Appendix A. Exact Search Strings

PubMed® search strategy (June 30, 2016)

KQ 1:

#1	"Varicose Veins"[Mesh] OR "Venous Insufficiency"[Mesh] OR "Venous Thromboembolism"[Mesh] OR "May-Thurner Syndrome"[Mesh] OR "Thrombophlebitis"[Mesh] OR "varicose vein"[tiab] OR "varicose veins"[tiab] OR varicosity[tiab] OR "venous ulcer"[tiab] OR "vein ulcer"[tiab] OR "varicose ulcer"[tiab] OR "venous ulcers"[tiab] OR "vein ulcers"[tiab] OR "varicose ulcers"[tiab] OR "stasis dermatitis"[tiab] OR "venous stasis"[tiab] OR "vein insufficiency"[tiab] OR "venous insufficiency"[tiab] OR "vein incompetence"[tiab] OR "venous incompetence"[tiab] OR "vein reflux"[tiab] OR "venous reflux"[tiab] OR "post-thrombotic syndrome"[tiab] OR "postthrombotic syndrome"[tiab] OR "venous obstruction"[tiab] OR "vein obstruction"[tiab] OR thrombophlebitis[tiab] OR "venous outflow disease"[tiab] OR "venous outflow obstruction"[tiab] OR "impaired venous outflow"[tiab] OR "post phlebitis"[tiab] OR "post phlebitic"[tiab] OR postphlebitic[tiab] OR postphlebitis[tiab] OR "post thrombotic"[tiab] OR postthrombosis[tiab] OR postthrombotic[tiab] OR "post thrombosis"[tiab] OR "chronic venous thrombosis"[tiab] OR "chronic vein thrombosis"[tiab] OR "May-Thurner Syndrome"[tiab] OR (("Venous Thrombosis"[Mesh] OR "deep vein thrombosis"[tiab] OR "venous thrombosis"[tiab] OR dvt[tiab]) AND chronic[tiab])
#2	"Varicose Veins/diagnosis"[Majr] OR "Venous Insufficiency/diagnosis"[Majr] OR "Venous Thromboembolism/diagnosis"[Majr] OR "May-Thurner Syndrome/diagnosis"[Majr] OR "Thrombophlebitis/diagnosis"[Majr] OR "Phlebography"[Mesh] OR "Ultrasonography"[Mesh] OR "Veins/ultrasonography"[Mesh] OR "Varicose Veins/ultrasonography"[Mesh] OR "Diagnostic Techniques and Procedures"[Mesh] OR phlebography[tiab] OR venography[tiab] OR "D-Dimer"[tiab] OR "villalta"[tiab] OR diagnosis[tiab] OR diagnostic[tiab]
#3	"Sensitivity and Specificity"[Mesh] OR "Diagnostic Errors"[Mesh] OR sensitivity[tiab] OR specificity[tiab] OR accuracy[tiab] OR "positive predictive value"[tiab] OR "negative predictive value"[tiab] OR "likelihood ratio"[tiab] OR (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR Clinical trial[pt] OR “clinical trial”[tiab] OR “clinical trials”[tiab] OR "evaluation studies"[pt] OR "evaluation studies as topic"[MeSH] OR "evaluation study"[tiab] OR evaluation studies[tiab] OR "intervention studies"[MeSH] OR "intervention study"[tiab] OR "intervention studies"[tiab] OR "case-control studies"[MeSH] OR "case-control"[tiab] OR "cohort studies"[MeSH] OR cohort[tiab] OR "longitudinal studies"[MeSH] OR "longitudinal”[tiab] OR longitudinally[tiab] OR "prospective"[tiab] OR prospectively[tiab] OR "retrospective studies"[MeSH] OR "retrospective"[tiab] OR "Cross-Sectional Studies"[Mesh] OR cross-sectional[tiab] OR "comparative study"[pt] OR "comparative study"[tiab] OR systematic[sb] OR "meta-analysis"[pt] OR "meta-analysis as topic"[MeSH] OR "meta-analysis"[tiab] OR "meta-analyses"[tiab]) NOT (Editorial[ptyp] OR Letter[pt] OR Case Reports[pt] OR Comment[pt]) NOT (animals[mh] NOT humans[mh]) AND English[la]
#4	#1 AND #2 AND #3
#5	#4, Limit: Publication Date from 2000/01/01 – present

KQs 2-3:

#1	"Varicose Veins"[Mesh] OR "Venous Insufficiency"[Mesh] OR "Venous Thromboembolism"[Mesh] OR "May-Thurner Syndrome"[Mesh] OR "Thrombophlebitis"[Mesh] OR "varicose vein"[tiab] OR "varicose veins"[tiab] OR varicosity[tiab] OR "venous ulcer"[tiab] OR "vein ulcer"[tiab] OR "varicose ulcer"[tiab] OR "venous ulcers"[tiab] OR "vein ulcers"[tiab] OR "varicose ulcers"[tiab] OR "stasis dermatitis"[tiab] OR "venous stasis"[tiab] OR "vein insufficiency"[tiab] OR "venous insufficiency"[tiab] OR "vein incompetence"[tiab] OR "venous incompetence"[tiab] OR "vein reflux"[tiab] OR "venous reflux"[tiab] OR "post-thrombotic syndrome"[tiab] OR "postthrombotic syndrome"[tiab] OR "venous obstruction"[tiab] OR "vein obstruction"[tiab] OR thrombophlebitis[tiab] OR "venous outflow disease"[tiab] OR "venous outflow obstruction"[tiab] OR "impaired venous outflow"[tiab] OR "post phlebitis"[tiab] OR "post phlebitic"[tiab] OR

	postphlebitic[tiab] OR postphlebitis[tiab] OR "post thrombotic"[tiab] OR postthrombosis[tiab] OR postthrombotic[tiab] OR "post thrombosis"[tiab] OR "chronic venous thrombosis"[tiab] OR "chronic vein thrombosis"[tiab] OR "May-Thurner Syndrome"[tiab] OR (("Venous Thrombosis"[Mesh] OR "deep vein thrombosis"[tiab] OR "venous thrombosis"[tiab] OR dvt[tiab]) AND chronic[tiab])
#2	"Varicose Veins/prevention and control"[Majr] OR "Varicose Veins/therapy"[Majr] OR "Venous Insufficiency/prevention and control"[Majr] OR "Venous Insufficiency/therapy"[Majr] OR "Venous Thromboembolism/therapy"[Majr] OR "Venous Thromboembolism/prevention and control"[Majr] OR "May-Thurner Syndrome/prevention and control"[Majr] OR "May-Thurner Syndrome/therapy"[Majr] OR "Thrombophlebitis/therapy"[Majr] OR "Thrombophlebitis/prevention and control"[Majr] OR "Anticoagulants"[Mesh] OR "Anticoagulants" [Pharmacological Action] OR "Diuretics"[Mesh] OR "Diuretics" [Pharmacological Action] OR "Platelet Aggregation Inhibitors"[Mesh] OR "Platelet Aggregation Inhibitors"[Pharmacological Action] OR "prasugrel"[Supplementary Concept] OR "Ticagrelor"[Supplementary Concept] OR "Prostaglandins I"[Mesh] OR "Sclerotherapy"[Mesh] OR "Sclerosing Solutions"[Mesh] OR "Stockings, Compression"[Mesh] OR "Intermittent Pneumatic Compression Devices"[Mesh] OR "Laser Therapy"[Mesh] OR "Catheter Ablation"[Mesh] OR "Ablation Techniques"[Mesh] OR "Vena Cava Filters"[Mesh] OR "Stents"[Mesh] OR "Tissue Plasminogen Activator"[Mesh] OR "Streptokinase"[Mesh] OR "Urokinase-Type Plasminogen Activator"[Mesh] OR "Mechanical Thrombolysis"[Mesh] OR "Bandages"[Mesh] OR "Pressure"[Mesh] OR "Wounds and Injuries/therapy"[Mesh] OR "Negative-Pressure Wound Therapy"[Mesh] OR "Skin Care"[Mesh] OR "Exercise"[Mesh] OR "Exercise Therapy"[Mesh] OR "Ligation"[Mesh] OR "Angioplasty"[Mesh] OR "Zinc Sulfate"[Mesh] OR "Hyperbaric Oxygenation"[Mesh] OR "Weight Loss"[Mesh] OR "Nutrition Therapy"[Mesh] OR "Smoking Cessation"[Mesh] OR "Ultrasonography"[Mesh] OR anticoagulants[tiab] OR Apixaban[tiab] OR Coumadin[tiab] OR dabigatran[tiab] OR edoxaban[tiab] OR Eliquis[tiab] OR Jantoven[tiab] OR Lixiana[tiab] OR Marevan[tiab] OR Pradaxa[tiab] OR Prazaxa[tiab] OR rivaroxaban[tiab] OR Savaysa[tiab] OR warfarin[tiab] OR Xarelto[tiab] OR coumarol[tiab] OR phenocoumarol[tiab] OR diuretics[tiab] OR Aldactone[tiab] OR amiloride[tiab] OR Aquatensen[tiab] OR bendroflumethiazide[tiab] OR bumetanide[tiab] OR Bumex[tiab] OR chlorothiazide[tiab] OR chlorthalidone[tiab] OR Demadex[tiab] OR Diuril[tiab] OR Dyrenium[tiab] OR Edecrin[tiab] OR Enduron[tiab] OR Esidrix[tiab] OR "ethacrynic acid"[tiab] OR furosemide[tiab] OR hydrochlorothiazide[tiab] OR HydroDIURIL[tiab] OR hydroflumethiazide[tiab] OR Hygroton[tiab] OR Lasix[tiab] OR Metahydrin[tiab] OR methyclothiazide[tiab] OR metolazone[tiab] OR Microzide[tiab] OR Midamor[tiab] OR Mykrox[tiab] OR Naqua[tiab] OR Naturetin[tiab] OR Oretic[tiab] OR Saluron[tiab] OR spironolactone[tiab] OR Thalitone[tiab] OR torsemide[tiab] OR triamterene[tiab] OR Trichlorex[tiab] OR trichlormethiazide[tiab] OR Zaroxolyn[tiab] OR antiplatelets[tiab] OR "platelet aggregation inhibitors"[tiab] OR Aspirin[tiab] OR Agrylin[tiab] OR anagrelide[tiab] OR Brilinta[tiab] OR cilostazol[tiab] OR clopidogrel[tiab] OR dipyridamole[tiab] OR Effient[tiab] OR Pentoxifylline[tiab] OR pentoxil[tiab] OR Persantine[tiab] OR Plavix[tiab] OR Pletal[tiab] OR prasugrel[tiab] OR ticagrelor[tiab] OR Ticlid[tiab] OR ticlopidine[tiab] OR trental[tiab] OR vorapaxar[tiab] OR Zontivity[tiab] OR epoprostenol[tiab] OR prostacyclins[tiab] OR "prostaglandins 1"[tiab] OR "prostaglandins I"[tiab] OR sclerotherapy[tiab] OR Asclera[tiab] OR Aethoxysklerol[tiab] OR "chromated glycerin"[tiab] OR Cyanoacrylate[tiab] OR Dermabond[tiab] OR polidocanol[tiab] OR Scleremo[tiab] OR Sclerodex[tiab] OR "sodium chloride"[tiab] OR "sodium tetradecyl sulfate"[tiab] OR Sotradecol[tiab] OR Varisolve[tiab] OR Varithena[tiab] OR compression[tiab] OR Flexitouch[tiab] OR CircuFlow[tiab] OR BioCryo[tiab] OR Flowtron[tiab] OR VPulse[tiab] OR "laser ablation"[tiab] OR VenaCure[tiab] OR "Pro V Laser"[tiab] OR CoolTouch[tiab] OR ELVes[tiab] OR "Lumenis Sharplan"[tiab] OR Medilas[tiab] OR "catheter ablation"[tiab] OR "closure catheter"[tiab] OR venefit[tiab] OR ("vena cava"[tiab] AND (filter[tiab] OR filters[tiab])) OR stenting[tiab] OR stent[tiab] OR stents[tiab] OR activase[tiab] OR alteplase[tiab] OR kinlytic[tiab] OR streptase[tiab] OR streptokinase[tiab] OR "tissue plasminogen activator"[tiab] OR urokinase[tiab] OR "mechanical thrombectomy"[tiab] OR ekosonic[tiab] OR trerotola[tiab] OR amplatzer[tiab] OR trellis[tiab] OR angiojet[tiab] OR penumbra[tiab] OR Exercise[tiab] OR "physical therapy"[tiab] OR "zinc sulfate"[tiab] OR "elastic stockings"[tiab] OR bandage[tiab] OR bandages[tiab] OR bandaged[tiab] OR "pressure"[tiab] OR "wound therapy"[tiab] OR "skin care"[tiab] OR (leg[tiab] AND elevat*[tiab]) OR ablation[tiab] OR phlebectomy[tiab] OR ligation[tiab] OR excision[tiab] OR ((hyperbaric[tiab] OR "high pressure"[tiab] OR "high tension"[tiab]) AND (oxygen[tiab] OR oxygenation[tiab])) OR HBO[tiab] OR HBOT[tiab] OR HBO2[tiab] OR HBO2T[tiab] OR "hyperbaric chamber"[tiab] OR "hyperbaric chambers"[tiab] OR boots[tiab] OR "wound vac"[tiab] OR "wound vacuum"[tiab] OR angioplasty[tiab] OR "weight loss"[tiab] OR diet[tiab] OR smoking[tiab] OR tobacco[tiab] OR ultrasound[tiab] OR thromboembolectomy[tiab]
#3	(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR Clinical trial[pt] OR "clinical trial"[tiab] OR "clinical trials"[tiab] OR "evaluation studies"[pt] OR "evaluation studies as topic"[MeSH] OR "evaluation study"[tiab] OR evaluation studies[tiab] OR

