent superficial phlebitis, recurrent/persistent hemorrhage, or recurrent/chronic ulceration
 - Failed 3 months of conservative therapy
 - U/S showing venous incompetence
 - Photographs of affected areas
 - Specific anatomic criteria for each procedure type

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Agency medical director concerns

- Safety = Medium
- Efficacy = High
- Cost = Medium

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Agency Medical Director Recommendations

- Cover all modalities with Prior Authorization
- Indications/eligibility
 - Varicose veins ≥ 3 mm AND
 - 3 months of conservative therapy (compression and elevation) without improvement AND
 - Symptoms of pain and/or swelling sufficient to interfere with instrumental ADLs, or presence of complications (ulceration, recurrent thrombophlebitis)
 - Exclusions: pregnancy, active infection, peripheral arterial disease, DVT
- Evidence insufficient to support selection of one modality over another; use will vary based on patient characteristics and preferences

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Questions?

More information:

<https://www.hca.wa.gov/about-hca/health-technology-assessment/varicose-veins>

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Order of Scheduled Presentations:

Selected treatments for varicose veins

Name	
1	Kathleen Gibson, MD, Lake Washington Vascular
2	Monte Madsen, Medtronic

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:

____ I receive current research support from Angiodynamics (endovascular lasers), Bayer (blood thinners), Medtronic (Venaseal and stents), and Bard (stents). I have had travel support from Medtronic and am a speaker for Bristol Myers Squibb (blood thinners). I am on the Scientific Advisory Board for Medtronic and am a consultant for BTG. _____

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 _____ 4/20/17 _____ Kathleen Gibson
 Signature Date Print Name

So we may contact you regarding this information, please provide the following:

Email Address: drgibson@lkwv.com _____

Phone Number: 206-714-7479 _____

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:

I am an employee of Medtronic Inc.

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:

Medtronic Inc. Clorsur Fast Thermal Ablation System

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

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

X [Signature] Apr. 28-2017 Monte A. Madsen
 Signature Date Print Name

So we may contact you regarding this information, please provide the following:

Email Address: monte.madsen@medtronic.com
 Phone Number: 651-202-0997

Selected Treatments for Varicose Veins

Hayes, Inc.
May 19, 2017

Shorthand and Abbreviations

- ▶ **AGREE** – Appraisal of Guidelines Research and Evaluation tool
- ▶ **AVVSS** – Aberdeen Varicose Vein Symptom Severity
- ▶ **BRAVVO**: Behavioural Recovery After treatment for Varicose Veins
- ▶ **CEAP** – Clinical, Etiologic, Anatomic, Pathophysiologic
- ▶ **CIVIQ** – Chronic Venous Insufficiency Quality-of-Life Questionnaire
- ▶ **CND** – cannot determine
- ▶ **CVD** – chronic venous disease
- ▶ **CVI** – chronic venous insufficiency
- ▶ **DVT** – deep vein thrombosis
- ▶ **EVA** – endovenous ablation
- ▶ **EVLA** – endovenous laser ablation
- ▶ **FDA** – Food and Drug Administration
- ▶ **FQ** – fair quality
- ▶ **FS** – foam sclerotherapy
- ▶ **GL** – guidelines
- ▶ **GQ** – good quality
- ▶ **GSV** – great saphenous vein
- ▶ **HL&S** – high ligation and stripping
- ▶ **(HR)QOL** – (health related) quality of life
- ▶ **HTA** – health technology assessment
- ▶ **L&S** – ligation and stripping
- ▶ **LS** – liquid sclerotherapy
- ▶ **PICOS** – population, intervention, comparator, outcomes, setting
- ▶ **PQ** – poor quality
- ▶ **RCT(s)** – randomized controlled trial(s)
- ▶ **RF** – radiofrequency
- ▶ **RFA** – radiofrequency ablation
- ▶ **SSV** – small saphenous vein
- ▶ **UGFS** – ultrasound-guided foam sclerotherapy
- ▶ **VCSS** – Venous Clinical Severity Score

Presentation overview



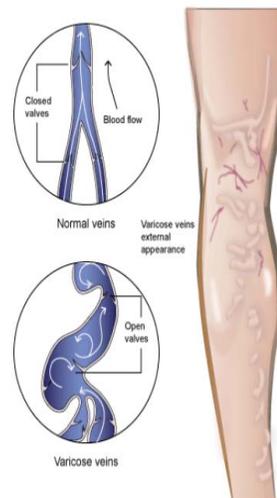
- ▶ Background ✓
- ▶ Objectives
- ▶ Methods
- ▶ Search Results and Findings
- ▶ Practice Guidelines and Payer Policies
- ▶ Overall Summary and Discussion

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Background – Varicose Veins

- ▶ Enlarged (≥ 3 mm) and tortuous vessels in presence of venous reflux
- ▶ Manifestation of chronic venous insufficiency (CVI), a category of chronic venous disease (CVD)
- ▶ CEAP (Clinical, Etiologic, Anatomic, Pathophysiologic) category C₂, and further described by characteristics from the other categories
- ▶ 5% to 30% of adult population; 25 million in U.S.

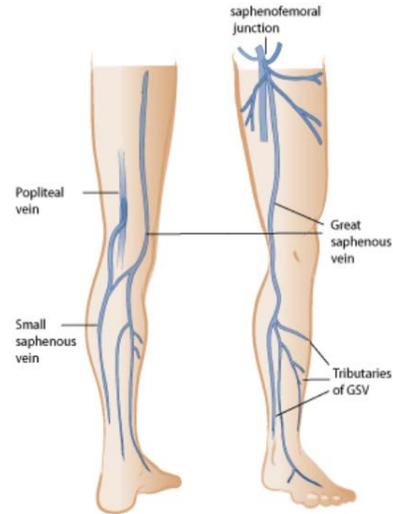


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Background – Varicose Veins

- ▶ **Location:** Anywhere, usually lower extremities; great saphenous vein (GSV) reflux most prevalent, small saphenous vein (SSV) reflux also occurs
- ▶ **Symptoms:** Cramping, throbbing, burning, swelling, heaviness or fatigue, skin discoloration, ulceration, thrombophlebitis
- ▶ **Risk factors:** Older age, a family history of the condition, obesity, pregnancy, inactivity, and prolonged standing or sitting



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Background – Varicose Veins

- ▶ **Goals and potential benefits of treatments:** Seal off damaged portions of veins, reduce or eliminate pain and discomfort, improve quality of life (QOL), prevent further varicose vein formation and more serious conditions such as venous leg ulcers, cosmetic improvements
- ▶ **Risks and potential harms of treatments:** Complications from groin incisions, pain, scarring, nerve damage, hematoma, deep vein thrombosis (DVT), long recovery periods with surgery, thrombophlebitis, vessel perforation, thermal injury to adjacent nerves, skin burns, nerve damage, discoloration

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Background – Treatments

- ▶ **Endovenous laser ablation (EVLA):** Removal or destruction of a vein or vein segment by means of laser light
- ▶ **Radiofrequency ablation (RFA):** Removal or destruction of a vein or vein segment by means of radiofrequency energy
- ▶ **Sclerotherapy:** Obliteration of a vein or vein segment by chemical introduction (liquid [LS] or foam [FS])
- ▶ **Phlebectomy:** Removal of a vein segment through small (1 to 3 millimeter) incisions with the aid of instruments
- ▶ **Ligation and stripping:** Traditional open surgical method of managing GSV and SSV varices by means of closing off a vein and removing it

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Presentation overview



- ▶ Background ✓
- ▶ Objectives ✓
- ▶ Methods
- ▶ Search Results and Findings
- ▶ Practice Guidelines and Payer Policies
- ▶ Overall Summary and Discussion

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Objectives

▶ Policy Context

- Treatments for varicose veins represent an area of substantial utilization in plans managed by the Washington State agencies
- A variety of treatments are available offering potential benefits such as reducing pain or discomfort and improving appearance
- Concerns: Uncertainty about safety, efficacy, and value of treatment options compared with traditional open surgery
- An evidence-based assessment of the comparative effectiveness, safety, and cost is warranted to guide coverage policy

▶ Key Questions

1. Effectiveness
2. Safety
3. Varying effectiveness and safety for subgroups
4. Cost implications

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Presentation overview



- ▶ Background ✓
- ▶ Objectives ✓
- ▶ Methods ✓
- ▶ Search Results and Findings
- ▶ Practice Guidelines and Payer Policies
- ▶ Overall Summary and Discussion

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Methods: PICOS

▶ PICOS

- **Population:** Adult patients being treated for varicose veins
- **Interventions:** EVLA, endovascular RFA, sclerotherapy (i.e., liquid or foam chemical ablation), ambulatory phlebectomy (i.e., stab phlebectomy or microphlebectomy)
- **Comparisons:** Vein ligation with or without stripping

