

Ambulatory Varicosity avulsion Later or Synchronised (AVULS): A Randomised Clinical Trial

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Mini Abstract

A randomised clinical trial comparing simultaneous endovenous ablation and phlebectomy with endovenous ablation and delayed phlebectomy successfully recruited and treated 101 patients. Combined endovenous ablation and phlebectomy delivers improved clinical outcomes and a reduced rate of need for further procedures, in addition to early Quality of Life improvements.

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Abstract

Objective

A randomised clinical trial assessing the difference in quality of life and clinical outcomes between delayed and simultaneous phlebectomies in the context of endovenous truncal vein ablation

Summary

Endovenous ablation has replaced open surgery as the treatment of choice for truncal varicose veins. Timing of varicosity treatment is controversial with delayed and simultaneous pathways having studies advocating their benefits. A previous small randomised study has shown improved outcomes for simultaneous treatment.

Methods

Patients undergoing local anaesthetic endovenous thermal ablation were randomised to either simultaneous phlebectomy or delayed varicosity treatment. Patients were reviewed at 6 weeks, 6 months and 1 year with clinical and quality of life scores completed, and were assessed at 6 weeks for need for further varicosity intervention, which was completed with either ultrasound guided foam sclerotherapy or local anaesthetic phlebectomy. Duplex ultrasound assessment of the treated trunk was completed at 6 months.

Results

101 patients were successfully recruited and treated out of 221 suitable patients from a screened population of 393. Patients in the simultaneous group (n=51) showed a significantly improved VCSS at all time points, 36% of the delayed group required further treatment compared to 2% of the simultaneous group ($p<0.001$). There were no DVTs, with 1 SVT in each group.

Conclusion

Combined endovenous ablation and phlebectomy delivers improved clinical outcomes and a reduced need for further procedures, as well as early quality of life improvements.

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Short Title
The AVULS Trial – Phlebectomy Timing

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Introduction

With the advent of endovenous ablation techniques, the treatment of the incompetent truncal veins has been intensively investigated with multiple studies showing benefit (1-3). This has led to clinicians moving away from surgical ligation of the saphenofemoral junction and stripping of the great saphenous vein, towards less invasive options. However the issue of residual varicosities has not been conclusively investigated and remains a matter of debate (4), (5).

Varicosities can be treated at the same sitting as truncal veins, either with phlebectomy or foam sclerotherapy; alternatively treatment of varicosities can be delayed for a period, when, in a number of patients the need for treatment will be reduced.

There are two schools of thought with regard to treating varicosities in those patients undergoing truncal vein ablation. The first suggests simultaneous truncal treatment and phlebectomy as a single procedure (6,7). The second advises delayed phlebectomy after monitoring for varicosity regression. If still present, these varicosities or REVAS (REsidual Varicosities After Surgery) can be addressed with either ambulatory phlebectomies or foam sclerotherapy (8) .

Previous work in laser ablation has shown that approximately 40% of patients with delayed phlebectomies require a second procedure, which was matched in a non-randomised cohort study in radiofrequency ablation (8,9). Carradice et al. showed that there was no difference in QOL outcome between the delayed or simultaneous varicosity treatment.

Advocates of the first option suggest that immediate treatment of surface varicosities is advantageous in that it ensures patients are treated in a single session and reduces the varicosity reservoir. However, this may increase operative time (9) , and could be over-treating patients whose varicosities may regress.

Avoiding potentially unnecessary phlebectomies reduces operative time and potentially outpatient discomfort. However, a variable number of patients do come back with troublesome residual varicosities, which require secondary procedures.

There are a number of variables that confound the picture. Patient factors such as age, body habitus and mobility will influence the result of any intervention on the venous system. Patient preference and expectations, as well as operator experience, may have an effect on patient and operator satisfaction. Pain levels experienced have been assessed only in the Hull study, which showed no statistical difference in pain or return to normal activities (9) .

The aim of this study is to ascertain the outcomes of delayed or simultaneous phlebectomy in the context of truncal vein ablation.

Methods

AVULS was a single centre randomised controlled trial with the aim of recruiting 240 patients into 2 arms. Patients undergoing local anaesthetic endothermal ablation of incompetent truncal veins were randomised into two groups one with simultaneous varicosity avulsion; and the other with delayed treatment of the varicosities.

Ethical Approval and Trial Registration

Ethical approval has been granted for the AVULS Trial by Brighton Research Ethics Committee Reference Number 11/H1107/3. The trial is registered with Current Controlled Trials - ISRCTN76821539 (10) .

Patient Selection

Consecutive patients presenting with symptomatic primary varicose veins due to reflux in the great saphenous vein (GSV) or small saphenous vein (SSV) were invited to participate. The study was set in the Local Anaesthetic Varicose Vein Unit (LAVVU) of the Department of Vascular Surgery at Charing Cross Hospital. Patients were followed up for 12 months post-procedure, with repeated quality of life measures at 6 weeks, 6 and 12 months and technical success appraisal at 6 months.

Patients were eligible if they have single truncal vein incompetence and visible symptomatic varicosities (>3mm) in the distribution of that target vein.

Patients were consented and completed quality of life questionnaires incorporating the Aberdeen Varicose Vein Questionnaire (AVVQ), EuroQol EQ-5D 5 level and EQ-VAS and Centre for Epidemiological Studies – Depression Score (CES-D). The consenting clinician completed the Venous Clinical Severity Score (VCSS), Clinical Etiological Anatomical Pathological stage (CEAP), VDS and also the estimated number of avulsions required.

Power Calculation

Aberdeen Varicose Vein Questionnaire:

Based on previous randomised clinical trials, an improvement of 10 points is predicted at 6 weeks with a standard deviation of 10 in patients who have concomitant phlebectomies. A difference of 5 points at 6 months is considered clinically significant. At 90% power and 5% significance, 64 patients per arm would be required.

Allowing for loss to follow-up and protocol violation, target recruitment was set at 120 per arm, or 240 in total

Reasons for declining AVULS

Patients who did not want to participate in the AVULS study were invited to offer a reason for declining to enter the study.

Randomisation

Following consenting and recruitment patients were randomised into concomitant or delayed phlebectomy groups on the day of treatment. Randomisation was via computerised allocation at a remote location provided by a randomisation service (Sealed Envelope, London, UK).

Treatment

Treatment was then performed according to standardised endovenous thermal ablation using radiofrequency ClosureFAST catheters under tumescent local anaesthesia using standard Covidien Venefit procedure (11) and multiple stab phlebectomies according to treatment arm. Number of phlebectomies and length of treatment were recorded. Phlebectomies were performed as previously described under local anaesthetic, using vein hook phlebectomy technique. The treatment was non-blinded as the use of phlebectomies cannot be hidden from either the practitioner or patient. Patients then received standardised above knee class II compression hosiery (20-30 mmHg) for 2 weeks post-operatively.

