

Figure 1: Diagram of model structure

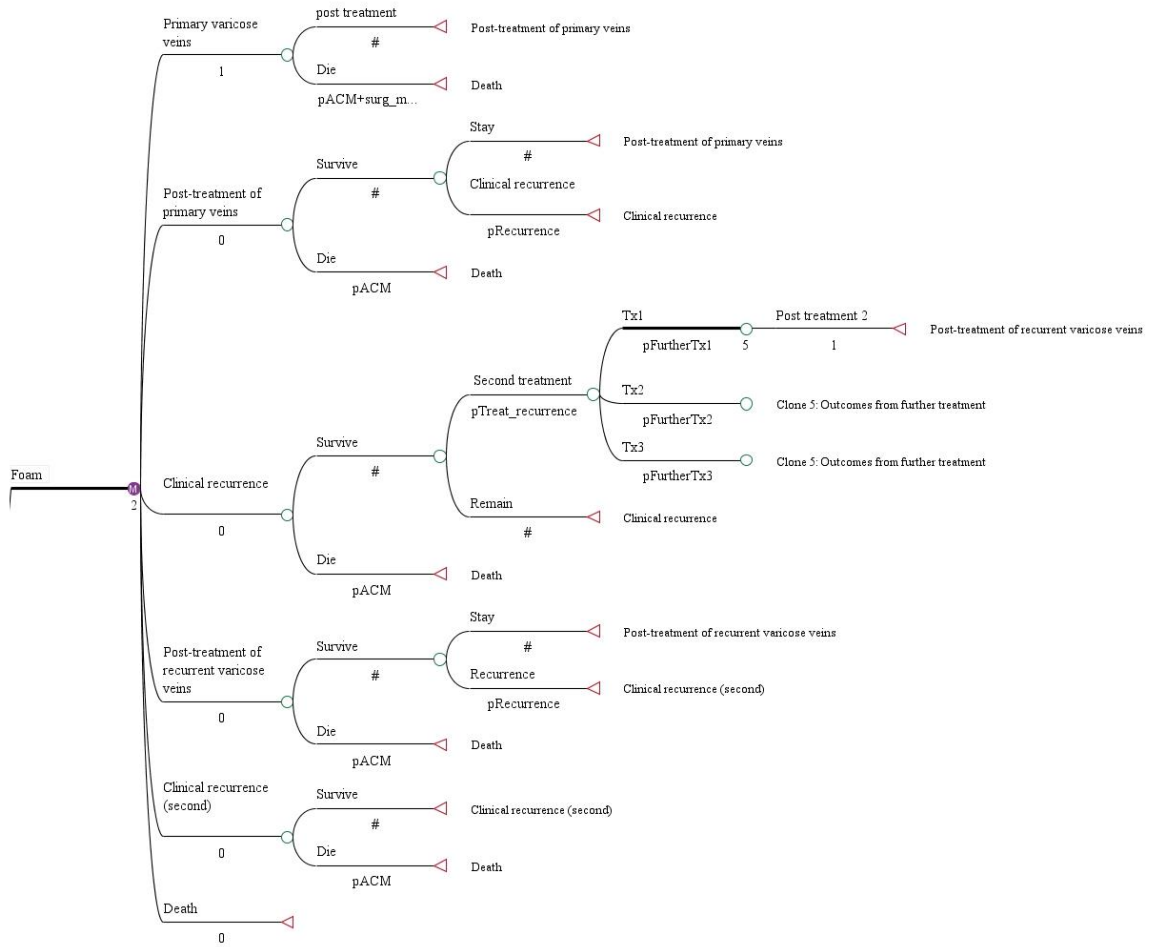


Figure 2: Cost-effectiveness acceptability curve based on 5 year time horizon

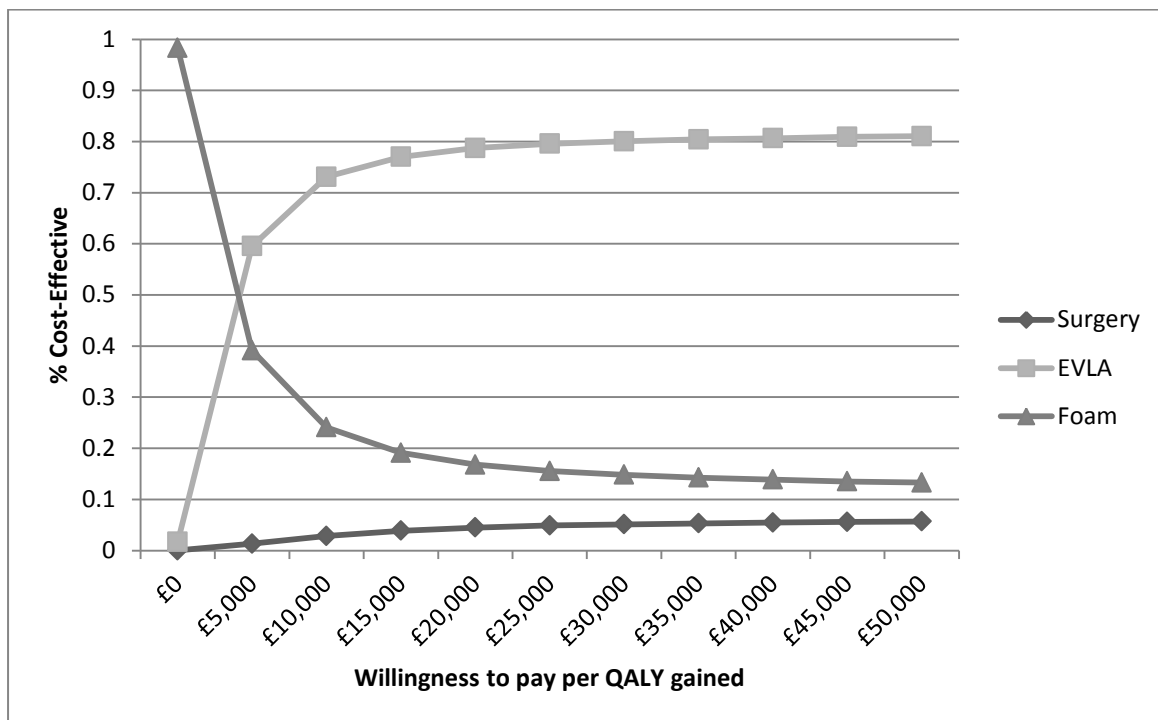


Table 1: Unit costs and recurrence probabilities applied in the analysis

Input variables	Point estimate	Estimated SEM	Distribution	Source
Unit costs				
<i>Nursing staff</i>				
	<i>Cost per hour</i>			
Band 2	£20	-	-	PSSRU, 2011
Band 3	£24	-	-	PSSRU, 2011
Band 4	£30	-	-	PSSRU, 2011
Band 5	£82	-	-	PSSRU, 2011
Band 6	£107	-	-	PSSRU, 2011
Band 7	£129	-	-	PSSRU, 2011
Band 8b (Consultant Nurse)	£147	-	-	PSSRU, 2011
<i>Medical staff</i>				
	<i>Cost per hour</i>			
Foundation Year 1	£33	-	-	PSSRU, 2011
Foundation Year 2 Core trainee, CCT	£42	-	-	PSSRU, 2011
Speciality trainee	£59	-	-	PSSRU, 2011
Staff Grade	£95	-	-	PSSRU, 2011
Associate Specialist	£131	-	-	PSSRU, 2011
Consultant Medical	£136	-	-	PSSRU, 2011
<i>Equipment</i>				
	<i>Cost per use</i>			
Ultrasound machine	£8.78	-	-	Participant centres
ECG, pulse oximeter, blood pressure monitor	£4.15	-	-	Participant centres
Laser generator ^a	£34.67	-	-	Participant centres
<i>Consumables</i>				
	<i>Cost per procedure</i>			
Surgery	£159.56	-	-	Participant centres
UGFS	£26.23	-	-	Participant centres
EVLA	£321.06	-	-	Participant centres
<i>Follow-up costs</i>				
GP visit	£36	-	-	PSSRU, 2011
Practice nurse visit	£12	-	-	PSSRU, 2011
Vascular surgery follow-up outpatient appointment	£123	-	-	Department of Health, 2011
Duplex scan	£53	-	-	Department of Health, 2011
Probabilities				
<i>Post treatment recurrence risks ^b</i>				
	<i>Monthly probability</i>			
Surgery	0.008818	0.00306	Beta	NICE, 2013
UGFS	0.0115	0.009929	Beta	NICE, 2013
EVLA	0.006532	0.003448	Beta	NICE, 2013

Notes: ^a The laser generator cost was only included in a sensitivity analysis (see text); ^a Monthly probabilities were transformed into six-month probabilities; - Unit costs were omitted from the model based probabilistic analysis.