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Methods: PICOS

▶ PICOS cont'd

- **Outcomes:**
 - Clinical outcomes (e.g., failure of procedure, recurrence, changes in symptoms)
 - Patient-centered outcomes (e.g., QOL, time to return to activities, pain)
 - AVVSS, SF-36, EQ-5D, EurQOL, CIVIQ, others
 - Adverse events (e.g., deep vein thrombosis [DVT], pulmonary embolism [PE], nerve damage, bleeding, infection)
 - Cost/cost-effectiveness
- **Study designs:** Systematic reviews, randomized controlled trials (RCTs), observational studies with $n > 500$ for KQ#2, modelling for KQ#4

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Methods: Literature Search

▶ Systematic reviews

- Databases searched: PubMed, Centre for Reviews and Dissemination (CRD), Canadian Agency for Technology and Health (CADTH), Cochrane Library, National Health Service – National Institute for Health Research (NIH–NIHR), National Institute for Health and Care Excellence (NICE); last search date March 6, 2017
- Exclusion criteria: Older reviews that have been updated or superseded by more recent reviews, no meta-analyses

▶ Primary data

- Databases searched: PubMed, Embase, manual searches of key sources; last search date March 9, 2017
- Exclusion criteria: Ineligible PICOS; data from publication already included in a selected systematic review

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Quality Assessment Aligns with GRADE System (Appendix III)

▶ Individual study appraisal

- *Are the findings valid?*
 - Study design, execution, and analysis (checklist)
 - Internal validity (minimization of bias)
 - *Good–Fair–Poor–Very Poor*

▶ Evaluation of **body of evidence** for each outcome

- *How **confident** are we that this evidence answers the Key Question?*
 - Domains:
 - Study design and weaknesses
 - Quantity/precision of data
 - Publication bias
 - Applicability to PICOS
 - Consistency of study findings
 - *High–Moderate–Low–Very Low*

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Presentation overview

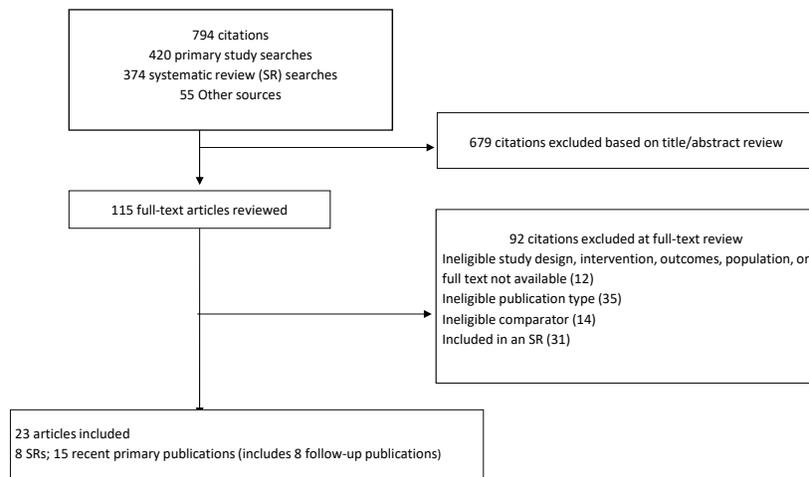


- ▶ Background ✓
- ▶ Objectives ✓
- ▶ Methods ✓
- ▶ Search Results and Findings ✓
- ▶ Practice Guidelines and Payer Policies
- ▶ Overall Summary and Discussion

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Search Results



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Study Characteristics

Systematic reviews (n=8)

Author (year), Funding Source	# Studies	Population
Carroll et al. (2013), NHS-NIHR HTA program (UK)	34 RCTs* <i>EVLA vs surgery (8)</i> <i>RFA vs surgery (6)</i> <i>FS vs surgery (10)</i>	Adults aged ≥ 16 yrs being tx'd for varicose veins
Nesbitt et al. (2014) [Cochrane Review], none	13 RCTs <i>EVLA vs surgery (8)</i> <i>RFA vs surgery (5)</i> <i>FS vs surgery (3)</i>	Men and women any age w/ varicose veins affecting the GSV system
Paravastu et al. (2016) [Cochrane Review], none	3 RCTs <i>EVLA vs surgery (2)</i> <i>RFA vs surgery (0)</i> <i>FS vs surgery (1)</i>	Men and women aged ≥ 18 yrs who received tx for SSV varices
Pan et al. (2014), NR	10 RCTs, 3 nonrandomized trials <i>EVLA vs surgery (13)</i>	Pts being tx'd for varicose veins

*Some of these studies compared the interventions of interest with treatments other than surgery and are not listed in this table.

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Study Characteristics

Systematic reviews (n=8), cont'd

Author (year), Funding Source	# Studies	Population
Rathbun et al. (2012), American College of Phlebology Foundation	104* (20 RCTs, 82 observational studies, 2 not classified) <i>FS vs surgery: A list of studies included in analyses was not provided</i>	Pts aged ≥ 19 yrs being tx'd for varicose veins, congenital venous malformations, or venous ulcers
Rigby et al. (2009), [Cochrane Review] Sheffield Vascular Institute, UK; NHS R&D HTA Programme, UK	9 RCTs <i>Sclerotherapy vs surgery (9)</i>	Pts being tx'd for cosmesis and/or symptomatic varicose veins
O'Donnell et al. (2016), none	7 RCTs <i>EVLA vs surgery or cryostripping (4)</i> <i>RFA vs surgery (3)</i>	Pts tx'd w/ EVA (EVLA or RFA) for GSV incompetence
Dermody et al. (2013), none	17 RCTs* <i>EVLA vs surgery (7)</i> <i>RFA vs surgery (5)</i>	EVLA/RFA/L&S to treat GSV incompetence

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Study Characteristics

Primary data (n=15)

- ▶ 8 follow-up publications
- ▶ 9 compared EVLA with surgery
- ▶ 5 compared sclerotherapy with surgery
- ▶ 1 compared RFA with surgery
- ▶ 2 U.S.-based cost studies
- ▶ Inclusion criteria: level of detail provided varied; some studies specified location of reflux and/or presence of symptoms, diameter or length of varicosity, CEAP classification
- ▶ Exclusion criteria: included but not limited to – previous surgical or other interventional tx, pregnancy, DVT, contraindications, deep vein insufficiency, veins unsuitable for technique, arterial disease

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Comparison # Studies, Quality	KQ#1 Results – Technical Failure
EVLA vs Surgery 4 GQ SRs Overall: Moderate Reduced w/ EVLA or similar	Carroll, 2013 (n=12 studies) <ul style="list-style-type: none"> • Pooled percentage: EVLA 1% (5/467); S/L 3% (20/681); <i>P</i>=NR Nesbitt, 2014 (n=6 studies) <ul style="list-style-type: none"> • OR=0.29 (95% CI, 0.14–0.60); <i>P</i>=0.0009 Paravastu, 2016 (n=3 studies) <ul style="list-style-type: none"> • OR=0.07 (95% CI, 0.02–0.22); <i>P</i><0.00001 Pan, 2014 (n=9 studies) <ul style="list-style-type: none"> • Pooled percentage (1–12 wks): EVLA 97.3%; HL&S 97.6%; <i>P</i>=NS • MA: RR=1.1 (95% CI, 0.62–1.397); <i>P</i>=0.72
RFA vs Surgery 2 GQ SRs Overall: Low No difference	Carroll, 2013 (n=12 studies) <ul style="list-style-type: none"> • Pooled percentage: RFA 4% (16/431); S/L 3% (20/681); <i>P</i>=NR Nesbitt, 2014 (n=5 studies) <ul style="list-style-type: none"> • OR=0.82 (95% CI, 0.07–10.10); <i>P</i>=0.88
Sclerotherapy vs Surgery 4 GQ SRs Overall: Low No difference	Carroll, 2013 (n=12 studies) <ul style="list-style-type: none"> • Pooled percentage: FS 7% (7/295); S/L 3% (20/681); <i>P</i>=NR Nesbitt, 2014 (n=2 studies) <ul style="list-style-type: none"> • OR=0.44 (95% CI, 0.12–1.57); <i>P</i>=0.20 Paravastu, 2016 (1 study) <ul style="list-style-type: none"> • OR=0.34 (95% CI, 0.06–2.10); <i>P</i>=0.25 Rathbun, 2012 (6 studies) <ul style="list-style-type: none"> • Anatomical closure (6 studies): RR=0.92 (95% CI, 0.86–0.97); <i>P</i>=0.0036 • Residual SF incompetence (4 studies): RR=0.92 (95% CI, 0.56–1.51); <i>P</i>=0.73