Follow-up

Patients were seen in the research clinic at 6 weeks, 6 months and 1 year post-operatively. At each clinic visit, clinical review was completed as were the quality of life questionnaires.

At the 6 week visit, the patient was assessed for the need for further intervention by an independent clinicians unaware of the initial treatment group. Intervention was offered if both patient and clinician identified symptomatic residual varicosities ($>3\text{mm}$). Full blinding was not possible due to residual healing wounds. This was offered as either foam sclerotherapy or multiple stab phlebectomies under local anaesthetic, as per local protocol. All further treatments were

completed as soon as possible after the 6 week visit and all before the 6 month visit. Phlebectomies were performed under local anaesthetic in an identical manner to the simultaneous treatment, with compression hosiery for two weeks post treatment (12), (13). Foam sclerotherapy was performed under ultrasound guidance according to standard empty vein technique using Air/Foam mix of 4:1 and eccentric foam compression, compression bandaging and stockings for 2 weeks post treatment (14,15).

At the 6 month follow-up a duplex ultrasound scan was completed to ensure closure of the treated truncal vein. This was categorised as fully occluded, predominantly occluded (<5cm sections of colour flow), predominantly patent (>5cm sections of colour flow) and fully patent. The duplex ultrasound was performed by an independent vascular scientist blinded to the treatment allocation.

Primary Endpoint

The primary endpoint of this study was disease specific quality of life improvement at 6 months post procedure assessed by the AVVQ

Secondary Endpoints

- The need for further procedures over the 6 month period
- Clinical disease severity assessed using the Venous Clinical Severity Score (VCSS)
- Generic quality of life assessed using the EQ-5D
- Anatomical success assessed with colour duplex at 6 months
- Level of depression assessed using CES-D

Statistical Methods

All data was entered into a bespoke database created in Microsoft Access version 14 (Microsoft, Redmond, Washington, USA). Statistical analysis was performed on SPSS version 22

(IBM, Armonk, New York, USA), Prism version 6 (Graphpad, La Jolla, California, USA) and Wizard Pro version 1.3.5 (Evan Miller, Chicago, Illinois, USA).

Results

From April 2011 until November 2012, 393 consecutive patients presenting to the Charing Cross Local Anaesthetic Varicose Vein Unit for treatment were screened for inclusion in the AVULS trial and 221 patients were suitable. The 172 patients ineligible for the trial included those with no visible varicosities but truncal reflux (88 = 22%), patients with visible varicosities but no truncal reflux (71 = 18%) and patients with mixed truncal disease with venous anatomy unsuitable for endovenous treatment (13 = 3%). Of the 221 patients eligible, 101 patients consented to randomisation. Of those refusing to participate in the trial, 95% gave wanting single sitting treatment as their reason. The final trial sample was 26% of the screened population and 46% of the suitable population. Recruitment was slower than anticipated and was stopped early in order to complete the 12-month follow-up of patients already enrolled with the available funding.

The baseline demographics are shown in Table 1, and as can be seen the groups were well matched, with no significant differences: Treatment characteristics are shown below in table 2. No baseline differences were seen between groups. All treatments were completed as per protocol.

Primary Outcome - AVVQ

Mean AVVQ decreased following treatment as shown by Figure 2. The mean baseline AVVQ was 22.54 (standard deviation, sd, 12.40), decreasing to 13.57 (12.04) at 6 weeks, 11.19 (10.08) at 6 months and 8.56 (7.83) at 1 year, which represents a symptomatic improvement of 62%. ($p < 0.001$). Mean change at 6 weeks, 6 months and 12 months was -8.86 (11.30), -10.00 (10.24) and -11.54 (7.76) respectively (negative change equates to an improvement in symptoms). The

improvement in scores continued throughout follow-up, with that at 12 months being significantly better to that at 6 weeks ($p=0.046$).

Both groups showed a significant improvement in symptoms from baseline at all time points ($p<0.0001$). There was a significant difference seen at 6 weeks, with the simultaneous group showing a 5.48 point improvement ($p=0.029$). However there was no significant difference at 6 months or 12 months. Table 3 demonstrates the AVVQ values.

When assessed between patients who did not need any further treatment after 6 weeks there was no significant difference seen between the groups at any time point.

When comparing the groups who did and did not need further treatment a large significant difference of 8.1 AVVQ points was found at 6 weeks ($p=0.004$). Though those patients requiring Further Treatment remained at higher symptom scores throughout, this difference was not statistically significant at 6 months or 12 months and is demonstrated by Table 4. Further treatment was completed before the 6 months review.

The final comparison for the AVVQ quality of life score was between those in the delayed group who needed further treatment compared to the simultaneous group. This showed a large significant difference at 6 weeks and 6 months in favour of simultaneous treatment. This is shown in Table 5 and Figure 4.

Secondary Outcomes

Need for Further Procedure

19 patient required further procedures, with 18 undergoing multiple stab phlebectomy and 1 opting for foam sclerotherapy of residual varicosities.

There was a significant difference in need for further treatment between the delayed and simultaneous groups - 18 (36%) required further treatment in the delayed group compared with 1 (2%) in the simultaneous group ($p<0.001$).

The odds ratio and relative risk of patients in the delayed group requiring further varicosity treatment were 27.78 and 18.36 respectively ($p < 0.0001$).

There was no difference between estimated number of multiple stab phlebectomies required prior to intervention (9.76 vs 8.24, $p = 0.171$) in the patient groups and there was no significant difference between the number of phlebectomies estimated as necessary prior to intervention and the number performed in patients requiring further treatment (9.0 vs 7.33, $p = 0.3479$).

All procedures were completed as soon as feasible after the 6 week review and no further procedures were needed after 6 months or 1 year.

Technical Success

At 6 months, 94% of patients had truncal vein complete ablation. No patient needed truncal retreatment and no cases of complete failure were found. 6 patients had areas of open truncal vein > 5 cm in length. There was no difference in treatment success between groups ($p = 0.849$).

Generic Quality of Life

There was a significant improvement in generic quality of life as measured by the EQ-5D QOL from baseline to 6 weeks (0.691 to 0.820, $p < 0.0001$) but not as measured by the EQ-VAS (76.24 to 79.45, $p = 0.157$). The significant improvement in EQ-5D QOL was maintained through to 12 months however there were no further significant differences seen between time groups. This improvement equates to a 21% improvement in QOL. This is shown in Figure 5.

Overall, EQ-5D results showed the same trends as found for the primary outcome of AVVQ.

Between treatment groups there was a significant difference in EQ-5D QOL at 6 weeks (Delayed 0.773, Simultaneous 0.866, $p = 0.033$) but this difference was lost as the follow-up progressed, as shown in Figure 6. There was no significant difference seen between groups for the EQ-VAS score.

For those patients not requiring further treatment, there was no significant difference seen between treatment arms.

