Editor's Choice – A Core Outcome Set for Clinical Studies on Chronic Venous Disease Involving the Deep Veins

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WHAT THIS PAPER ADDS

Chronic venous disease (CVD) has a significant impact on a patient's quality of life; however, inconsistent outcome reporting has impeded the establishment of best practices. This study establishes the first core outcome set for CVD involving the deep veins. It provides seven general core outcomes to be reported in all future clinical research evaluating interventions for CVD involving the deep veins, alongside six procedure specific core outcomes for invasive interventions. This will help to standardise outcome reporting and is an important step towards comparative analyses and improving patient outcomes.

Objective: Chronic venous disease (CVD) is a debilitating disease that results in significant morbidity and costs. A lack of standardised outcome reporting has made it difficult to evaluate the impact of interventions for CVD involving the deep veins. This study aimed to develop a core outcome set (COS) for studies evaluating interventions for this subset of CVD.

Methods: The COS was developed using the Core Outcome Measures in Effectiveness Trials (COMET) methodology. A systematic review and interviews with 19 patients experiencing post-thrombotic syndrome after deep vein thrombosis generated a longlist of outcomes, which was then refined by a steering group. Each outcome was rated on importance by patients and healthcare practitioners using a 9 point Likert scale within a Delphi survey. Outcomes not meeting consensus criteria in the first round were re-prioritised in a second round. Outcomes meeting the criteria for being critically important were discussed in a final meeting between patients and international experts to develop the COS.

Results: The review and interviews generated 80 outcomes, which entered the Delphi process. In total, 233 stakeholders responded in the first round and 143 in the second round. Consensus was reached on 29 outcomes deemed critically important. These outcomes were discussed in the final meeting to yield seven general outcomes and six procedure specific outcomes, since some outcomes were not relevant to all patients with CVD. The general outcomes were death, lower limb ulceration, venous thromboembolism, bleeding, quality of life, limb pain, and oedema or limb swelling. The procedure specific outcomes were device migration, device mechanical failure, patency, technical and/or procedural success, re-intervention, and vascular complications.

Conclusion: A COS was developed for studies evaluating interventions for CVD involving the deep veins, comprising seven general outcomes and six procedure specific outcomes. Reporting these outcomes will promote comparison of interventions for CVD involving the deep veins.

Keywords: Chronic venous disease, Consensus, Core outcome set, Delphi technique, Treatment outcome
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INTRODUCTION

Chronic venous disease (CVD) represents a global health concern with an estimated prevalence of 46 — 84% across all stages.[1] It is characterised by leg symptoms, such as the sensation of swelling, heaviness, itching, burning pain, claudication, and cramps, with more symptoms described in the SYM Vein Consensus statement.[2] In severe cases, CVD may manifest as venous ulceration in 0.6% of the population.[3] The classification of its diverse clinical findings, aetiology, anatomy, and pathophysiology is commonly addressed using the CEAP (clinical, etiological, anatomical, and pathophysiological) classification system.[4]

CVD results in significant disability, with a large impact on quality of life and high economic burden.[5,6] Specifically, 10.4% of individuals with CVD have lost workdays owing to their symptoms, and venous ulceration has high incremental healthcare costs.[7,8]

In some patients, CVD affects the deep veins beneath the deep fascia. In primary disease, degeneration of the valve or vein wall causes pathological reflux. In contrast, in secondary aetiology, deep vein thrombosis (DVT) may result in obstruction, incomplete recanalisation, and/or valve incompetence. A patient with prior DVT experiencing symptoms at least three to six months after the initial phase may be diagnosed with post-thrombotic syndrome (PTS) using tools such as the Villalta score. Congenital aetiologies may also contribute, including venous agenesis.

Current management of CVD involving the deep veins includes compression therapy, medical treatments, and invasive interventions such as stents. However, trials have been too heterogeneous to compare using meta-analysis, partly attributable to inconsistent outcome reporting.[9,10]

Inconsistent outcome reporting in other fields has been addressed by the international Core Outcome Measures in Effectiveness Trials (COMET) initiative.[11] The COMET initiative outlines the development process for a core outcome set (COS) representing a minimum set of outcomes to report when studying a condition.[12] To date, this approach has developed a number of COSs for routine care, with several in the surgical field.[13,14] Although some have focused on vascular disease, none have addressed CVD involving the deep veins.[15—17]