	"intervention studies"[MeSH] OR "intervention study"[tiab] OR "intervention studies"[tiab] OR "case-control studies"[MeSH] OR "case-control"[tiab] OR "cohort studies"[MeSH] OR cohort[tiab] OR "longitudinal studies"[MeSH] OR "longitudinal"[tiab] OR longitudinally[tiab] OR "prospective"[tiab] OR prospectively[tiab] OR "retrospective studies"[MeSH] OR "retrospective"[tiab] OR "follow up"[tiab] OR "comparative study"[pt] OR "comparative study"[tiab] OR systematic[subset] OR "meta-analysis"[pt] OR "meta-analysis as topic"[MeSH] OR "meta-analysis"[tiab] OR "meta-analyses"[tiab]) NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp]) NOT (animals[mh] NOT humans[mh]) AND English[la]
#4	#1 AND #2 AND #3
#5	#4, Limit: Publication Date from 2000/01/01 – present

Embase® search strategy (June 30, 2016)

Platform: Embase.com

KQ 1:

#1	'varicosis'/de OR 'leg varicosis'/exp OR 'spider vein'/exp OR 'vein insufficiency'/exp OR 'venous thromboembolism'/de OR 'lower extremity deep vein thrombosis'/exp OR 'thrombophlebitis'/exp OR 'leg thrombophlebitis'/exp OR 'postthrombosis syndrome'/exp OR "varicose vein":ab,ti OR "varicose veins":ab,ti OR varicosity:ab,ti OR "venous ulcer":ab,ti OR "vein ulcer":ab,ti OR "varicose ulcer":ab,ti OR "venous ulcers":ab,ti OR "vein ulcers":ab,ti OR "varicose ulcers":ab,ti OR "stasis dermatitis":ab,ti OR "venous stasis":ab,ti OR "vein insufficiency":ab,ti OR "venous insufficiency":ab,ti OR "vein incompetence":ab,ti OR "venous incompetence":ab,ti OR "vein reflux":ab,ti OR "venous reflux":ab,ti OR "post thrombotic syndrome":ab,ti OR "postthrombotic syndrome":ab,ti OR "venous obstruction":ab,ti OR "vein obstruction":ab,ti OR thrombophlebitis:ab,ti OR "venous outflow disease":ab,ti OR "venous outflow obstruction":ab,ti OR "impaired venous outflow":ab,ti OR "post phlebitis":ab,ti OR "post phlebitic":ab,ti OR postphlebitic:ab,ti OR postphlebitis:ab,ti OR "post thrombotic":ab,ti OR postthrombosis:ab,ti OR postthrombotic:ab,ti OR "post thrombosis":ab,ti OR "chronic venous thrombosis":ab,ti OR "chronic vein thrombosis":ab,ti OR "May Thurner Syndrome":ab,ti OR (('deep vein thrombosis'/exp OR "deep vein thrombosis":ab,ti OR "venous thrombosis":ab,ti OR dvt:ab,ti) AND chronic:ab,ti)
#2	'varicosis'/exp/mj/dm_di OR 'vein insufficiency'/exp/mj/dm_di OR 'venous thromboembolism'/de/mj/dm_di OR 'lower extremity deep vein thrombosis'/exp/mj/dm_di OR 'leg thrombophlebitis'/exp/mj/dm_di OR 'postthrombosis syndrome'/exp/mj/dm_di OR 'phlebography'/exp OR 'echography'/de OR 'D dimer'/exp OR phlebography:ab,ti OR venography:ab,ti OR "D Dimer":ab,ti OR "villalta":ab,ti OR diagnosis:ab,ti OR diagnostic:ab,ti
#3	('sensitivity and specificity'/exp OR 'predictive value'/exp OR 'diagnostic error'/exp OR sensitivity:ab,ti OR specificity:ab,ti OR accuracy:ab,ti OR misdiagnos*:ab,ti OR 'predictive value':ab,ti OR 'likelihood ratio':ab,ti OR 'randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR random*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR (cross NEAR/1 over*):ab,ti OR placebo*:ab,ti OR (doubl* NEAR/1 blind*):ab,ti OR (singl* NEAR/1 blind*):ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR 'clinical study'/exp OR ‘clinical trial’:ti,ab OR ‘clinical trials’:ti,ab OR 'controlled study'/exp OR 'evaluation'/exp OR ‘evaluation study’:ab,ti OR ‘evaluation studies’:ab,ti OR 'cross-sectional study'/exp OR ‘intervention study’:ab,ti OR ‘intervention studies’:ab,ti OR ‘case control’:ab,ti OR 'cohort analysis'/exp OR cohort:ab,ti OR "cross sectional":ab,ti OR longitudinal*:ab,ti OR prospective:ab,ti OR prospectively:ab,ti OR retrospective:ab,ti OR 'follow up'/exp OR ‘follow up’:ab,ti OR 'comparative effectiveness'/exp OR 'comparative study'/exp OR ‘comparative study’:ab,ti OR ‘comparative studies’:ab,ti OR 'evidence based medicine'/exp OR ‘systematic review’:ab,ti OR ‘meta-analysis’:ab,ti OR ‘meta-analyses’:ab,ti) NOT ('case report'/exp OR 'case study'/exp OR 'editorial'/exp OR 'letter'/exp OR 'note'/exp OR 'conference abstract'/exp)
#4	#1 AND #2 AND #3
#5	#4 AND [embase]/lim NOT [medline]/lim AND [humans]/lim AND [english]/lim
#6	#5 AND [2000-2016]/py

KQs 2-3:

#1	'varicosis'/de OR 'leg varicosis'/exp OR 'spider vein'/exp OR 'vein insufficiency'/exp OR 'venous thromboembolism'/de OR 'lower extremity deep vein thrombosis'/exp OR 'thrombophlebitis'/exp OR 'leg thrombophlebitis'/exp OR 'postthrombosis syndrome'/exp OR "varicose vein":ab,ti OR "varicose veins":ab,ti OR varicosity:ab,ti OR "venous ulcer":ab,ti OR "vein ulcer":ab,ti OR "varicose ulcer":ab,ti OR "venous ulcers":ab,ti OR "vein ulcers":ab,ti OR "varicose ulcers":ab,ti OR "stasis dermatitis":ab,ti OR "venous stasis":ab,ti OR "vein insufficiency":ab,ti OR "venous insufficiency":ab,ti OR "vein incompetence":ab,ti OR "venous incompetence":ab,ti OR "vein reflux":ab,ti OR "venous reflux":ab,ti OR "post thrombotic syndrome":ab,ti OR "postthrombotic syndrome":ab,ti OR "venous obstruction":ab,ti OR "vein obstruction":ab,ti OR thrombophlebitis:ab,ti OR "venous outflow disease":ab,ti OR "venous outflow obstruction":ab,ti OR "impaired venous outflow":ab,ti OR "post phlebitis":ab,ti OR "post phlebitic":ab,ti OR postphlebitic:ab,ti OR postphlebitis:ab,ti OR "post thrombotic":ab,ti OR postthrombosis:ab,ti OR postthrombotic:ab,ti OR "post thrombosis":ab,ti OR "chronic venous thrombosis":ab,ti OR "chronic vein thrombosis":ab,ti OR "May Thurner Syndrome":ab,ti OR (('deep vein thrombosis'/exp OR "deep vein thrombosis":ab,ti OR "venous thrombosis":ab,ti OR dvt:ab,ti) AND chronic:ab,ti)
#2	'varicosis'/exp/mj/dm_dt,dm_su,dm_th,dm_rh,dm_rt,dm_dm,dm_pc OR 'vein insufficiency'/exp/mj/dm_dt,dm_su,dm_th,dm_rh,dm_rt,dm_dm,dm_pc OR 'venous thromboembolism'/mj/dm_dt,dm_su,dm_th,dm_rh,dm_rt,dm_dm,dm_pc OR 'lower extremity deep vein thrombosis'/exp/mj/dm_dt,dm_su,dm_th,dm_rh,dm_rt,dm_dm,dm_pc OR 'thrombophlebitis'/exp/mj/dm_dt,dm_su,dm_th,dm_rh,dm_rt,dm_dm,dm_pc OR 'leg thrombophlebitis'/exp/mj/dm_dt,dm_su,dm_th,dm_rh,dm_rt,dm_dm,dm_pc OR 'postthrombosis syndrome'/exp/mj/dm_dt,dm_su,dm_th,dm_rh,dm_rt,dm_dm,dm_pc OR 'anticoagulant agent'/exp OR 'diuretic agent'/exp OR 'antithrombocytic agent'/exp OR 'prasugrel'/exp OR 'ticagrelor'/exp OR 'prostaglandin'/exp OR 'sclerotherapy'/exp OR 'sclerosing agent'/exp OR 'compression stocking'/exp OR 'intermittent pneumatic compression device'/exp OR 'low level laser therapy'/exp OR 'ablation catheter'/exp OR 'ablation therapy'/exp OR 'vena cava filter'/exp OR 'stent'/exp OR 'tissue plasminogen activator'/exp OR 'streptokinase'/exp OR 'urokinase'/exp OR 'mechanical thrombectomy'/exp OR 'bandages and dressings'/exp OR 'pressure'/exp OR 'wound care'/exp OR 'skin care'/exp OR 'exercise'/exp OR 'kinesiotherapy'/exp OR 'ligation'/exp OR 'angioplasty'/exp OR 'zinc sulfate'/exp OR 'hyperbaric oxygen'/exp OR 'weight reduction'/exp OR 'diet therapy'/exp OR 'smoking cessation'/exp OR 'echography'/exp OR 'catheter'/exp OR anticoagulants:ab,ti OR Apixaban:ab,ti OR Coumadin:ab,ti OR dabigatran:ab,ti OR edoxaban:ab,ti OR Eliquis:ab,ti OR Jantoven:ab,ti OR Lixiana:ab,ti OR Marevan:ab,ti OR Pradaxa:ab,ti OR Prazaxa:ab,ti OR rivaroxaban:ab,ti OR Savaysa:ab,ti OR warfarin:ab,ti OR Xarelto:ab,ti OR coumarol:ab,ti OR phenocoumarol:ab,ti OR diuretics:ab,ti OR Aldactone:ab,ti OR amiloride:ab,ti OR Aquatensen:ab,ti OR bendroflumethiazide:ab,ti OR bumetanide:ab,ti OR Bumex:ab,ti OR chlorothiazide:ab,ti OR chlorthalidone:ab,ti OR Demadex:ab,ti OR Diuril:ab,ti OR Dyrenium:ab,ti OR Edecrin:ab,ti OR Enduron:ab,ti OR Esidrix:ab,ti OR "ethacrynic acid":ab,ti OR furosemide:ab,ti OR hydrochlorothiazide:ab,ti OR HydroDIURIL:ab,ti OR hydroflumethiazide:ab,ti OR Hygroton:ab,ti OR Lasix:ab,ti OR Metahydrin:ab,ti OR methyclothiazide:ab,ti OR metolazone:ab,ti OR Microzide:ab,ti OR Midamor:ab,ti OR Mykrox:ab,ti OR Naqua:ab,ti OR Naturetin:ab,ti OR Oretic:ab,ti OR Saluron:ab,ti OR spironolactone:ab,ti OR Thalitone:ab,ti OR torsemide:ab,ti OR triamterene:ab,ti OR Trichlorex:ab,ti OR trichlormethiazide:ab,ti OR Zaroxolyn:ab,ti OR antiplatelets:ab,ti OR "platelet aggregation inhibitors":ab,ti OR Aspirin:ab,ti OR Agrylin:ab,ti OR anagrelide:ab,ti OR Brilinta:ab,ti OR cilostazol:ab,ti OR clopidogrel:ab,ti OR dipyridamole:ab,ti OR Effient:ab,ti OR Pentoxifylline:ab,ti OR pentoxil:ab,ti OR Persantine:ab,ti OR Plavix:ab,ti OR Pletal:ab,ti OR prasugrel:ab,ti OR ticagrelor:ab,ti OR Ticlid:ab,ti OR ticlopidine:ab,ti OR trental:ab,ti OR vorapaxar:ab,ti OR Zontivity:ab,ti OR epoprostenol:ab,ti OR prostacyclins:ab,ti OR "prostaglandins 1":ab,ti OR prostaglandins:ab,ti OR sclerotherapy:ab,ti OR Asclera:ab,ti OR Aethoxysklerol:ab,ti OR "chromated glycerin":ab,ti OR Cyanoacrylate:ab,ti OR Dermabond:ab,ti OR polidocanol:ab,ti OR Scleremo:ab,ti OR Sclerodex:ab,ti OR "sodium chloride":ab,ti OR "sodium tetradecyl sulfate":ab,ti OR Sotradecol:ab,ti OR Varisolve:ab,ti OR Varithena:ab,ti OR compression:ab,ti OR Flexitouch:ab,ti OR CircuFlow:ab,ti OR BioCryo:ab,ti OR Flowtron:ab,ti OR VPulse:ab,ti OR "laser ablation":ab,ti OR VenaCure:ab,ti OR "Pro V Laser":ab,ti OR CoolTouch:ab,ti OR ELVes:ab,ti OR "Lumenis Sharplan":ab,ti OR Medilas:ab,ti OR "catheter ablation":ab,ti OR "closure catheter":ab,ti OR venefit:ab,ti OR ("vena cava":ab,ti AND (filter:ab,ti OR filters:ab,ti)) OR stenting:ab,ti OR stent:ab,ti OR stents:ab,ti OR activase:ab,ti OR alteplase:ab,ti OR kinlytic:ab,ti OR streptase:ab,ti OR streptokinase:ab,ti OR "tissue plasminogen activator":ab,ti OR urokinase:ab,ti OR "mechanical thrombectomy":ab,ti OR ekosonic:ab,ti OR trerotola:ab,ti OR amplatzer:ab,ti OR trellis:ab,ti OR