Comparing those requiring further treatment to those not requiring further treatment showed a significant difference at 6 weeks, with those needing further treatment having a significantly worse QOL (0.719 vs 0.846, $p=0.018$). This difference was not seen at 6 months or 12 months.

Comparing those in the delayed group who required further treatment to the simultaneous group shows a similar picture - a significant difference at 6 weeks in favour of simultaneous treatment (0.720 vs 0.866, $p=0.024$) however this difference in QOL was not seen at 6 months or 12 months. This is shown in Figure 7.

Clinical Disease Severity

CEAP

CEAP is a non-reactive clinical staging measure, however, it does provide an overview of the cohort.

Median CEAP at baseline was 4 (inter-quartile range 3-4), decreasing to 2 (2-4) at 6 weeks, 2 (1-4) at 6 months and 1(1-3) at 12 months. This was a significant improvement from baseline ($p<0.0001$), and is shown in Figure 8.

This represents an improvement in clinical signs from venous eczema to thread veins at 1 year.

When looking at the simultaneous and delayed groups, there was a significant higher CEAP score in the delayed group at 6 weeks ($p=0.006$) and 6 months ($p=0.003$), however by 1 year this was no longer significantly different ($p=0.117$). This is shown in Figure 9.

This represents an improvement for the delayed group from venous eczema to varicosities, compared to from venous eczema to thread veins in the simultaneous group.

VCSS

Treatment led to a significant reduction in VCSS from a baseline of 7.368 (2.556) to 3.011 (2.193) at 6 weeks, 2.557 (2.319) at 6 months and 1.978 (2.390) at 12 months ($p < 0.0001$). This represents a 73% decrease in clinical score. Patients continued to improve after 6 weeks, with 12 month scores being significantly lower than 6 weeks score ($p = 0.031$).

Treatment groups were well matched at baseline (Delayed 7.696 versus Simultaneous 7.061, $p = 0.229$) and showed a significant difference in VCSS levels at all follow-up points as shown in Table 6 and Figure 10 ($p = 0.001$ at 6 weeks, $p = 0.012$ at 6 months and $p = 0.011$ at 12 months).

When comparing those patients who needed no further treatment, a significant difference between the delayed and the simultaneous groups was seen at 6 weeks (3.72 vs 2.22, $p = 0.004$), 6 months (3.21 vs 1.90, $p = 0.022$) and 12 months (2.83 vs 1.14, $p = 0.013$), again in favour of the simultaneous group.

Assessing those patients who did and did not require further treatment, no statistical difference was seen at any follow-up time-point. At 6 weeks the further treatment group scored 3.82 vs 2.8 ($p = 0.082$), at 6 months scored 3.07 vs 2.34 ($p = 0.371$) and at 12 months scored 2.27 vs 1.80 ($p = 0.537$).

Finally, assessing the group of the delayed arm that required further treatment versus the simultaneous arm, a significant difference in favour of the simultaneous arm was found at 6 weeks (3.81 vs 2.26, $p = 0.006$), but at 6 months (3.15 vs 1.90, $p = 0.080$) and 12 months (2.27 vs 1.14, $p = 0.088$) this was no longer significant ($p = 0.080$ and $p = 0.088$).

Depressive Symptoms - CES-D

CES-D results are tabulated in Table 7. There was no significant difference seen between baseline and 6 weeks for the CES-D score, though there was a 24% reduction ($p = 0.0636$). There

was a significant improvement between baseline and 6 months (24%, $p=0.0199$). However at 12 months this difference had reduced and was not significant (17%, $p=0.2657$).

No significant difference was seen during follow-up in the delayed group. There was a significant improvement at 6 weeks in the simultaneous group ($p=0.0361$) but this was no longer significant by 6 months ($p=0.0796$) or 12 months ($p=0.6600$).

No significant difference was seen between groups at any time point during follow-up (Figure 11).

Complications

Two episodes of superficial venous thrombosis occurred, one in each group. No other complications were reported by patients. No DVTs were recorded.

Discussion

Endovenous management of varicose veins in the outpatient setting is a successful and safe procedure with increasing uptake (16,17). This study provides further evidence of excellent results with endovenous ablation at up to 1 year after treatment in both clinical (73% improvement) and disease specific QOL (62% improvement) scoring systems. Additionally generic QOL scores improved by 21%. Both simultaneous phlebectomy and delayed phlebectomy groups showed excellent overall improvements. Minimal complications were seen, with only two SVT episodes observed, one in each group. This study provides further evidence that both simultaneous and delayed treatment pathways are safe and feasible. The improvements after treatment show a significant improvement in patient morbidity following outpatient treatment of a common condition. Disease specific clinical and quality of life scores show greater improvement than generic quality of life scores as would be expected by a more sensitive tailored assessment, however a 20% improvement in quality of life post treatment of a single condition indicates excellent improvement.

The main finding of this study is that simultaneous treatment of incompetent truncal veins and varicose tributary veins provides improved clinical outcomes which persist up to one year after treatment. Quality of life values are improved at 6 weeks in both disease specific and generic scoring systems. These changes normalise by 6 months after adjunctive treatment was completed. The simultaneous group showed an improved VCSS score out to 1 year compared to the delayed group and even when comparing only those patients who did not require further treatment. CEAP scores were significantly different at 6 weeks and 6 months between the two groups, however this measure is not designed to assess clinical change, and improvements in clinical score are slow to occur. Additionally, patients with lipodermatosclerosis or venous ulcers cannot improve beyond C4 (venous skin changes) and C5 stages (healed venous ulcer) respectively. Venous eczema however can resolve and is also termed C4 (C4a).

Understandably, no significant difference was seen in the QOL tools, as these patients were happy with their outcome. Most interesting is how the "under-treated" group fared - those in the delayed group who underwent further treatment. In these 18 patients whilst the clinical score was no longer significantly different to the simultaneous arm after further treatment ($p=0.080$ at 6 months and 0.088 at 12 months), the AVVQ remained significantly worse until 1 year.

Depression screening scores (CES-D) improved overall at 6 months by 24%, before regressing to 17% improvement, a non significant improvement on pre-treatment values. Interestingly, delayed patients displayed no significant difference in scores at the time points, with simultaneous patients only improved at 6 weeks. This may indicate that patients experience a greater mental-health "bounce" from a larger procedure, and the improvement offered by delayed treatment is too gradual to be assessed with the numbers achieved in this study.

Patients undergoing delayed treatment in this study had a significantly higher rate of further intervention (36% vs 2%, Relative Risk 18.36). Advocates of delayed phlebectomies cite "over-treatment" as a prime concern (18), however in a time of austerity (19) one must also consider "under-treatment" and its sequelae as shown by this study's worse outcomes in those patients needing further treatment. With recent long term cohort data indicating that superficial venous disease has a progressive nature (20-22), and good outcomes from ascending theory evangelists (23), the fact that patients receive both better clinical outcomes and the treatment that they prefer with simultaneous treatment may become a key driver to better healthcare.