The aim of the current study was to develop a COS for studies evaluating interventions to manage CVD involving the deep veins, including compression, anticoagulation, and deep venous interventions. This used a similar protocol and framework employed in the COS for diabetes related foot ulceration.[17]

METHODS

Study design, ethics, and sponsorship

This was an observational study with a pre-defined data collection and analysis protocol. The COS was developed in four phases using the COMET methodology and in line with previous work.[12,17] The study received approval from the West of Scotland Research Ethics Committee (REC reference 22/WS/0172; protocol no. 2022-1912; IRAS ID 312226) and sponsorship from the University of Bristol (Bristol, UK). The study was pre-registered with the COMET initiative.[18] The COS has been reported according to the Core Outcome Set-STAndards for Reporting (COS-STAR) Statement.[19] Written informed consent was collected before participant involvement in each stage.

Scope of the core outcome set

The COS was designed for use in clinical research studies evaluating interventions for CVD involving the deep veins in adults.

Phase I: generation of the longlist of outcomes

Systematic review. A previously published systematic review provided a list of 62 outcomes for consideration in the COS.[20]

Patient interviews. To capture additional outcomes, semi-structured patient interviews were conducted. This included adult patients with PTS identified from vascular outpatient clinics within the Bristol, Bath, and Weston Vascular Network. This network covers a broad geographical region handling secondary and tertiary vascular referrals. Nineteen patients with PTS secondary to iliofemoral DVT were sampled, ensuring good coverage of experiences. Patient recruitment concluded with outcome saturation, defined as no new outcomes in the preceding two interviews. Interviews were conducted using Microsoft Teams with a topic guide designed by a qualitative research specialist. Interviews were transcribed and two independent researchers extracted the outcomes using thematic analysis.

Steering committee review. The steering committee (G.H., A.S., B.A.O., and R.J.H.) reviewed the longlist of outcomes and adjusted the phrasing and descriptors of these outcomes for interpretability (Supplementary Table S1). Only 'General quality of life' was not taken forward due to the preferred inclusion of 'Disease specific quality of life', which has a more complete association with the CVD stage.[6]

Phase II: Delphi process

First round. The longlist of outcomes entered a Delphi survey, delivered using the Research Electronic Data Capture (REDCap) platform hosted by the University of Bristol.[21,22]

An anonymous survey link was shared with patients with CVD involving the deep veins across the Bristol, Bath, and Weston Vascular Network and through Thrombosis UK, HaemSTAR, and on social media.

To access the survey, patients read an information sheet and confirmed that they suffered from CVD involving the deep veins. To ensure reliability, the survey was distributed only to patients in the Bristol, Bath, and Weston Vascular Network who had been reviewed in clinic. Distribution to the HaemSTAR/Thrombosis UK mailing lists included only previously signed up patients. The survey was also

