BJD
British Journal of Dermatology

A core outcome domain set for clinical research on capillary malformations (the COSCAM project): an e-Delphi process and consensus meeting*

Ginger Beau Langbroek,[1,2] Albert Wolkerstorfer,[3] Sophie E.R. Horbach,[2] Phyllis I. Spuls,[3] Kristen M. Kelly,[4] Susan J. Robertson,[5] M. Ingmar van Raath,[6] Firas Al-Niaimi,[7,8] Taro Kono,[9] Pablo Boixeda,[10] Hans J. Laubach,[11] Ashraf M. Badawi,[12,13] Agneta Troilius Rubin,[14] Merete Haedersdal,[15] Woraphong Manuskiatti,[16] Chantal M.A.M. van der Horst,[2] D.T. Ubbink[1] and on behalf of the COSCAM study group

[1]Department of Surgery, Amsterdam University Medical Centers, location AMC, University of Amsterdam, Amsterdam, the Netherlands
[2]Department of Plastic, Reconstructive and Hand Surgery, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, the Netherlands
[3]Department of Dermatology, Amsterdam University Medical Centers, Amsterdam Public Health, Immunity and Infections, University of Amsterdam, Amsterdam, the Netherlands
[4]Department of Dermatology, University of California Irvine, Irvine, CA, USA
[5]Department of Dermatology, Murdoch Children's Research Institute, The Royal Children's Hospital, Melbourne, VIC, Australia
[6]Department of Plastic, Reconstructive, and Hand Surgery, Maastricht University Medical Center, Maastricht University, Maastricht, the Netherlands
[7]Private dermatological practice, London, UK
[8]Department of Dermatology, University of Aalborg, Aalborg, Denmark
[9]Department of Plastic Surgery, Tokai University School of Medicine, Shimokasuya, Isehara, Kanagawa, Japan
[10]Department of Dermatology, Hospital Ramon y Cajal, Madrid, Spain
[11]Department of Dermatology, Geneva University Hospitals (HUG), Geneva, Switzerland
[12]Department of Dermatology, Szeged University, Szeged, Hungary
[13]Department of Medical Laser Applications, National Institute of Laser Enhanced Sciences, Cairo University, Giza, Egypt
[14]Department of Dermatology, Skåne University Hospital, Malmö, Sweden
[15]Department of Dermatology, University of Copenhagen, Bispebjerg Hospital, Copenhagen, NV, Denmark
[16]Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Linked Comment: H. Rönsch and J. Kottner. Br J Dermatol 2022; **187**:629–630.

Summary

Background There is limited evidence on the best available treatment options for capillary malformations (CMs), mainly due to the absence of uniform outcome measures in trials on therapies. A core outcome set (COS) enables standard reporting of trial outcomes, which facilitates comparison of treatment results.
Objectives To develop a core outcome domain set (CDS), as part of a core outcome set (COS), for clinical research on CMs.
Methods Sixty-seven potentially relevant outcome subdomains were recognized based on the literature, focus group sessions, and input from the COSCAM working group. These outcome subdomains were presented in an online Delphi study to CM experts (medical specialists and authors of relevant literature) and (parents of) patients with CM (international patient associations). During three e-Delphi study rounds, the participants repeatedly scored the importance of these outcome subdomains on a seven-point Likert scale. Participants could also propose other relevant outcome subdomains. Consensus was defined as ≥ 80% agreement as to the importance of an outcome subdomain among both stakeholder groups. The CDS was finalized during an online consensus meeting.
Results In total 269 participants from 45 countries participated in the first e-Delphi study round. Of these, 106 were CM experts from 32 countries, made up predominantly of dermatologists (59%) and plastic surgeons (18%). Moreover, 163 (parents of) patients with CM from 28 countries participated, of whom 58%

Correspondence:
Ginger Beau Langbroek.
Email: g.b.langbroek@amsterdamumc.nl

Accepted for publication
26 June 2022

C.M.A.M.H. and D.T.U. are joint senior and last authors.

Contributors to the COSCAM project are listed in Appendix S1 (see Supporting Information).

*Plain language summary available online

[Correction added on 13 October 2022, after first online publication: The affiliations for the first author have been updated and the sequence for the rest of the affiliations were reordered accordingly.]

DOI 10.1111/bjd.21723

had Sturge–Weber syndrome. During the two subsequent e-Delphi study rounds, 189 and 148 participants participated, respectively. After the entire consensus process, consensus was reached on 11 outcome subdomains: colour/redness, thickness, noticeability, distortion of anatomical structures, glaucoma, overall health-related quality of life, emotional functioning, social functioning, tolerability of intervention, patient satisfaction with treatment results, and recurrence.

Conclusions We recommend the CDS to be used as a minimum reporting standard in all future trials of CM therapy. Our next step will be to select suitable outcome measurement instruments to score the core outcome subdomains.

What is already known about this topic?

- Besides physical and functional sequelae, capillary malformations (CMs) often cause emotional and social burden.
- The lack of uniform outcome measures obstructs proper evaluation and comparison of treatment strategies. As a result, there is limited evidence on the best available treatment options.
- The development of a core outcome set (COS) may improve standardized reporting of trial outcomes.

What does this study add?

- A core outcome domain set (CDS), as part of a COS, was developed for clinical research on CMs.
- International consensus was reached on the recommended core outcome subdomains to be measured in CM trials: colour/redness, thickness, noticeability, distortion of anatomical structures, glaucoma, overall health-related quality of life, emotional functioning, social functioning, tolerability of intervention, patient satisfaction with treatment results, and recurrence.
- This CDS enables the next step in the development of a COS, namely to reach consensus on the core outcome measurement instruments to score the core outcome subdomains.

What are the clinical implications of this work?

- The obtained CDS will facilitate standardized reporting of treatment outcomes, thereby enabling proper comparison of treatment results.
- This comparison is likely to provide more reliable information for patients about the best available treatment options.