This study provides further evidence that simultaneous treatment of truncal veins and varicosities leads to improved early disease specific quality of life with improved clinical status as found by Carradice et al in the previous randomised study specifically addressing this question (9). That study of 50 patients using laser ablation found that clinical severity (as assessed by VCSS) was not significantly different at 1 year, but did show early improvement in favour of simultaneous treatment. Our present study replicates these outcomes with early QOL improvement but adds extended clinical improvement.

The odds ratio of patients undergoing adjunctive procedures in the delayed phlebectomy group in the Carradice trial was 16.67 (66% in delayed group vs 4% in simultaneous group) with a relative risk of 16.67, which is in keeping with the risk profile seen in our current study. In our study, patients who underwent delayed treatment had an Odds Ratio of 28.125 ($p < 0.0001$) and Relative Risk of 18.360 ($p < 0.0001$) of requiring further treatment, with 36% requiring further treatment compared to 2% in the simultaneous group. It is interesting that despite a decrease in overall percentage requiring re-intervention the risk statistics are in fact increased. The patient demographic reported by Carradice et al had a far lower disease burden than that reported in this

study (AVVQ 13 vs 23 and VCSS 4 vs 7.4). This may be secondary to change in referral practice in the intervening 5 years or a different burden of disease in our local geographical area.

This study was powered to detect a 5 point difference in AVVQ at 6 months between groups, and thus required a recruitment target of 128 patients with 100% follow-up. Allowing for loss to follow-up, target recruitment was 240. 81% of recruited patients were follow-up up to the primary endpoint at 6 months. A significant limitation of this study is the failure to reach target recruitment over the 18 month recruitment period. The target was not achieved due to patient preference for single sitting treatment despite equipoise from the researchers and careful consenting for both the trial and the procedure - >50% of the suitable population refused randomisation due to a preference for simultaneous treatment. At 6 weeks the difference in AVVQ was 5.48 and at 6 months 3.47. It is possible therefore that this lack of significance is a Type 2 error. Alternatively, as all patients requiring further treatment would have both received and recovered from the second intervention by 6 months, it may not be possible to achieve this difference. A clearer picture may have been found if a further review at 6 weeks post re-intervention had been undertaken. Carradice et al. also set their reintervention review at 6 weeks, and reassessed at 3 months, finding the same early quality of life improvements as this trial. Using a longer time delay such as 3 months between initial treatment and possible further intervention may have offered better differentiation between groups and comparison between trials.

Operating time was not recorded in this study, however all patients participating in the trial were scheduled as \pm phlebectomies and booked onto standardised morning lists in single slots. The morning day case lists catered for a maximum of 6 patients per session, based on one surgeon completing all tasks (consent, positioning, preparation and treatment including ultrasonography). Those undergoing adjunctive procedures were booked into similar single slots, however previous work on anaesthetic time reduction in general anaesthetic cases has found that large reductions in

treatment time are required to allow extra case throughput (24,25) , due to the logistical time involved in moving, positioning and preparing the patient. This is even more vital in the context of local anaesthetic procedures where the patient must not feel rushed.

Initial adjunctive procedures were not completed with foam sclerotherapy, though this is standard in some centres (26,27) . This may provide a more time-efficient option, especially as tumescentless ablation techniques become more accepted and commonplace, as phlebectomies would require further injections of local anaesthetic, rendering the major selling point of these new techniques obsolete.

Conclusion

This study lends further weight to the argument that one stage treatment is not only the patients preference but also in their best interests with improved early quality of life and prolonged improved clinical status. The clinical improvement is upheld even in those in the delayed group who do not need further varicosity treatment.

This study would therefore suggest that simultaneous treatment of truncal veins and varicosities represents the optimal management of patients with symptomatic varicose vein disease. However, larger scale studies are required to confirm these results.

Further work into cost-effectiveness, operating time and pain profile would allow clear guidance on not only the patient's ideal treatment pathway, but also the most efficient.

Crucially the final decision on treatment pathway remains with the clinician and the patient as both simultaneous and delayed pathways offer good outcomes overall with excellent complication profiles.

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Figure Legends

Figure 1: AVULS Trial Consort Diagram

Figure 2: Aberdeen Varicose Vein Questionnaire (AVVQ) over the course of treatment.

Figure 3: Aberdeen Varicose Vein Questionnaire (AVVQ) over the course of treatment showing delayed and simultaneous groups.

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Figure 7: EQ-5D QOL Outcomes for patients comparing Further treatment in the delayed group and the Simultaneous Groups.

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Table Legends

Table 1: Baseline Demographics

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Table 4: AVVQ for no further treatment needed and further treatment needed groups.

Table 5: AVVQ values for the Delayed and requiring further treatment group and the Simultaneous group

Table 6: VCSS Outcomes over duration of follow-up.

Table 7: CES-D Scores during Follow-up.

	Overall	Delayed	Simultaneous
Patients (n)	101	50	51
M:F	44:57	22:28	22:29
Age	52.9	53.9	52.0
BMI > 30	24%	26%	22%
BMI	28.28	29.13	27.52
CEAP (Median)	4	4	4
Maximal Vein Diameter	9.04	8.97	9.11
AVVQ Baseline	22.52	21.80	23.20
VCSS Baseline	7.56	7.80	7.30
EQ-5D QOL Baseline	0.691	0.695	0.688
EQ-5D VAS Baseline	75.68	74.76	77.30
CES-D Baseline	11.68	12.26	11.14

Table 1: Baseline Demographics

	Overall	Delayed	Simultaneous
Patients (n)	101	50	51
Trunks Treated (Median)	1.10 (1)	1.08 (1)	1.11 (1)
Cycles Completed (Median)	6.71 (7)	6.93 (7)	6.49 (6)
Vein Length Treated (Median)	46.97 (49)	48.51 (49)	45.43 (42)
Pre-Operative Estimated Phlebectomies (Median)	9.00 (8)	9.76 (10)	8.24 (6)
Phlebectomies Completed (Median)	6.84 (6)	-	6.84 (6)
Further Phlebectomies (Median)	7.33 (9)	7 (9)	10 (10)

Table 2: Completed Treatment Details

Table 3

AVVQ	Overall	Delayed	Simultaneous	Difference	p
Baseline	22.54 (12.40)	22.69 (11.67)	22.39 (13.17)	0.30	0.908
6 Weeks	13.57 (12.04)	16.34 (12.62)	10.86 (10.91)	5.48	0.029
6 Months	11.19 (10.08)	12.93 (11.05)	9.46 (8.80)	3.47	0.120
12 Months	8.56 (7.83)	9.48 (9.61)	7.60 (5.43)	1.88	0.387

Table 3: AVVQ Results between groups

Table 4

AVVQ	No Further Treatment Needed	Further Treatment Needed	Difference	p
Baseline	22.08 (12.38)	24.70 (12.63)	2.62	0.937
6 Weeks	11.97 (11.18)	20.07 (13.53)	8.1	0.010
6 Months	10.24 (9.86)	15.48 (10.26)	5.24	0.069
12 Months	8.05 (6.98)	10.73 (10.96)	2.68	0.335

Table 4: AVVQ for no further treatment needed and further treatment needed groups.