	angiojet:ab,ti OR penumbra:ab,ti OR Exercise:ab,ti OR "physical therapy":ab,ti OR "zinc sulfate":ab,ti OR "elastic stockings":ab,ti OR bandage:ab,ti OR bandages:ab,ti OR bandaged:ab,ti OR "pressure":ab,ti OR "wound therapy":ab,ti OR "skin care":ab,ti OR (leg:ab,ti AND elevat*:ab,ti) OR ablation:ab,ti OR phlebectomy:ab,ti OR ligation:ab,ti OR excision:ab,ti OR ((hyperbaric:ab,ti OR "high pressure":ab,ti OR "high tension":ab,ti) AND (oxygen:ab,ti OR oxygenation:ab,ti)) OR HBO:ab,ti OR HBOT:ab,ti OR HBO2:ab,ti OR HBO2T:ab,ti OR "hyperbaric chamber":ab,ti OR "hyperbaric chambers":ab,ti OR boots:ab,ti OR "wound vac":ab,ti OR "wound vacuum":ab,ti OR angioplasty:ab,ti OR "weight loss":ab,ti OR diet:ab,ti OR smoking:ab,ti OR tobacco:ab,ti OR ultrasound:ab,ti OR thromboembolectomy:ab,ti
#3	('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR random*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR (cross NEAR/1 over*):ab,ti OR placebo*:ab,ti OR (doubl* NEAR/1 blind*):ab,ti OR (singl* NEAR/1 blind*):ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR 'clinical study'/exp OR ‘clinical trial’:ti,ab OR ‘clinical trials’:ti,ab OR 'controlled study'/exp OR 'evaluation'/exp OR ‘evaluation study’:ab,ti OR ‘evaluation studies’:ab,ti OR ‘intervention study’:ab,ti OR ‘intervention studies’:ab,ti OR ‘case control’:ab,ti OR 'cohort analysis'/exp OR cohort:ab,ti OR longitudinal*:ab,ti OR prospective:ab,ti OR prospectively:ab,ti OR retrospective:ab,ti OR 'follow up'/exp OR ‘follow up’:ab,ti OR 'comparative effectiveness'/exp OR 'comparative study'/exp OR ‘comparative study’:ab,ti OR ‘comparative studies’:ab,ti OR 'evidence based medicine'/exp OR ‘systematic review’:ab,ti OR ‘meta-analysis’:ab,ti OR ‘meta-analyses’:ab,ti) NOT ('case report'/exp OR 'case study'/exp OR 'editorial'/exp OR 'letter'/exp OR 'note'/exp OR 'conference abstract'/exp)
#4	#1 AND #2 AND #3
#5	#4 AND [embase]/lim NOT [medline]/lim AND [humans]/lim AND [english]/lim
#6	#5 AND [2000-2016]/py

Cochrane search strategy (June 30, 2016)

Platform: Wiley

Database searched: Cochrane Database of Systematic Reviews

#1	[mh "varicose veins"] or [mh "venous insufficiency"] or [mh "venous thromboembolism"] or [mh "may-thurner syndrome"] or [mh thrombophlebitis]
#2	"Varicose Veins":ab,ti,kw or "varicosity":ab,ti,kw or "venous ulcer":ab,ti,kw or "vein ulcer":ab,ti,kw or "varicose ulcer":ab,ti,kw or "venous ulcers":ab,ti,kw or "vein ulcers":ab,ti,kw or "varicose ulcers":ab,ti,kw or "stasis dermatitis":ab,ti,kw or "venous stasis":ab,ti,kw or "vein insufficiency":ab,ti,kw or "venous insufficiency":ab,ti,kw or "vein incompetence":ab,ti,kw or "venous incompetence":ab,ti,kw or "vein reflux":ab,ti,kw or "venous reflux":ab,ti,kw or "post-thrombotic syndrome":ab,ti,kw or "postthrombotic syndrome":ab,ti,kw or "venous obstruction":ab,ti,kw or "vein obstruction":ab,ti,kw or thrombophlebitis:ab,ti,kw or "venous outflow disease":ab,ti,kw or "venous outflow obstruction":ab,ti,kw or "impaired venous outflow":ab,ti,kw or "post phlebitis":ab,ti,kw or "post phlebitic":ab,ti,kw or postphlebitic:ab,ti,kw or postphlebitis:ab,ti,kw or "post thrombotic":ab,ti,kw or postthrombosis:ab,ti,kw or postthrombotic:ab,ti,kw or "post thrombosis":ab,ti,kw or "chronic venous thrombosis":ab,ti,kw or "chronic vein thrombosis":ab,ti,kw or "chronic deep vein thrombosis":ab,ti,kw or "chronic dvt":ab,ti,kw or "May-Thurner Syndrome":ab,ti,kw
#3	[mh "venous thrombosis"]
#4	chronic:ab,ti,kw
#5	#3 AND #4
#6	#1 OR #2 OR #5
#7	#6, Limits: 2000/01/01and Cochrane Reviews

Gray Literature Searches

ClinicalTrials.gov (September 26, 2016)

Conditions	varicose veins OR venous insufficiency OR venous thromboembolism OR may-thurner OR thrombophlebitis OR deep vein thrombosis OR peripheral venous disease
Recruitment	Completed studies
Study Results	All studies
Study type	Interventional studies
Age group	Adult (18–65), Senior (66+)
Phase	Phase 2, Phase 3, Phase 4

Total number of results: 285

WHO: International Clinical Trials Registry Platform Search Portal (September 26, 2016)

Title: venous disease
OR
Condition: venous disease
Recruiting status: All

Total number of results: 37 records for 31 trials

National Guidelines Clearinghouse (September 26, 2016)

Platform: www.guideline.gov

Keyword	venous disease AND extremity
Clinical Specialty	Cardiology, Internal Medicine, Surgery (For the original search, these terms were searched in an OR combination. Due to a change in the database format that no longer allowed OR functionality, the Sep 2016 update searches were performed individually.)

Total number of results: 94

Appendix B. Data Abstraction Elements

Study Characteristics

- Study Identifiers
  - Study Name or Acronym
  - NCT number or other trial registry identifier
  - Last name of first author
- Additional Articles Used in This Abstraction
- Study Sites
  - Single center, Multicenter, Unclear/Not reported
  - Number of sites
- Geographic Location (Select all that apply)
  - US, Canada, UK/Europe, Latin America, Middle East (includes Israel), Asia, Africa, Australia/NZ, Unclear/Not reported
- Study Design
  - RCT
  - Observational
- Funding Source (Select all that apply)
  - Government, Industry, Non-government/non-industry, Unclear/Not reported
- Setting (Select all that apply)
  - Primary care, Specialty Care (e.g. surgery, cardiology, vein clinic), Other, Unclear/Not reported
- Diagnostic tool or criteria used in the study
- Study Enrollment/Study Completion
  - N enrolled/included
  - N completed
- Key Question Applicability (Select all that apply)
  - KQ1, KQ2, KQ3
- Study patient population defined as
  - Symptomatic, Asymptomatic, Unclear/Not reported
- Conditions described in patient population
  - LE varicose veins, LE chronic venous insufficiency/reflux/incompetency, LE venous thrombosis/obstruction, Post-thrombotic syndrome, Unclear/Not reported
- Comments

Baseline Characteristics

- Record the following elements for Total Population, Arm 1, Arm 2, Arm 3, Arm 4, Arm 5, and Arm 6 (as applicable)
  - Number of Patients (N and %)
  - Male and Female (N and %)
  - Age in years
    - Mean
    - Median
    - Standard Deviation
    - Min

        - Max
        - 25% IQR
        - 75% IQR
        - Categorical
        - Other, specify
    - Race/Ethnicity (N and %)
        - Hispanic or Latino
        - Black/African American
        - American Indian or Alaska Native
        - Asian
        - Native Hawaiian or Pacific Islander
        - White
        - Multiracial
        - Other
    - Body Weight
        - Reported (describe), NR or Unclear
    - CEAP Classification
        - Reported (describe), NR or Unclear
    - VCSS Classification
        - Reported (describe), NR or Unclear
    - Villalta Score
        - Reported (describe), NR or Unclear
    - Severity of Disease
        - Reported (describe), NR or Unclear
    - Anatomic Segment
        - Reported (describe), NR or Unclear
    - Known Malignancy
        - Reported (describe), NR or Unclear
    - Presence of LE Ulcer
        - Reported (describe), NR or Unclear
- Were there relevant differences noted between groups in any other baseline characteristic? (Yes/No)
    - If yes, describe the differences.
- Comments

KQ 2-3 Intervention Characteristics

- Intervention Descriptors (For each Arm)
    - Describe the intervention received by each patient group.
- Indicate components of the intervention (For each Arm – representing main categories)
    - Placebo or Control
    - Lifestyle Interventions
    - Medical Therapy
    - Local Skin Care/Wound Care
    - Mechanical Compression Therapy
    - Invasive Surgical/Endovascular Procedures
- Specify applicable components from the selected main categories (For each Arm)

- Placebo or Control
  - Placebo
  - Usual care control/ optimal medical therapy
  - Other, specify
- Lifestyle Intervention
  - Smoking cessation
  - Leg elevation
  - Weight reduction
  - Exercise
  - Other, specify
- Medical Therapy
  - Diuretics
  - Anticoagulants
  - Aspirin
  - Pentoxifylline
  - Prostacyclins
  - Zinc sulfate
  - Warfarin
  - Apixaban
  - Rivaroxaban
  - Edoxaban
  - Dabigatran
  - Other, specify
- Mechanical Compression Therapy (indicate mmHg where applicable)
  - Pump
  - Wrap
  - Other, specify
  - Unclear/NR
- Invasive/Endovascular Procedures
  - Ablation - Chemical/Mechanicochemical
  - Ablation - Laser
  - Ablation - Radiofrequency
  - Ablation - Thermal
  - Angioplasty
  - Cryostripping
  - Phlebectomy
  - Sclerotherapy - Foam
  - Sclerotherapy - Glue
  - Sclerotherapy - Liquid
  - Stenting
  - Surgical stripping
  - Surgical thromboembolectomy
  - Ultrasound accelerated thrombolysis (e.g. Ekosonic)
  - Venous excision
  - Venous ligation
  - Other, specify

- Comments

KQ 1 Interventions/ Outcomes

- Indicate/ describe diagnostic tests applied
- Indicate/ describe gold standard used
- Findings for outcomes of interest
    - Sensitivity
    - Specificity
    - Positive predictive value
    - Negative predictive value
    - Inter-rater reliability
    - Internal consistency
    - Test-retest reliability
    - False positives
    - False negatives
    - Positive likelihood ratio
    - Negative likelihood ratio
- Comments

KQ 2 and KQ 3 Outcomes

- Select the outcome reported on this form:
    - Adverse effects of treatment:
        - Adverse drug reactions
        - Bleeding (including intracranial bleeding)
        - Venous wound infection
        - Contrast Nephropathy
        - Radiation-related injuries
        - Exercise-related harms
        - Periprocedural complications (vessel dissection, vessel perforation, and AV fistula)
        - Thrombophlebitis
        - Venous thromboembolic events (including PE)
        - Venous thrombosis (including stent thrombosis)
        - Death
    - Changes on standardized symptom scores
        - Symptom score used
            - Villalta
            - CEAP
            - VCSS
            - Other, specify
    - Patient-reported quality of life (including AVVQ)
        - Was a summary score reported? (Yes/No)
        - Were subscores for that QOL measure reported? (Yes/No)
            - What subscores were reported?
    - Qualitative reduction in LE edema
    - Qualitative reduction in LE pain

    - Improvement in LE venous hemodynamics/reflux severity as measured by air plethysmography, duplex ultrasonography, or invasive venography
    - Venous wound healing
    - Recurrent ulceration
    - Repeat intervention
    - LE Amputation
- Is this outcome form for a subgroup of interest? (Yes/No)
    - What subpopulation is this outcome reported for on this form?
        - Age
        - Sex
        - Race/ethnicity
        - Body weight
        - CEAP classification
        - VCSS classification
        - Villalta score
        - Severity of Disease
        - Anatomic segment affected
        - Known malignancy
        - Presence of LE Ulcer
- Any additional description/ clarification of the outcome reported on this form
- Total N Analyzed for this outcome
- Timepoint reported on this form
    - Short-term (<30 days)
    - Intermediate-term (31 days to 6 months)
    - Long-term (6+ months)
- Specify actual timing of the outcome (Day(s)/Week(s)/Month(s)/Year(s))
- For each arm:
    - N Analyzed (enter UNK if unknown)
    - Unadjusted Result
        - Number of patients with outcome
        - % of patients with outcome
        - Events/denominator
        - Odds ratio
        - Hazard ratio
        - Relative risk
        - Mean
        - Median
        - Mean within group change
        - Mean between group change
        - Other (specify)
    - Unadjusted Result Variability
        - 95% CI
        - IQR
        - Standard Error (SE)
        - Standard Deviation (SD)
        - Other % CI (specify)

        - Other (specify)
    - Unadjusted Result, p-value between groups
    - Unadjusted Result, Reference group (for comparison between groups)
    - Adjusted Result
        - Number of patients with outcome
        - % of patients with outcome
        - Events/denominator
        - Odds ratio
        - Hazard ratio
        - Relative risk
        - Mean
        - Median
        - Mean within group change
        - Mean between group change
        - Other (specify)
    - Adjusted Result Variability
        - 95% CI
        - IQR
        - Standard Error (SE)
        - Standard Deviation (SD)
        - Other % CI (specify)
        - Other (specify)
    - Adjusted Result, p-value between groups
    - Adjusted Result, Reference group (for comparison between groups)
    - If adjusted data is recorded, indicate the adjustments applied
- Comments

Quality

- Study Type (select one):
    - RCT
    - Observational
        - Cohort
        - Case-control
- If RCT, select Yes/No/Unclear for each of the following questions:
    - Sequence generation
        - Was the allocation sequence generated adequately (e.g., random number table, computer-generated randomization)?
    - Allocation concealment
        - Was the allocation of treatment adequately concealed (e.g., pharmacy-controlled randomization or use of sequentially numbered sealed envelopes)?
    - Blinding of participants, personnel and outcome assessors
        - Was knowledge of the allocated intervention adequately prevented during the study?
    - Incomplete outcome data
        - Were incomplete outcome data adequately addressed?