Capillary malformations (CMs) are caused by a hyperdilation of capillaries and postcapillary venules in the dermis or subcutaneous tissue.[1,2] They are commonly known as port-wine stains or birthmarks and have been associated with somatic mosaic mutations in the *GNAQ*, *GNA11* and *PIK3CA* genes.[3–6] Besides physical and functional effects, CMs often lead to decreased emotional and social overall health-related quality of life, as most are visibly located in the head and neck region.[7–12]

Multiple therapeutic strategies are available, including cosmetic camouflage, medical tattooing, surgical excision, and laser and light therapies.[13] Even though pulsed-dye laser is still the treatment of choice, its effectiveness in terms of clearance rate has barely improved over the last three decades.[14] Due to this and frequent post-treatment lesion recurrences, patients with CMs are left with a desire for improved treatment regimens.[15] Novel therapies might be promising, but they have no permanent place in the CM treatment palette yet.[16–19]

Currently, there is no consensus on which outcomes should be measured when evaluating treatment results.[20] This hampers the evaluation and comparison of treatment modalities and, as a result, there is limited evidence available on the best treatment options.[13] A core outcome set (COS) facilitates standard reporting of trial outcomes and, by including patients in the development process, incorporates patient-relevant outcomes. A COS, containing a core outcome domain set (CDS)

and a core outcome measurement set, includes a minimum set of outcomes that should be measured and reported in clinical research when studying a specific health condition.[21,22] So, a COS involves *what* to measure (outcome domains and subdomains) and *how* to measure (outcome measurement instruments). COS development has become an essential part in conducting meaningful research in the field of dermatology.[23] Over the last few years, a rise in dermatological COSs has become evident, for example in peripheral vascular malformations, congenital melanocytic naevi, and vitiligo.[24–26] Moreover, a dermatology-specific framework was recently developed to support COS developers in this field.[27]

The Core Outcome Set for Capillary Malformations (COSCAM) project was initiated, as currently no COS exists for CMs. We have previously reported on the methods to develop the CDS for CMs, including the results of the first development stage.[28] The objective of this study was to finalize the second development stage, in order to reach international consensus on the CDS for clinical research on CMs.

Patients and methods

Scope and methodological guidelines

Our previously published protocol describes our methods in detail.[28] The CDS is focused on patients of any age with any form of CM. It is intended for use in clinical research on CMs with any type of intervention, including watchful waiting. This study was registered on the CS-COUSIN website (http://cs-cousin.org/coscam) and the COMET website (http://www.comet-initiative.org/Studies/Details/1599). The guidelines of the COMET initiative, CS-COUSIN, COS-STAD and HOME initiative roadmap were followed.[23,29–31] The study results are reported according to the COS-STAR checklist.[32]

Stakeholders and recruitment

Two main stakeholder groups were included: patients with CM (and their caregivers or parents) and experts in CM. Both groups were considered the most essential stakeholders in CM clinical research and were therefore included. Patients with CM were invited to participate via the COSCAM steering group, participating CM experts, national and international patient organizations, and the social media channels (Facebook or Instagram) of the various patient organizations. CM experts were sought among authors of published CM literature, through personal networks of the COSCAM steering group and contact lists of the International Society of the Study for Vascular Anomalies, and through the OVAMA (Outcome Measures for Vascular Malformations) project participant list (See the protocol for details on stakeholder eligibility and recruitment).[28]

Identification of potential core outcome subdomains

The protocol describes the first CDS development stage in detail. In brief, potential core outcome subdomains were retrieved from a systematic review (n = 16), focus group sessions (n = 20) and discussions with the COSCAM founding group (n = 38).[20] Seven outcome subdomains overlapped (Figure 1). As suggested by Lange *et al.*, the relatively broad outcome domains (such as clinical assessment) were specified by more precise subdomains (such as redness). For definitions see Table S1 in the Supporting Information.[27] Subsequently, a final list with 67 potentially relevant outcome subdomains was generated (Table S2; see Supporting Information).

Selection of core outcome subdomains: e-Delphi study

An international modified e-Delphi study was conducted to evaluate the importance of the potential core outcome subdomains. The potential core outcome subdomains, written in lay language, formed the material for online surveys in Dutch and English (Google Forms; and Paperform Pty Ltd, Sydney, NSW, Australia). To prevent overlap, these outcome subdomains were presented on either a first or second level in the e-Delphi study together with their corresponding definitions. This resulted in 43 outcome subdomains that were presented in the first e-Delphi round (Figure 1). Before the first round, one Dutch patient and one American patient checked the surveys for readability and comprehensibility.

A total of 3–4 weeks was anticipated to complete each survey per study round. This deviated from our previously published protocol, in which a period of 4–6 weeks was foreseen. In each round, a maximum of three reminders were sent. A response rate of ≥ 70% compared with the previous study round was maintained.

During the first round, we collected the baseline characteristics of both stakeholder groups, as described in our study protocol.[28] Both stakeholder groups were asked to rate the importance of the potential core outcome subdomains. Only during this round, participants were able to suggest other potentially relevant outcome subdomains. Before being introduced in the second study round for evaluation, the suggested outcome subdomains were checked by the COSCAM founding group to determine whether they could measure treatment effect and if they were truly new outcome subdomains. In the subsequent rounds, participants received feedback on the scores of the previous study round for each stakeholder group. The outcome subdomains on which no consensus was reached were then re-evaluated.

The consensus definitions are specified in detail in our protocol.[28] Briefly, the importance of the proposed outcome subdomains was rated on a seven-point Likert scale. If ≥ 80% of both stakeholder groups scored in the outcome subdomain a six or seven, the outcome subdomain was deemed 'important' or 'crucial', respectively. These were included in the CDS. Outcome subdomains were excluded from the CDS if ≥ 80% of both stakeholder groups scored a one or two on the Likert scale. After the third round, outcome subdomains were categorized as 'included in the CDS' (consensus on the importance in both stakeholder groups), 'excluded from the CDS' (consensus on nonimportance in both stakeholder groups) or 'undecided' (no consensus on the importance reached yet, or consensus reached in only one stakeholder group).

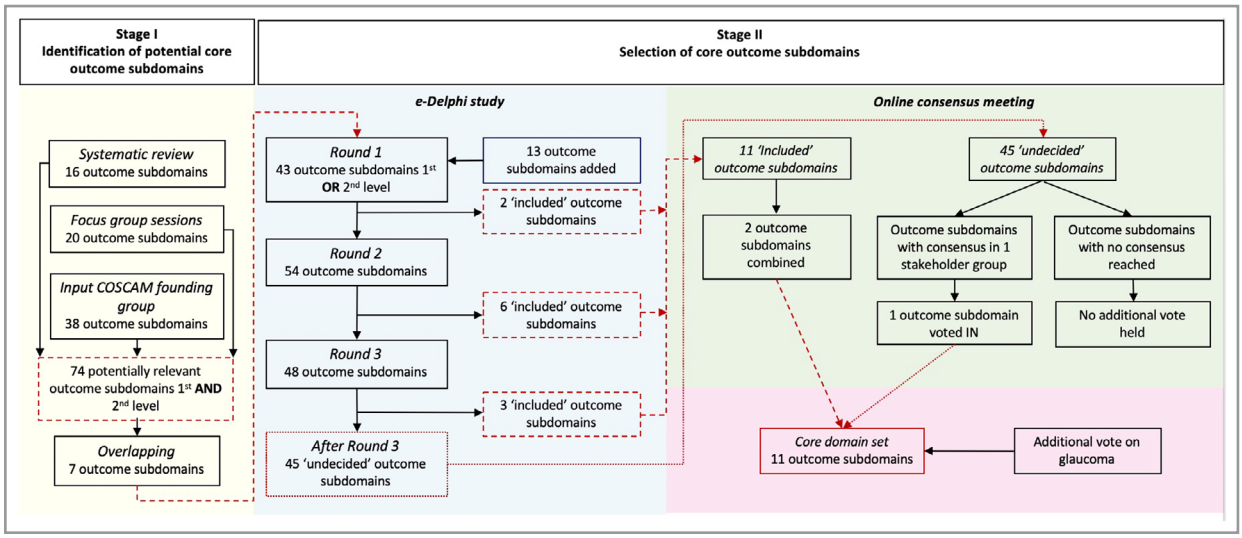

Figure 1 Overview of the core domain set development stages.