Table 2: Estimated EQ-5D utility values and 6 month costs (including initial treatment) applied in the Markov model

Outcome	Complete case data		Multiple imputation data		Assumed distributional form
	Mean	Standard error	Mean	Standard error	
<i>EQ-5D at baseline</i> (across all treatment groups)	0.790	0.009	-	-	Beta
QALYs at 6 months					
Surgery	0.432	0.006 ^a	0.435	0.006 ^a	Beta
UGFS (increment) ^c	-0.005	0.010 ^b	-0.011	0.009 ^b	Normal
EVLA (increment)	0.011	0.006 ^b	0.007	0.007 ^b	Normal
EQ-5D at 6 months					
Surgery	0.884	0.0104 ^a	0.888	0.011 ^a	Beta
UGFS (increment)	-0.009	0.018 ^b	-0.020	0.023 ^b	Normal
EVLA (increment)	0.016	0.0121 ^b	0.011	0.016 ^b	Normal
Costs at 6 months					
Surgery	£1,110	£80 ^a	£1,047	£80 ^a	Gamma
UGFS (increment)	-£655	£85 ^b	-£579	£75 ^b	Normal
EVLA (increment)	-£160	£83 ^b	-£98	£79 ^b	Normal

^a Cluster bootstrapped standard error

^b Cluster robust standard error

^c The estimated 6 month utility and cost increments associated with UGFS and EVLA, compared to surgery.

Table 3: Model based incremental cost-effectiveness analysis (over a 5 year time horizon)

Strategy	Cost (£)	Incremental cost (£)	QALYs	Incremental QALYs	Incremental cost per QALY	Probability cost-effective at Rc £20,000
UGFS	664	-	4.000	-	-	0.168
EVLA	1,095	431	4.119	0.118	£3,640	0.787
Surgery	1,300	206	4.040	-0.078	Dominated	0.045

Note: Rc is ceiling ratio of WTP per QALY gained

Table 4: Model based incremental cost-effectiveness analysis (over a 5 year time horizon)

Strategy	Cost (£)	Incremental cost (£)	QALYs	Incremental QALYs	Incremental cost per QALY	Probability cost-effective at Rc £20,000
UGFS	664	-	4.000	-	-	0.168
EVLA	1,095	431	4.119	0.118	£3,640	0.787
Surgery	1,300	206	4.040	-0.078	Dominated	0.045

Note: Rc is ceiling ratio of WTP per QALY gained

Appendix

Supplementary Table 1: NHS resource use costs and outcomes by intention to treat

		Randomised to EVLA			Randomised to UGFS			Randomised to surgery		
	N									
Treatment received										
Presented for EVLA	N, %	203	96.7		6	2.9		8	3.8	
Presented for UGFS	N, %	46	21.9		191	92.3		9	4.23	
Number of UGFS treatments	N, mean n, SD	46	1.07	0.25	191	1.15	0.39	9	1.00	0.00
Presented for surgery	N, %	3	1.4		3	1.5		183	85.9	
No recorded treatment	N, %	5	2.4		10	4.8		17	8.0	
Treatment durations										
Cumulative procedure time										
-EVLA	N, mean, SD	194	59.41	28.48	204	0.86	7.11	212	1.63	9.17
- UGFS	N, mean, SD	197	4.41	11.50	185	29.34	18.08	212	0.89	4.72
-Surgery	N, mean, SD	209	0.69	7.08	207	1.07	8.95	197	62.60	34.06
Treatment costs										
Staff procedure costs										
- EVLA	N, mean, SD	194	£326	£154	204	£5	£43	212	£10	£58
- UGFS	N, mean, SD	197	£19	£52	185	£137	£91	212	£4	£20
- Surgery	N, mean, SD	209	£6	£64	207	£10	£88	197	£615	£362
Recovery time costs	N, mean, SD	209	£32	£10	207	£4	£11	198	£74	£37
Consumable costs	N, mean, SD	210	£322	£58	207	£50	£60	213	£150	£58
Theatre use	N, mean, SD	193	£31	£96	185	£14	£46	196	£231	£122
Equipment costs	N, mean, SD	210	£11	£4	207	£10	£4	213	£4	£2
Prep costs	N, mean, SD	210	£29	£12	207	£28	£12	213	£29	£9
Cost of overnight stay	N, mean, SD	210	0	0	207	0	0	213	£22	£77
Total treatment costs										
- EVLA	N, mean, SD	194	£699	£195	204	£11	£90	212	£23	£126
- UGFS	N, mean, SD	197	£33	£79	185	£214	£111	212	£6	£33