- Selective outcome reporting
  - Are reports of the study free of suggestion of selective outcome reporting?
- Other sources of bias
  - Was the study apparently free of other problems that could put it at a high risk of bias?

- If cohort, select the most appropriate option for each statement:
  - Selection bias
    - Representativeness of the exposed cohort…
      - truly representative of the average peripheral venous disease patient in the community
      - somewhat representative of the average peripheral venous disease patient in the community
      - selected group of users (e.g. nurses, volunteers)
      - no description of the derivation of the cohort
    - Selection of the non-exposed cohort…
      - drawn from the same community as the exposed cohort
      - drawn from a different source
      - no description of the derivation of the non-exposed cohort
    - Ascertainment of exposure…
      - secure record (e.g. surgical records)
      - structured interview
      - written self-report
      - no description
    - Demonstration that outcome of interest was not present at start of study? (Yes/No)
  - Comparability
    - Comparability of cohorts on the basis of the design or analysis…
      - study controls for underlying severity of disease and anatomic location
      - study controls for any additional factor
  - Outcome
    - Assessment of outcome…
      - independent blind assessment
      - record linkage
      - self-report
      - no description
    - Was follow-up long enough for outcome to occur (Yes/No)?
    - Adequacy of follow up of cohorts…
      - complete follow up - all subjects accounted for
      - subjects lost to follow up unlikely to introduce bias - small number lost - > 90% follow up, or description provided of those lost
      - follow up rate < 90% and no description of those lost
      - no statement
- If case-control, select the most appropriate option for each statement:
  - Selection bias

        - Is the case definition adequate?
            - yes, with independent validation
            - yes, e.g. record linkage or base on self-reports
            - no description
        - Representativeness of the cases…
            - consecutive or obviously representative series of cases
            - potential for selection biases or not stated
        - Selection of Controls
            - community controls
            - hospital controls
            - no description
        - Definition of Controls
            - no history of disease (endpoint)
            - no description of source
    - Comparability
        - Comparability of cases and controls on the basis of the design or analysis
            - study controls for underlying severity of disease and anatomic location
            - study controls for any additional factor
    - Exposure
        - Ascertainment of exposure…
            - secure record (e.g. surgical records)
            - structured interview where blind to case/control status
            - interview not blinded to case/control status
            - written self-report or medical record only
            - no description
        - Was there the same method of ascertainment for cases and controls (Yes/No)?
        - Non-Response rate…
            - same rate for both groups
            - non respondent described
            - rate different and no designation
- Overall Study Risk of Bias Rating (Good/Fair/Poor)
    - **Good** (low risk of bias). These studies have the least bias, and the results are considered valid. These studies adhere to the commonly held concepts of high quality, including the following: a clear description of the population, setting, approaches, and comparison groups; appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; a low dropout rate; and clear reporting of dropouts.
    - **Fair**. These studies are susceptible to some bias, but not enough to invalidate the results. They do not meet all the criteria required for a rating of good quality because they have some deficiencies, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

- **Poor** (high risk of bias). These studies have significant flaws that may have invalidated the results. They have serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.
- If the study is rated as "Fair" or "Poor," provide rationale.

- Outcome-specific quality rating
  - Should any of the outcomes abstracted for this study should be assigned a quality rating DIFFERENT from the overall study rating? (No/Yes)
    - If yes, provide the outcome(s), rating(s) and rationale(s).
- For KQ1 Studies Only:
  - QUADAS-2 Tool for Quality Assessment of Studies of Diagnostic Accuracy.
    - Domain 1: Patient Selection
      - Was a consecutive or random sample of patients enrolled? (Yes/No/Unclear)
      - Was a case-control design avoided? (Yes/No/Unclear)
      - Did the study avoid inappropriate exclusions? (Yes/No/Unclear)
      - Summary: Could the selection of patients have introduced bias? (Risk: Low, High, Unclear)
    - Domain 2: Index Tests
      - Were the index test results interpreted without knowledge of the reference standard? (Yes/No/Unclear)
      - If a threshold was used, was it pre-specified? (Yes/No/Unclear)
      - Summary: Could the conduct or interpretation of the index test have introduced bias? (Risk: Low, High, Unclear)
    - Domain 3: Reference Standards
      - Is the reference standard likely to correctly classify the target condition? (Yes/No/Unclear)
      - Were the reference standard results interpreted without knowledge of the results of the index test? (Yes/No/Unclear)
      - Summary: Could the reference standard, its conduct, or its interpretation have introduced bias? (Risk: Low, High, Unclear)
    - Domain 4: Flow and Timing
      - Was there an appropriate interval between index test(s) and reference standard? (Yes/No/Unclear)
      - Did all patients receive a reference standard? (Yes/No/Unclear)
      - Did all patients receive the same reference standard? (Yes/No/Unclear)
      - Were all patients included in the analysis? (Yes/No/Unclear)
      - Summary: Could the patient flow have introduced bias? (Risk: Low, High, Unclear)
  - Overall QUADAS-2 Study Rating (Low/Medium/High risk of bias)
    - **Low risk of bias.** No major features that risk biased results. RCTs are considered a high-quality study design, but studies that include consecutive patients representative of the intended sample for whom diagnostic uncertainty exists may also meet this standard. A "low risk" study avoids the multiple biases to which medical test studies are subject

(e.g., use of an inadequate reference standard, verification bias), and key study features are clearly described, including the comparison groups, outcomes measurements, and characteristics of patients who failed to have actual state (diagnosis or prognosis) verified.
        - **Medium risk of bias.** Susceptible to some bias, but flaws not sufficient to invalidate the results. The study does not meet all the criteria required for a rating of low risk, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.
        - **High risk of bias.** Significant flaws imply biases of various types that may invalidate the results. The study has significant biases determined a priori to be major or "fatal" (i.e., likely to make the results either uninterpretable or invalid).
        - If the study is rated as "Medium" or "High" risk of bias, provide rationale.
    - QUADAS-2 outcome-specific quality rating
        - Should any of the outcomes abstracted for this study should be assigned a quality rating DIFFERENT from the overall study rating? (No/Yes)
            - If yes, provide the outcome(s), rating(s) and rationale(s).
- Comments

Applicability – Use the PICOTS format to identify specific issues, if any, which may limit the applicability of the study.

- Population (P)
    - Narrow eligibility criteria and exclusion of those with comorbidities
    - More complex patients than typical of the community
    - Run-in period with high exclusion rate for non-adherence or side effects
    - Narrow or unrepresentative severity, stage of illness, or comorbidities
- Intervention (I)
    - Diagnostic tools used differently than as recommended or commonly used in practice
    - Dosing not reflective of current practice
    - Co-intervention that are likely to modify the effectiveness of therapy
    - Highly selected intervention team or level of training/proficiency not widely available
    - Follow-up not reflective of current practice
- Comparator (C)
    - Diagnostic tools used differently than as recommended or commonly used in practice
    - Comparator unclear
    - Inadequate comparison therapy or use of a substandard alternative therapy
- Outcomes (O)
    - Composite outcomes that mix outcomes of different significance
    - Short-term follow-up
    - Surrogate outcomes
- Timing (T)
    - Duration of participant followup was inadequate

- Setting (S)
    - Study conducted solely outside the US
    - Study was conducted only at a single site
- Any other concerns regarding the applicability of this study? (Yes/No)
    - If yes, describe.
- Comments

Appendix C. List of Included Studies

Abela R, Liamis A, Prionidis I, et al. Reverse foam sclerotherapy of the great saphenous vein with sapheno-femoral ligation compared to standard and invagination stripping: a prospective clinical series. Eur J Vasc Endovasc Surg 2008;36(4):485-90. DOI: 10.1016/j.ejvs.2008.06.029. PMID: 18718769.

Aguilar-Ferrandiz ME, Castro-Sanchez AM, Mataran-Penarrocha GA, et al. A randomized controlled trial of a mixed Kinesio taping-compression technique on venous symptoms, pain, peripheral venous flow, clinical severity and overall health status in postmenopausal women with chronic venous insufficiency. Clin Rehabil 2014;28(1):69-81. DOI: 10.1177/0269215512469120. PMID: 23426563.

Aguilar-Ferrandiz ME, Castro-Sanchez AM, Mataran-Penarrocha GA, et al. Effects of kinesio taping on venous symptoms, bioelectrical activity of the gastrocnemius muscle, range of ankle motion, and quality of life in postmenopausal women with chronic venous insufficiency: a randomized controlled trial. Arch Phys Med Rehabil 2013;94(12):2315-28. DOI: 10.1016/j.apmr.2013.05.016. PMID: 23769763.

Aguilar-Ferrandiz ME, Moreno-Lorenzo C, Mataran-Penarrocha GA, et al. Effect of a mixed kinesio taping-compression technique on quality of life and clinical and gait parameters in postmenopausal women with chronic venous insufficiency: double-blinded, randomized controlled trial. Arch Phys Med Rehabil 2014;95(7):1229-39. DOI: 10.1016/j.apmr.2014.03.024. PMID: 24732169.

Al Shammeri O, AlHamdan N, Al-Hothaly B, et al. Chronic Venous Insufficiency: prevalence and effect of compression stockings. Int J Health Sci (Qassim) 2014;8(3):231-6. PMID: 25505858.

Almeida JI, Kaufman J, Gockeritz O, et al. Radiofrequency endovenous ClosureFAST versus laser ablation for the treatment of great saphenous reflux: a multicenter, single-blinded, randomized study (RECOVERY study). J Vasc Interv Radiol 2009;20(6):752-9. DOI: 10.1016/j.jvir.2009.03.008. PMID: 19395275.

Antoch G, Pourhassan S, Hansen O, et al. Comparison of colour Doppler ultrasonography, ascending phlebography and clinical examination in the diagnosis of incompetent calf perforating veins. Br J Surg 2002;89(2):192-3. DOI: 10.1046/j.0007-1323.2001.02003.x. PMID: 11856132.

Barwell JR, Davies CE, Deacon J, et al. Comparison of surgery and compression with compression alone in chronic venous ulceration (ESCHAR study): randomised controlled trial. Lancet 2004;363(9424):1854-9. DOI: 10.1016/s0140-6736(04)16353-8. PMID: 15183623.

Basela H, Aydina C, Aya Y, et al. Endovenous laser ablation (EVLA) versus high ligation and striping (HL/S): Two-years follow up. Eastern Journal of Medicine 2011;17(2):83-87.

Belcaro G, Cesarone M, Di Renzo A, et al. Treatments for varicose veins: Surgery, sclerotherapy, foamsclerotherapy and combined (surgery+sclerotherapy) options. A 10-year, prospective, randomised, controlled, follow-up study. The VEDICO* trial and EST (European Sclerotherapy Trial). Angeiologie 2003;55(1):29-36.

Belcaro G, Cesarone MR, Di Renzo A, et al. Foam-sclerotherapy, surgery, sclerotherapy, and combined treatment for varicose veins: a 10-year, prospective, randomized, controlled, trial (VEDICO trial). Angiology 2003;54(3):307-15. PMID: 12785023.

Belcaro G, Dugall M and Corsi M. Superficial venous incompetence: Low-cost outpatient mini-surgery, sclerotherapy and combined procedure as a management plan. Costs and efficacy. A 20-year, follow-up registry. Minerva Chir 2015; PMID: 26046959.

Belcaro G, Nicolaides AN, Ricci A, et al. Endovascular sclerotherapy, surgery, and surgery plus sclerotherapy in superficial venous incompetence: a randomized, 10-year follow-up trial--final results. Angiology 2000;51(7):529-34. PMID: 10917577.

Benarroch-Gampel J, Sheffield KM, Boyd CA, et al. Analysis of venous thromboembolic events after saphenous ablation. Journal of Vascular Surgery: Venous and Lymphatic Disorders 2013;1(1):26-32.

Biemans AA, Kockaert M, Akkersdijk GP, et al. Comparing endovenous laser ablation, foam sclerotherapy, and conventional surgery for great

saphenous varicose veins. J Vasc Surg 2013;58(3):727-34.e1. DOI: 10.1016/j.jvs.2012.12.074. PMID: 23769603.

Bootun R, Lane T, Dharmarajah B, et al. Intra-procedural pain score in a randomised controlled trial comparing mechanochemical ablation to radiofrequency ablation: The Multicentre Venefit versus ClariVein(R) for varicose veins trial. Phlebology. 2016;31(1):61-5. doi: 10.1177/0268355514551085. PMID: 25193822.

Bountouroglou DG, Azzam M, Kakkos SK, et al. Ultrasound-guided foam sclerotherapy combined with sapheno-femoral ligation compared to surgical treatment of varicose veins: early results of a randomised controlled trial. Eur J Vasc Endovasc Surg 2006;31(1):93-100. DOI: 10.1016/j.ejvs.2005.08.024. PMID: 16233981.

Brittenden J, Cotton SC, Elders A, et al. A randomized trial comparing treatments for varicose veins. N Engl J Med 2014;371(13):1218-27. DOI: 10.1056/NEJMoa1400781. PMID: 25251616.

Brittenden J, Cotton SC, Elders A, et al. Clinical effectiveness and cost-effectiveness of foam sclerotherapy, endovenous laser ablation and surgery for varicose veins: results from the Comparison of LAser, Surgery and foam Sclerotherapy (CLASS) randomised controlled trial. Health Technol Assess 2015;19(27):1-342. DOI: 10.3310/hta19270. PMID: 25858333.