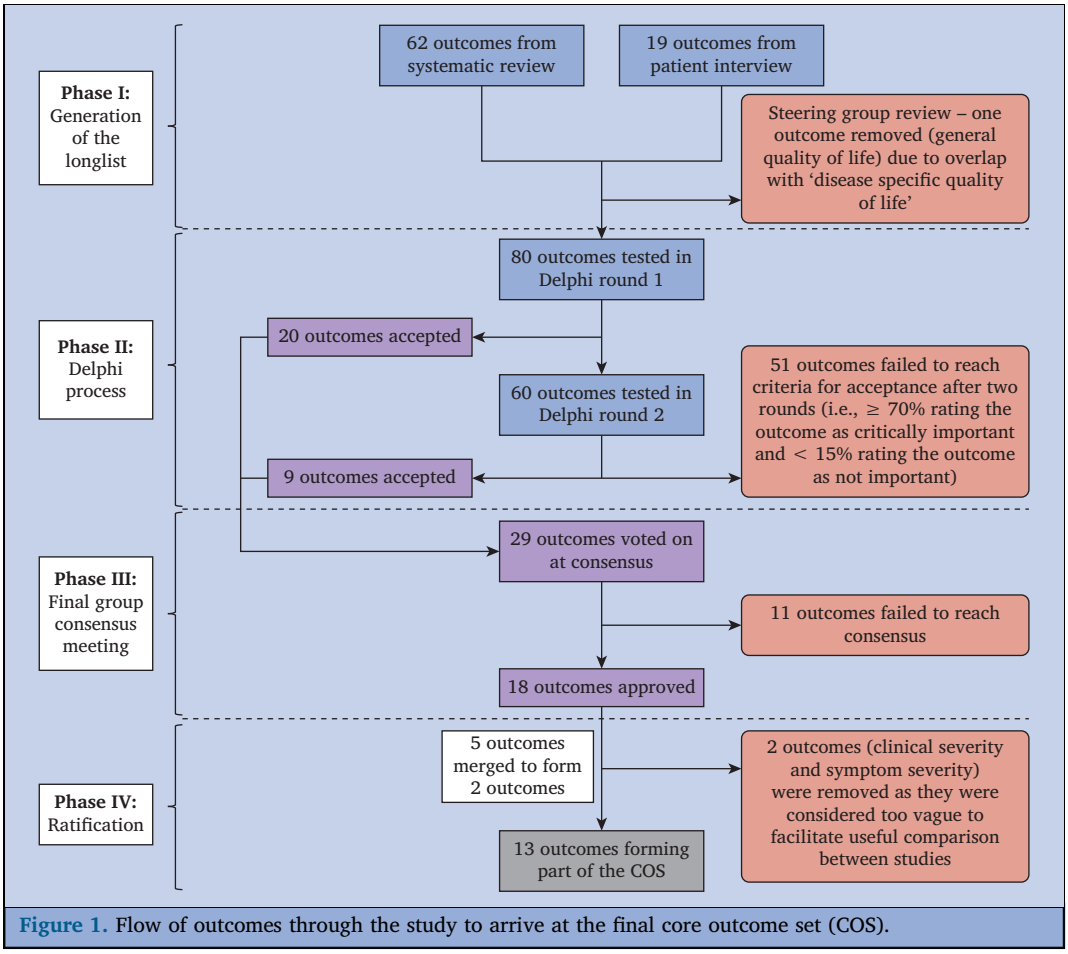

Figure 1. Flow of outcomes through the study to arrive at the final core outcome set (COS).

explained directly to patients from Thrombosis UK in an online meeting. Only patients from the UK were included, due to ethics constraints.[23] Healthcare practitioner (HCP) responses were captured by circulation using professional mailing lists of the following vascular societies: the European Society for Vascular Surgery (ESVS), Venous Special Interest Group (Vascular Research UK), Vascular Society of Great Britain and Ireland (VSGBI), Royal Society of Medicine (RSM), Society of Vascular Nurses, Legs Matter, Lindsay Leg Club, UK Vascular Clinical Trials Network, and the UK Thrombosis Research Network (UK-TReN).

The longlist of outcomes was presented in five standard core areas: death; physiological and clinical; life impact; resource use; and adverse events.[12] Participants rated the importance of each outcome on a Likert scale from 1 (not important) to 9 (critically important). Due to disease and/or intervention variability, participants were advised to leave blank outcomes they did not understand. During the analysis, records with incomplete data were therefore included (Supplementary Tables S2 and S3); however, sensitivity analysis of complete records yielded similar results (Supplementary Tables S4 and S5).

In agreement with Delphi recommendations, outcomes rated as critical (7 — 9) by $\geq$ 70% and not important (1 — 3) by $<$ 15% of respondents were considered for discussion at phase III.[11] Meanwhile, outcomes rated as critical (7 — 9) by $<$ 15% and not important (1 — 3) by $\geq$ 70% of respondents were discarded. Remaining outcomes were forwarded to the second round of the Delphi survey. Duplicate responses with fewer recorded answers were removed.

Second round. Those who participated in the first round were given a personalised link to the second round. Bar charts summarised the responses from first round participants alongside a median score for each outcome. Participants were reminded how they rated the outcome in the first round to facilitate a move towards consensus.[24] A clarifying email and up to three general reminder emails were sent to non-responders. Individualised emails to HCP non-responders were also used to ensure follow through.

Outcomes were again subjected to the above criteria to determine progression to phase III.

Phase III: consensus group meeting

A final consensus meeting was held online over Microsoft Teams (Microsoft, Redmond, Washington, USA). This group included local patient representatives selected to include a range of experiences, alongside a group of Key Opinion Leaders within the European Research Hub and ESVS, interventional radiologists, haematologists, and vascular scientist experts. The experts represented an international, interdisciplinary panel with substantial balanced experience in managing CVD involving the deep veins.

Outcomes that had reached consensus as critically important during phase II were voted on using anonymous Mentimeter software (Mentimeter, Stockholm, Sweden). Participants were given three options pertaining to the COS: must include, must exclude, and unsure. Outcomes voted in by $\geq$ 70% and out by $<$ 15% were recommend for inclusion in the COS. After discussion, stakeholders were asked whether they wanted to reconsider any other outcomes.