Selection of core outcome subdomains: consensus meeting

Following the third e-Delphi round, an online consensus meeting was organized to reach consensus on the final CDS. The consensus rules were identical to those in the e-Delphi study. Stakeholders who completed the second e-Delphi round were invited to participate in this meeting. An online date planner was sent to pick a date based on the availability of the stakeholders.

Two members of the COSCAM steering group (A.W. and G.B.L.) chaired the meeting and one expert (P.I.S.) provided methodological support. During the meeting, stakeholders discussed and voted on the 'included' outcome subdomains as well as the 'undecided' outcome subdomains on which only one stakeholder group reached consensus. Stakeholders also had the opportunity to discuss and, if necessary, vote on the 'undecided' outcome subdomains on which no consensus had been reached yet in both stakeholder groups, and make suggestions on the outcome subdomain definitions. Revoting on any of the latter outcome subdomains would be initiated only when there were strong advocates during the meeting to do so. The final IN or OUT vote was held separately per stakeholder group via an online poll to select the definitive core outcome subdomains of the CDS. The CDS was categorized according to the framework by Lange *et al.*[27]

Statistical analyses

Microsoft Excel was used for data analyses. Categorical data were presented as absolute numbers and percentages. The percentage agreement in each e-Delphi round was calculated for all outcome subdomains and rounded to the nearest whole percentage. Subanalyses for 'included' outcome subdomains of patients with Sturge–Weber syndrome (SWS) were presented descriptively. Absolute numbers of IN and OUT votes were presented for the consensus meeting. All results were calculated separately per stakeholder group.

Ethics and consent

The medical ethics review board of the Amsterdam University Medical Center, location AMC, approved this study (W20_351#20.389). Stakeholders gave online consent for their data to be used anonymously at the first online survey.

Results

Participant characteristics

In total 269 participants from 45 countries participated in the first study round. Of these, 163 were (parents of) patients with CM from 28 countries. Of all participating patients, 95 (58%) had SWS. Some patients had a CM in combination with a venous malformation (n = 18), an arteriovenous malformation (n = 4), a lymphatic malformation (n = 1) or combinations of these (n = 24). In addition, 106 CM experts from 32 countries participated, of whom the majority were dermatologists (59%) or plastic surgeons (18%). Most physicians had 15–20 years (21%) or > 20 years (39%) of experience in the field of CMs. Tables 1 and 2 present the participant characteristics of the first e-Delphi round, and Table 3 shows the number of participants and response rates per e-Delphi round. Overall, the response rate was ≥ 70% in each round. Participant characteristics of round 3 can be found in Table S3 (see Supporting Information).

e-Delphi study

Table 4 shows the results of each stakeholder group per e-Delphi round. Of the list with comments and suggested outcome subdomains during the first round, 13 outcome subdomains were eventually added to the second round (a full list with comments and suggested outcome subdomains is given in Table 5 and Appendix S2; see Supporting Information).

Table 1 Complete overview of the characteristics of patients with capillary malformations (CMs) in e-Delphi round 1

Characteristics of patients[a]		n (%)
Total group		163 (100)
Age ranges		
0 to < 5 years		11 (6·7)
5 to < 10 years		15 (9·2)
10 to < 18 years		32 (19·6)
18 to < 35 years		34 (20·9)
35 to < 50 years		35 (21·5)
> 50 years		36 (22·1)
Educational level[b]		
Primary school		52 (31·9)
High school		26 (16·0)
Associate degree		25 (15·3)
University		60 (36·8)
Continent	Country of residence	
Africa	Ethiopia	1 (0·6)
	South Africa	2 (1·2)
Asia	India	1 (0·6)
	Japan	3 (1·8)
	Malaysia	1 (0·6)
	Philippines	2 (1·2)
	Russia	1 (0·6)
	Saudi Arabia	1 (0·6)
	Singapore	1 (0·6)
	Thailand	3 (1·8)
Australasia	Australia	10 (6·1)
Europe	Spain	8 (4·9)
	Austria	1 (0·6)
	Belgium	4 (2·5)
	Denmark	1 (0·6)
	Finland	1 (0·6)
	France	3 (1·8)
	Germany	2 (1·2)
	Italy	5 (3·1)
	Netherlands	25 (15·3)
	Norway	1 (0·6)
	Romania	1 (0·6)
	UK	10 (6·1)
North America	Canada	3 (1·8)
	Mexico	2 (1·2)
	Puerto Rico	1 (0·6)
	USA	68 (41·7)
South America	Argentina	1 (0·6)
Skin type		
Type I		26 (16·0)
Type II		63 (38·7)
Type III		52 (31·9)
Type IV		15 (9·2)
Type V		6 (3·7)
Type VI		1 (0·6)
Location of CM		
Head and neck		106 (65·0)
Mixed locations		46 (28·2)
Lower extremities		7 (4·3)
Trunk		2 (1·2)
Upper extremities		2 (1·2)
Presence of skin/soft tissue hypertrophy		
Yes		33 (20·2)
No		130 (79·8)
Sturge–Weber syndrome		
Yes		95 (58·3)
No		56 (34·4)
I don't know		12 (7·4)
CM combined with another type of vascular malformation		
No		76 (46·6)
I don't know		40 (24·5)
Combination		24 (14·7)
Venous malformation		18 (11·0)
Arteriovenous malformation		4 (2·5)
Lymphatic malformation		1 (0·6)
Previous therapies		
Laser therapy		86 (52·8)
Camouflage		6 (3·7)
Surgery		3 (1·8)
Combination of therapies		25 (15·3)
Other		4 (2·5)
No		39 (23·9)
Currently undergoing therapy		
Yes		55 (33·7)
No		108 (66·3)

[a]The data refer to the patients with the CMs, not to their parents or caregivers. [b]Educational levels were similar for all countries, except for Dutch patients. The Dutch 'MBO' and 'HBO' educational levels were categorized in the 'associate degree' group.

After the third round, consensus was reached for 'thickness', 'noticeability', 'facial deformity', 'overgrowth of underlying structures', 'glaucoma', 'overall health-related quality of life', 'emotional functioning', 'social functioning', 'tolerability of the intervention', 'patient satisfaction with treatment results' and 'recurrence'.

Subanalysis showed that in the SWS group consensus was also reached for 'physical functioning', 'occupational functioning', 'cognitive functioning', 'coping' and 'pain'.