Table 5

AVVQ	Delayed & Further Treatment Needed	Simultaneous	Difference	p
Baseline	24.76 (13.04)	22.39 (13.17)	2.37	0.534
6 Weeks	20.56 (13.77)	10.86 (10.91)	9.7	0.005
6 Months	15.74 (10.59)	9.46 (8.80)	6.28	0.033
12 Months	10.73 (10.96)	7.60 (5.43)	3.13	0.258

Table 5: AVVQ values for the Delayed and requiring further treatment group and the Simultaneous group

Table 6

VCSS	Overall	Delayed	Simultaneous	Difference	p
Baseline	7.32 (2.55)	7.65 (2.59)	7.00 (2.50)	0.65	0.212
6 Weeks	2.99 (2.191)	3.76 (2.18)	2.26(1.96)	1.50	<0.001
6 Months	2.56 (2.356)	3.20 (2.45)	1.90 (2.09)	1.30	0.012
12 Months	1.90 (2.234)	2.62 (2.46)	1.14 (1.72)	1.48	0.011

Table 6: VCSS Outcomes over duration of follow-up.

CES-D	Overall	Delayed	Simultaneous	Difference	p
Baseline	11.68 (10.32)	12.26 (11.41)	11.14 (9.29)	1.12	0.598
6 Weeks	8.85 (10.14)	10.81 (10.53)	7.02 (9.53)	3.79	0.082
6 Months	8.22 (9.07)	8.82 (8.96)	7.65 (9.26)	1.17	0.574
12 Months	9.66 (10.02)	9.32 (8.16)	9.96 (11.58)	0.64	0.829

Table 7: CES-D Scores during Follow-up.