Campos W, Jr., Torres IO, da Silva ES, et al. A prospective randomized study comparing polidocanol foam sclerotherapy with surgical treatment of patients with primary chronic venous insufficiency and ulcer. Ann Vasc Surg 2015;29(6):1128-35. DOI: 10.1016/j.avsg.2015.01.031. PMID: 26004968.

Carpentier PH, Blaise S, Satger B, et al. A multicenter randomized controlled trial evaluating balneotherapy in patients with advanced chronic venous insufficiency. J Vasc Surg 2014;59(2):447-454.e1. DOI: 10.1016/j.jvs.2013.08.002. PMID: 24135621.

Carradice D, Mekako AI, Hatfield J, et al. Randomized clinical trial of concomitant or sequential phlebectomy after endovenous laser therapy for varicose veins. Br J Surg 2009;96(4):369-75. DOI: 10.1002/bjs.6556. PMID: 19283745.

Carradice D, Mekako AI, Mazari FA, et al. Clinical and technical outcomes from a randomized clinical trial of endovenous laser ablation compared with conventional surgery for great saphenous varicose veins. Br J Surg 2011;98(8):1117-23. DOI: 10.1002/bjs.7615. PMID: 21638277.

Carradice D, Mekako AI, Mazari FA, et al. Randomized clinical trial of endovenous laser ablation compared with conventional surgery for great saphenous varicose veins. Br J Surg 2011;98(4):501-10. DOI: 10.1002/bjs.7394. PMID: 21283981.

Carruthers TN, Farber A, Rybin D, et al. Interventions on the superficial venous system for chronic venous insufficiency by surgeons in the modern era: an analysis of ACS-NSQIP. Vasc Endovascular Surg 2014;48(7-8):482-90. DOI: 10.1177/1538574414561226. PMID: 25487248.

Christenson JT, Gueddi S, Gemayel G, et al. Prospective randomized trial comparing endovenous laser ablation and surgery for treatment of primary great saphenous varicose veins with a 2-year follow-up. J Vasc Surg 2010;52(5):1234-41. DOI: 10.1016/j.jvs.2010.06.104. PMID: 20801608.

Clarke-Moloney M, O'Brien JF, Grace PA, et al. Health-related quality of life during four-layer compression bandaging for venous ulcer disease: a randomised controlled trial. Ir J Med Sci 2005;174(2):21-5. PMID: 16094908.

Coccheri S, Scondotto G, Agnelli G, et al. Randomised, double blind, multicentre, placebo controlled study of sulodexide in the treatment of venous leg ulcers. Thromb Haemost 2002;87(6):947-52. PMID: 12083500.

Darwood RJ, Theivacumar N, Dellagrammaticas D, et al. Randomized clinical trial comparing endovenous laser ablation with surgery for the treatment of primary great saphenous varicose veins. Br J Surg 2008;95(3):294-301. DOI: 10.1002/bjs.6101. PMID: 18278775.

De Franciscis S, Gasbarro V, Amato B, et al. Hemodynamic surgery versus conventional surgery in chronic venous disease: A multicenter retrospective study. Acta Phlebologica 2013;14(3):109-114.

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Appendix D. List of Excluded Studies

All studies listed below were reviewed in their full-text version and excluded for the reasons cited. Reasons for exclusion signify only the usefulness of the articles for this study and are not intended as criticisms of the articles.

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Appendix E. Key to Included Primary and Companion Articles

Study Designation	Primary Abstracted Article	Companion Articles
CLASS (The Comparison of LAser, Surgery and foam Sclerotherapy)	Brittenden, 2014[1]	Brittenden, 2015[2]
EASI Study (The Efficacy and Safety of Aethoxysklerol®, Sotradecol® and Isotonic Saline for the Sclerotherapy of Telangiectasias and Reticular Varicose Veins)	Rabe, 2010[3]	None
ESCHAR Trial (The Effect of Surgery and Compression on Healing And Recurrence)	Barwell, 2004[4]	Gohel, 2007[5] Gohel, 2005[6] Gohel, 2005[7]
Evlt Versus Vnus Endovenous Randomised Trial study	Nordon, 2011[8]	None
EVOLVeS (EndoVenous radiofrequency Obliteration versus Ligation and Vein Stripping)	Lurie, 2003[9]	Lurie, 2011[10] Lurie, 2005[11]
HELP-1 (The Hull Endovenous Laser Project 1)	Carradice, 2011[12]	Carradice, 2011[13]
HELP-2 (The Hull Endovenous Laser Project 2)	Samuel, 2013[14]	Nandhra, 2015[15]
LARA (The Laser And Radiofrequency Ablation study)	Goode, 2010[16]	None
LAST Trial (Laser Ablation versus STeam ablation)	van den Bos, 2014[17]	None
MAGNA Trial	Biemans, 2013[18]	van der Velden, 2015[19]
REACTIV (The Randomised and	Michaels, 2006[20]	None
	Michaels, 2006[21]	None

Study Designation	Primary Abstracted Article	Companion Articles
Economic Assessment of Conservative and Therapeutic Interventions for Varicose Veins)	Michaels, 2006[22]	Michaels, 2006[23]
RECOVERY study	Almeida, 2009[24]	None
RELACS (The Randomized study comparing Endovenous Laser Ablation with Crossectomy and Stripping of the great saphenous vein	Rass, 2012[25]	Rass, 2015[26]
SUAVIS (The SUlodexide Arterial Venous Italian Study)	Coccheri, 2002[27]	None
VALVV Study (VNUS ClosureFAST radiofrequency Ablation versus 980nm Laser for Varicose Veins)	Shepherd, 2010[28]	Shepherd, 2015[29]
VANISH-1	King, 2015[30]	None
VANISH-2	Todd, 2014[31]	None
Varithena 013	Gibson, 2016[32]	None
Varithena 017	Vasquez, 2016[33]	None
VeCLOSE Trial	Morrison, 2015[34]	None
VEDICO (VEnous DIsease COntrol Trial)	Belcaro, 2003[35]	Belcaro, 2003[36]
None	Bountouroglou, 2006[37]	Kalodiki, 2012[38]
None	Disselhoff, 2008[39]	Disselhoff, 2009[40] Disselhoff, 2011[41]
None	Flessenkamper, 2013[42]	Flessenkamper, 2016[43]
None	Kalteis, 2008[44]	Kalteis, 2015[45]
None	Lane, 2016[46]	Bootun, 2016[47]
None	Lattimer, 2013[48]	Lattimer, 2012[49]
None	Pronk, 2010[50]	Gauw, 2016[51]

Study Designation	Primary Abstracted Article	Companion Articles
None	Rasmussen, 2011[52]	Rasmussen, 2013[53]
None	Rasmussen, 2007[54]	Rasmussen, 2010[55] Rasmussen, 2013[56]
None	Rautio, 2002[57]	Perala, 2005[58]
None	van Gent, 2006[59]	van Gent, 2015[60]
None	Zamboni, 2003[61]	Zamboni, 2004[62]
None	Abela, 2008[63]	None
None	Aguilar-Ferrandiz, 2014[64]	None
None	Aguilar-Ferrandiz, 2014[65]	None
None	Aguilar-Ferrandiz, 2013[66]	None
None	Al Shammeri, 2014[67]	None
None	Antoch, 2002[68]	None
None	Basela, 2011[69]	None
None	Belcaro, 2000[70]	None
None	Belcaro, 2015[71]	None
None	Benarroch-Gampel, 2013[72]	None
None	Campos, 2015[73]	None
None	Carpentier, 2014[74]	None
None	Carradice, 2009[75]	None
None	Carruthers, 2014[76]	None
None	Christenson, 2010[77]	None
None	Clarke-Moloney, 2005[78]	None
None	Darwood, 2008[79]	None
None	De Franciscis, 2013[80]	None
None	de Roos, 2003[81]	None
None	del Rio Sola, 2012[82]	None
None	Depalma, 2000[83]	None
None	Elderman, 2014[84]	None
None	Figueiredo, 2009[85]	None
None	Franek, 2006[86]	None
None	Gale, 2010[87]	None
None	Garg, 2011[88]	None
None	Ginsberg, 2001[89]	None
None	Guest, 2003[90]	None
None	Hamel-Desnos, 2010[91]	None
None	Helmy ElKaffas, 2011[92]	None
None	Holmes, 2014[93]	None
None	Houtermans-Auckel, 2009[94]	None
None	Jull, 2009[95]	None
None	Kahle, 2004[96]	None
None	Kahn, 2011[97]	None
None	Kayilioglu, 2016[98]	None

Study Designation	Primary Abstracted Article	Companion Articles
None	Klem, 2009[99]	None
None	Kumar, 2002[100]	None
None	Kurstjens, 2016[101]	None
None	Lee, 2008[102]	None
None	Liu, 2011[103]	None
None	Liu, 2011[104]	None
None	Mantoni, 2002[105]	None
None	Massenburg, 2015[106]	None
None	Menyhei, 2008[107]	None
None	Meyer, 2000[108]	None
None	Moreno-Moraga, 2014[109]	None
None	Mousa, 2016[110]	None
None	Mozafar, 2014[111]	None
None	Nelson, 2007[112]	None
None	Nikolovska, 2002[113]	None
None	Noppeney, 2016[114]	None
None	Obi, 2015[115]	None
None	O'Hare, 2010[116]	None
None	O'Sullivan, 2000[117]	None
None	Pares, 2010[118]	None
None	Rabahie, 2011[119]	None
None	Raju, 2013[120]	None
None	Roopram, 2013[121]	None
None	Schouten, 2006[122]	None
None	Sell, 2014[123]	None
None	Serra, 2015[124]	None
None	Shadid, 2012[125]	None
None	Stotter, 2006[126]	None
None	Subramonia, 2001[127]	None
None	Theivacumar, 2008[128]	None
None	Vandongen, 2000[129]	None
None	Vanscheidt, 2002[130]	None
None	Viarengo, 2007[131]	None
None	Wang, 2016[132]	None
None	Wong, 2012[133]	None
None	Wozniak, 2015[134]	None
None	Wright, 2006[135]	None
None	Yang, 2013[136]	None
None	Yin, 2015[137]	None
None	Yin, 2015[138]	None

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Appendix F. Characteristics of Included Studies

Appendix Table F-1. Study Characteristics—KQ 1

Author, Year	Study Details	Diagnostic Method(s)	Outcomes Results
Antoch, 2002[1]	Study Design: Observational Quality: Fair QUADAS-2: Medium risk of bias Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 50 N Completed: 50 % Female: Unclear/NR Mean Age: 51	Color doppler ultrasonagraphy vs. Ascending phlebography vs. Surgical Evaluation (gold standard)	For color doppler ultrasound: Sensitivity=80%; Specificity=74%, Accuracy not reported individually; Ascending phlebography: Sensitivity=66%; Clinical examination: Sensitivity=79%
Depalma, 2000[2]	Study Design: Observational Quality: Fair QUADAS-2: Medium risk of bias Location: U.S. <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 33 N Completed: 33 % Female: 0% Mean Age: 55	Color doppler ultrasound vs. Ascending and descending phlebography (gold standard)	For complete occlusion: Sensitivity=100%; Specificity=100%; For postphlebetic changes: Sensitivity=63%; Specificity=100%; PPV=100%; NPV=53%; For reflux detection: Sensitivity=82%; Specificity=75%; PPV=96%; NPV=37%; For saphenous reflux: Sensitivity=95%; Specificity=100%

Author, Year	Study Details	Diagnostic Method(s)	Outcomes Results
Kayilioglu, 2016[3]	Study Design: Observational Quality: Good QUADAS-2: Low risk of bias Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE venous thrombosis/ obstruction; PTS Total N: 86 N Completed: 86 % Female: 26.7% Mean Age: 40.3	Doppler ultrasound vs. Venography + IVUS (gold standard)	Sensitivity=62.5%; Specificity=71.0%; PPV=73.0%; NPV=60.0%
Kurstjens, 2016[4]	Study Design: Observational Quality: Fair QUADAS-2: Low risk of bias Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic; Asymptomatic Condition(s): LE venous thrombosis/ obstruction; PTS Total N: 262 N Completed: 248 % Female: 62.5% Mean Age: 45.5	Air Plethysmography vs. Doppler ultrasound + MRV vs. Doppler ultrasound + CTV (3 limbs) vs. Doppler ultrasound (10 limbs) (gold standard unclear)	Outflow fraction by APG: Sensitivity=34.8%, Specificity=87.5%, PPV=89.9%, NPV=29.6%, LR(+)=2.78, LR(-)=0.75 Ejection fraction by APG: Sensitivity=64.3%, Specificity=48.3%, PPV=78.8%, NPV=31.2%, LR(+)=1.24, LR(-)=0.74 Residual volume fraction by APG: Sensitivity=44.7%, Specificity=46.7%, PPV=71.4%, NPV=22.1%, LR(+)=0.84, LR(-)=1.19"