Eventually, none of the outcome subdomains reached consensus on 'nonimportance'. Both the 11 'included' and the 45 'undecided' outcome subdomains were discussed in the consensus meeting (Figure 1).

Consensus meeting

During the consensus meeting, a total of 61 participants with various geographical backgrounds joined, including six patients, eight parents or caregivers and 47 experts (Appendix S1). Throughout the meeting and polls, the number of participants varied. It was decided during the meeting that a minimum of eight patients (or parents/caregivers) would need to participate during the voting, otherwise the meeting would be closed. This was not defined in the study protocol. Table 5 presents the results of the votes and comments raised during the meeting.

Table 2 Complete overview of the characteristics of experts in capillary malformations (CMs) in e-Delphi round 1

Characteristics of experts		n (%)
Total group		106 (100)
Specialty		
Dermatology		63 (59·4)
Plastic surgery		19 (17·9)
Other		5 (4·7)
Otolaryngology		4 (3·8)
Paediatrics		4 (3·8)
Paediatric surgery		3 (2·8)
No specialty		3 (2·8)
Vascular surgery		2 (1·9)
Intervention radiology		1 (0·9)
Ophthalmology		1 (0·9)
Oral and maxillofacial surgery		1 (0·9)
Continent	Country of residence	
Africa	Egypt	2 (1·9)
Asia	China	3 (2·8)
	India	1 (0·9)
	Iran	1 (0·9)
	Iraq	2 (1·9)
	Japan	6 (5·7)
	Saudi Arabia	1 (0·9)
	South Korea	1 (0·9)
	Thailand	1 (0·9)
Australasia	Australia	12 (11·3)
	New Zealand	1 (0·9)
Europe	Belgium	2 (1·9)
	Finland	1 (0·9)
	France	3 (2·8)
	Germany	2 (1·9)
	Greece	1 (0·9)
	Ireland	2 (1·9)
	Italy	4 (3·8)
	Lithuania	1 (0·9)
	Poland	1 (0·9)
	Scotland	1 (0·9)
	Spain	12 (11·3)
	Sweden	1 (0·9)
	Switzerland	1 (0·9)
	The Netherlands	10 (9·4)
	UK	7 (6·6)
North America	Canada	3 (2·8)
	USA	16 (15·1)
South America	Aruba	1 (0·9)
	Brazil	1 (0·9)
	Chile	4 (3·8)
	Peru	1 (0·9)
Years of experience in the field of CMs		
0 to < 5 years		9 (8·5)
5 to < 10 years		15 (14·2)
10 to < 15 years		19 (17·9)
15 to < 20 years		22 (20·8)
> 20 years		41 (38·7)
Type of hospital		
University hospital		80 (75·5)
Urban hospital		5 (4·7)
Private clinic		9 (8·5)
Mixed		12 (11·3)
Member of multidisciplinary working group		
Yes		77 (72·6)
No		22 (20·8)
Maybe		7 (6·6)
Number of new patients visiting the hospital annually		
0–20		12 (11·3)
20–100		53 (50·0)
100–200		21 (19·8)
200–400		14 (13·2)
> 400		6 (5·7)
Number of new patients with CM treated annually		
0–20		25 (23·6)
20–100		58 (54·7)
100–200		13 (12·3)
200–400		7 (6·6)
> 400		3 (2·8)
Types of vascular malformations treated		
Only CMs		12 (11·3)
Combinations		94 (88·7)

Table 3 Number of participants and response rates (RRs) per e-Delphi study round

Round 1	
Patients	163
Experts	106
Total (RR)	269 (unknown)[a]
Round 2	
Patients	99
Experts	90
Total (RR)	189 (70)
Round 3	
Patients	65
Experts	83
Total (RR)[b] (RR)[c]	148 (78) (55)

[a]The RR of the first round could not be determined, as participants were invited via various ways, including open invitations via social media accounts of patient organizations and personal contacts of CM experts. [b]Percentage relative to the previous round; and [c]percentage relative to the first round.

Of the 'included' outcome subdomains during the e-Delphi study, 'glaucoma', 'facial deformity', 'overgrowth of underlying structures' and 'recurrence' were revoted on during the meeting. Glaucoma was revoted on as only a minority of the patients have (an increased risk for) glaucoma: that is, patients with a CM in which any part of the forehead is involved, including the upper eyelids.[33] Furthermore, current therapies for CMs do not have any effect on glaucoma. Despite elaborate discussions on the pros and cons, 'glaucoma' remained in the CDS after revoting. Furthermore, due to overlap it was suggested to combine 'facial deformity' and 'overgrowth of

Table 4 Overview of the outcome subdomains that were rated as 'important' or 'crucial' by each stakeholder group per e-Delphi study round

Outcome Domain	Outcome subdomains rated as important or crucial by a stakeholder group	First round		Second round		Third round	
		Patients	Experts	Patients	Experts	Patients	Experts
Clinical assessment	General appearance	58%	92%	74%	96%	78%	92%
	Colour	58%	92%	74%	89%	69%	90%
	Texture	65%	73%	75%	69%	77%	58%
	Thickness	62%	80%	80%	83%	IN	IN
	Size	61%	70%	69%	59%	71%	49%
	Skin stiffness	54%	25%	58%	18%	57%	11%
	Noticeability	60%	87%	74%	90%	80%	90%
	Facial deformity[a]	n/a	n/a	85%	92%	IN	IN
	Overgrowth of underlying structures[a]	n/a	n/a	87%	88%	IN	IN
Signs and symptoms	Bleeding	60%	64%	72%	47%	66%	33%
	Pain	62%	58%	74%	46%	75%	36%
	Itching	44%	31%	44%	13%	46%	10%
	Pyogenic granuloma	61%	57%	69%	38%	65%	24%
	Glaucoma[a]	n/a	n/a	80%	81%	IN	IN
	Infections[a]	n/a	n/a	61%	31%	65%	10%
	Eczema in the birthmark[a]	n/a	n/a	48%	17%	48%	2%
	Headache[a]	n/a	n/a	68%	30%	57%	19%
	Sensibility problems[a]	n/a	n/a	64%	30%	55%	14%
Health-related quality of life	Overall health-related quality of life	80%	88%	IN	IN	IN	IN
	Emotion functioning	85%	86%	IN	IN	IN	IN
	Cognitive functioning	67%	44%	72%	41%	85%	31%
	Social functioning	77%	88%	83%	91%	IN	IN
	Occupational (role) functioning	72%	66%	79%	68%	86%	67%
	Physical functioning	74%	66%	82%	77%	89%	77%
	Family impact	57%	51%	61%	42%	55%	30%
	Perception of cosmetic results	53%	76%	64%	81%	69%	82%
	Perception of functional results	62%	69%	72%	61%	77%	52%
	Perception of symptoms related to CMs	59%	59%	73%	38%	60%	46%
	Perception of CM severity	63%	71%	75%	67%	75%	59%
	Coping	63%	66%	71%	58%	82%	45%
Treatment	Adherence to treatment	60%	69%	70%	72%	75%	76%
	Number of required treatment procedures	56%	75%	68%	77%	75%	76%
	Total duration of treatment process[a]	n/a	n/a	59%	53%	55%	30%
	Tolerability of the intervention	67%	77%	73%	88%	80%	88%
	Patient satisfaction with treatment results	74%	91%	85%	94%	IN	IN
	Recurrence[a]	n/a	n/a	77%	88%	82%	80%
Adverse events	Pain	72%	79%	78%	77%	78%	72%
	Bruising	58%	39%	46%	23%	51%	13%
	Wound	62%	74%	67%	63%	60%	43%
	Hypopigmentation	42%	67%	44%	54%	40%	35%
	Hyperpigmentation	50%	59%	54%	49%	54%	40%
	Hypertrophic scarring	61%	86%	65%	84%	69%	77%
	Atrophic scarring	52%	75%	57%	67%	60%	43%
	Blistering	61%	55%	58%	32%	57%	16%
	Crusting	53%	47%	58%	24%	58%	6%
	Swelling	56%	35%	56%	10%	60%	4%
	Textural changes	62%	57%	66%	34%	68%	19%
	Bleeding	66%	56%	69%	27%	60%	20%
	Pyogenic granuloma	64%	45%	68%	26%	68%	13%
	Adverse events of anaesthetics	57%	54%	58%	42%	62%	28%
	Burning of skin[a]	n/a	n/a	62%	34%	65%	17%
	Itching[a]	n/a	n/a	47%	13%	42%	4%
	Infection[a]	n/a	n/a	65%	37%	66%	17%
	Eczema in birthmark[a]	n/a	n/a	55%	21%	46%	7%
Practical issues	Treatment costs	63%	59%	61%	56%	72%	52%
	Number of hospital visits	55%	60%	58%	49%	62%	34%