- Surgery	N, mean, SD	209	£9	£94	207	£14	£121	197	£876	£457
Total treatment cost ^a	N, mean, SD	183	£737	£204	182	£245	£161	195	£916	£412
Follow-up costs										
Routine assessment for residual veins ^b	N, mean, SD	210	£115	£84	207	£131	£77	213	£10	£41
Unplanned outpatient attendances	N, mean, SD	210	£39	£97	207	£31	£149	213	£34	£103
Admissions	N, mean, SD	199	£0	£0	195	£0	£0	183	£7	£49
Primary care	N, mean, SD	170	£16	£43	168	£16	£42	156	£26	£47
Total NHS costs (excluding all theatre costs)	N, mean, SD	142	£951	£179	144	£453	£225	141	£1,113	£332
Total NHS costs (including theatre costs)	N, mean, SD	142	£975	£205	144	£465	£239	141	£1,367	£404
EQ-5D values										
Baseline	N, mean, SD	206	0.792	0.169	202	0.793	0.187	207	0.777	0.184
6 Weeks	N, mean, SD	184	0.894	0.145	181	0.853	0.172	164	0.864	0.180
6 Months	N, mean, SD	172	0.903	0.171	167	0.884	0.192	151	0.872	0.212
Total QALYs	N, mean, SD	155	0.443	0.071	159	0.431	0.078	139	0.426	0.086

^a Based on complete case data and excluding additional overheads associated with use of theatre

^b Assumes that patients who attended a 6 week assessment post EVLA/ UGFS, but did not require further UGFS treatment, would incur the cost of an outpatient appointment and duplex scan in routine practice.

Appendix

Supplementary Table 2: Results of deterministic sensitivity analyses

Strategy	Cost (£)	Incremental cost (£)	QALYs	Incremental QALYs	Incremental cost per QALY	Probability cost-effective at Rc £20,000
Scenario 1: Including additional overhead costs for procedures carried out in theatre						
UGFS	684	-	4.000	-	-	0.174
EVLA	1,122	438	4.119	0.118	£3,703	0.8
Surgery	1,561	439	4.040	-0.078	Dominated	0.027
Scenario 2: Cost and utility inputs based on full multiple imputation analysis						
UGFS	677	-	3.975	-	-	0.114
EVLA	1,094	417	4.116	0.142	£2,943	0.769
Surgery	1,237	144	4.057	-0.060	Dominated	0.116
Scenario 3: Cost and utility inputs based on multiple imputation analysis, with participants receiving no treatment and follow-up dropped						
UGFS	665	-	3.996	-	-	0.174
EVLA	1,097	432	4.115	0.119	£3,626	0.738
Surgery	1,272	175	4.044	-0.071	Dominated	0.088
Scenario 4: Applying cost and utility input parameter values based only on patients with unilateral disease and no simultaneous treatment to contralateral leg						
UGFS	646	-	3.990	-	-	0.172
EVLA	1,081	436	4.138	0.148	£2,947	0.778
Surgery	1,233	152	4.037	-0.101	Dominated	0.051
Scenario 5: Applying cost and utility input parameter values based only on patients with unilateral disease and great saphenous vein involvement						
UGFS	646	-	3.929	-	-	0.115
EVLA	1,085	439	4.107	0.179	£2,456	0.784
Surgery	1,251	166	4.039	-0.069	Dominated	0.102
Scenario 6: 60% of patients with clinical recurrence proceed to further treatment						
UGFS	622	-	3.995	-	-	0.168
EVLA	1,066	444	4.115	0.120	£3,702	0.786
Surgery	1,262	196	4.035	-0.080	Dominated	0.046
Scenario 7: 90% of patients with clinical recurrence proceed to further treatment						
UGFS	706	-	4.006	-	-	0.168
EVLA	1,124	418	4.123	0.117	£3,576	0.788
Surgery	1,339	215	4.045	-0.077	Dominated	0.044
Scenario 8: All patients with clinical recurrence receive conventional surgery						
UGFS	734	-	3.999	-	-	0.169
EVLA	1,143	409	4.118	0.119	£3,451	0.785
Surgery	1,363	221	4.039	-0.079	Dominated	0.046
Scenario 9: All patients with clinical recurrence receive UGFS						
UGFS	603	-	3.997	-	-	0.17
EVLA	1,053	450	4.116	0.119	£3,768	0.786
Surgery	1,245	192	4.037	-0.079	Dominated	0.045
Scenario 10: Application of NHS reference cost (£1,216) to all treatments for clinical recurrence						
UGFS	755	-	4.000	-	-	0.169