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Comparison # Studies, Quality	KQ#1 Results – Technical Recurrence
<p>EVLA vs Surgery 5 GQ SRs, 3 FQ RCTs, 1 PQ RCT</p> <p>Overall: Moderate No difference</p>	<p>Carroll, 2013 (n=23 studies, network MA)</p> <ul style="list-style-type: none"> 2 yr HR=0.84 (95% CrI, 0.44–1.81); 1 yr HR=0.77 (95% CrI, 0.37–1.54); 6 mo HR=0.70 (95% CrI, 0.27–1.45) <p>Nesbitt, 2014 (n=7 studies)</p> <ul style="list-style-type: none"> OR=0.72 (95% CI, 0.43–1.22); P=0.22 <p>Paravastu, 2016 (n=1 & 2 studies)</p> <ul style="list-style-type: none"> 1 yr OR=0.24 (95% CI, 0.07–0.77); P=0.016; 2 yr OR=0.43 (95% CI, 0.16–1.15); P=0.09 <p>Pan, 2014 (n=5 & 6 studies)</p> <ul style="list-style-type: none"> 1 yr RR=0.65 (95% CI, 0.41–1.02); P=0.06; 2 yr RR=0.65 (95% CI, 0.37–1.12); P=0.12 <p>O'Donnell, 2016</p> <ul style="list-style-type: none"> Pooled percentage: EVLA (4 studies), 12.5% (95% CI, 8.9–16.5); RFA (3 studies), 12.4% (95% CI, 7.3–18.6); L/S (5 studies), 7.2% (95% CI, 4.4–10.6); P=0.32 for EVLA and RFA combined compared w/ L&S <p>van der Velden, 2015 (n=135 pts; 147 legs at 5 yrs)</p> <ul style="list-style-type: none"> EVLA 23%; surgery 14.5%; P=NR <p>Gauw, 2016 (n=112 pts at 5 yrs)</p> <ul style="list-style-type: none"> EVLA 49%; SFL&S, 23%; log-rank test; P=0.02 <p>Kalteis, 2015 (n=72 at 5 yrs)</p> <ul style="list-style-type: none"> No recurrence HL+EVLA 43%; HL&S 67%; P=0.049 <p>Mozafar, 2014 (n=65)</p> <ul style="list-style-type: none"> 12 mos: 6.7% EVLA; 11.7% HL; P=NR

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Comparison # Studies, Quality	KQ#1 Results – Technical Recurrence cont'd
<p>RFA vs Surgery 2 GQ SRs</p> <p>Overall: Low No difference</p>	<p>Carroll, 2013 (n=23 studies, network MA)</p> <ul style="list-style-type: none"> 2 yr HR=0.94 (95% CrI, 0.42–2.51); 1 yr HR=0.93 (95% CrI, 0.42–2.22); 6 mo HR=0.92 (95% CrI, 0.39–2.11) <p>Nesbitt, 2014 (n=4 studies)</p> <ul style="list-style-type: none"> OR=0.82 (95% CI, 0.49–1.39)
<p>Sclerotherapy vs Surgery 4 GQ SRs, 2 FQ RCTs</p> <p>Overall: Low No difference</p>	<p>Carroll, 2013 (n=23 studies, network MA)</p> <ul style="list-style-type: none"> 2 yr HR=0.92 (95% CrI, 0.43–1.60); 1 yr HR=1.02 (95% CrI, 0.49–1.84); 6 mo HR=1.12 (95% CrI, 0.53–2.27) <p>Nesbitt, 2014 (n=3 studies)</p> <ul style="list-style-type: none"> OR=1.74 (95% CI, 0.97–3.12); P=0.06 <p>Paravastu, 2016 (1 study)</p> <ul style="list-style-type: none"> OR=1.19 (95% CI, 0.29–4.92); P=NR <p>Rigby, 2009 (5 studies)</p> <ul style="list-style-type: none"> Benefit w/ sclerotherapy at 1 yr, then favoring surgery or no difference at 2, 3, and 5 yrs <p>van der Velden, 2015 (n=146 legs at 5 yrs)</p> <ul style="list-style-type: none"> Recurrence at 5 yrs: FS 77%; surgery 14.5%; P<0.001 <p>Michaels, 2006 (n=77 randomized, 52 at 1 yr)</p> <ul style="list-style-type: none"> No difference at 1, 2, or 3 yrs

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Comparison # Studies, Quality	KQ#1 Results – Symptomatic Recurrence
EVLA vs Surgery 5 GQ SRs, 4 FQ RCTs Overall: Moderate No difference	<p>Carroll, 2013 (n=3 studies)</p> <ul style="list-style-type: none"> Differences between grps NS <p>Nesbitt, 2014 (n=3 studies)</p> <ul style="list-style-type: none"> OR=0.87 (95% CI, 0.47–1.62); <i>P</i>=0.67 <p>Paravastu, 2016 (n=1 study)</p> <ul style="list-style-type: none"> OR=0.54 (95% CI, 0.17 to 1.75); <i>P</i>=NR <p>Pan, 2014 (n=5 & 6 studies)</p> <ul style="list-style-type: none"> 1 yr RR=0.83 (95% CI, 0.39–1.77); <i>P</i>=0.63; 2 yr RR=0.85 (95% CI, 0.64–1.11); <i>P</i>=0.23 <p>O'Donnell, 2016</p> <ul style="list-style-type: none"> EVLA (5 studies): 20.6% (95% CI, 17.0–24.3); RFA (3 studies): 21.4% (95% CI, 14.8–28.8); surgery (6 studies): 19.2% (95% CI, 15.5–23.2); <i>P</i>=0.98 for EVLA and RFA combined compared w/ surgery <p>Rass, 2015 (RELACS) (n=281 legs at 5 yrs)</p> <ul style="list-style-type: none"> EVLA 45%; HL/S 54%; <i>P</i>=0.152 <p>Flessenkamper, 2016 (n=81 pts at 72 mos)</p> <ul style="list-style-type: none"> No difference in time to clinical recurrence w/in 6-yr f/u; <i>P</i>=0.5479 <p>Kalteis, 2015 (n=72 at 5 yrs)</p> <ul style="list-style-type: none"> Visible recurrence: HL+EVLA 40%; HL/S 55%; <i>P</i>=NR <p>Gauw, 2016 (n=112 pts at 5 yrs)</p> <ul style="list-style-type: none"> Clinical recurrence at 5 yrs: 33% EVLA, 17% SFL&S; <i>P</i>=0.04

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Comparison # Studies, Quality	KQ#1 Results – Symptomatic Recurrence cont'd
RFA vs Surgery 2 GQ SRs Overall: Low No difference	<p>Carroll, 2013 (n=2 studies)</p> <ul style="list-style-type: none"> Differences between grps NS <p>Nesbitt, 2014 (n=1 study)</p> <ul style="list-style-type: none"> OR=2.00 (95% CI, 0.30–13.26); <i>P</i>=NR
Sclerotherapy vs Surgery 1 GQ SRs, 2 FQ RCTs Overall: Very low Mixed	<p>Nesbitt, 2014 (n=1 study)</p> <ul style="list-style-type: none"> OR=1.28 (95% CI, 0.66–2.49); <i>P</i>=NR <p>Michaels, 2006 (n=77 randomized, 52 at 1 yr)</p> <ul style="list-style-type: none"> At 1 yr, no visible varicosities in 76% of surgery grp vs 39% of L&S grp (<i>P</i><0.05) <p>Rasmussen, 2013b (n=247 pts; 284 legs at 3 yrs)</p> <ul style="list-style-type: none"> Recurrence, n (Kaplan–Meier estimate): UGFS 20 (19.1%); surgery 22 (20.2%); <i>P</i>=NS

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Comparison # Studies, Quality	KQ#1 Results – Change in Symptom Severity
EVLA vs Surgery 1 GQ SR, 3 FQ RCTs, 1 PQ RCT Overall: Low No difference	Carroll, 2013 (n=6 studies, network MA) <ul style="list-style-type: none"> VCSS, MD=-0.10 (95% CrI, -0.94 to 0.73) van der Velden, 2015 (n=135 pts; 147 legs) <ul style="list-style-type: none"> Distribution of class C: EVLA OR=1.3 (95% CI, 1.1-1.5); surgery OR=1.4 (95% CI, 1.2-1.6); P=NS Rasmussen, 2013 (n=247 pts; 284 legs at 3 yrs) <ul style="list-style-type: none"> VCSS, mean (SD): EVLA 0.34 (1.3); surgery 0.3 (0.5); P=NS Rass, 2015 (n=281 legs at 5 yrs) <ul style="list-style-type: none"> HVVSS: EVLA 3.00±2.87; HL&S 3.16±3.48; P=0.789 Mozafar, 2014 (n=65) <ul style="list-style-type: none"> AVVSS: Lower in EVLA than HL at 12 mos (P=0.019) and 18 mos (P=0.008)
RFA vs Surgery 2 GQ SRs, 1 FQ RCT Overall: Low No difference	Carroll, 2013 (n=6 studies, network MA) <ul style="list-style-type: none"> VCSS, MD=0.15 (95% CrI, -0.50 to 0.95) Nesbitt, 2014 (3 studies) <ul style="list-style-type: none"> No overall differences between grps Rasmussen, 2013b (n=247 pts; 287 legs at 3 yrs) <ul style="list-style-type: none"> VCSS, mean (SD): RFA 0.44 (1.82); surgery 0.3 (0.5)