CM, capillary malformation; n/a, not applicable. Items highlighted in green indicate consensus reached on the importance of an outcome subdomain. [a]Outcome subdomains proposed by stakeholders during the first e-Delphi round.

Table 5 Results and comments from the online consensus meeting

Outcome domains	Outcome subdomains	Results after last e-Delphi round	Votes	Final results	Comments from consensus meeting
Clinical assessment	General appearance	?	Vote IN: patients 6/10 (60%), experts 22/41 (54%)	OUT	This outcome subdomain is covered by noticeability
	Colour	?	Vote IN: patients 10/10 (100%), experts 36/38 (95%)	IN	
	Texture	−	~	OUT	
	Thickness	+	n/a	IN	
	Size	−	~	OUT	
	Skin stiffness	−	~	OUT	
	Noticeability	+	n/a	IN	
	Facial deformity[a]	+	Vote for combining into 'distortion of anatomical contours': patients 9/11 (82%), experts 36/41 (88%)	IN ('distortion of anatomical contours')	Overlap with overgrowth of underlying structures, new vote was suggested to combine both
	Overgrowth of underlying structures[a]	+	Vote for combining into 'distortion of anatomical contours': patients 9/11 (82%), experts 36/41 (88%)	IN ('distortion of anatomical contours')	Overlap with facial deformity, new vote was suggested to combine both
Signs and symptoms	Bleeding	−	~	OUT	
	Pain	−	~	OUT	
	Itching	−	~	OUT	
	Pyogenic granuloma	−	~	OUT	
	Glaucoma[a]	+	Vote to remove glaucoma from the CDS: patients 8/11 (73%), experts 35/41 (85%)	IN	Glaucoma only occurs in a minority of the patients with CMs and it is debatable if it really is an outcome subdomain
	Infections[a]	−	~	OUT	
	Eczema in the birthmark[a]	−	~	OUT	
	Headache[a]	−	~	OUT	
	Sensibility problems[a]	−	~	OUT	
Health-related quality of life	Overall health-related quality of life	+	n/a	IN	
	Emotional functioning	+	n/a	IN	
	Cognitive functioning	?	Votes IN: patients 5/9 (56%), experts 2/36 (6%)	OUT	It is rarely affected by CMs
	Social functioning	+	n/a	IN	
	Occupational (role) functioning	?	Votes IN: patients 11/11 (100%), experts 13/35 (37%)	OUT	
	Physical functioning	?	Votes IN: patients 6/8 (75%), experts 10/37 (27%)	OUT	It is only relevant in a selected group of patients with CMs
	Family impact	−	~	OUT	
	Perception of cosmetic results	?	Votes IN: patients 9/10 (90%), experts 25/37 (68%)	OUT	
	Perception of functional results	−	~	OUT	
	Perception of symptoms related to CMs	−	~	OUT	
	Perception of CM severity	−	~	OUT	
	Coping	?	Votes IN: patients 10/10 (100%), experts 7/37 (19%)	OUT	

(continued)

Table 5 (continued)

Outcome domains	Outcome subdomains	Results after last e-Delphi round	Votes	Final results	Comments from consensus meeting
Treatment	Adherence to treatment	–	~	OUT	
	Number of required treatment procedures	–	~	OUT	
	Total duration of treatment process[a]	–	~	OUT	
	Tolerability of intervention	+	n/a	IN	
	Patient satisfaction with treatment results	+	n/a	IN	
	Recurrence[a]	+	Vote to remove 'recurrence' from the core domain set: patients 2/10 (20%), experts 12/38 (32%)	IN	Some see recurrence as a separate outcome subdomain that should be covered by a measurement instrument, yet others see it as a repeated measurement of other core outcome subdomains
Adverse events	Pain	–	~	OUT	
	Bruising	–	~	OUT	
	Wound	–	~	OUT	
	Hypopigmentation	–	~	OUT	
	Hyperpigmentation	–	~	OUT	
	Hypertrophic scarring	–	~	OUT	
	Atrophic scarring	–	~	OUT	
	Blistering	–	~	OUT	
	Crusting	–	~	OUT	
	Swelling	–	~	OUT	
	Textural changes	–	~	OUT	
	Bleeding	–	~	OUT	
	Pyogenic granuloma	–	~	OUT	
	Adverse events of anaesthetics	–	~	OUT	
	Burning of skin[a]	–	~	OUT	
	Itching[a]	–	~	OUT	
	Infection[a]	–	~	OUT	
	Eczema in birthmark[a]	–	~	OUT	
Practical issues	Treatment costs	–	~	OUT	
	Number of hospital visits	–	~	OUT	

CM, capillary malformation; 'n/a', not applicable. [a]Outcome subdomains suggested in the first e-Delphi round. '+' included in the core domain set. '?' undecided outcome subdomains with consensus in only one stakeholder group. '–' undecided outcome subdomains with no consensus reached in both stakeholder groups. '~' no vote was held during the consensus meeting, as this outcome subdomain was not found important enough by both stakeholder groups during the e-Delphi study and there were no strong advocates during the consensus meeting to open a vote.

underlying structures' into 'distortion of anatomical structures'. After voting, this newly combined outcome subdomain was included in the CDS. It was also discussed whether 'recurrence' is a separate outcome subdomain or if it is defined as repeated measurements of other core outcome subdomains and should therefore be removed from the CDS. A revote was held and it was kept in the CDS.