Author, Year	Study Details	Diagnostic Method(s)	Outcomes Results
Lee, 2008[5]	Study Design: Observational Quality: Fair QUADAS-2: Medium risk of bias Location: Asia <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE varicose veins Total N: 100 N Completed: 100 % Female: 55% Mean Age: 54.9	3-D CTV vs. Doppler Sonography (gold standard)	GSV: Sensitivity=98.2%; Specificity=83.3%; SSV: Sensitivity=53.3%; Specificity=94.9%
Mantoni, 2002[6]	Study Design: Observational Quality: Fair QUADAS-2: Medium risk of bias Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 39 N Completed: 38 % Female: 39% Mean Age: 67	Ascending phlebography vs. Descending phlebography vs. Continuous wave Doppler vs. Ambulatory strain gauge plethysmography vs. Triplex ultrasound (TUS) (gold standard)	For common and superficial venous system: Sensitivity=86%(AP), 70%(CWD), 4%(ASGP); Specificity=0%(AP), 38%(CWD), 100%(ASGP). For popliteal vein: Sensitivity=83%(AP), 48%(CWD), 5%(ASGP); Specificity=17%(AP), 75%(CWD), 100%(ASGP)
Massenburg, 2015[7]	Study Design: Observational Quality: Fair QUADAS-2: Medium risk of bias Location: U.S. <u>Population</u> Symptom Status: Symptomatic; LE venous thrombosis/obstruction Total N: 46 N Completed: 46 % Female: 58%, 64% Mean Age: 64, 59	Magnetic resonance venography vs. Invasive venography + IVUS (gold standard)	Sensitivity=100%; Specificity=22.7%; PPV=58.5%; NPV=100%; False Positive rate=41.5%

Author, Year	Study Details	Diagnostic Method(s)	Outcomes Results
Meyer, 2000[8]	Study Design: Observational Quality: Poor QUADAS-2: High risk of bias Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 87 N Completed: 87 % Female: 50.4% Mean Age: 56	Duplex ultrasound vs. Ascending phlebography vs. Surgical evaluation (gold standard)	Cockett I (p=1.0); Cockett II (p= 0.569); Cockett III (p=1.0)
Mousa, 2016[9]	Study Design: Observational Quality: Fair QUADAS-2: Medium risk of bias Location: U.S. <u>Population</u> Symptom Status: Symptomatic Condition(s): LE venous thrombosis/ obstruction; PTS Total N: 36 N Completed: 36 % Female: 72.2% Median Age: 61.2	Doppler ultrasound vs. Venography + IVUS (gold standard)	The area under the curve for using CFV reflux vales (by VDUS) to predict IVUS iliac stenosis was 0.77 (P=.001) determined by ROC curve analysis

Author, Year	Study Details	Diagnostic Method(s)	Outcomes Results
Rabahie, 2011[10]	Study Design: Observational Quality: Fair QUADAS-2: Medium risk of bias Location: Latin America <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 30 N Completed: 30 % Female: 90% Mean Age: 53.7	Color doppler ultrasound vs. Surgical evaluation (gold standard)	GSV: Sensitivity=70.3%; False-negative rate=29.7%

Abbreviations: CTV=computed tomography venography; IVUS=intravascular ultrasound; GSV=great saphenous vein; LE=lower extremity; MRV=magnetic resonance venography; NR=not reported; PTS=Post-thrombotic Syndrome

Appendix Table F-2. Study Characteristics—KQ 2

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Abela, 2008[11]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 82 N Completed: 82 % Female: 61% Median Age: 44	High Ligation + Invagination Stripping vs. High Ligation + Foam Sclerotherapy	Clinical assessment; Ultrasound	Bleeding
Aguilar-Ferrandiz, 2013[12]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 123 N Completed: 123 % Female: 100%, 100% Mean Age: 66.05, 63.32	Mixed Kinesio Taping vs. Placebo Taping	Clinical assessment	Patient-reported QOL (including AVVQ); Changes on standardized symptom scores; Qualitative reduction in LE edema; Recurrent ulceration; Qualitative reduction in LE pain

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Aguilar-Ferrandiz, 2014[13]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 120 N Completed: 104 % Female: 100%, 100% Mean Age: 64.4, 66.48	Mixed Kinesio Taping vs. Placebo Taping	Clinical assessment	Patient-reported QOL); Changes on standardized symptom scores; Qualitative reduction in LE edema; Improvement in LE venous hemodynamics/reflux severity; Qualitative reduction in LE pain
Aguilar-Ferrandiz, 2014[14]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic; Asymptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 130 N Completed: 130 % Female: 100%, 100% Mean Age: 64.4, 66.48	Mixed Kinesio Taping vs. Placebo Taping	Clinical assessment	Changes on standardized symptom scores; Patient-reported QOL

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Al Shammeri, 2014[15]	Study Design: RCT Quality: Poor Location: Middle East <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 100 N Completed: 75 % Female: 75.4% Mean Age: 43.9	Compression Stockings vs. Standard Medical Therapy	Unclear/NR	Changes on standardized symptom scores
Almeida, 2009[16] RECOVERY	Study Design: RCT Quality: Poor Location: U.S.,UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 69 N Completed: 69 % Female: 82.9%, 75.6% Mean Age: 51.6, 52.4	EVLA vs. RFA	Ultrasound	Thrombophlebitis; Changes on standardized symptom scores; Patient-reported QOL; Venous thromboembolic events; Thrombophlebitis

Author, Year **Trial** **Companion Articles**	**Study Details***	**Interventions**	**Diagnostic Method(s) and Criteria**	**Outcomes (Subgroups analyzed)**
Barwell, 2004[17] ESCHAR Companions: Gohel, 2007[18] Gohel, 2005[19] Gohel, 2005[20]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 500 N Completed: 460 % Female: 60%, 56% Median Age: 74, 72	Mechanical Compression vs. Surgical Stripping + Avulsions + Compression	Clinical assessment; Ultrasound	Venous wound healing; Death; Venous wound infection; Venous thrombosis; Bleeding; Improvement in LE venous hemodynamics/reflux severity
Basela, 2011[21]	Study Design: RCT Quality: Poor Location: Middle East <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 174 N Completed: 174 % Female: 40%, 40% Mean Age: 32.8, 34.45	High Ligation + Stripping vs. EVLA	Clinical assessment; Ultrasound	Bleeding; Qualitative reduction in LE edema; Radiation-related injuries; Improvement in LE venous hemodynamics/reflux severity; Thrombophlebitis; Venous wound infection

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Belcaro, 2000[22]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 150 N Completed: 121 % Female: 44%, 48% Mean Age: 52, 53	High Ligation + Stripping vs. Liquid/Foam Sclerotherapy	Ultrasound	Improvement in LE venous hemodynamics/reflux severity
Belcaro, 2003[23] VEDICO Companions: Belcaro, 2003[24]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE varicose veins Total N: 887 N Completed: 749 % Female: 67%, 69%, 68%, 70%, 69%, 68% Mean Age: 44.4, 45, 44, 45, 42, 42	Ligation + Stripping vs. High Ligation + Stripping vs. Stripping vs. Foam Sclerotherapy +/- Ligation	Ultrasound	Improvement in LE venous hemodynamics/reflux severity

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Belcaro, 2015[25]	Study Design: Observational Quality: Poor Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 852 N Completed: 711 % Female: 55.7%, 53.9%, 52.2%, 43.9% Mean Age: 43.2, 44.2, 43.7, 44.7	Mini-ligation vs. Ligation + Stripping vs. Compression Sclerotherapy vs. Mini-ligation + Sclerotherapy.	Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Repeat intervention, Venous thrombosis
Benarroch-Gampel, 2013[26]	Study Design: Observational Quality: Fair Location: U.S. <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 3,874 N Completed: 3,874 % Female: 70.9%, 29% Mean Age: 53.8, 51.8	EVLA +/- Phlebectomy vs. RFA +/- Phlebectomy	Unclear/NR	Venous thromboembolic events (Anatomic Segment)

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Biemans, 2013[27] MAGNA Trial Companions: van der Velden, 2015[28]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 240 N Completed: 223 % Female: 69%, 68%, 68% Mean Age: 49, 56	EVLA vs. Foam Sclerotherapy vs. High Ligation + Stripping	Ultrasound	Venous wound infection; Venous thromboembolic events; Periprocedural complications; Repeat intervention; Venous thrombosis; Patient-reported QOL; Changes on standardized symptom scores
Bountouroglou, 2006[29] Companions: Kalodiki, 2012[30]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 73 N Completed: 59 % Female: 74%, 59% Median Age: 49, 47	Surgical Stripping + Venous ligation vs. Foam sclerotherapy + venous ligation	Unclear/NR	Periprocedural complications; Bleeding; Repeat intervention; Venous thromboembolic events; Improvement in LE venous hemodynamics/reflux severity; Thrombophlebitis; Changes on standardized symptom scores; Patient-reported QOL

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Brittenden, 2014[31] CLASS Companions: Brittenden, 2015[32]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 798 N Completed: 670 % Female: 57.1%, 56.6%, 56.4% Mean Age: 49.7, 49, 49.2	High Ligation + Stripping vs. EVLA vs. Foam Sclerotherapy	Ultrasound	Patient-reported QOL; Changes on standardized symptom score;s Improvement in LE venous hemodynamics/reflux severity
Campos, 2015[33]	Study Design: RCT Quality: Good Location: Latin America <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 58 N Completed: 51 % Female: 82%, 65% Mean Age: 46.7, 52	High Ligation + Stripping vs. Foam Sclerotherapy + Ligation	Ultrasound	Venous wound healing; Recurrent ulceration; Changes on standardized symptom scores; Patient-reported QOL

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Carpentier, 2014[34]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 425 N Completed: 390 % Female: 56%, 57% Mean Age: 65.1, 63.5	Bathing therapy (Balneotherapy) vs. Waitlist Control Group	Clinical assessment; Ultrasound	Recurrent ulceration; Exercise-related harms; Venous thromboembolic events; Changes on standardized symptom scores; Patient-reported QOL (CEAP Classification)
Carradice, 2009[35]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 50 N Completed: 41 % Female: 68%, 84% Mean Age: 51.1, 52.4	EVLA vs. EVLA + Phlebectomy	Ultrasound	Patient-reported QOL; Changes on standardized symptom scores; Repeat intervention

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Carradice, 2011[36] HELP-1 Companions: Carradice, 2011[37]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 280 N Completed: 237 % Female: 66%, 61% Mean Age: 49	Phlebectomy + Surgical Stripping + Ligation vs. EVLA + Phlebectomy	Ultrasound	Patient-reported QOL; Changes on standardized symptom scores; Periprocedural complications; Bleeding; Thrombophlebitis; Qualitative reduction in LE pain; Venous thromboembolic events
Carruthers, 2014[38]	Study Design: Observational Quality: Fair Location: U.S. <u>Population</u> Symptom Status: Symptomatic Condition(s): Unclear/NR Total N: 4,366 N Completed: 4,366 % Female: 66.4% Mean Age: 52.4	High Ligation + Stripping vs. RFA vs. EVLA	ICD-9 codes	Periprocedural complications; Venous thrombosis

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Christenson, 2010[39]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 204 N Completed: 200 % Female: NR Mean Age: 46.3, 44.6	Ligation +Stripping vs. Foam Sclerotherpy	Ultrasound, CEAP grade 2-6	Changes on standardized symptom scores; Patient-reported QOL; Improvement in LE venous hemodynamics/reflux severity; Repeat intervention; Qualitative reduction in LE pain; Venous thromboembolic events; Bleeding; Periprocedural complications; Thrombophlebitis; Radiation-related injuries
Clarke-Moloney, 2005[40]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 200 N Completed: 180 % Female: NR Age: NR	Compression vs. Compression	Clinical assessment	Patient-reported QOL; Venous wound healing

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Coccheri, 2002[41] SUAVIS	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 235 N Completed: 230 % Female: 56%, 52% Mean Age: 63.18, 64.18	Sulodexide + Compression vs. Placebo + Compression	Clinical assessment	Venous wound healing
Darwood, 2008[42]	Study Design: RCT Quality: Poor Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 136 N Completed: 103 % Female: 45%, 38%, 36% Median Age: 42, 52, 49	High Ligation + Stripping vs. EVLA	Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Thrombophlebitis; Periprocedural complications; Bleeding; Qualitative reduction in LE pain; Patient-reported QOL; Changes on standardized symptom scores

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
De Franciscis, 2013[43]	Study Design: Observational Quality: Poor Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 11,026 N Completed: 11,026 % Female: 68%, 59% Median Age:45, 46.5	RFA +/- Phlebectomy vs. EVLA +/- Phlebectomy	Clinical assessment; Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Qualitative reduction in LE pain; Qualitative reduction in LE edema
de Roos, 2003[44]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE varicose veins Total N: 82 N Completed: 80 % Female: 98% Mean Age: 42.1	Phlebectomy vs. Liquid Sclerotherapy	Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Bleeding; Thrombophlebitis; Repeat intervention

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
del Rio Sola, 2012[45]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 51 N Completed: 51 % Female: 44%, 68% Mean Age: 60.5, 58.59	Aspirin + Compression vs. Compression	Clinical assessment	Recurrent Ulceration
Disselhoff, 2008[46] Companions: Disselhoff, 2009[47] Disselhoff, 2011[48]	Study Design: RCT Quality: Good; Fair for 5 year outcomes Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 120 N Completed: 111 % Female: 68%, 70% Mean Age: 46, 49	EVLA vs. Cryostripping	Ultrasound	Changes on standardized symptom scores; Qualitative reduction in LE pain; Improvement in LE venous hemodynamics/reflux severity; Venous thrombosis; Repeat intervention

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Elderman, 2014[49]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 111 N Completed: 79 % Female: 82%, 80% Mean Age: 54.87, 50.93	EVLA vs. EVLA + Compression	Clinical assessment; Ultrasound	Patient-reported QOL; Qualitative reduction in LE pain
Figueiredo, 2009[50]	Study Design: RCT Quality: Fair Location: Latin America <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE varicose veins Total N: 60 N Completed: 56 % Female: 79%, 85% Mean Age: 49, 53	High Ligation + Stripping vs. Foam Sclerotherapy	CEAP great C5EpAsPr (healed venous ulcer)	Changes on standardized symptom scores