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Comparison # Studies, Quality	KQ#1 Results – Change in Symptom Severity cont'd
Sclerotherapy vs Surgery 2 GQ SRs, 3 FQ RCTs Overall: Very low Mixed	Carroll, 2013 (n=6 studies, network MA) <ul style="list-style-type: none"> VCSS, MD=-1.63 (95% CrI, -2.90 to -0.42) Nesbitt, 2014 (2 studies) <ul style="list-style-type: none"> No difference Rasmussen, 2013b (n=247 pts; 284 legs at 3 yrs) <ul style="list-style-type: none"> VCSS, mean (SD): FS 0.15 (0.4); surgery 0.3 (0.5) van der Velden, 2015 (n=129 pts; 146 legs) <ul style="list-style-type: none"> No difference at 5 yrs in C class distribution between the tx grps Yin, 2017 (n=177) <ul style="list-style-type: none"> VCSS, median (IQR) at 6 mos: UGFS 4 (4); surgery 4 (3); P=0.869; at 12 mos: UGFS 2 (1); 3 surgery (2); P=0.006

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Comparison # Studies, Quality	KQ#1 Results – Pain
EVLA vs Surgery 4 GQ SRs Overall: Very low Mixed	Carroll, 2013 (n=9 studies, network MA) <ul style="list-style-type: none"> Pain w/in 7–14 days: MD=0.10 (95% CrI, –0.49 to 0.64) Nesbitt, 2014 <ul style="list-style-type: none"> Described results from studies measuring pain as inconclusive Paravastu, 2016 (n=2 studies) <ul style="list-style-type: none"> Mixed results Pan, 2014 (n=8 studies) <ul style="list-style-type: none"> 3 studies found > pain in HL&S grp than EVLA grp; 4 studies found no difference; 1 study reported significantly > pain in the EVLA grp
RFA vs Surgery 2 GQ SRs Overall: Moderate Benefit w/ RFA	Carroll, 2013 (n=9 studies, network MA) <ul style="list-style-type: none"> MD=–1.26 (95% CrI, –1.95 to –0.61) Nesbitt, 2014 (4 studies) <ul style="list-style-type: none"> 3 studies < pain in RFA grp ($P<0.001$); 1 study NS difference
Sclerotherapy vs Surgery 2 GQ SRs Overall: Very low No difference	Carroll, 2013 (n=9 studies, network MA) <ul style="list-style-type: none"> MD=–0.80 (95% CrI, –1.93 to 0.30) Nesbitt, 2014 (2 studies) <ul style="list-style-type: none"> 1 study, no difference; 1 study significantly < pain in FS grp ($P<0.001$)

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Comparison # Studies, Quality	KQ#1 Results – Time to Return to Work or Normal Activity
EVLA vs Surgery 4 GQ SRs, 1 FQ RCT Overall: Low Benefit w/ EVLA	Carroll, 2013 (n=6 studies) <ul style="list-style-type: none"> 1 study, < time in surgery grp; 1 study, < time in EVLA grp; 2 studies, no difference; 2 studies, $P=NR$ Nesbitt (2014) (n=6 studies) <ul style="list-style-type: none"> 6 studies summarized as generally < time for the EVLA grp Paravastu (2016) (n=2 studies) <ul style="list-style-type: none"> < time for EVLA grp Pan (2014) (n=7 studies) <ul style="list-style-type: none"> Time to return to normal activities (5 studies): No difference Time to return to work: 2 studies, < time in EVLA grp; 3 studies, no difference; 1 study, < time in surgery grp Cotton, 2016 (n=415 at 6 wks) <ul style="list-style-type: none"> BRAVVO: < time for EVLA grp for 13 of 15 behaviors
RFA vs Surgery 2 GQ SRs Overall: Low Benefit w/ RFA	Carroll, 2013 (n=4 studies) <ul style="list-style-type: none"> 1 study, $P=NS$; 3 studies, < time in RFA grp Nesbitt (2014) (n=5 studies) <ul style="list-style-type: none"> < time in RFA grp, $P=NR$

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Comparison # Studies, Quality	KQ#1 Results – Time to Return to Work or Normal Activity cont'd
Sclerotherapy vs Surgery 2 GQ SRs, 2 FQ RCTs Overall: Low Benefit w/FS	<p>Carroll, 2013 (n=3 studies)</p> <ul style="list-style-type: none"> 1 study, $P=NR$ 2 studies, < time in FS grp, $P<0.001$ <p>Nesbitt, 2014 (n=1 study)</p> <ul style="list-style-type: none"> Return to work < time in FS grp, median 2.9 vs 4.3 days, $P=NR$ Return to normal activities < time in FS grp, median 1 vs 4 days, $P=NR$ <p>Cotton, 2016 (n=473 at 6 wks)</p> <ul style="list-style-type: none"> BRAVVO: < time for UGFS grp for 13 of 15 behaviors <p>Yin, 2017 (n=177)</p> <ul style="list-style-type: none"> Avg time to return to normal activities, days (range): UGFS 5.4 (3–14); surgery 9.6 (7–18); $P<0.001$

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Comparison # Studies, Quality	KQ#1 Results – Quality of Life
EVLA vs Surgery 2 GQ SRs, 5 FQ RCTs Overall: Moderate No difference	<p>Nesbitt, 2014 (n=5 studies)</p> <ul style="list-style-type: none"> No difference <p>Paravastu, 2016</p> <ul style="list-style-type: none"> AVVQ at 6 wks (2 studies): MD=0.15 (95% CI, -1.65 to 1.95); $P=0.87$; at 1 yr (1 study): MD=-1.08 (95% CI, -3.39 to 1.23); $P=NR$ EQ-5D (2 studies): No difference <p>Rasmussen, 2013b (n=247 pts; 284 legs at 3 yrs)</p> <ul style="list-style-type: none"> AVVSS, mean (SD): EVLA 4.61 (5.8); surgery 4.0 (4.87) <p>Flessenkamper, 2014 (n=343)</p> <ul style="list-style-type: none"> FLQA-V: No difference <p>van der Velden, 2015 (n=114 pts)</p> <ul style="list-style-type: none"> CIVIQ and EQ-5D scores: No difference at 5 yrs <p>Rass, 2015 (n=281 legs at 5 yrs)</p> <ul style="list-style-type: none"> CIVIQ-2 scores: No difference Pt satisfaction: EVLA 1.28±0.51; HL&S 1.39±0.58; $P=0.078$ <p>Kalteis, 2015 (n=72 at 5 yrs)</p> <ul style="list-style-type: none"> CIVIQ-2: EVLA 94; HL&S 93; $P=NR$ Pt satisfaction: EVLA 87%; HL&S 88% rated good or very good; $P=NR$

Key to QOL scales: AVVQ, Aberdeen Varicose Veins Questionnaire; AVVSS, Aberdeen Varicose Vein Symptom Severity; CIVIQ, Chronic Venous Insufficiency Quality-of-Life Questionnaire; EQ-5D, EuroQoL Group 5-dimension Questionnaire; FLQA, Freiburg Life Quality Assessment

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Comparison # Studies, Quality	KQ#1 Results – Quality of Life
RFA vs Surgery 1 GQ SR, 1 RCT Overall: Very low Mixed	Nesbitt, 2014 (n=3 studies) <ul style="list-style-type: none"> 2 studies, no difference; 1 study reported no difference at 3 wks, then better CIVIQ-2 scores for RFA at 1 and 2 yrs Rasmussen, 2013b (n=247 pts; 287 legs at 3 yrs) <ul style="list-style-type: none"> AVVSS, mean (SD): 4.43 (6.58); surgery 4.0 (4.87)
Sclerotherapy vs Surgery 1 GQ SRs, 4 FQ RCTs Overall: Low No difference	Nesbitt, 2014 (n=3 studies) <ul style="list-style-type: none"> NS differences Michaels, 2006 (n=49 pts at 1 yr) <ul style="list-style-type: none"> SF-36 1 and 2 yrs: No difference EQ-5D mean (SD) 1 yr: L&S 0.80 (0.14); surgery 0.85 (0.20); $P<0.05$; 2 yrs: L&S 0.74 (0.11); surgery 0.84 (0.32); $P=NS$ EuroQOL VAS mean (SD) 1 yr: LS 0.77 (0.18); surgery 0.83 (0.14); $P<0.05$; 2 yrs: LS 0.77 (0.13); surgery 0.83 (0.13); $P=NS$ Rasmussen, 2013b (n=247 pts; 284 legs at 3 yrs) <ul style="list-style-type: none"> AVVSS, mean (SD): 4.76 (5.71), surgery 4.0 (4.87) van der Velden, 2015 (n=111) <ul style="list-style-type: none"> CIVIQ: FS 0.98 (95% CI, 0.16–1.79); surgery 0.44 (95% CI, –0.41 to 1.29); $P=NR$ EQ-5D: FS 0.01 (95% CI, 0.01–0.02); surgery 0.02 (95% CI, 0.01–0.02); $P=NR$ Yin, 2017 (n=177) <ul style="list-style-type: none"> AVVQ: No difference at 6 or 12 mos Pt satisfaction (12 mos): UGFS 92.3%; surgery 86.5%; $P=NS$