Of the 'undecided' outcome subdomains, only the outcome subdomains with consensus in one stakeholder group (n = 7) were voted on. Eventually, only 'colour/redness' was included in the CDS. The 'undecided' outcome subdomains with no consensus in both stakeholder groups (n = 38) were discussed but not voted on, as there were no strong advocates during the meeting to revote.

Additional vote on glaucoma

Because there were still strong advocates after the consensus meeting that 'glaucoma' might not be an outcome measure for CMs and that it is not applicable to all patients with CM, the COSCAM steering group and the CS-COUSIN Methods advisory group were consulted. Based on these deliberations different conditions were proposed in which glaucoma should be considered as an outcome measure and when it should be assessed in clinical research (Figure 2). These conditions were approved by an online vote, in which a total of 94 participants responded, including 61 experts, 20 patients and 13 parents/caregivers (Appendix S1).

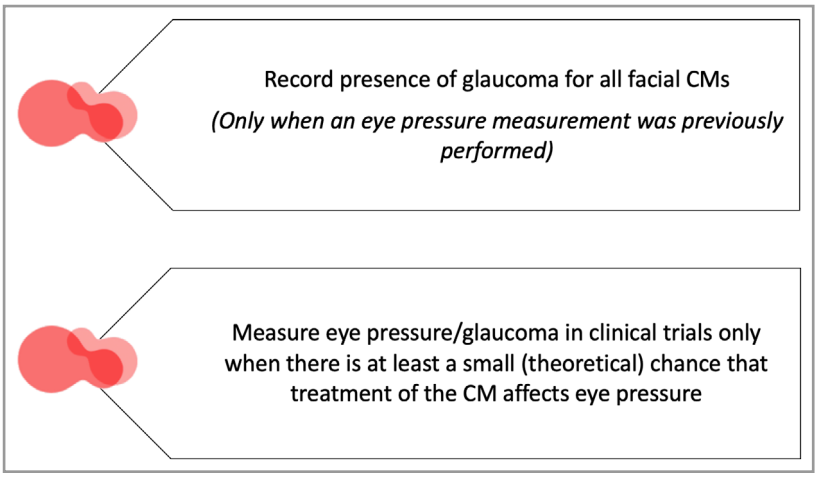

Figure 2 Conditions for glaucoma. CM, capillary malformation.

Table 6 Final core outcome domain set for capillary malformations in clinical research

Core area	Outcome domain	Subdomain first level	Subdomain second level
(Skin) pathophysiological manifestations	Clinical assessment	Appearance	Colour/redness Thickness Noticeability Distortion of anatomical structures
		Signs and symptoms	Glaucoma[a]
Life impact	Quality of life	Overall QoL	Overall health-related QoL
		Functioning	Emotional functioning Social functioning
	Treatment	Tolerability of intervention	
		Patient satisfaction with treatment results	Satisfaction with cosmetic and/or functional outcome
		Recurrence	

QoL, quality of life. [a]Should only be measured based on the proposed conditions.

Final core domain set

Following the consensus process, the final CDS consisted of three outcome domains containing 11 outcome subdomains (Table 6).

Discussion

Through this international e-Delphi study, involving a large group of patients (and parents or caregivers) and experts, we identified the core outcome subdomains for CMs by applying transparent predefined methods. The final inclusion of 11 core outcome subdomains belonging to only a limited number of outcome domains makes the CDS feasible to be used in future CM research.

Expectedly, 'overall health-related quality of life', 'emotional functioning' and 'social functioning' were included in the CDS. CMs are well known to affect quality of life due to their disfiguring appearance, specifically when located in the head and neck region.[7,34] Wanitphakdeedecha *et al.* found a statistically significant difference between quality-of-life scores of patients with a facial CM and patients without a facial CM or with no CM.[35] They concluded that patients with facial CMs are more likely to encounter discrimination than patients with nonfacial CMs. In addition, 'recurrence' was ranked as a crucial outcome subdomain. This was foreseen, as CMs often recur and re-darken after laser therapy.[36,37]

Notably, 'colour/redness' was only voted in the CDS during the consensus meeting. It was anticipated that its importance would already become clear at the start of the e-Delphi study, as for years treatment effects have been evaluated by colour measurements and degrees of colour improvement. Its inclusion in the CDS is therefore justifiable and preferable, as colour can be more easily (and objectively) measured, compared with, for example, the more subjective 'patient satisfaction with treatment results'. However, the latter patient-reported outcome subdomain is an essential constituent of our CDS, as it supports future treatment outcomes to better match the patient's needs and goals.

We have recommended practical conditions in which 'glaucoma' should be measured in future CM clinical trials. Previous research concluded that outcomes should be feasible to

measure and responsive to interventions.[38] As glaucoma is only present in a minority of patients with CM and current CM therapies do not affect glaucoma, we believe this might decrease the uptake of our CDS. Our proposed conditions will make our CDS more suitable and will promote its implementation. The OCOMEN project has provided a similar practical solution to such a problem.[39]

Overall, our CDS is similar to those of other cosmetically burdensome dermatological conditions, such as vitiligo, in which 'repigmentation' and 'tolerability of treatment' are also included.[24] However, in our CDS no adverse events are included. This may be due to the fact that adverse events are not that common after (laser) therapy and were possibly not deemed important enough to be measured in all future clinical trials on CMs.[13] Yet, our core outcome subdomains are the minimum set that should be measured in clinical trials on therapies. Researchers are free to measure additional outcomes, such as adverse events, that may be important depending on the study objective and type of treatment.

The methods used in this study are in harmony with internationally agreed standards for COS development, namely the guidelines of the COMET initiative and CS-COUSIN.[23,31] Moreover, our project is one of the first to use the recently developed framework for dermatological COSs, which facilitated the categorization of outcomes into core areas, outcome domains and subdomains.[27] Compared with other previously conducted dermatological COS development projects, our study included a relatively large group of participants from 45 countries and six continents, albeit mostly limited to small numbers of participants per country.[24,40] Especially during the first e-Delphi round a large number of patients participated. In contrast, during the second and third rounds, a drop in the number of stakeholders became evident despite frequent survey reminders.

Despite preceding efforts to identify potentially relevant outcome subdomains during stage 1, as many as 13 new ones were suggested during round 1 and were partly eventually included in the CDS. These outcome subdomains might have been missed due to the relatively small number of participants during the focus groups and discussions with the founding group. Also, some outcome subdomains were first seen as subitems of an outcome subdomain, whereas later on they were considered as separate outcome subdomains. This shows the subjective character of classifying outcomes.