Phase IV: ratification

Outcomes included in the COS by the consensus group were discussed amongst the steering group (R.J.H., B.A.O., and G.H.) and were consolidated. The final list of core outcomes was shared with the consensus group attendees, who made no further changes.

Statistical analysis

Results were analysed using descriptive statistics. Demographic age statistics were presented as the median and interquartile range (IQR).

RESULTS

The flow of outcomes through the study is shown in Figure 1.

Phase I: generation of the longlist of outcomes

In total, 19 patients (median age 42 years, IQR 32, 50 years) were interviewed. Most patients were female (n = 12; 63%). All patients suffered from PTS following iliofemoral DVT, with three patients secondarily developing varicose veins and two developing venous ulceration. At the time of interview, all patients had required anticoagulation and compression therapy, nine had venous stenting, and one had thrombolysis without stent insertion.

Nineteen outcomes were identified during patient interviews and were combined with the 62 outcomes from the previously published systematic review with one exception as previously described. This longlist was reviewed by the steering group and the descriptions refined to improve interpretability (Supplementary Table S1).

Phase II: Delphi process

Eighty outcomes proceeded to the Delphi survey. The first round of this process ran from November 2023 to March 2024, whilst the second round was completed in May 2024. Three hundred and sixteen people clicked onto the survey, 64 did not answer any questions, and 19 were duplicate records. This left 233 responses (109 fully complete and 124 partially complete). Most HCPs were from the UK, with 18 other countries also represented (Table 1). All responses were analysed, and 20 outcomes meeting criteria were accepted to be discussed at consensus, whilst outcomes not meeting criteria were put forward to the second round (Table 2).

All 233 first round engagers were emailed to complete the second round. Of these, 143 responded (98 fully complete and 45 partially complete) corresponding to a 61.4% second round response rate.

Table 1. Clinician demographics in the first and second rounds of the Delphi process.

Demographic	First round (n = 124)	Second round (n = 77)
Location		
UK	83 (66.9)	43 (56)
Italy	7 (5.6)	7 (9)
Greece	4 (3.2)	4 (5)
Germany	3 (2.4)	3 (4)
Sweden	4 (3.2)	3 (4)
USA	4 (3.2)	3 (4)
Ireland	6 (4.8)	2 (3)
Romania	3 (2.4)	2 (3)
Argentina	1 (0.8)	1 (1)
Australia	1 (0.8)	1 (1)
Denmark	1 (0.8)	1 (1)
France	1 (0.8)	1 (1)
Hungary	1 (0.8)	1 (1)
Moldova	1 (0.8)	1 (1)
Netherlands	1 (0.8)	1 (1)
North Macedonia	1 (0.8)	1 (1)
Portugal	1 (0.8)	1 (1)
Spain	1 (0.8)	1 (1)
Role		
Doctor	92 (74.2)	65 (84)
Nurse	27 (21.8)	8 (10)
Industry expert	3 (2.4)	3 (4)
Allied professional	2 (1.6)	1 (1)
Specialty		
Vascular surgery	97 (78.2)	62 (81)
Haematology or thrombosis	9 (7.3)	6 (8)
Industry expert	3 (2.4)	3 (4)
Interventional radiology	7 (5.6)	2 (3)
Vascular medicine	2 (1.6)	1 (1)
General practice	3 (2.4)	1 (1)
Transfusion medicine	1 (0.8)	1 (1)
Tissue viability	2 (1.6)	1 (1)
Grade		
Consultant	83 (66.9)	59 (77)
Registrar	6 (4.8)	3 (4)
Staff grade	2 (1.6)	2 (3)
Not relevant or not stated	33 (26.6)	13 (17)
Years of specialty experience		
<5	15 (12.1)	8 (10)
5–10	15 (12.1)	7 (9)
11–20	42 (33.9)	31 (40)
>20	52 (41.9)	31 (40)

Data are presented as n (%).

The results from the second round of the Delphi were analysed, and nine more outcomes proceeded to the consensus meeting (Table 2). One outcome, 'Contralateral DVT', failed the first round and was on criteria borderline in the second round. Due to similarity with other venous thromboembolism (VTE) outcomes, it was discussed at the consensus meeting but not voted upon.