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Flessenkamper, 2013[51] REVAS Companions: Flessenkamper, 2016[52]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 449 N Completed: 449 % Female: 70% Mean Age: 48	High Ligation + Stripping vs. EVLA vs. EVLA + Ligation	Clinical assessment; Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Changes on standardized symptom scores; Venous thrombosis; Periprocedural complications; Qualitative reduction in LE pain; Bleeding
Franek, 2006[53]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 110 N Completed: 110 % Female: 63%, 52% Mean Age: 65, 61	Compression + drug therapy vs. High Ligation + Stripping + Phlebectomy + Compression + Drug Therapy	Clinical assessment; Ultrasound	Venous wound healing

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Gale, 2010[54]	Study Design: RCT Quality: Fair Location: U.S. <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 118 N Completed: 106 % Female: 75%, 63%, 83% Mean Age: 49, 46, 54	EVLA vs. RFA	Ultrasound	Venous thrombosis; Improvement in LE venous hemodynamics/reflux severity; Changes on standardized symptom scores; Patient-reported QOL; Periprocedural complications; Repeat intervention
Gibson, 2016[55] Varithena 013	Study Design: RCT Quality: Good Location: U.S. <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins, LE chronic venous insufficiency/reflux/incompetency Total N: 77 N Completed: 77 % Female: 80.5% Mean Age: 45.1	Varithena 1% (Foam Sclerotherapy) vs. Placebo saline injections	CEAP grade 2-5	Venous thrombosis; Changes on standardized symptom scores; Patient-reported QOL; Qualitative reduction in LE pain; Qualitative reduction in LE edema

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Goode, 2010[56] LARA	Study Design: RCT Quality: Poor Location: UK/Europe <u>Population</u> Symptomatic; Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 66 N Completed: 66 % Female: 68%, 65% Mean Age: 48.6, 45	EVLA vs. RFA	Ultrasound	Improvement in LE venous hemodynamics/reflux severity
Guest, 2003[57]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 76 N Completed: 76 % Female: 59%, 67% Mean Age: 68, 67	High Ligation + Stripping or SEPS vs. Compression	Clinical assessment; Ultrasound	Death; Venous wound infection; Venous wound healing; Patient-reported QOL

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Hamel-Desnos, 2010[58]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic; Condition(s): LE varicose veins Total N: 60 N Completed: 60 % Female: 97%, 87% Mean Age: 53, 61	Foam Sclerotherapy vs. Foam Sclerotherapy + Compression	Clinical assessment; Ultrasound	Changes on standardized symptom scores
Helmy ElKaffas, 2011[59]	Study Design: RCT Quality: Poor Location: Africa <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 180 N Completed: 178 % Female: 47%, 50% Mean Age: 33.1, 34.9	High Ligation + Stripping vs. RFA	Ultrasound	Thrombophlebitis; Bleeding; Venous thromboembolic events; Changes on standardized symptom scores; Improvement in LE venous hemodynamics/reflux severity; Qualitative reduction in LE pain; Periprocedural complications

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Houtermans-Auckel, 2009[60]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 104 N Completed: 96 % Female: 63%, 73% Mean Age: 49, 50	GSV Stripping + Elastic Bandaging for 3 days vs. Elastic bandaging for 4 weeks	Clinical assessment; Ultrasound	Qualitative reduction in LE edema; Changes on standardized symptom scores
Jull, 2009[61]	Study Design: RCT Quality: Fair Location: Australia/N.Z. <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 40 N Completed: 39 % Female: 68% Mean Age: 54.6	Exercise + Compression vs. Usual Care + Compression	Clinical assessment	Venous wound healing; Exercise-related harms

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Kahle, 2004[62]	Study Design: RCT Quality: Poor Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 25 N Completed: 25 % Female: 72% Mean Age: 55.5	Compression vs. Sclerotherapy + Compression	Ultrasound	Improvement in LE venous hemodynamics/reflux severity
Kalteis, 2008[63]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 100 N Completed: 95 % Female: 79%, 71% Mean Age: 46, 46.5	Compression + Stripping vs. Compression + EVLA	Ultrasound	Bleeding; Patient-reported QOL; Qualitative reduction in LE pain; Qualitative reduction in LE edema; Thrombophlebitis; Improvement in LE venous hemodynamics/reflux severity; Venous thrombosis; Changes on standardized symptom scores; Repeat intervention

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
King, 2015[64] VANISH-1	Study Design: RCT Quality: Good Location: U.S. <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 284 N Completed: 279 % Female: 74.6% Mean Age: 48.9	Sclerotherapy vs. Placebo	Ultrasound	Changes on standardized symptom scores; Improvement in LE venous hemodynamics/reflux severity; Patient-reported QOL
Klem, 2009[65]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 536 N Completed: 445 % Female: 79%, 71% Mean Age: 56, 54	High Ligation + Stripping vs. High Ligation + Cryostripping	Clinical assessment; Ultrasound	Patient-reported QOL; Changes on standardized symptom scores

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Kumar, 2002[66]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 100 N Completed: 92 % Female: NR Mean Age: 72, 65, 73, 69	Compression vs. Compression	Clinical assessment	Venous wound healing; Recurrent ulceration
Lane, 2016[67] Companions: Bootun, 2016[68]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 170 N Completed: 121 % Female: 58.8% Median Age: 50	Mechanical Endovenous Ablation (MOCA) vs. RFA	Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Patient-reported QOL; Changes on standardized symptom scores; Thrombophlebitis; Venous thrombosis (including stent thrombosis)

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Lattimer, 2013[69] Companions: Lattimer, 2012[70]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 110 N Completed: 90 % Female: 61%, 54% Mean Age: 47.3, 49.6	EVLA vs. Sclerotherapy	Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Patient-reported QOL; Changes on standardized symptom scores; Venous thrombosis; Repeat intervention; Qualitative reduction in LE pain; Bleeding; Periprocedural complications;
Liu, 2011[71]	Study Design: RCT Quality: Fair Location: Asia <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 134 N Completed: 134 % Female: 57%, 52% Mean Age: 39.58, 41.02	EVLA vs. EVLA + Phlebectomy	Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Thrombophlebitis; Qualitative reduction in LE edema; Venous wound infection; Qualitative reduction in LE pain; Periprocedural complications; Bleeding; Thrombophlebitis

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Liu, 2011[72]	Study Design: RCT Quality: Poor Location: Asia <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 60 N Completed: 54 % Female: NR Age: NR	Stripping + Ligation vs. Foam Sclerotherapy + Ligation	Ultrasound	Changes on standardized symptom scores; Patient-reported QOL; Improvement in LE venous hemodynamics/reflux severity; Periprocedural complications; Bleeding; Thrombophlebitis; Repeat intervention
Lurie, 2003[73] EVOLVeS Companions: Lurie, 2011[74] Lurie, 2005[75]	Study Design: RCT Quality: Fair Location: U.S.,UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 85 N Completed: 80 % Female: 73%, 72% Mean Age: 49, 47	High Ligation + Stripping vs. RFA	Ultrasound	Periprocedural complications; Patient-reported QOL; Improvement in LE venous hemodynamics/reflux severity; Changes on standardized symptom scores; Bleeding; Venous wound infection; Venous thrombosis

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Menyhei, 2008[76]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 160 N Completed: 146 % Female: 66%, 70% Median Age: 47, 46	High Ligation + Stripping vs. High Ligation + Cyrostripping	Clinical assessment; Ultrasound	Patient-reported QOL
Michaels, 2006[77] REACTIV	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic; Asymptomatic Condition(s): LE varicose veins Total N: 77 N Completed: 52 % Female: 93%, 83% Mean Age: 47, 45.1	High Ligation + Stripping vs. Foam Sclerotherapy + Ligation	Clinical assessment; Ultrasound	Venous wound infection; Patient-reported QOL; Qualitative reduction in LE pain; Repeat intervention

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Michaels, 2006[78] REACTIV Companions: Michaels, 2006[79]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic; Asymptomatic Condition(s): LE varicose veins Total N: 246 N Completed: 182 % Female: 71%, 79% Mean Age: 49.5, 49	High Ligation + Stripping vs. Conservative Therapy	Clinical assessment; Ultrasound	Venous wound infection; Patient-reported QOL; Qualitative reduction in LE pain
Michaels, 2006[80] REACTIV	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic; Asymptomatic Condition(s): LE varicose veins Total N: 34 N Completed: 34 % Female: 68% Mean Age: 47.5	Lifestyle Intervention vs. Sclerotherapy with Sodium Tetradecylsuflate	Clinical assessment; Ultrasound	Patient-reported QOL; Qualitative reduction in LE pain

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Moreno-Moraga, 2014[81]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins Total N: 320 N Completed: 298 % Female: NR Age: NR	Foam Sclerotherapy vs. YAG Laser + Foam Sclerotherapy	Ultrasound	Periprocedural complications; Qualitative reduction in LE pain; Patient-reported QOL; Improvement in LE venous hemodynamics/reflux severity (Severity of Disease)
Morrison, 2015[82] VeCLOSE Trial	Study Design: RCT Quality: Fair Location: U.S. <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 242 N Completed: 222 % Female: 77%, 82% Mean Age: 49, 50.5	Cyanoacrylate embolization vs. RFA	Ultrasound	Changes on standardized symptom scores; Patient-reported QOL; Qualitative reduction in LE pain; Thrombophlebitis; Bleeding

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Mozafar, 2014[83]	Study Design: RCT Quality: Poor Location: Middle East <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins Total N: 65 N Completed: 65 % Female: 73.3%, 71.4% Age: NR	High Ligation + Stripping vs. EVLA	Unclear/NR	Qualitative reduction in LE pain; Patient-reported QOL; Recurrent ulceration; Venous thrombosis; Changes on standardized symptom scores
Nelson, 2007[84]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins Total N: 245 N Completed: 245 % Female: 67% Mean Age: 70	Pentoxifylline vs. Bandages/Wound Care	Clinical assessment	Venous wound healing; Adverse drug reactions
Nikolovska, 2002[85]	Study Design: RCT Quality: Poor Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 80 N Completed: 80 % Female: 45%, 48% Mean Age: 61.5, 61.2	Pentoxifylline + Local Therapy vs. Local Therapy	Clinical assessment	Recurrent ulceration

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Noppeney, 2016[86]	Study Design: Observational Quality: Poor Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): Unclear/NR Total N: 89,647 N Completed: 36,096 % Female: 69.3% Mean Age: 52.8	Surgery (venous ligation plus stripping) vs. RFA vs. EVLA	Not Reported	Periprocedural Complications
Nordon, 2011[87] Evlt Versus Vnus Endovenous Randomised Trial study	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins Total N: 159 N Completed: 138 % Female: 68%, 57% Mean Age: 46.7, 46.9	EVLA vs. RFA	Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Qualitative reduction in LE pain; Thrombophlebitis; Venous thrombosis; Patient-reported QOL; Periprocedural complications

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Obi, 2015[88]	Study Design: Observational Quality: Poor Location: U.S. <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 979 N Completed: 979 % Female: 71% Mean Age: 52.4	RFA vs. EVLA + Compression	Ultrasound	Changes on standardized symptom scores; Venous thromboembolic events; Venous wound infection; Venous thrombosis; Bleeding; Periprocedural complications;
O'Hare, 2010[89]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 40 N Completed: 33 % Female: NR Median Age: 69	4 Layer Compression vs. 4 Layer Compression + Sclerotherapy	Ultrasound	Venous wound healing; Venous thromboembolic events; Improvement in LE venous hemodynamics/reflux severity

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Pares, 2010[90]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE varicose veins Total N: 501 N Completed: 501 % Female: 66%, 66%, 80% Mean Age: 49.54, 50, 48.76	RFA +/- Phlebectomy vs. EVLA +/- Phlebectomy	Clinical assessment; Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Venous thromboembolic events;) Periprocedural complications; Thrombophlebitis; Death; Bleeding
Pronk, 2010[91] Companions: Gauw, 2016[92]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 130 legs N Completed: 130 legs % Female: 78%, 74% Mean Age: 50, 49	Foam sclerotherapy + surgical stripping vs. EVLA + Foam Sclerotherapy	Ultrasound	Qualitative reduction in LE pain; Patient-reported QOL; Venous thromboembolic events; Venous thrombosis; Changes on standardized symptom scores; Improvement in LE venous hemodynamics/reflux severity; Repeat intervention (CEAP Classification)

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Rabe, 2010[93] EASI Study	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE varicose veins Total N: 316 N Completed: 266 % Female: 97.5% Mean Age: 43.5	Polidocanol (Foam Sclerotherapy) vs. Sodium Tetradecyl Sulphate (Foam Sclerotherapy) vs. Placebo saline injections	Ultrasound	Periprocedural complications; Bleeding
Rasmussen, 2007[94] Companions: Rasmussen, 2010[95] Rasmussen, 2013[96]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 121 N Completed: 88 % Female: 73%, 66% Mean Age: 54, 53	High Ligation + Stripping vs. EVLA	Ultrasound	Thrombophlebitis; Patient-reported QOL; Repeat intervention; Changes on standardized symptom scores; Improvement in LE venous hemodynamics/reflux severity

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Rasmussen, 2011[97] Companions: Rasmussen, 2013[98]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 500 N Completed: 433 % Female: 72%, 70%, 76%, 77% Mean Age: 52, 51, 51, 50	High Ligation + Stripping vs. EVLA vs. Sclerotherapy vs. RFA	Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Venous thrombosis; Venous thromboembolic events; Bleeding; Qualitative reduction in LE pain; Changes on standardized symptom scores; Patient-reported QOL; Repeat intervention
Rass, 2012[99] RELACS Companions: Rass, 2015[100]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 400 N Completed: 346 % Female: 67%, 70% Mean Age: 47.9, 48	High Ligation + Stripping vs. EVLA	Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Patient-reported QOL; Qualitative reduction in LE pain; Venous thrombosis; Thrombophlebitis; Bleeding; Venous wound infection; Changes on standardized symptom scores; Repeat intervention;