Key to QOL scales: AVVSS, Aberdeen Varicose Vein Symptom Severity; AVVQ, Aberdeen Varicose Veins Questionnaire; CIVIQ, Chronic Venous Insufficiency Quality-of-Life Questionnaire; EQ-5D, EuroQoL Group 5-dimension Questionnaire; FLQA, Freiburg Life Quality Assessment; SF-36, SF-36 Health Survey

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Comparison # Studies, Quality	KQ#1 Results – Reintervention
EVLA vs Surgery 3 GQ SRs, 3 FQ RCTs Overall: Low No difference	Nesbitt, 2014 (n=2 studies) <ul style="list-style-type: none"> Reintervention due to technical failure: EVLA 13%; surgery 8.8%; $P=NR$; EVLA 3.5%; 1.4% surgery; $P=NR$ Paravastu, 2016 (n=1 study) <ul style="list-style-type: none"> Reintervention due to technical failure: EVLA 4 pts; surgery 3 pts; $P=NR$ O'Donnell, 2016 <ul style="list-style-type: none"> Pooled percentages, EVLA (5 studies) 27.2% (95% CI, 23.3–31.3); RFA (1 study) 16.2% (95% CI, 10.4–35.9); surgery (4 studies): 17.3% (95% CI, 13.6–21.4); $P=0.74$ for EVLA and RFA combined vs surgery van der Velden, 2015 (n=135 pts; 147 legs) <ul style="list-style-type: none"> Reintervention at 5 yrs: 10% in EVLA and surgery grps Rass, 2015 (n=281 legs at 5 yrs) <ul style="list-style-type: none"> Types of reintervention for recurrence (n=69 EVLA; n=70 HL/S): "Wait and see" – EVLA 49%; HL/S 67%; $P=0.040$ Gauw, 2016 (n=121 legs at 5 yrs) <ul style="list-style-type: none"> Did not receive reintervention: EVLA 70%; SF/L 80%; $P=0.20$

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Comparison # Studies, Quality	KQ#1 Results – Reintervention cont'd
RFA vs Surgery 2 GQ SRs Overall: Very low CND	Nesbitt, 2014 (n=2 studies) <ul style="list-style-type: none"> Reintervention due to technical failure: RFA 0%; surgery 7.4%; <i>P</i>=NR; RFA 13.3%; 15.4% surgery; <i>P</i>=NR O'Donnell, 2016 <ul style="list-style-type: none"> Reoperation pooled percentages: EVLA (5 studies) 27.2% (95% CI, 23.3–31.3); RFA (1 study): 16.2% (95% CI, 10.4–35.9); surgery (4 studies): 17.3% (95% CI, 13.6–21.4); <i>P</i>=0.74 for EVLA and RFA combined vs surgery
Sclerotherapy vs Surgery 1 GQ SRs, 3 FQ RCTs Overall: Very low CND	Nesbitt, 2014 (n=2 studies) <ul style="list-style-type: none"> Reintervention due to technical failure: FS 18.8%; surgery 5.6%; <i>P</i>=NR; FS 3.5%; no data for surgery grp; <i>P</i>=NR Rasmussen, 2013b (n=247 pts; 284 legs at 3 yrs) <ul style="list-style-type: none"> Retreatment, n (Kaplan–Meier estimate): UGFS 37 (31.6%); surgery 18 (15.5%); <i>P</i><0.0001 van der Velden, 2015 (129 pts; 146 legs at 5 yrs) <ul style="list-style-type: none"> FS 32%; surgery 10% (limbs); log rank test; <i>P</i><0.001 Yin, 2017 (n=177) <ul style="list-style-type: none"> Reintervention due to technical failure: UGFS 29; surgery 34; <i>P</i>=0.506

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Comparison # Studies	KQ#2 Results – DVT and PE
EVLA vs Surgery 4 GQ SRs, 1 PQ RCT, 2 FQ obs	Carroll, 2013; Dermody, 2013; Pan, 2014; Paravastu, 2016 <ul style="list-style-type: none"> 4 SRs report low rates of DVT and PE and NS differences between grps Mozafar, 2014 (n=65) <ul style="list-style-type: none"> 0 DVT events in both grps Carruthers, 2014 (n=4366 pts) <ul style="list-style-type: none"> 50% decrease in odds of DVT after surgery vs EVA (EVLA and RFA pts combined); adjusted OR=0.52 (95% CI, 0.28–0.97); <i>P</i>=0.040; 21 (0.8%) DVT events in the open surgery grp vs 28 (1.6%) events in the EVA grp; <i>P</i>=0.027 O'Donnell, 2015 (n=131,887) <ul style="list-style-type: none"> DVT w/in 30 days of EVLA was 701 of 22,980 (3.05%) compared w/ 277 of 11,529 (2.40%) w/in 30 days of surgery for varicose veins (<i>P</i>=NR) PE w/in 30 days of EVLA was 58 of 22,980 (0.25%) and was 33 of 11,529 (0.29%) w/in 30 days of surgery (<i>P</i>=NR)

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Comparison # Studies	KQ#2 Results – DVT and PE cont'd
RFA vs Surgery 2 GQ SRs, 1 FQ obs	<p>Carroll, 2013; Dermody, 2013</p> <ul style="list-style-type: none"> 2 SRs report low rates of DVT and PE and NS differences between grps <p>Carruthers, 2014 (n=4366 pts)</p> <ul style="list-style-type: none"> 50% decrease in odds of DVT after surgery vs EVA (EVLA and RFA pts combined); adjusted OR=0.52 (95% CI, 0.28–0.97); <i>P</i>=0.040; 21 (0.8%) DVT events in the open surgery grp vs 28 (1.6%) events in the EVA grp; <i>P</i>=0.027 <p>O'Donnell, 2015 (n=131,887)</p> <ul style="list-style-type: none"> DVT w/in 30 days of RFA was 954 of 21,637 (4.41%) compared w/ 277 of 11,529 (2.40%) w/in 30 days of surgery for varicose veins (<i>P</i>=NR) PE w/in 30 days of RFA was 68 of 21,637 (0.31%) and was 33 of 11,529 (0.29%) w/in 30 days of surgery (<i>P</i>=NR)
Sclerotherapy vs Surgery 2 GQ SRs, 1 FQ RCT; 1 FQ obs	<p>Carroll, 2013; Rathbun, 2012</p> <ul style="list-style-type: none"> 1 SR found 13 DVTs after FS and 1 after surgery across 3 studies; 1 SR found NS difference <p>Yin, 2017 (n=177)</p> <ul style="list-style-type: none"> 2 DVT events in surgery grp and 1 in FS grp (<i>P</i>=NR), 0 PE events <p>O'Donnell, 2015 (n=131,887)</p> <ul style="list-style-type: none"> DVT w/in 30 days of sclerotherapy was 104 of 12,708 (0.82%) compared w/ 277 of 11,529 (2.40%) w/in 30 days of surgery (<i>P</i>=NR) PE w/in 30 days of sclerotherapy was 19 of 12,708 (0.15%) and was 33 of 11,529 (0.29%) w/in 30 days of surgery (<i>P</i>=NR)

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Comparison # Studies	KQ#2 Results – Nerve Damage
EVLA vs Surgery 4 GQ SRs, 1 FQ RCT	<p>Carroll, 2013; Dermody, 2013; Pan, 2014; Paravastu, 2016</p> <ul style="list-style-type: none"> 4 SRs suggest better outcomes w/ EVLA <p>Gauw, 2016 (n=121 at 5 yrs)</p> <ul style="list-style-type: none"> 1 (2%) occurrence of persistent neurosensory deficit in surgery grp at 5 yrs and none in the EVLA grp
RFA vs Surgery 2 GQ SRs	<p>Carroll, 2013; Dermody, 2013</p> <ul style="list-style-type: none"> 2 SRs provide mixed results from RCTs
Sclerotherapy vs Surgery 2 GQ SRs, 1 FQ RCT	<p>Carroll, 2013; Nesbitt, 2014</p> <ul style="list-style-type: none"> 15 of 363 (4.1%) cases of nerve damage in the surgery grps compared w/ 3 of 418 (0.7%) in the FS grps from 3 studies; <i>P</i>=NR <p>Yin, 2017 (n=177)</p> <ul style="list-style-type: none"> 9 pts w/ paresthesia after surgery vs 0 after FS; <i>P</i>=NR