Phase III: consensus group meeting

An online final consensus meeting was attended by 12 HCPs considered international experts on CVD and four patient

Table 2. Percentage of participants rating outcomes as critically important (7 − 9 on a Likert scale) and not important (1 − 3 on a Likert scale) in the first and second rounds of the Delphi survey.

Outcome by domain	First round (n = 233)		Second round (n = 143)		Voted on at consensus meeting?
	Critical	Not important	Critical	Not important	
Death					
Death	71	7	Accepted round 1		Yes
Physiological and clinical					
Claudication	64	5	61	4	–
Clinical severity	73	7	Accepted round 1		Yes
Vascular complications	78	2	Accepted round 1		Yes
Contralateral deep vein thrombosis	65	7	70	5	*
Device misplacement	74	5	Accepted round 1		Yes
Device mechanical failure	78	2	Accepted round 1		Yes
Device migration or embolism	82	1	Accepted round 1		Yes
Haemodynamic indices	39	12	23	15	–
Heaviness	36	10	25	10	–
Ipsilateral deep vein thrombosis	77	2	Accepted round 1		Yes
Oedema	59	4	71	1	Yes
Paraesthesia	46	8	38	12	–
Pulmonary embolism	90	0	Accepted round 1		Yes
Technical or procedural success	76	1	Accepted round 1		Yes
Treatment durability	75	1	Accepted round 1		Yes
Varicose veins	42	15	33	11	–
Vessel rupture or perforation	63	6	65	5	–
Unspecified VTE	66	3	82	1	Yes
Symptom severity	79	0	Accepted round 1		Yes
Allergic reaction	58	6	54	9	–
General or unspecified bleeding	58	6	65	4	–
Access site bleeding	47	6	35	6	–
Brain haemorrhage or haematoma	88	3	Accepted round 1		Yes
Gastrointestinal bleeding	78	3	Accepted round 1		Yes
Epistaxis	38	13	16	20	–
Epidural bleed or haematoma	83	3	Accepted round 1		Yes
Haemorrhagic menstrual bleeding	42	10	24	15	–
Haematological complications	51	5	46	10	–
Lymphatic complications	47	10	39	7	–
Retinal haemorrhage	58	8	53	9	–
General or unspecified pain	44	11	42	6	–
Limb pain	60	3	72	2	Yes
Back pain	37	13	31	6	–
Ulcer healing or recurrence	66	4	72	5	Yes
Skin complications	43	11	40	12	–
Skin signs or symptoms	40	13	33	9	–
Cardiopulmonary complications	70	2	74	1	Yes
Nervous system complications	54	6	58	6	–
Infective complications	52	5	59	2	–
Surgical site infection	55	6	58	5	–
Renal complications	57	4	57	6	–
Patency	76	2	Accepted round 1		Yes
Clinical improvement	75	4	Accepted round 1		Yes
Ulcer odour	23	28	15	20	–
Ulcer pain	41	9	32	6	–
Levels of exudate	30	20	11	14	–
Breathlessness	53	15	56	11	–
Life impact					
Disease specific quality of life	79	2	Accepted round 1		Yes
Disability	74	1	Accepted round 1		Yes
General health	62	1	63	2	–
Social functioning	54	4	60	3	–
Emotional functioning	52	6	60	4	–
Psychological impacts	53	5	56	4	–
Mental health	55	4	59	4	–
Physical functioning	67	1	75	0	Yes
Re-intervention	66	1	73	2	Yes
Amputation	86	3	Accepted round 1		Yes

Continued

Table 2-*continued*

Outcome by domain	First round (n = 233)		Second round (n = 143)		Voted on at consensus meeting?
	Critical	Not important	Critical	Not important	
Compliance	63	1	68	3	–
Satisfaction	62	2	67	3	–
Radiation exposure	36	13	25	12	–
Impact on family	35	12	32	8	–
Role functioning	54	4	58	1	–
Ambulatory status	61	1	74	1	Yes
Time to leg fatigue	42	5	42	5	–
Sexual functioning	35	10	18	9	–
Sleep disturbance	45	6	36	5	–
Resource use					
Duration of intervention	36	14	9	18	–
Hospital re-admission	53	7	50	7	–
Length of hospital stay	38	12	33	10	–
Healthcare contacts	36	12	34	8	–
Cost or economic	36	22	23	12	–
Effectiveness of pain relief	67	2	71	1	Yes
Compression therapy	55	8	59	7	–
Leg elevation	42	12	34	7	–
Need for surgical intervention	58	4	64	2	–
Need for antibiotic therapy	36	15	27	9	–
Wound care	43	10	31	5	–
Adverse events					
General or composite adverse events	61	4	57	4	–
VTE recurrence	85	1	Accepted round 1		Yes