A known limitation in COS studies is the problem of possibly having a different set of participants in the Delphi study than in the consensus meeting, which might affect the final CDS. During our consensus meeting, a relatively low and inconsistent number of patients participated compared with the number of participating experts. The discussions during the meeting might therefore have been more expert led. Yet, the number of patients during our consensus meeting is similar to that of other COS development projects.[25,39] We believe that, as long as no decision to include or exclude an outcome subdomain was overturned by the small patient cohort, it is inconsequential. Furthermore, a clear predominance of patients with SWS was evident during both the e-Delphi rounds and the consensus meeting, which could have biased the results. The inclusion of 'glaucoma' in our CDS is likely to be a consequence of this. The CDS was developed to be applicable to all patients with all types of CMs. We hope that the small number of participants per country, the inclusion of few patients with skin types V and VI, and the relatively large number of patients from the USA and the Netherlands will not impact the applicability of the CDS.

Especially during the COVID-19 pandemic, the use of an online consensus meeting allowed us to meet with patients with CM (or parents or guardians) and CM experts from all over the world. Yet, international time differences might have discouraged participants to join. Moreover, participants may have been less engaged than in a face-to-face meeting. Still, we believe online consensus meetings are an effective way to discuss and directly vote on the outcome subdomains, provided that they are executed with a predefined meeting agenda.

In conclusion, we recommend using our CDS as a minimum reporting standard for clinical research on all types of CMs. The next step in the COSCAM project is to define the core outcome measurement set. Previous research sought to identify the most appropriate outcome measurement instruments for CMs, but the authors concluded that further evaluation of the measurement properties is needed.[41] The developed CDS will now provide a better guide for this process. Future research is thus needed to further define the core outcome subdomains and determine the *how* and *when* to measure them.

Acknowledgments

First, we thank all of the stakeholders who contributed to this study. We also would like to thank the following (inter)national patient organizations that provided help with patient recruitment: the Dutch HEVAS Association, the Dutch Wijnvlek-Sturge Weber Association, the VASCAPA Association, the Sturge Weber Foundation UK and USA, the Sturge Weber Association Germany, Spain and Italy, and the Birthmark Support Group UK. We also owe our gratitude to the patients who provided feedback on the first Delphi survey and participated in the focus group sessions. Lastly, many thanks to the CS-COUSIN methods working group (Kim Thomas, Jochen Schmitt, Jamie Kirkham, Toni Lange, Murad Alam, Christian Apfelbacher, Joanne Chalmers, Jan Kottner and Phyllis Spuls), Anne Fledderus for providing methodological support, and Timothy van Asbeck for his linguistic advice.

Funding sources

None.

Conflicts of interest

A.W. reports a lecture honorarium to the institution from Candela. P.I.S. has performed consultancies in the past for

Sanofi and AbbVie (unpaid), has received departmental independent research grants for the TREAT NL registry, for which she is Chief Investigator, from pharma companies since December 2019, and is involved in performing clinical trials with many pharmaceutical companies that manufacture drugs used for the treatment of conditions such as psoriasis and atopic dermatitis, for which financial compensation is paid to the department or hospital. K.M.K. reports grants from Biophotas, personal fees from IQVIA, personal fees from FDZJ, grants from Orlucent, nonfinancial support from Sciton, and grants and nonfinancial support from Michaelson Diagnostics, outside the submitted work; and is secretary for the American Society for Laser Medicine and Surgery. S.J.R. reports personal fees from Candela (Syneron Medical HK Ltd), outside the submitted work. P.B. reports consulting fees, payment for lectures and nonfinancial support from Cynosure. H.J.L. reports payment or honoraria for lectures, presentations, speakers' bureaus or educational events. A.T.R. is chair of the Multidisciplinary Vascular Anomaly Group at Skåne University Hospital, Malmö, Sweden. M.H. reports grants from LEO Pharma, nonfinancial support from Cherry Imaging, nonfinancial support from Cynosure-Hologic, grants and nonfinancial support from Lutronic, grants and nonfinancial support from Mirai Medical, nonfinancial support from Perfaction Technologies, nonfinancial support from miraDry–Sientra, and grants and nonfinancial support from Venus Concept, outside the submitted work. The other authors declare they have no conflicts of interest.

Ethics statement

The medical ethics review committee of the Academic Medical Center, the Netherlands, has confirmed that the Medical Research Involving Human Subjects Act (WMO) does not apply to this study and an official approval of this study by the committee was not required (reference number W20_351 #20.389).