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Comparison # Studies	KQ#2 Results – Infection
EVLA vs Surgery 4 GQ SRs, 1 FQ obs	<p>Carroll, 2013; Dermody, 2013; Pan, 2014; Paravastu, 2016</p> <ul style="list-style-type: none"> 4 SRs suggest better outcomes w/ EVLA Pooled incidence of infection: L&S 2.1% (95% CI, 1.3–3.1) vs 12 EVLA 0.7% (95% CI, 0.3–1.3); $P=0.006$ 2 MAs: OR=0.24 (95% CI, 0.10–0.58); $I^2=0\%$; RR=0.28 (95% CI, 0.11–0.70); $I^2=0\%$ <p>Carruthers, 2014 (n=4366)</p> <ul style="list-style-type: none"> Increased odds of infection after surgery compared w/ EVA adjusted OR=2.56 (95% CI, 1.19–5.50); $P=0.016$ (EVLA and RFA pts were combined for this analysis)
RFA vs Surgery 2 GQ SRs, 1 FQ obs	<p>Carroll, 2013; Dermody, 2013</p> <ul style="list-style-type: none"> Pooled incidence of infection: L&S 2.1% (95% CI, 1.3–3.1) vs RFA 1.0% (95% CI, 0.3–2.0); $P=0.094$ <p>Carruthers, 2014 (n=4366)</p> <ul style="list-style-type: none"> Increased odds of infection after surgery compared w/ EVA adjusted OR=2.56 (95% CI, 1.19–5.50); $P=0.016$ (EVLA and RFA pts were combined for this analysis)
Sclerotherapy vs Surgery 1 GQ SR, 1 FQ RCT	<p>Carroll, 2013</p> <ul style="list-style-type: none"> 1 SR (1 study) higher infection rate in FS grp; $P=NR$ <p>Yin, 2017 (n=177)</p> <ul style="list-style-type: none"> Surgery 5 vs FS 0; $P=NR$

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Comparison # Studies	KQ#2 Results – Other Complications
EVLA vs Surgery 4 GQ SRs, 1 FQ RCT, 1 PQ RCT	<p>Carroll, 2013; Dermody, 2013; Pan, 2014; Paravastu, 2016</p> <ul style="list-style-type: none"> 4 SRs suggest similar or better outcomes w/ EVLA <p>Mozafar, 2014 (n=65)</p> <ul style="list-style-type: none"> Bruising: HL&S 12 (34.3%) vs EVLA 5 (16.7%); $P=NS$; dysesthesia at 18 mos HL&S 3 (8.6%) vs EVLA 2 (6.7%); $P=NS$; skin discoloration; $P=NS$ <p>Rass, 2015 (RELACS trial) (n=281 at 5 yrs)</p> <ul style="list-style-type: none"> Dysesthesia at 5 yrs EVLA 3% vs HL&S 2%; $P=NS$; hyperpigmentation at 5 yrs EVLA 0%, HL/S 1%; $P=NS$
RFA vs Surgery 2 GQ SRs	<p>Carroll, 2013; Dermody, 2013</p> <ul style="list-style-type: none"> 2 SRs suggest lower rates of bruising and hematoma and higher rates of superficial thrombosis and phlebitis after RFA
Sclerotherapy vs Surgery 2 GQ SRs, 1 FQ RCT	<p>Carroll, 2013; Nesbitt, 2014; Rathbun, 2012</p> <ul style="list-style-type: none"> 3 SRs suggest lower rates of bruising and hematoma and higher rates of phlebitis after FS, similar rates of skin discoloration <p>Yin, 2017 (n=177)</p> <ul style="list-style-type: none"> Minor complications: FS 27.7% vs HL&S 21.6%; $P=0.406$; major complications: FS, 3.1% vs HL&S, 2.7%; $P=0.897$; 0 hematoma in FS grp and 5 in surgery grp; pts w/ pain needing oral analgesics (n=5), saccular thrombophlebitis (n=10), and hyperpigmentation (n=3) were reported in the FS grp; none of these events were reported in the surgery grp

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# Studies	KQ#3 Results – Subgroup Analyses
4 GQ SRs; 1 FQ RCT	<p>Dermody, 2013; Nesbitt, 2014; O'Donnell, 2016; Paravastu, 2016;</p> <ul style="list-style-type: none"> 4 SRs described in KQ#1 and KQ#2 focused specifically on varicosities of either the GSV or SSV <p>Yin, 2017</p> <ul style="list-style-type: none"> 1 recent RCT enrolled only pts w/ severe lower extremity varicosis (C₄-C₆)
0	<ul style="list-style-type: none"> No studies were identified that reported comparative subgroup analyses by previous tx, ethnicity, comorbidities, or other clinical history or pt characteristics

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# Studies	KQ#4 Results – Cost
3 SRs	<p>Carroll, 2013</p> <ul style="list-style-type: none"> 2 economic analyses conducted along w/ RCTs, and 2 modelling studies Differences in costs and benefits between txs are small and sensitive to assumptions; cost-effectiveness of the different procedures in relation to each other is likely to be uncertain and vary by local costs <p>Nesbitt, 2014</p> <ul style="list-style-type: none"> 2 studies FS vs surgery; decreased costs w/ FS 2 studies EVLA vs surgery; slightly higher costs w/ EVLA 3 studies RFA vs surgery; procedural costs were similar for both tx grps; 1 study reported slightly higher costs w/ RFA and 2 reported slightly higher costs w/ surgery Overall, costs varied, and no study reported estimates of costs of additional procedures for residual or recurrent varices <p>Rigby, 2009</p> <ul style="list-style-type: none"> Data on cost-effectiveness were not adequately reported or were outdated Sclerotherapy was cheaper in terms of cost to the hospital and to the pt, measured in terms of money and days off work
2 U.S.-based cost analyses	<p>Eidson, 2011 and Lin, 2014</p> <ul style="list-style-type: none"> Minimally invasive txs were associated w/ lower costs than surgery 1 study compared average direct costs 1 study calculated costs per case and net profit/loss Studies examined different tx settings

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Presentation overview



- ▶ Background ✓
- ▶ Objectives ✓
- ▶ Methods ✓
- ▶ Search Results and Findings ✓
- ▶ Practice Guidelines and Payer Policies ✓
- ▶ Overall Summary and Discussion

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Practice Guidelines

- ▶ Generally recommend EVLA or RFA over surgery unless endovenous thermal ablation is not appropriate for the patient.
- ▶ Sclerotherapy and phlebectomy are also recommended in some clinical situations but not always as a first choice of treatment.
- ▶ Endovenous treatments are not recommended during pregnancy.
- ▶ Phlebectomy is often considered as a concomitant treatment along with other techniques.

8 Practice Guidelines

ACR Appropriateness Criteria: Radiologic management of lower-extremity venous insufficiency (2012)

Recommendations state that EVLA or RFA is “usually appropriate” in several specific clinical situations described, and “usually not appropriate” during pregnancy. Surgical vein stripping and injection sclerotherapy were classified as “may be appropriate” for the same clinical scenarios, except pregnancy, for which these were also rated as “not usually appropriate.”

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8 Practice Guidelines cont'd	
<i>Society for Vascular Surgery (SVS) and the American Venous Forum (AVF): the care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines (2011)</i>	The 2011 clinical practice guidelines of the SVS and AVF Venous Guideline Committee recommend EVLA, RFA, and FS as effective alternatives to stripping and other modalities.
<i>Management of venous leg ulcers: clinical practice guidelines of the Society for Vascular Surgery (SVS) and the American Venous Forum (AVF): (2014)</i>	The 2014 GLs on management of venous leg ulcers aim to address the twofold goal of venous leg ulcer treatment, which includes ulcer healing and prevention of ulcer recurrence. The GL authors note that, in general, they found the quality of the available evidence for operative or endovascular management was largely limited to level "C" because of a lack of RCTs evaluating treatment techniques. The GLs generally, with a few exceptions, suggest or recommend the use of ablation followed by compression for specific types of venous incompetence and reflux occurring with venous leg ulcers.
<i>Diagnosis and management of varicose veins in the legs: National Institute for Health and Care Excellence (NICE) guideline (National Clinical Guideline Centre, 2013)</i>	The NICE recommended a treatment hierarchy for confirmed varicose veins and truncal reflux: RFA/EVLA > UGFS > surgery. During pregnancy, consideration should be given to compression hosiery instead of interventional treatment (except in exceptional circumstances).

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8 Practice Guidelines cont'd	
<i>Management of chronic venous disease: clinical practice guidelines of the European Society for Vascular Surgery (ESVS) (2015)</i>	<ul style="list-style-type: none"> • Recommends against sclerotherapy for first-choice treatment except in elderly and frail patients with venous ulcers; sclerotherapy is recommended as a second-choice treatment for some CEAP classifications or for more advanced stages of CVD for patients not eligible for surgery or endovascular ablation. • Recommends endovenous thermal ablation techniques in preference to surgery and sclerotherapy for patients with GSV reflux, and endovenous thermal ablation should be considered for patients with SSV reflux. • Recommends surgical treatment for noncomplicated varicose veins instead of conservative treatment; when surgical treatment is performed, high ligation and stripping is recommended instead of high ligation alone; surgical stripping of the saphenous vein without high ligation leaving a 2 centimeter stump may be considered. • Concomitant phlebectomies should be considered when performing endovenous thermal ablation for truncal reflux; ambulatory phlebectomy should be considered to treat tributary varicose veins. • EVLA, RFA, UGFS, or phlebectomies should be considered for treating recurrent varicose veins; extensive redo surgery is not recommended as first choice for patients with recurrent varicose veins.