Data are presented as percentages. Of the 233 entries in the first round, 109 were complete and 124 were partial. Of the 143 entries in the second round, 98 were complete and 45 were partial. VTE = venous thromboembolism.
* Contralateral deep vein thrombosis was discussed but not voted on at the final consensus meeting.

representatives. The HCPs included eight vascular surgeons, two haematologists or cardiovascular specialists, and two interventional radiologists. Represented countries included the UK, Belgium, France, Greece, Ireland, Italy, Spain, and the Netherlands.

Twenty nine outcomes were formally voted on (Table 3). Seventeen met the criteria after the consensus meeting vote. Alongside these successful outcomes, 'Oedema' (which did not meet criteria in the vote) was later re-discussed and recommended unanimously for inclusion in the COS.

Some outcomes were specific to endovascular procedures, including intravascular thrombolysis, thrombectomy, venoplasty, and stent placement. These were separated into a list of procedure specific outcomes. This was because, whilst some outcomes may be crucial to capture when assessing a stent, they would be laboursome for studies focused on conservative therapy.

Phase IV: ratification

In the final phase, three outcomes were merged under a 'Venous thromboembolism' core outcome and two were merged under a 'Bleeding' core outcome. 'Ulcer healing or recurrence' was renamed to better apply to patients without an ulcer in the first instance, and 'Device migration or embolism' was shortened to eliminate redundancy. 'Disease specific quality of life' was broadened to avoid biasing how investigators should measure quality of life. 'Symptom severity' and 'Clinical severity' were removed as these outcomes were considered too vague to be usefully included without recommending how they should be measured. This converged to a list of seven universal core outcomes (Table 4): (1) death; (2) lower limb ulceration; (3) VTE; (4) bleeding; (5) quality of life; (6) limb pain; and (7) oedema or limb swelling.

The six procedure specific core outcomes were: (1) device migration; (2) device mechanical failure; (3) patency; (4) technical or procedural success; (5) re-intervention; and (6) vascular complications (including access site complications, venous aneurysm formation, and venous perforation or rupture).

The descriptions of these outcomes as presented throughout the process can be found in Supplementary Table S1.

DISCUSSION

Key findings

Seven universal core outcomes were recommended to be reported in all studies evaluating interventions for CVD involving the deep veins. A further six procedure specific outcomes should also be reported if a study was to evaluate an endovascular intervention.

The decision to have a separate list of procedure specific outcomes was driven by the wide existing reporting of

Table 3. Percentage of members of the final consensus meeting rating outcomes to be included in or excluded from the core outcome set (COS).

Outcome by domain	Include	Exclude	Unsure	Recommended for inclusion in COS
Death				
Death	86	14	0	Yes
Physiological/clinical				
Clinical severity	86	7	7	Yes
Vascular complications	80	13	7	Yes
Device misplacement	63	0	38	–
Device mechanical failure	100	0	0	Yes
Device migration or embolism	94	0	6	Yes
Ipsilateral deep vein thrombosis	88	6	6	Yes
Oedema	36	57	7	Yes*
Pulmonary embolism	73	13	13	Yes
Technical or procedural success	100	0	0	Yes
Treatment durability	19	25	56	–
Unspecified VTE	60	13	27	–
Symptom severity	86	7	7	Yes
Brain haemorrhage or haematoma	87	7	7	Yes
Gastrointestinal bleeding	73	0	27	Yes
Epidural bleed or haematoma	67	0	33	–
Limb pain	73	13	13	Yes
Ulcer healing or recurrence	86	14	0	Yes
Cardiopulmonary complications	44	44	13	–
Patency	100	0	0	Yes
Clinical improvement	71	21	7	–
Life impact				
Disease specific quality of life	93	0	7	Yes
Disability	31	46	23	–
Physical functioning	33	47	20	–
Re-intervention	100	0	0	Yes
Amputation	40	60	0	–
Ambulatory status	8	62	31	–
Resource use				
Effectiveness of pain relief	7	87	7	–
Adverse events				
VTE recurrence	93	0	7	Yes

COS = core outcome set; VTE = venous thromboembolism.
* Oedema was later re-discussed and recommended unanimously.

outcomes such as 'Patency'.[20] These outcomes are significant for the development of management guidelines for endovascular procedures.[25] However, it is unrealistic to recommend capturing these outcomes for studies evaluating conservative therapies. This separation strategy has previously been successfully employed in other fields where the outcomes of interest varied by context.[15]

Importantly, the COS outcomes are a minimum standard. Studies using the COS should also consider why a patient is seeking treatment and capture additional outcomes to determine benefit to individual patients.