Figure 1

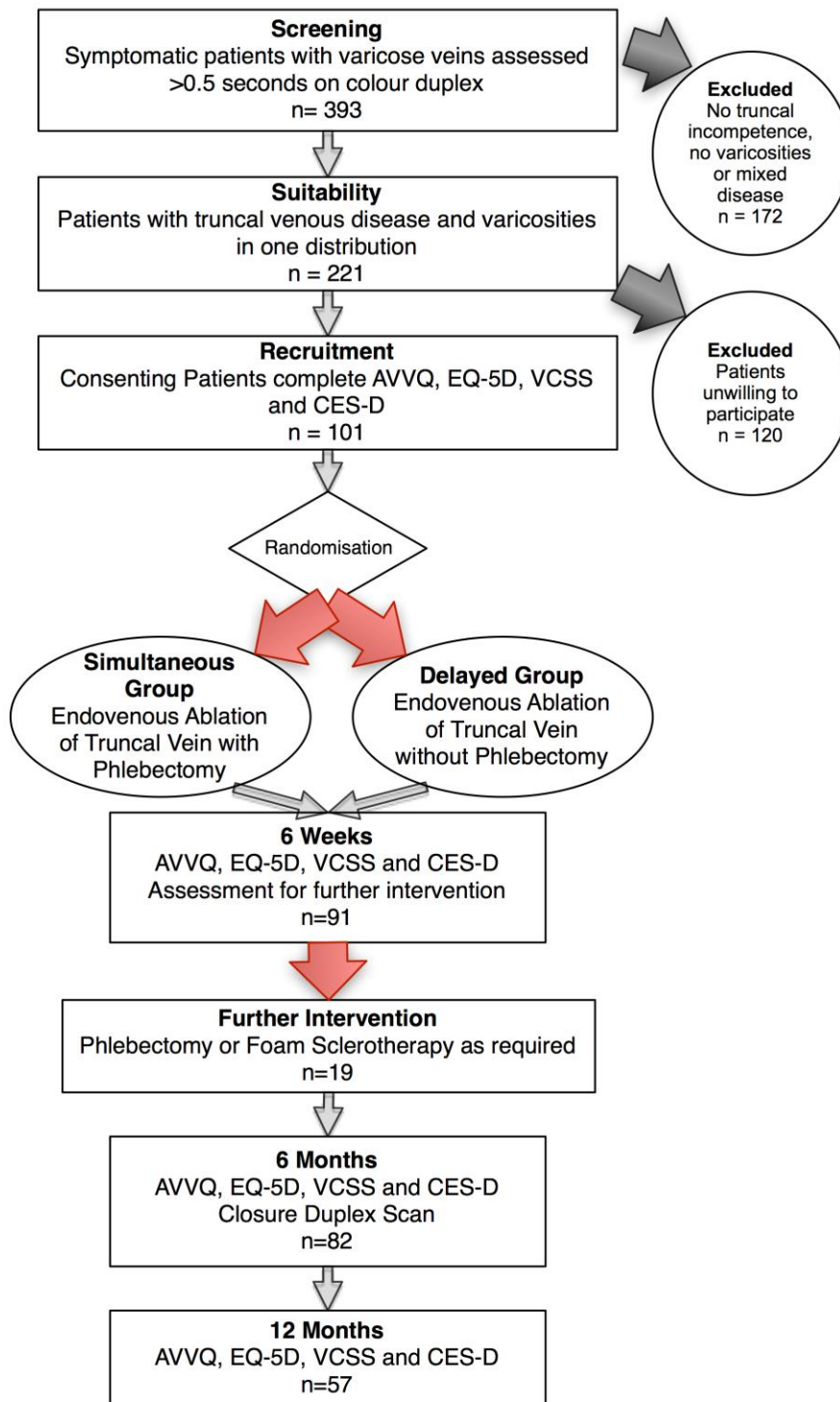


Figure 1: AVULS Trial Consort Diagram

Figure 2

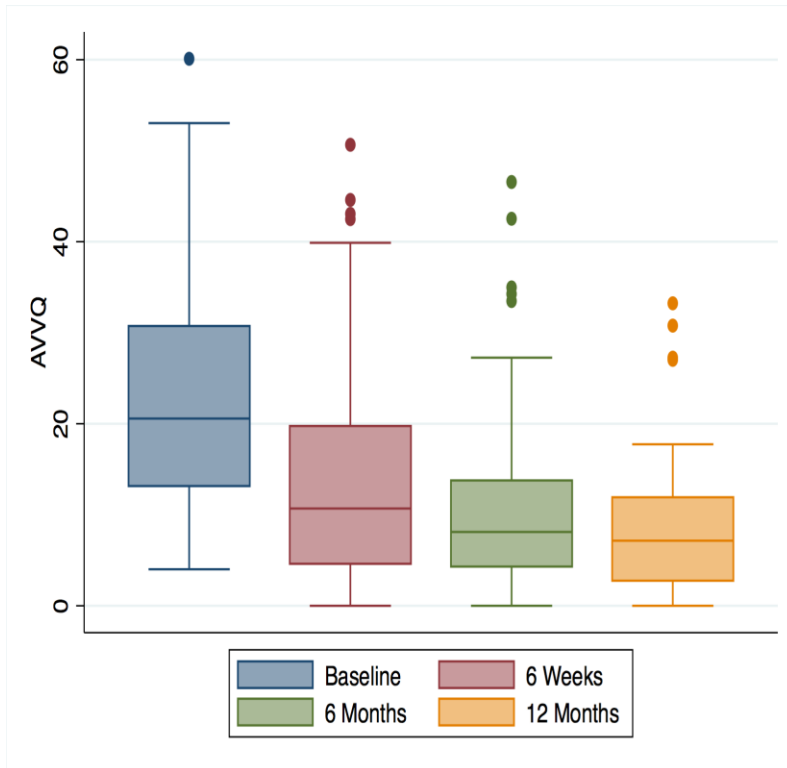


Figure 2: Aberdeen Varicose Vein Questionnaire (AVVQ) over the course of treatment.

Figure 3

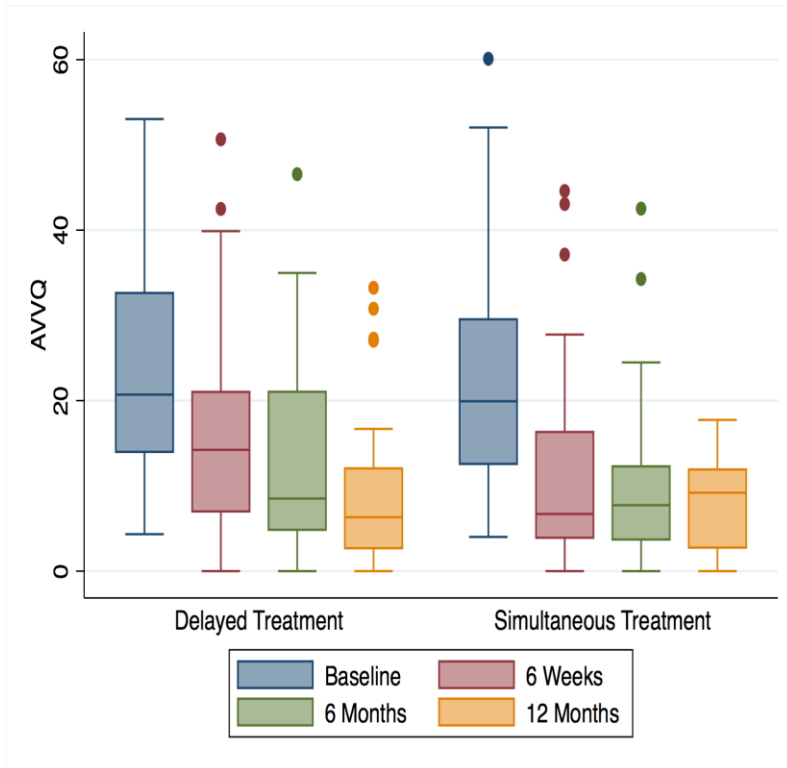


Figure 3: Aberdeen Varicose Vein Questionnaire (AVVQ) over the course of treatment showing delayed and simultaneous groups.

Figure 4

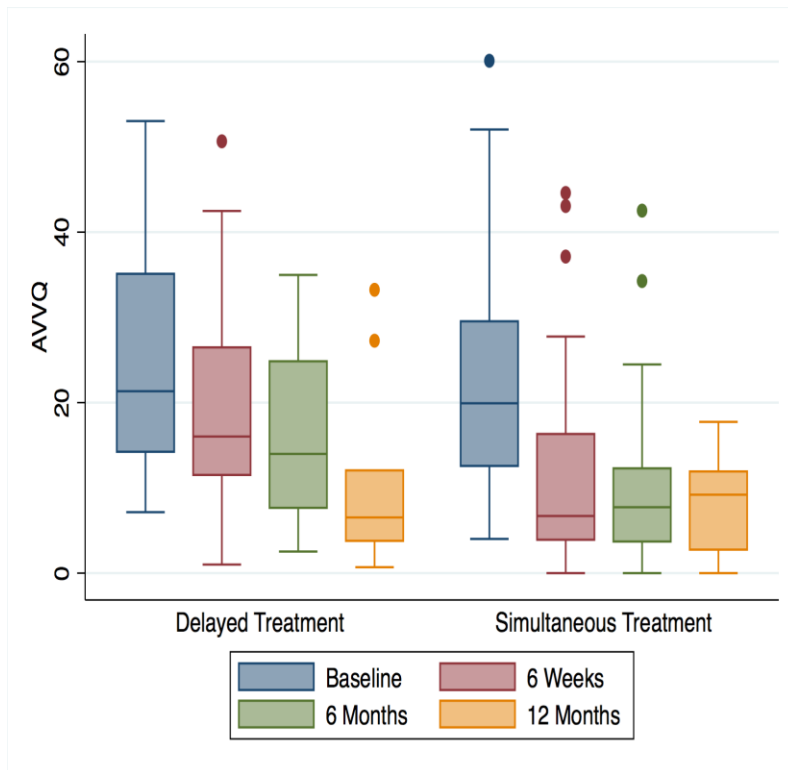


Figure 4: AVVQ values for the Delayed and requiring further treatment group and the Simultaneous group