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1 Mulliken JB, Burrows PE, Fishman SJ. *Mulliken and Young's Vascular Anomalies: Hemangiomas and Malformations*, 2nd edn. Oxford: Oxford University Press, 2013.
2 Schneider BV, Mitsuhashi Y, Schnyder UW. Ultrastructural observations in port wine stains. *Arch Dermatol Res* 1988; **280**:338–45.
3 Shirley MD, Tang H, Gallione CJ *et al.* Sturge–Weber syndrome and port-wine stains caused by somatic mutation in *GNAQ*. *N Engl J Med* 2013; **368**:1971–9.
4 Jordan M, Carmignac V, Sorlin A *et al.* Reverse phenotyping in patients with skin capillary malformations and mosaic *GNAQ* or *GNA11* mutations defines a clinical spectrum with genotype–phenotype correlation. *J Invest Dermatol* 2020; **140**:1106–10.
5 Vahidnezhad H, Youssefian L, Uitto J. Klippel–Trenaunay syndrome belongs to the PIK3CA-related overgrowth spectrum (PROS). *Exp Dermatol* 2016; **25**:17–19.
6 Kahana M, Feldman M, Abudi Z *et al.* The incidence of birthmarks in Israeli neonates. *Int J Dermatol* 1995; **34**:704–6.
7 Hagen SL, Grey KR, Korta DZ *et al.* Quality of life in adults with facial port-wine stains. *J Am Acad Dermatol* 2017; **76**:695–702.
8 Geronemus RG, Ashinoff R. The medical necessity of evaluation and treatment of port-wine stains. *J Dermatol Surg Oncol* 1991; **17**:76–9.
9 Dowling MB, Zhao Y, Darrow DH. Orodental manifestations of facial port-wine stains. *J Am Acad Dermatol* 2012; **67**:687–93.
10 Eivazi B, Roessler M, Pfutzner W *et al.* Port-wine stains are more than skin-deep! Expanding the spectrum of extracutaneous manifestations of nevi flammei of the head and neck. *Eur J Dermatol* 2012; **22**:246–51.
11 Stevenson RF, Thomson HG, Morin JD. Unrecognized ocular problems associated with port-wine stain of the face in children. *Can Med Assoc J* 1974; **111**:953–4.
12 Mills CM, Lanigan SW, Hughes J *et al.* Demographic study of port wine stain patients attending a laser clinic: family history, prevalence of naevus anaemicus and results of prior treatment. *Clin Exp Dermatol* 1997; **22**:166–8.
13 Cinkara G, Langbroek GB, van der Horst C *et al.* Therapeutic strategies for untreated capillary malformations of the head and neck region: a systematic review and meta-analyses. *Am J Clin Dermatol* 2021; **22**:603–14.
14 van Raath MI, Chohan S, Wolkerstorfer A *et al.* Port wine stain treatment outcomes have not improved over the past three decades. *J Eur Acad Dermatol Venereol* 2019; **33**:1369–77.
15 van Raath MI, Bambach CA, Dijksman LM *et al.* Prospective analysis of the port-wine stain patient population in the Netherlands in light of novel treatment modalities. *J Cosmet Laser Ther* 2018; **20**:77–84.
16 Greveling K, Prens EP, van Doorn MB. Treatment of port wine stains using pulsed dye laser, erbium YAG laser, and topical rapamycin (sirolimus) – a randomized controlled trial. *Lasers Surg Med* 2017; **49**:104–9.
17 Griffin TD Jr, Foshee JP, Finney R *et al.* Port wine stain treated with a combination of pulsed dye laser and topical rapamycin ointment. *Lasers Surg Med* 2016; **48**:193–6.
18 Tremaine AM, Armstrong J, Huang YC *et al.* Enhanced port-wine stain lightening achieved with combined treatment of selective photothermolysis and imiquimod. *J Am Acad Dermatol* 2012; **66**:634–41.
19 van Raath MI, van Amesfoort JE, Hermann M *et al.* Site-specific pharmaco-laser therapy: a novel treatment modality for refractory port wine stains. *J Clin Transl Res* 2019; **5**:1–24.
20 van Raath MI, Chohan S, Wolkerstorfer A *et al.* Clinical outcome measures and scoring systems used in prospective studies of port wine stains: a systematic review. *PLOS ONE* 2020; **15**:e0235657.
21 Williamson PR, Altman DG, Blazeby JM *et al.* Developing core outcome sets for clinical trials: issues to consider. *Trials* 2012; **13**:132.
22 Chiarotto A, Ostelo RW, Turk DC *et al.* Core outcome sets for research and clinical practice. *Braz J Phys Ther* 2017; **21**:77–84.
23 Prinsen CAC, Spuls PI, Kottner J *et al.* Navigating the landscape of core outcome set development in dermatology. *J Am Acad Dermatol* 2019; **81**:297–305.
24 Eleftheriadou V, Thomas K, van Geel N *et al.* Developing core outcome set for vitiligo clinical trials: international e-Delphi consensus. *Pigment Cell Melanoma Res* 2015; **28**:363–9.
25 Horbach SER, van der Horst C, Blei F *et al.* Development of an international core outcome set for peripheral vascular malformations: the OVAMA project. *Br J Dermatol* 2018; **178**:473–81.

26 Oei W, Fledderus AC, Korfage I *et al*. Protocol for the development of core set of domains of the core outcome set for patients with congenital melanocytic naevi (OCOMEN project). *J Eur Acad Dermatol Venereol* 2020; **34**:267–73.
27 Lange T, Kottner J, Weberschock T *et al*. Outcome assessment in dermatology clinical trials and Cochrane reviews: call for a dermatology-specific outcome taxonomy. *J Eur Acad Dermatol Venereol* 2021; **35**:523–35.
28 Langbroek GB, Wolkerstorfer A, Horbach SER *et al*. Development of a core outcome domain set for clinical research on capillary malformations (the COSCAM project). *J Eur Acad Dermatol Venereol* 2021; **35**:1888–95.
29 Schmitt J, Apfelbacher C, Spuls PI *et al*. The Harmonizing Outcome Measures for Eczema (HOME) roadmap: a methodological framework to develop core sets of outcome measurements in dermatology. *J Invest Dermatol* 2015; **135**:24–30.
30 Kirkham JJ, Davis K, Altman DG *et al*. Core Outcome Set-STAndards for Development: the COS-STAD recommendations. *PLOS Med* 2017; **14**:e1002447.
31 Prinsen CA, Vohra S, Rose MR *et al*. Core Outcome Measures in Effectiveness Trials (COMET) initiative: protocol for an international Delphi study to achieve consensus on how to select outcome measurement instruments for outcomes included in a 'core outcome set'. *Trials* 2014; **15**:247.
32 Kirkham JJ, Gorst S, Altman DG *et al*. Core Outcome Set-STAndards for Reporting: the COS-STAR Statement. *PLOS Med* 2016; **13**:e1002148.
33 Waelchli R, Aylett SE, Robinson K *et al*. New vascular classification of port-wine stains: improving prediction of Sturge–Weber risk. *Br J Dermatol* 2014; **171**:861–7.
34 Lanigan SW, Cotterill JA. Psychological disabilities amongst patients with port wine stains. *Br J Dermatol* 1989; **121**:209–15.
35 Wanitphakdeedecha R, Sudhipongpracha T, Ng JNC *et al*. Self-stigma and psychosocial burden of patients with port-wine stain: a systematic review and meta-analysis. *J Cosmet Dermatol* 2021; **20**:2203–10.
36 Michel S, Landthaler M, Hohenleutner U. Recurrence of port-wine stains after treatment with the flashlamp-pumped pulsed dye laser. *Br J Dermatol* 2000; **143**:1230–4.
37 Huikeshoven M, Koster PH, de Borgie CA *et al*. Redarkening of port-wine stains 10 years after pulsed-dye-laser treatment. *N Engl J Med* 2007; **356**:1235–40.
38 Tong A, Crowe S, Gill JS *et al*. Clinicians' and researchers' perspectives on establishing and implementing core outcomes in haemodialysis: semistructured interview study. *BMJ Open* 2018; **8**: e021198.
39 Fledderus AC, Pasmans S, Wolkerstorfer A *et al*. Domains and outcomes of the core outcome set of congenital melanocytic naevi for clinical practice and research (the OCOMEN project): part 2. *Br J Dermatol* 2021; **185**:970–7.
40 Schmitt J, Langan S, Stamm T *et al*. Core outcome domains for controlled trials and clinical recordkeeping in eczema: international multiperspective Delphi consensus process. *J Invest Dermatol* 2011; **131**:623–30.
41 van Raath MI, Chohan S, Wolkerstorfer A *et al*. Treatment outcome measurement instruments for port wine stains: a systematic review of their measurement properties. *Dermatology* 2021; **237**:416–32.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Appendix S1 COSCAM project contributors.

Appendix S2 List with comments and suggested outcome subdomains during e-Delphi round 1.

Table S1 Outcome definitions consistent with the suggested hierarchy by Lange *et al*.[27]

Table S2 Potentially relevant outcome domains and subdomains for capillary malformations in clinical research.

Table S3 Complete overview of participant characteristics in e-Delphi round 3.

Video S1 Supporting Information