Strategy	Cost (£)	Incremental cost (£)	QALYs	Incremental QALYs	Incremental cost per QALY	Probability cost-effective at Rc £20,000
EVLA	1,157	402	4.119	0.118	£3,401	0.046
Surgery	1,383	225	4.040	-0.078	Dominated	0.786
Scenario 11: Two year delay between clinical recurrence and receiving further treatment						
UGFS	605	-	3.987	-	-	0.172
EVLA	1,049	444	4.108	0.122	£3,656	0.782
Surgery	1,242	192	4.027	-0.081	Dominated	0.047
Scenario 12: Allowing any number of repeat treatments for subsequent clinical recurrences, with a 10 year time horizon						
UGFS	927	-	7.283	-	-	0.164
EVLA	1,285	358	7.478	0.196	£1,831	0.765
Surgery	1,547	262	7.345	-0.134	Dominated	0.071
Scenario 13: Assuming no difference in post treatment utility scores between alternatives						
UGFS	664	-	4.033	-	-	0.549
EVLA	1,095	431	4.052	0.019	£22,268	0.378
Surgery	1,300	206	4.039	-0.013	Dominated	0.073
Scenario 14: Assume no difference in post treatment utility scores between alternatives, with 10 year time horizon						
UGFS	815	-	7.311	-	-	0.42
EVLA	1,238	424	7.365	0.054	£7,881	0.454
Surgery	1,475	237	7.328	-0.036	Dominated	0.127
Scenario 15: Utility inputs based on participant responses to the SF-36 (scored using the SF-6D)						
UGFS	665	-	3.706	-	-	0.216
EVLA	1,095	431	3.772	0.066	£6,503	0.782
Surgery	1,301	205	3.706	-0.066	Dominated	0.003
Scenario 16: Equal recurrence rates applied following EVLA and surgery						
UGFS	664	-	4.002	-	-	0.169
EVLA	1,095	431	4.119	0.117	£3,691	0.78
Surgery	1,255	160	4.053	-0.066	Dominated	0.052
Scenario 17: Analysis conducted over a 10 year time horizon						
UGFS	817	-	7.314	-	-	0.251
EVLA	1,240	422	7.409	0.094	£4,474	0.440
Surgery	1,476	237	7.406	-0.003	Dominated	0.309
Scenario 18: Applying separate outpatient appointment and duplex scan costs prior to all top-up foam treatments						
UGFS	694	-	4.000	-	-	0.169
EVLA	1,137	443	4.119	0.118	£3,744	0.783
Surgery	1,305	169	4.040	-0.078	Dominated	0.048
Scenario 19: As per scenario 18 plus apportioned laser generator costs (£35 per EVLA procedure)						
UGFS	796	-	4.000	-	-	0.173
EVLA	1,172	£476	4.119	0.118	£4,024	0.777
Surgery	1,308	£136	4.040	-0.078	Dominated	0.050
Scenario 20: Removal of all follow-up assessment costs						
UGFS	£490	-	4.000	-	-	0.172
EVLA	£946	£456	4.119	0.118	£3,856	0.794

Strategy	Cost (£)	Incremental cost (£)	QALYs	Incremental QALYs	Incremental cost per QALY	Probability cost-effective at Rc £20,000
Surgery	£1,278	£332	4.040	-0.078	Dominated	0.034
Scenario 21: Costing EVLA with the same staffing profile as UGFS						
UGFS	£649	-	4.000	-	-	0.151
EVLA	£918	£269	4.119	0.118	£2,277	0.816
Surgery	£1,287	£368	4.040	-0.078	Dominated	0.033
Scenario 22: Alternative model structure based on transitions between clinical severity states						
UGFS	667	-	4.022	-	-	0.302
EVLA	1,096	429	4.063	0.042	£10,329	0.397
Surgery	1,301	205	4.070	0.006	£31,977	0.301
Scenario 23: Alternative model structure based on transitions between clinical severity states plus costing assumptions of scenario 19						
UGFS	699	-	4.021	-	-	0.308
EVLA	1,188	£488	4.064	0.043	£11,418	0.364
Surgery	1,309	£122	4.069	0.005	£22,137	0.328

Note: Rc is ceiling ratio of WTP per QALY gained