Figure 5

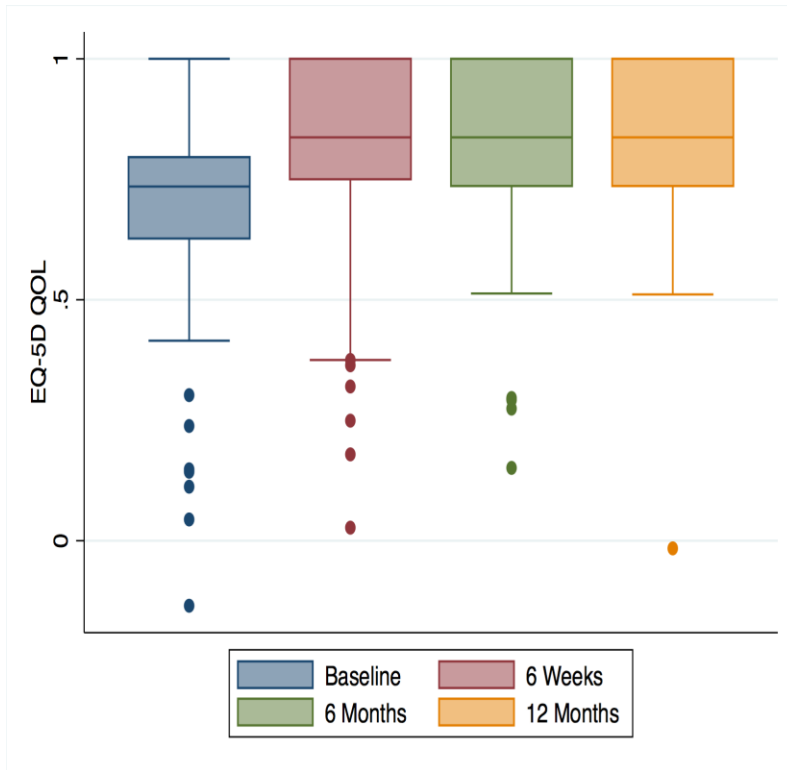


Figure 5: EQ-5D QOL for total cohort over follow-up

Figure 6

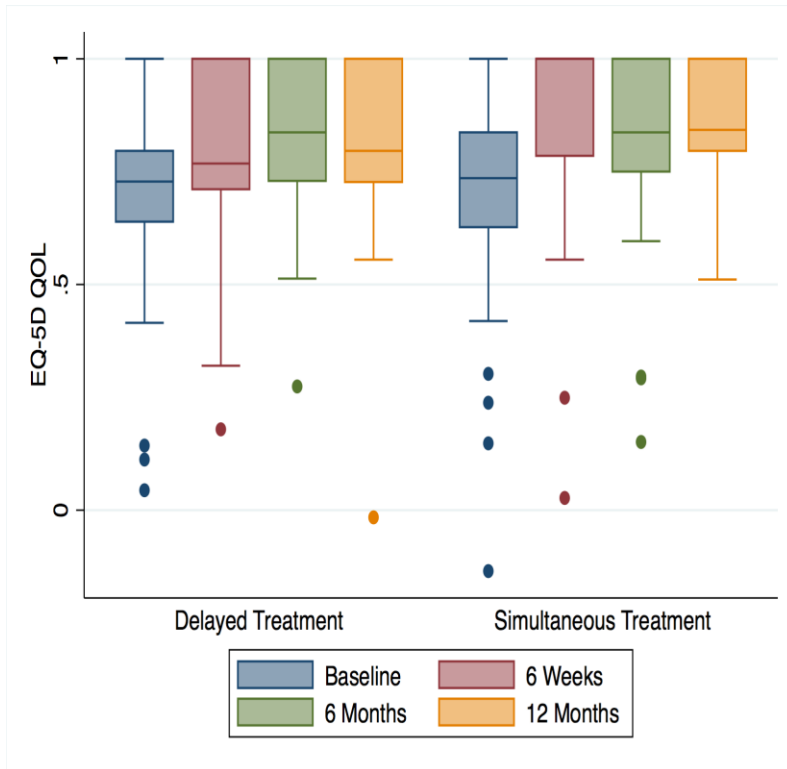


Figure 6: EQ-5D Generic Quality of Life Outcomes for Simultaneous and Delayed Groups

Figure 7

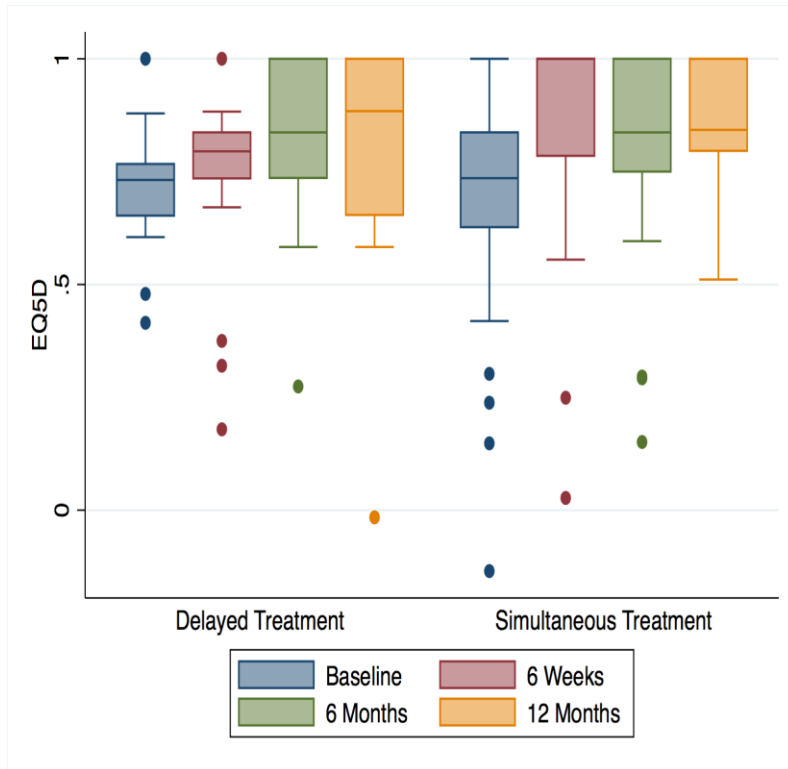


Figure 7: EQ-5D QOL Outcomes for patients comparing Further treatment in the delayed group and the Simultaneous Groups.

Figure 8

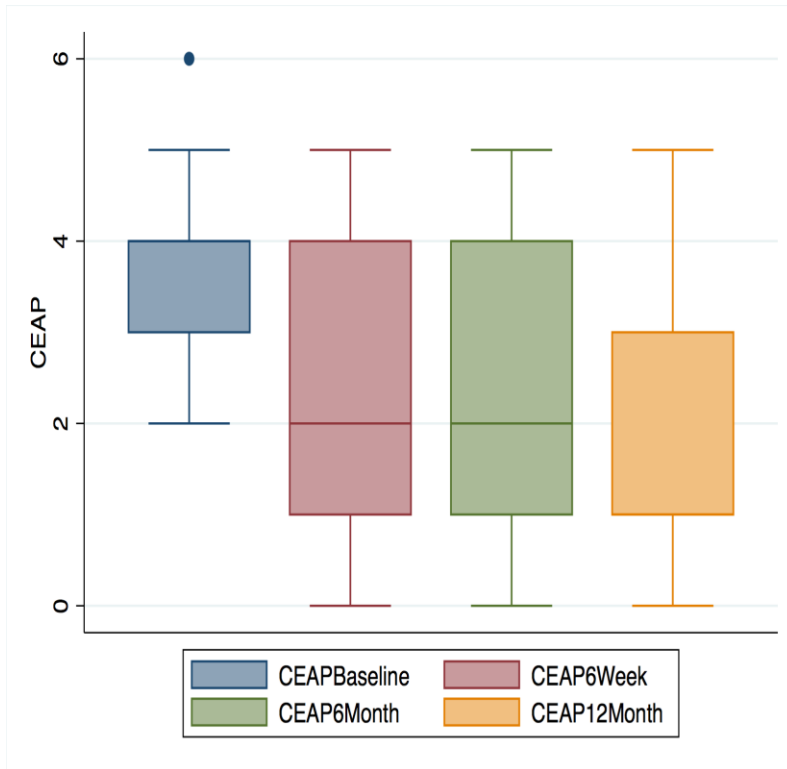


Figure 8: Overall CEAP status of the treated cohort.