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Rautio, 2002[101] Companions: Perala, 2005[102]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 33 N Completed: 28 % Female: 93%, 92% Mean Age: 33, 38	Surgical Stripping vs. Endovenous obliteration	Ultrasound	Changes on standardized symptom scores; Patient-reported QOL; Repeat intervention; Thrombophlebitis
Roopram, 2013[103]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 189 N Completed: 175 % Female: 73%, 54% Mean Age: 51	High Ligation + Stripping vs. EVLA	Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Qualitative reduction in LE pain; Patient-reported QOL

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Samuel, 2013[104] HELP-2 Companions: Nandhra, 2015[105]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 106 N Completed: 106 % Female: 75.5%, 64.2% Mean Age: 47.5, 47.8	High Ligation + Stripping vs. EVLA	Unclear/NR	Improvement in LE venous hemodynamics/reflux severity; Patient-reported QOL; Qualitative reduction in LE pain
Schouten, 2006[106]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 40 N Completed: 40 % Female: 75%, 70% Mean Age: 39.5, 46.5	High Ligation + Stripping vs. High Ligation + Cryostripping	Ultrasound	Bleeding; Periprocedural complications; Thrombophlebitis; Qualitative reduction in LE pain; Exercise-related harms

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Sell, 2014[107]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 153 N Completed: 145 % Female: 90%, 86% Mean Age: 46, 48	High Ligation + Stripping +/- Phlebectomy/Excision vs. Compression	Clinical assessment; Ultrasound	Changes on standardized symptom scores; Patient-reported QOL
Serra, 2015[108]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 284 N Completed: 284 % Female: 78% Mean Age: 69.5	Nadroparin vs. No Anticoagulants	Clinical assessment; Ultrasound	Venous wound healing; Recurrent ulceration (Age)

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Shadid, 2012[109]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 460 N Completed: 390 % Female: 74%, 72% Mean Age: 55.8, 54.6	Foam Sclerotherapy vs. High Ligation + Stripping +/- Phlebectomy	Clinical assessment; Ultrasound	Changes on standardized symptom scores; Patient-reported QOL; Repeat intervention; Improvement in LE venous hemodynamics/reflux severity; Periprocedural complications; Bleeding; Qualitative reduction in LE pain; Thrombophlebitis; Venous thromboembolic events (Anatomic Segment)
Shepherd, 2010[110] VALVV Companions: Shepherd, 2015[111]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 131 N Completed: 115 % Female: 70%, 66% Mean Age: 49, 48	RFA vs. EVLA + Compression	Ultrasound	Patient-reported QOL; Changes on standardized symptom scores; Qualitative reduction in LE pain; Venous thromboembolic events; Bleeding;) Periprocedural complications

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Stötter, 2006[112]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 60 N Completed: 57 % Female: 70%, 75%, 70% Age: NR	High Ligation + Stripping vs. RFA	Clinical assessment; Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Qualitative reduction in LE pain; Bleeding
Subramonia, 2010[113]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 93 N Completed: 88 % Female: 72%, 66% Median Age: 47, 45	High Ligation + Stripping vs. RFA	Ultrasound	Patient-reported QOL

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Theivacumar, 2008[114]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 65 N Completed: 65 % Female: 59%, 62%, 55% Median Age: 40, 42,46	EVLA vs. EVLA + Sclerotherapy	Unclear/NR	Patient-reported QOL; Repeat intervention; Improvement in LE venous hemodynamics/reflux severity
Todd, 2014[115] VANISH-2	Study Design: RCT Quality: Good Location: U.S. <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 235 N Completed: 230 % Female: 72.8% Mean Age: 50.8	Sclerotherapy vs. Placebo	Ultrasound	Changes on standardized symptom scores; Improvement in LE venous hemodynamics/reflux severity; Patient-reported QOL

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
van den Bos, 2014[116] LAST	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 237 N Completed: 227 % Female: 57.5%, 65.2% Mean Age: 55, 56	EVLA vs. Thermal Ablation	Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Changes on standardized symptom scores; Patient-reported QOL; Venous thrombosis; Thrombophlebitis; Bleeding
van Gent, 2006[117] Companions: van Gent, 2015[118]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 170 (200 limbs) N Completed: 143 (196 limbs) % Female: NR Mean Age: 64, 68	SEPS + High Ligation + Stripping vs. Conservative/ Compression	Clinical assessment; Ultrasound	Death; Recurrent ulceration; Venous wound healing (Presence of LE Ulcer)

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Vandongen, 2000[119]	Study Design: RCT Quality: Poor Location: Australia/N.Z. <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 153 N Completed: 78 % Female: 54% Mean Age: 67	Below-Knee Compression Stockings vs. No Compression Therapy	Clinical assessment; Ultrasound (76% of patients)	Recurrent Ulceration
Vanscheidt, 2002[120]	Study Design: RCT Quality: Good Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 254 N Completed: 226 % Female: 79% Mean Age: 55.1	Medication vs. Placebo + Compression	Clinical assessment; Ultrasound	Adverse drug reactions; Qualitative reduction in LE pain; Qualitative reduction in LE edema

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Vasquez, 2016[121] Varithena 017	Study Design: RCT Quality: Fair Location: U.S. <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins, LE chronic venous insufficiency/reflux/incompetency Total N: 118 N Completed: 112 % Female: 69% Mean Age: 52	Thermal Ablation + 0.5% Polidocanol microfoam (PEM) vs. Thermal Ablation + 1% Polidocanol microfoam vs. Thermal Ablation + placebo injection	CEAP grade 2-5; Clinical assessment	Venous thrombosis; Changes on standardized symptom scores; Patient-reported QOL; Thrombophlebitis; Repeat intervention; Improvement in LE venous hemodynamics/reflux severity
Viarengo, 2007[122]	Study Design: RCT Quality: Fair Location: Latin America <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 52 N Completed: 52 % Female: 72%, 78% Mean Age: 60.7, 57.4	Compression vs. EVLA + Compression	Ultrasound	Venous wound healing; Qualitative reduction in LE pain; Thrombophlebitis; Venous thromboembolic events; Periprocedural complications; Recurrent ulceration

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Wang, 2016[123]	Study Design: RCT Quality: Fair Location: Asia <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 150 N Completed: 150 % Female: 36% Mean Age: 46.5	High Ligation + Stripping vs. EVLA vs. CHIVA	CEAP grade 2-6	Improvement in LE venous hemodynamics/reflux severity; Thrombophlebitis; Bleeding
Wong, 2012[124]	Study Design: RCT Quality: Good Location: Asia <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 321 N Completed: 276 % Female: 36% Mean Age: 71.7	Mechanical Compression vs. Placebo/Control therapy	Clinical assessment; Ultrasound	Qualitative reduction in LE pain; Patient-reported QOL; Venous wound healing

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Wozniak, 2015[125]	Study Design: RCT Quality: Fair Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 102 N Completed: 102 % Female: 83%, 78% Mean Age: 51.44, 53.04	High Ligation + Stripping vs. Thermal Ablation (Steam)	CEAP grades 2-6	Qualitative reduction in LE edema; Changes on standardized symptom scores; Venous thrombosis; Venous thromboembolic events; Improvement in LE venous hemodynamics/reflux severity
Wright, 2006[126]	Study Design: RCT Quality: Poor Location: UK/Europe <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 710 N Completed: 645 % Female: 68%, 64%, 75% Mean Age: 50.4, 49, 49.6	High Ligation + Stripping vs. Foam Sclerotherapy + Ligation vs. Liquid/Foam Sclerotherapy	Clinical assessment; Ultrasound	Improvement in LE venous hemodynamics/reflux severity; Qualitative reduction in LE pain; Venous thrombosis; Bleeding

Author, Year Trial Companion Articles	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Yang, 2013[127]	Study Design: RCT Quality: Fair Location: Asia <u>Population</u> Symptom Status: Symptomatic Condition(s): LE varicose veins; LE chronic venous insufficiency/reflux/incompetency Total N: 200 N Completed: 183 % Female: 51%, 55% Median Age: 59, 58	High Ligation + Stripping +/- Phlebectomy vs. High Ligation + Endovenous Microwave Therapy	Clinical assessment; Ultrasound	Periprocedural complications; Repeat intervention; Patient-reported QOL; Changes on standardized symptom scores
Zamboni, 2003[128] Companions: Zamboni, 2004[129]	Study Design: RCT Quality: Poor Location: UK/Europe <u>Population</u> Symptom Status: Unclear/NR Condition(s): LE chronic venous insufficiency/reflux/incompetency Total N: 45 N Completed: 45 % Female: 60% Mean Age: 63	CHIVA + Compression vs. Compression	Clinical assessment; Ultrasound	Repeat intervention; Venous wound healing; Recurrent ulceration; Improvement in LE venous hemodynamics/reflux severity

* = Multiple values are listed for percent female and age in instances where baseline data is reported by study arm rather than for the total population.
Abbreviations: CEAP=Clinical, Etiologic, Anatomic, Pathophysiologic; CHIVA=Cure conservatrice et Hémodynamique de l'Insuffisance Veineuse en Ambulatoire; EVLA = Endovenous Laser Ablation; LE=lower extremity; NR=not reported; QOL=quality of life; RFA=Radiofrequency Ablation; SEPS=subfascial endoscopic perforating vein surgery

Appendix Table F-3. Study Characteristics—KQ 3

Author, Year	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Garg, 2011[130]	Study Design: Observational Quality: Fair Location: U.S. Population Symptom Status: Unclear/NR Condition(s): LE venous thrombosis/ obstruction; PTS Total N: 60 N Completed: 60 % Female: 56 Mean Age: 43	Palma vein Procedure vs. Endophlebectomy and patch angioplasty with stent	Obstruction of iliofemoral veins and IVC, using MRV, ultrasound or CTV	Improvement in LE venous hemodynamics/reflux severity
Ginsberg, 2001[131]	Study Design: RCT Quality: Poor Location: Canada Population Symptom Status: Symptomatic Condition(s): PTS Total N: 35 N Completed: Unclear/NR % Female: 60% Mean Age: 46, 51.6, 54.6, 39.5	Compression Therapy (thigh and calf) vs. Placebo/Control (thigh and calf)	Postphlebitic syndrome, Chronic (>1 month in duration), typical symptoms including pain and swelling >= 6 months after proximal DVT.	Death
Holmes, 2014[132]	Study Design: RCT Quality: Good Location: U.S. Population Symptom Status: Symptomatic Condition(s): LE venous thrombosis/ obstruction; PTS Total N: 31 N Completed: 31 % Female: 53%,62% Mean Age: 47, 49	Complex lymphedema therapy (CLT) vs. Compression therapy	Prior history of DVT and clinical diagnosis of PTS	Changes on standardized symptom scores Patient-reported QOL

Author, Year	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Kahn, 2011[133]	Study Design: RCT Quality: Good Location: Canada <u>Population</u> Symptom Status: Symptomatic Condition(s): PTS Total N: 43 N Completed: 39 % Female: 55% Mean Age: 44.9, 48.14	Patient Education vs. Exercise Training	Symptomatic DVT >= 6 months, and symptoms with Villalta score >= 5	Changes on standardized symptom scores Patient-reported QOL
O'Sullivan, 2000[134]	Study Design: Observational Quality: Poor Location: U.S. <u>Population</u> Symptom Status: Symptomatic Condition(s): PTS Total N: 20 N Completed: 20 % Female: 77% Mean Age: 43	Stent + Lysis vs. Stent	Ultrasound, CTV, MRV, or invasive venography showing L iliac vein thrombosis +/- involvement of femoral and popliteal segments. Also needed symptoms with at least one of the following: edema, pain, venous claudication, and /or phlegmasia.	Changes on standardized symptom scores, Improvement in LE venous hemodynamics/reflux severity
Raju, 2013[135]	Study Design: Observational Quality: Poor Location: U.S. <u>Population</u> Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/ incompetency Total N: 192 N Completed: 192 % Female: 50% Age: 59	EVLA vs. EVLA + Stent vs. Stent	Patients with CEAP6 (failed conservative therapy). Swelling, pain; venography + intravascular ultrasound were used to look for obstruction.	Venous wound healing

Author, Year	Study Details*	Interventions	Diagnostic Method(s) and Criteria	Outcomes (Subgroups analyzed)
Yin, 2015[136]	Study Design: Observational Quality: Fair Location: Asia. Population Symptom Status: Symptomatic Condition(s): LE venous thrombosis/ obstruction; PTS Total N: 216 N Completed: 216 % Female: 59% Median Age: 46, 42	Endovascular Stent vs. Compression Therapy	PTS with iliofemoral obstruction (>50% stenosis or occlusion on venography) and mod/severe symptoms (Villalta score >=10)	Changes on standardized symptom scores Qualitative reduction in LE edema Qualitative reduction in LE pain (subgroup: Villalta Score)
Yin, 2015[137]	Study Design: Observational Quality: Fair Location: Asia. Population Symptom Status: Symptomatic Condition(s): LE chronic venous insufficiency/reflux/ incompetency; PTS Total N: 207 N Completed: 207 % Female: 66% Mean Age: 50.1, 51.9	EVLA vs. EVLA + Stent	Phlebography and ultrasound were used to diagnose May-Thurner syndrome	Recurrent ulceration Improvement in LE venous hemodynamics/reflux severity Patient-reported QOL

* = Multiple values are listed for percent female and age in instances where baseline data is reported by study arm rather than for the total population.
Abbreviations: Abbreviations: CEAP=Clinical, Etiologic, Anatomic, Pathophysiologic; CHIVA=Cure conservatrice et Hémodynamique de l'Insuffisance Veineuse en Ambulatoire; CTV=computed tomography venography; DVT=deep vein thrombosis; EVLA = Endovenous Laser Ablation; IVUS=intravascular ultrasound; LE=lower extremity; MRV=magnetic resonance venography; NR=not reported; QOL=quality of life; PTS=Post-thrombotic Syndrome

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