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8 Practice Guidelines cont'd	
<i>American College of Phlebology Guidelines – treatment of refluxing accessory saphenous veins (Gibson et al., 2016)</i>	The group's recommendation is that patients with symptomatic incompetence of the accessory GSV be treated with endovenous thermal ablation (EVLA or RFA) or with UGFS to reduce symptoms.
<i>Performance of endovenous foam sclerotherapy in the USA for the treatment of venous disorders: ACP/SVM/AVF/SIR quality improvement guidelines (2014)</i>	The GLs state that endovenous FS is effective for treating primary and recurrent GSV, SSV, and accessory varicose veins. However, no RCTs were available for assessment and the group could not draw conclusions about the comparative efficacy or safety of FS and endovenous thermal ablation.
<i>Treatment of superficial venous disease of the lower leg (ACP, 2014)</i>	<ul style="list-style-type: none"> • Generally recommend EVLA or RFA as preferred treatment instead of surgery, except when veins are not amenable to endovenous procedures; recommends against compression therapy as a prerequisite for symptomatic venous disease when treatments such as endovenous ablation are appropriate. • Recommends treating visible symptomatic tributary veins with stab phlebectomy, LS, or FS; non-visible symptomatic tributary veins should be treated with UGFS or FS.

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Payer Policies

- ▶ Information about coverage policies was sought from these 5 payer organizations: **Aetna, Centers for Medicare & Medicaid Services (CMS), Group Health Cooperative, Oregon Health Evidence Review Commission (HERC), and Regence Group.**
- ▶ Only the Oregon HERC did not have a published coverage policy available for review.
- ▶ The remaining organizations have coverage policies for varicose vein treatment, including EVLA, RFA, sclerotherapy, and/or phlebectomy. Each policy describes specific diagnostic, symptom, and/or prior treatment criteria that must be met for coverage eligibility.
- ▶ Some details may vary, but common elements of the coverage policies include documentation of venous incompetence; minimum size requirements for varicose veins; presence of 1 or more symptoms; some circumstances may require a minimum time period for trial of conservative therapies, sclerotherapy (LS and FS), and phlebectomy as adjunct treatments.

Presentation overview



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Quality of the Body of Evidence

High

- ▶ Reliable evidence reflecting the true effect
- ▶ Unlikely to change with future studies

Moderate

- ▶ Reasonable confidence that the results represent the true direction of effect
- ▶ The effect estimate might change with future studies

Low

- Little confidence due to poor quality and/or mixed results and/or a paucity of studies
- Future studies are likely to change the estimates and possibly the direction

Very Low

- No confidence in any result found (e.g., paucity of data)
- Data are such that we cannot make a statement on the findings

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Summary: KQ#1

- ▶ EVLA is similar to or better than surgery for many clinical and patient-centered outcomes (moderate-quality evidence); evidence for some outcomes such as pain and time to return to activities is mixed or inconclusive.
- ▶ RFA is similar to or better than surgery for many outcomes and may be associated with less postoperative pain than surgery (low-quality evidence).
- ▶ Evidence suggests similarities in some clinical and patient-centered outcomes between sclerotherapy and surgery (low-quality evidence); it is difficult to draw conclusions about several outcomes because of a lack of sufficient or consistent data.
- ▶ No eligible studies comparing phlebectomy with surgery; phlebectomy may have been an adjunctive treatment in studies of the other interventions.

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Summary: KQ#2

- ▶ EVLA, RFA, and sclerotherapy are relatively safe compared with surgery—few significant differences were reported (moderate-quality evidence).
 - ▶ Rates of serious complications are low and similar when compared with surgery. However, results from 2 large observational studies suggest that the risk of DVT after procedures such as EVLA and RFA may need further investigation.
 - ▶ More common complications include bruising, phlebitis, hematoma, and infection.

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Summary: KQ#3 and KQ#4

- ▶ KQ#3: Results and conclusions from publications reporting results among patients being treated either for GSV or SSV varices are discussed in KQ#1 and KQ#2; no other subgroup analyses were identified.
- ▶ KQ#4: Conclusions from systematic reviews evaluating economic outcomes suggest that available economic data and analyses are limited by variations in reporting, lack of applicability to settings outside of the UK or Europe, poor methodological quality, and inadequate reporting or out-of-date information.
- ▶ KQ#4: 2 U.S.-based cost analyses reported that the minimally invasive varicose vein treatments were associated with lower costs than surgery.

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Summing up . . .

▶ Evidence base

- Limitations include lack of reporting of statistical test results; methodological limitations of individual studies; few studies for some comparisons and some outcomes; lack of sufficient or consistent data for some outcomes; and obvious or potential heterogeneity within the body of evidence with respect to aspects such as treatment delivery, comparators, and methods.

▶ Gaps

- Future studies are needed that address the methodological limitations of individual studies such as variation in outcome definitions and metrics, more consistent performance and reporting of statistical analyses, and better reporting or conduct of randomization procedures.

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Thank you

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FINAL Key Questions and Background

Selected Endovascular and Surgical Interventions for Treating Varicose Veins

Varicose veins are a common condition, affecting approximately 25 million people in the United States. The National Heart, Lung, and Blood Institute provides the following information about varicose veins. Varicose veins are swollen, twisted veins visible under the surface of the skin. Veins have one-way valves that help keep blood flowing toward the heart. If the valves are weak or damaged, blood can back up and pool in veins. This causes the veins to swell, which can lead to varicose veins. These veins usually occur in the legs, but can also form in other parts of the body.

Many factors can raise a person's risk for varicose veins. Examples of these factors include family history, older age, gender, pregnancy, overweight or obesity, lack of movement, and leg trauma.

Sometimes varicose veins cause pain, blood clots, skin ulcers, or other problems. Varicose veins can lead to dermatitis. Dermatitis can cause bleeding or skin ulcers if the skin is scratched or irritated. Varicose veins also can lead to a condition called superficial thrombophlebitis, a blood clot in a vein close to the surface of the skin. This type of blood clot may cause pain and other problems in the affected area.

Varicose veins are treated with lifestyle changes and medical procedures. The goals of treatment are to relieve symptoms, prevent complications, and improve appearance. Medical procedures are done either to remove varicose veins or to close them. Examples of medical procedures are:

- Sclerotherapy: Injection of a liquid (or foam) chemical to close off a varicose vein
- Endovenous ablation: Lasers or radiowaves to create heat to close off a varicose vein
- Ambulatory phlebectomy: Small cuts in the skin to remove small varicose veins
- Vein stripping and ligation: Tying shut and removing veins through small cuts in the skin

Policy Context

A variety of treatments for varicose veins are available. Treatment goals include reducing pain or discomfort and for cosmetic reasons. The topic is identified based on uncertainties related to the safety, efficacy, and value of the certain procedures, including chemical ablation, stab phlebectomy, and laser ablation.

Scope of This HTA

Population: Adult patients being treated for varicose veins.

Interventions: Endovascular laser ablation (EVLA), endovascular radiofrequency ablation (RFA), sclerotherapy (i.e., liquid or foam chemical ablation), ambulatory phlebectomy (i.e., stab phlebectomy or microphlebectomy)

Comparators: Any of the interventions listed above compared with vein ligation with or without stripping

Outcomes:

- Clinical outcomes: Failure of the procedure, second or additional procedures after failure of initial procedure, technical recurrence, symptomatic recurrence, second or additional procedures to treat recurrence, changes in symptom scores measured by validated scales (e.g., Venous Clinical Severity Score [VCSS])
- Patient-centered outcomes: Patient satisfaction/quality of life (QOL); time to return to work or normal activity; pain
- Adverse events: Nerve damage, skin burns, deep venous thermal injury, deep vein thrombosis, pulmonary embolism, transient ischemic attacks, stroke, bleeding, infection, thrombophlebitis, headache, visual disturbance, skin staining, pain at injection site, back pain, anaphylaxis, lymph leak, cellulitis
- Cost/cost-effectiveness outcomes

Settings: Inpatient or outpatient

Study Designs: For clinical effectiveness (key questions 1 and 3), good-quality systematic reviews and randomized controlled trials (RCTs); for harms (key questions 2 and 3) in addition to good-quality systematic reviews and RCTs, large observational studies including registry data (n≥500), may be employed; similarly, for key question 4, observational and modelling studies may be also be employed.