Figure 9

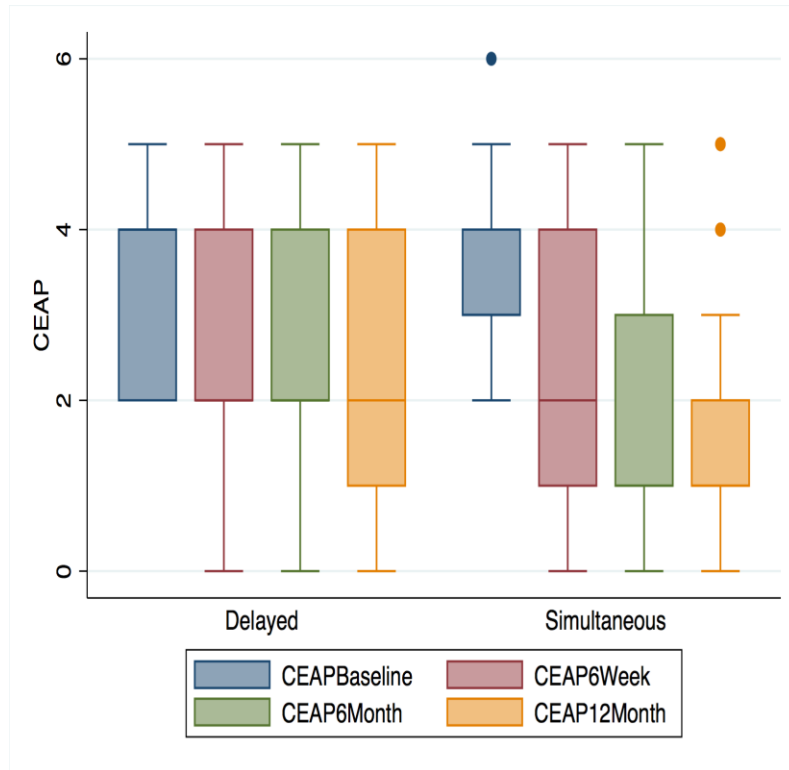


Figure 9: CEAP for the Delayed and Simultaneous Treatment Arms.

Figure 10

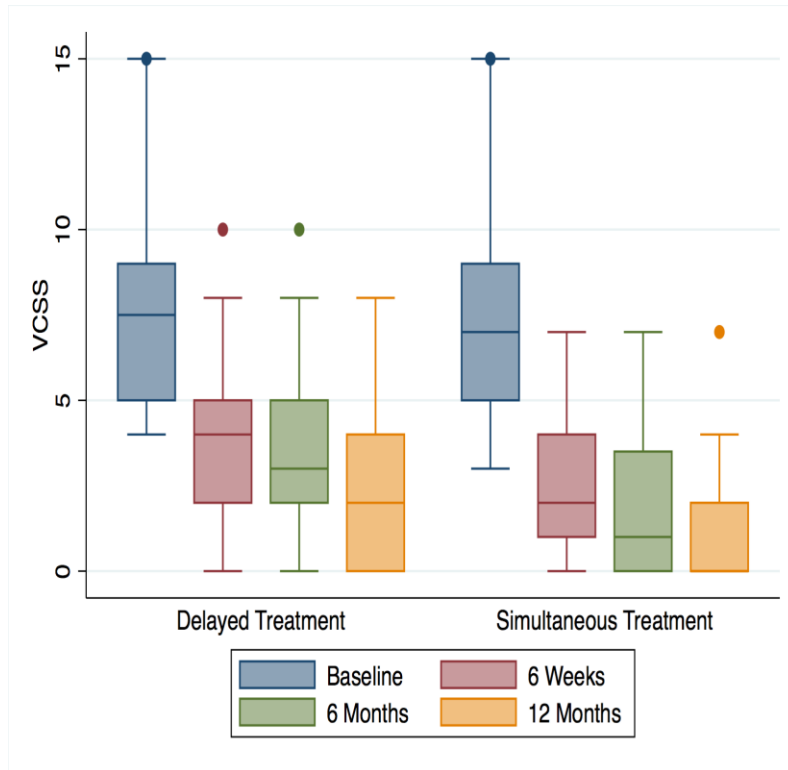


Figure 10: Mean VCSS in Delayed and Simultaneous Treatment Groups

Figure 11

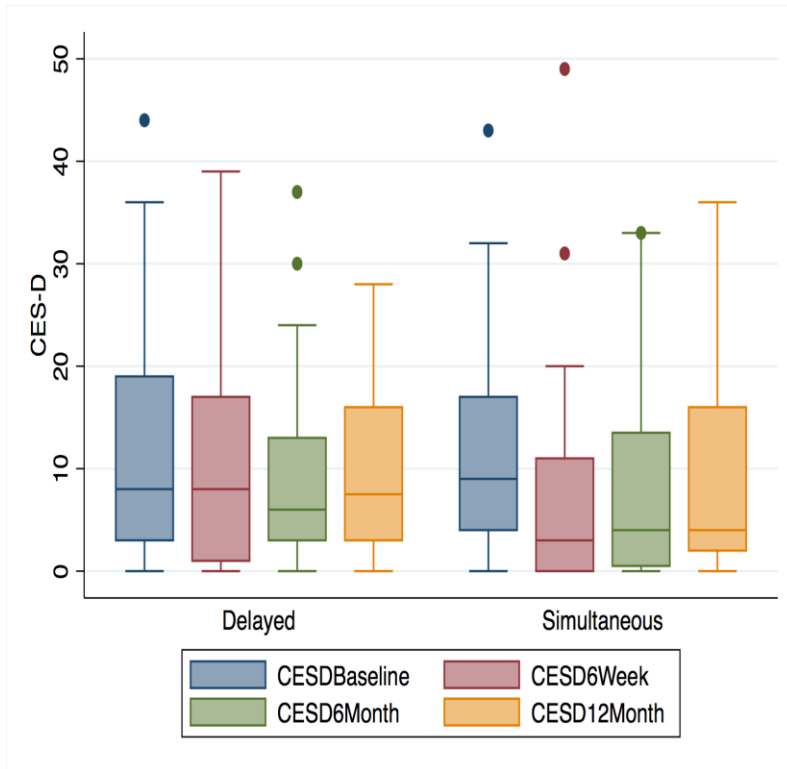


Figure 11: CES-D Scores during follow-up for Delayed and Simultaneous Groups