Table 4. Final recommended core outcome set for use in clinical research studies evaluating all potential interventions for chronic deep venous disease in adults.

General outcomes
Death
Lower limb ulceration
Venous thromboembolism
Bleeding
Quality of life
Limb pain
Limb swelling or oedema
Procedure specific outcomes
Device migration
Device mechanical failure
Patency
Technical or procedural success
Re-intervention
Vascular complications

Ratification of the core outcome set

The final group meeting in phase III achieved a balanced consideration of each outcome. This respected the Delphi consensus phase whilst consolidating outcomes into a practical list of outcomes similar in size to other surgical COSs.[13,26]

Several outcomes were grouped together into the core outcomes 'Bleeding' and 'Venous thromboembolism'. This was done because both are important to consider when considering anticoagulation or endovascular interventions.[27] However, they are relatively rare, therefore it was thought sufficient to capture them as a group rather than subdivide

them into the individual locations that a bleeding event or VTE could occur.[28,29]

The group argued that 'Disease specific quality of life' should be broadened to a 'Quality of life' outcome on the basis that many measures of quality of life deteriorate with increasing CVD severity.[6] Moreover, other studies have shown that there is no consensus on how quality of life should be captured.[30] General measures of quality of life have the benefit of being validated across several populations, whilst disease specific measures are more sensitive to individual patient change. It was therefore decided to keep the broad outcome 'Quality of life' until future core measurement sets decide the most relevant measure to use.

There was extensive discussion on the outcomes 'Clinical severity', 'Symptom severity', and 'Clinical improvement'. Concern was raised that the vagueness of the terms severity or improvement would impede the purpose of a COS to facilitate comparison between studies. In some cases, researchers have handled this issue by providing examples of symptoms to record or by using Likert scales.[13,31,32] Indeed, some members of the consensus group pointed towards the Villalta score. However, the symptoms in the Villalta score are not specific to CVD involving the deep veins.[30] Moreover, Villalta symptoms such as heaviness and paraesthesia were rated as critical by 25% and 38% of respondents, respectively, in the second round of the Delphi. It was therefore decided to exclude clinical severity, symptom severity, and clinical improvement, prioritising inclusion of individual symptoms regarded as critically important in the Delphi process.

Ambulatory status, Disability, and Physical functioning were considered important components of Quality of life, which had already been captured. The outcome Cardiopulmonary complications was thought to be more often a comorbidity rather than an outcome.[7] Amputation was rejected on the grounds that it was a rare outcome not conceivably linked to intervention for CVD involving the deep veins. Finally, Treatment durability and Device misplacement were rejected because they are directly related to technical or procedural success.

After the initial vote, haematology experts highlighted the high prevalence of oedema as an outcome.[33] Oedema also forms part of the CEAP classification and is key to the Widmer classification system.[34] Patient representatives also stated that management of oedema was key to their decision-making. There was unanimous agreement after this that Oedema should be included in the COS.

Limitations

The Delphi process helped narrow the initial longlist of 80 outcomes to a manageable list of 29. However, no outcomes met the pre-defined criteria for automatic rejection, and successive rounds resulted in even more outcomes being regarded as critically important, similar to prior studies.[35,36]

Furthermore, despite reminders being sent before the conclusion of the second round, the response rate was 61.4%, similar to previous studies.[23] This was perhaps due to the large size of the longlist that passed through the Delphi process.[37]

To address these limitations in the future, a more refined Delphi process seeking to first discover the symptoms experienced by patients might be useful.[38] Another approach might use best to worse scaling, which has been effective in other settings.[39]

A further limitation was the inability to verify the severity of CVD involving the deep veins experienced by Delphi patient respondents. Despite this, patients in phase I were interviewed in depth, and patients were again involved in phase III in extensive outcome discussions. This ensured that the patient input to the development of the COS had both breadth and depth.

Finally, there is a limitation in implementing some of the recommended outcomes. In keeping with COMET guidelines and previous approaches, it is not suggested how the outcomes should be measured.[40] However, differences in measurement tools (e.g., SF-36 or VEINES-QoL/Sym) can interfere with comparability even in studies implementing the COS. This limitation will resolve with the publication of future core measurement sets.