Key Questions

1. Among patients being treated for varicose veins, what is the clinical effectiveness of endovascular laser ablation, radiofrequency ablation, sclerotherapy, or ambulatory phlebectomy compared with ligation with or without stripping?
2. Among patients being treated for varicose veins, what are the harms associated with endovascular laser ablation, radiofrequency ablation, sclerotherapy, or ambulatory phlebectomy compared with ligation with or without stripping?
3. Among patients being treated for varicose veins, does the effectiveness or risk of adverse events of laser ablation, radiofrequency ablation, sclerotherapy, or ambulatory phlebectomy compared with ligation with or without stripping vary by clinical history (e.g., comorbidities, previous treatment of varicose veins), patient characteristics (e.g., age, sex, body mass index (BMI), smoking history)?
4. What are the cost implications and cost-effectiveness of endovascular laser ablation, radiofrequency ablation, sclerotherapy, or ambulatory phlebectomy compared with ligation with or without stripping for patients being treated for varicose veins?

Public Comment & Response

See **Draft Key Questions: Public Comment and Response** document published separately.

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-effective¹ as expressed by the following standards²:

- 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 harms³:

- 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.
- 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

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>

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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 evidence⁴ 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.

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

⁴ Based on GRADE recommendation: <http://www.gradeworkinggroup.org/FAQ/index.htm>

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.

Clinical Committee Findings and Decisions

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?

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.

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

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public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Discussion Document: What are the key factors and health outcomes and what evidence is there? (Applies to the population in the PICO for this review)

Safety Outcomes	Importance of Outcome	Safety Evidence / Confidence in Evidence
Adverse events		
Deep vein thrombosis		
Pulmonary embolism		
Nerve damage		
Bleeding		
Infection		
Other complications		

Efficacy – Effectiveness Outcomes	Importance of Outcome	Efficacy / Effectiveness Evidence
Change in symptoms		
Procedure failure/technical failure		
Technical recurrence		
Symptom recurrence		
Quality of life		
Return to activities, work		
Pain		
Symptom severity		
Repeat procedures		

Cost Outcomes	Importance of Outcome	Cost Evidence
Cost-utility		
Cost-effectiveness		
Direct cost		

Special Population / Considerations Outcomes	Importance of Outcome	Special Populations/ Considerations Evidence
Age		
Gender		
Prior treatment		
Comorbidities		
Clinical history		

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Other patient characteristics		
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For Safety: Is there sufficient evidence that the technology is safe for the indications considered?

Unproven (no)	Less (yes)	Equivalent (yes)	More in some (yes)	More in all

For Efficacy/Effectiveness: Is there sufficient evidence that the technology has a meaningful impact on patients and patient care?

Unproven (no)	Less (yes)	Equivalent (yes)	More in some (yes)	More in all

For Cost Outcomes/Cost-Effectiveness: Is there sufficient evidence that the technology is cost-effective for the indications considered?

Unproven (no)	Less (yes)	Equivalent (yes)	More in some (yes)	More in all

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.

Next Step: Proposed Findings and Decision and Public Comment

At the next public meeting the committee will review the proposed findings and decision and consider any public comments as appropriate prior to a vote for final adoption of the determination.

- 1) Based on public comment was evidence overlooked in the process that should be considered?
- 2) Does the proposed findings and decision document clearly convey the intended coverage determination based on review and consideration of the evidence?

Next Step: Final Determination

Following review of the proposed findings and decision document and public comments:

Final Vote

Does the committee approve the Findings and Decisions document with any changes noted in discussion?

If yes, the process is concluded.

If no, or an unclear (i.e., tie) outcome Chair will lead discussion to determine next steps.

Medicare and Coverage Guidelines

[From the Final Evidence Report, page 85]

Centers for Medicare & Medicaid Services (CMS)

No CMS National Coverage Determination (NCD) for treatment of varicose veins was identified on January 10, 2017 (search National Coverage Documents by the keywords varicose or vein in all documents at: <https://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

Guidelines

[From page 34 of Final Evidence Report]

Table 9. Summary of Practice Guideline Recommendations

Key: CEAP, Clinical, Etiologic, Anatomic, Pathophysiologic; CVD, chronic venous disease; EVLA, endovenous laser ablation; FS, foam sclerotherapy; GL(s), guideline(s); GSV, great saphenous vein; RCTs, randomized controlled trials; RFA, radiofrequency ablation; SSV, small saphenous vein; UGFS, ultrasound-guided foam sclerotherapy

Quality of Individual GLs, Title (Author, Year)	Recommendations
<p>Good</p> <p><i>Society for Vascular Surgery (SVS) and the American Venous Forum (AVF): the care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines</i> (Gloviczki et al., 2011)</p>	<p>The 2011 clinical practice guidelines of the SVS and AVF Venous Guideline Committee recommend EVLA, RFA, and FS as effective alternatives to stripping and other modalities.</p>
<p>Good</p> <p><i>Management of venous leg ulcers: clinical practice guidelines of the Society for Vascular Surgery (SVS) and the American Venous Forum (AVF):</i> (O'Donnell et al., 2014)</p>	<p>The 2014 GLs on management of venous leg ulcers aim to address the twofold goal of venous leg ulcer treatment, which includes ulcer healing and prevention of ulcer recurrence. The GL authors note that, in general, they found the quality of the available evidence for operative or endovascular management was largely limited to level "C" because of a lack of RCTs evaluating treatment techniques. The GLs generally, with a few exceptions, suggest or recommend the use of ablation followed by compression for specific types of venous incompetence and reflux occurring with venous leg ulcers.</p>
<p>Good</p> <p><i>Diagnosis and management of varicose veins in the legs: National Institute for Health and Care Excellence (NICE) guideline</i> (National Clinical Guideline Centre, 2013)</p>	<p>The NICE recommended a treatment hierarchy for confirmed varicose veins and truncal reflux: RFA/EVLA > UGFS > surgery. During pregnancy, consideration should be given to compression hosiery instead of interventional treatment (except in exceptional circumstances).</p>
<p>Good</p> <p><i>Management of chronic venous disease: clinical practice guidelines</i></p>	<ul style="list-style-type: none"> • Recommends against sclerotherapy for first-choice treatment except in elderly and frail patients with venous ulcers; sclerotherapy is recommended as a

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Quality of Individual GLs, Title (Author, Year)	Recommendations
<i>of the European Society for Vascular Surgery (ESVS) (Wittens et al., 2015)</i>	<p>second-choice treatment for some CEAP classifications or for more advanced stages of CVD for patients not eligible for surgery or endovascular ablation.</p> <ul style="list-style-type: none"> • Recommends endovenous thermal ablation techniques in preference to surgery and sclerotherapy for patients with GSV reflux, and endovenous thermal ablation should be considered for patients with SSV reflux. • Recommends surgical treatment for non-complicated varicose veins instead of conservative treatment; when surgical treatment is performed, high ligation and stripping is recommended instead of high ligation alone; surgical stripping of the saphenous vein without high ligation leaving a 2 cm stump may be considered. • Concomitant phlebectomies should be considered when performing endovenous thermal ablation for truncal reflux; ambulatory phlebectomy should be considered to treat tributary varicose veins. • EVLA, RFA, UGFS, or phlebectomies should be considered for treating recurrent varicose veins; extensive redo surgery is not recommended as first choice for patients with recurrent varicose veins.
<p>Fair</p> <p><i>American College of Phlebology Guidelines – treatment of refluxing accessory saphenous veins (Gibson et al., 2016)</i></p>	<p>The group’s recommendation is that patients with symptomatic incompetence of the accessory GSV be treated with endovenous thermal ablation (EVLA or RFA) or with UGFS to reduce symptoms.</p>
<p>Fair</p> <p><i>Performance of endovenous foam sclerotherapy in the USA for the treatment of venous disorders: ACP/SVM/AVF/SIR quality improvement guidelines (Rathbun et al., 2014)</i></p>	<p>The GLs state that endovenous FS is effective for treating primary and recurrent GSV, SSV, and accessory varicose veins. However, no RCTs were available for assessment and the group could not draw conclusions about the comparative efficacy or safety of FS and endovenous thermal ablation.</p>
<p>Poor</p> <p><i>Treatment of superficial venous disease of the lower leg (ACP, 2014)</i></p>	<ul style="list-style-type: none"> • Generally recommend EVLA or RFA as preferred treatment instead of surgery, except when veins are not amendable to endovenous procedures; recommends against compression therapy as a prerequisite for symptomatic venous disease when treatments such as endovenous ablation are appropriate. • Recommends treating visible symptomatic tributary veins with stab phlebectomy, liquid sclerotherapy, or FS; non-visible symptomatic tributary veins should be treated with UGFS or FS.
<p>Fair</p> <p><i>ACR Appropriateness Criteria: Radiologic management of lower-extremity venous insufficiency (Rochon et al., 2012)</i></p>	<p>Recommendations state that EVLA or RFA is “usually appropriate” in several specific clinical situations described, and “usually not appropriate” during pregnancy. Surgical vein stripping and injection sclerotherapy were classified as “may be appropriate” for the same clinical scenarios, except pregnancy for which these were also rated as “not usually appropriate.”</p>