Despite this, the current COS remains useful in structuring study planning. Researchers should use it as a guide to check that they have captured sufficient data on items that are important to patients and clinicians. Moreover, COSs in the past have improved the reporting of outcomes despite lack of specific measurement recommendations.[12]

Impact and implementation strategy

Previous studies have shown that lack of awareness of COSs is a key reason for their reduced uptake.[41] To maximise uptake, this COS will be shared as part of the Venous Registry in the European Society for Vascular Surgery and key international societies. To validate the usefulness of the COS, future systematic reviews of trials and observational studies will be required to determine uptake of the COS accordingly.

To maximise the utility of the COS, there is also a need to build consensus around how best to measure the outcomes reported here. This will require a second Delphi based process focused on difficult to define items such as quality of life and limb pain. Ultimately, this COS is intended to facilitate a meta-analysis of studies by standardising outcome reporting. To evaluate the success of the COS, it is therefore desirable for studies to acknowledge where the COS has changed their selection of primary and secondary outcomes.

In summary, this study has developed a COS that can be used for studies evaluating interventions for CVD involving the deep veins using the robust COMET methodology. The broad inclusion of stakeholders ensures that the recommended outcomes are relevant and realistic. Ultimately, this will allow better comparison between CVD studies in the future.

CONFLICT OF INTEREST

No conflict of interest to declare.

FUNDING

This study received no funding.

DATA SHARING

Access to raw data is available upon request.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2025.04.005.

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COUP D'OEIL

Popliteal Vein Aneurysm with Thrombosis

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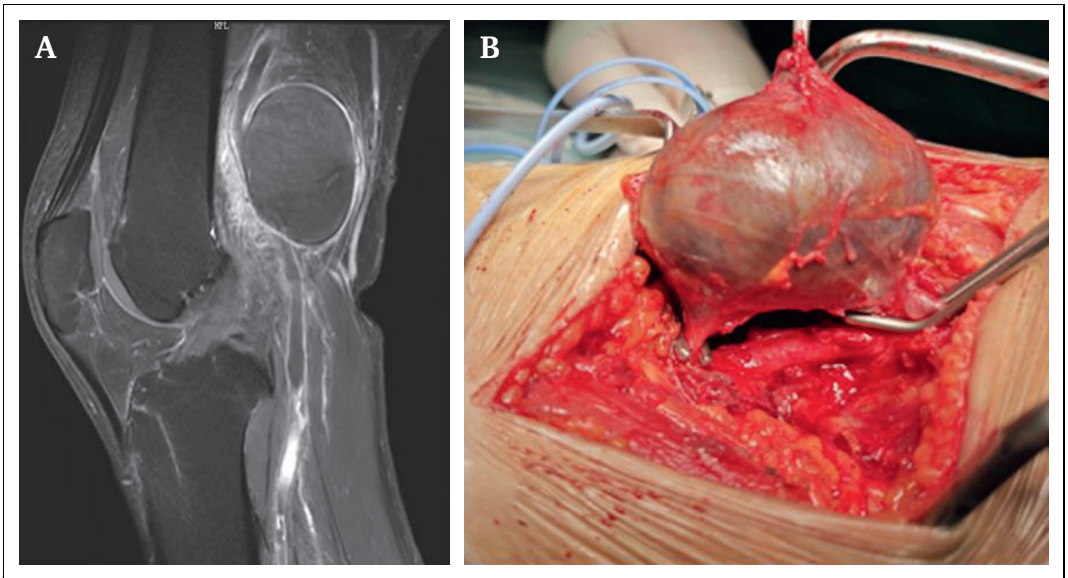

A 69 year old male presented with acute onset right popliteal fossa pain and ipsilateral calf swelling persisting for 24 hours, with no history of trauma. Examination revealed a soft, mobile mass in the right popliteal fossa. Magnetic resonance imaging revealed a thrombosed giant popliteal venous aneurysm (PVA) measuring 6.0 cm × 4.5 cm (A). To reduce the risk of fatal pulmonary embolism, a prophylactic retrievable inferior vena cava filter was deployed. Surgical intervention involved complete thrombus excision (B), PVA wall trimming, and venous reconstruction. The symptoms resolved without complications and the patient was discharged on rivaroxaban 20 mg daily for six months.

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