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Published in:
British Journal of Dermatology

DOI (link to publication from Publisher):
10.1093/bjd/ljac145

Publication date:
2023

Document Version
Publisher's PDF, also known as Version of record

Br J Dermatol 2023; **188**:628–635
https://doi.org/10.1093/bjd/ljac145
Advance access publication date: 26 January 2023

BJD
British Journal of Dermatology
Outcomes and Qualitative Research

Core outcome domains for lichen sclerosus: a CORALS initiative consensus statement

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Linked Article: Thorlacius *Br J Dermatol* 2023; **188**:587–588.

Abstract

Background Lichen sclerosus (LS) is a chronic inflammatory condition mainly affecting genital skin. It causes distressing symptoms that impact daily quality of life (QoL). It causes progressive anatomical changes and a potential risk of cancer. Published randomized controlled trials are of varying methodological quality and difficult to combine in meta-analyses. This is partly due to lack of agreed outcome measures to assess treatment response. Identification of core outcome sets (COSs), which standardize key outcomes to be measured in all future trials, is a solution to this problem.

Objectives To obtain international agreement on which outcome domains should be measured in interventional trials of genital LS.

Methods Recommended best practice for COS domain development was followed: (i) identification of potential outcome domains: a long list was generated through an up-to-date LS literature search, including information collected during the LS priority-setting partnership; (ii) provisional agreement of outcome domains: a three-stage multi-stakeholder international electronic-Delphi (e-Delphi) consensus study; (iii) final agreement of outcome domains: online consensus meeting with international stakeholders including anonymized voting.

Results In total, 123 participants (77 patients, 44 health professionals, 2 researchers) from 20 countries completed three rounds of the e-Delphi study. Eleven outcome domains were rated as 'critical' and were discussed at the online consensus meetings. The first set of consensus meetings involved 42 participants from 12 countries. Consensus was met for 'symptoms' (100% agreed) and 'QoL – LS-specific' (92% agreed). After the second set of meetings, involving 29 participants from 12 countries, 'clinical (visible) signs' also met consensus (97% agreed).

Conclusions The international community has agreed on three key outcome domains to measure in all future LS clinical trials. We recommend that trialists and systematic reviewers incorporate these domains into study protocols with immediate effect. CORALS will now work with stakeholders to select an outcome measurement instrument per prioritized core domain.

What is already known about this topic?

- Agreement of outcomes is an international priority area for lichen sclerosus (LS) research.
- Core outcome sets (COSs) reduce research waste by ensuring that outcomes measured in randomized controlled trials (RCTs) (of a specific condition) can be compared and combined in meta-analyses to provide a stronger treatment evidence base.
- There is currently no COS for genital LS trials.

Accepted: 17 December 2022

What does this study add?

- CORALS provides international multi-stakeholder consensus on core outcome domains for clinical trials in genital LS.
- The core domains are relevant to all people with genital LS: males, females, adults and children.
- The three internationally agreed core domains are: clinical (visible) signs, symptoms and quality of life specific to LS.

What are the clinical implications of the work?

- Implementation of the core domains into the protocols of RCTs and systematic reviews will ensure that outcomes of importance to patients and health professionals are measured in future LS research.

Core outcome sets (COSs) aim to reduce research waste by ensuring that outcomes measured in randomized controlled trials (RCTs) of a specific condition can be compared and combined in meta-analyses to provide a stronger treatment evidence base.[1] COSs ensure that all trials of a particular condition measure the same key outcomes so that they are comparable. However, it does not prevent researchers from measuring other additional outcomes relevant to their specific study.[2] There is an international movement to promote COSs, supported by initiatives such as COMET (Core Outcome Measures for Effectiveness Trials),[3] CROWN (Core Outcomes for Women's and Neonatal Health)[4] and C3 (the CHORD COUSIN Collaboration).[5] Leading peer-reviewed journals support implementation of COSs by ensuring that if one exists, the core outcomes are reported in published research.[6] There is considerable variation in outcome measurement for vulval disease.[7] Lichen sclerosus (LS) is an important, albeit under-recognized, condition which affects at least 1% of women of all ages[8–10] but also affects children and men, and usually runs a chronic course. An estimated 3–5% of cases develop malignancy.[11,12] LS has a significant impact on quality of life (QoL) and affects psychosocial and sexual wellbeing.[13–15] Lack of validated outcome measures and heterogeneity in published RCTs limits high-quality evidence to guide clinical practice.[16] Agreement regarding outcomes has been identified as a need in an international priority-setting partnership.[17] Due to an increase of trials testing new treatments for LS, such as laser, platelet-rich plasma and alternative topical treatments, which may be costly and/or have potentially serious side-effects, the need to standardize outcome measurement in LS is paramount.

CORALS (Core Outcomes for Research in Lichen Sclerosus) is an initiative led by a multi-stakeholder steering group which aims to create, via international consensus, a COS for future genital LS trials. COS development takes place in two stages: (i) agreement of core outcome domains and (ii) agreement of core outcome measurement instruments.

The aim of this stage of CORALS was to obtain international agreement on which 'domains' should be measured as a minimum requirement in interventional trials of genital LS.

Methods

A multidisciplinary steering group with representation from dermatology, gynaecology, nursing, urology, patients (male and female) and methodologists, with independent oversight from a C3 representative, was formed to drive this initiative forward. Ethical approval was obtained from the Faculty of Medicine and Health Sciences Research Ethics Committee of the University of Nottingham (Ref. 376-1908). Online consent was obtained for participation in the electronic-Delphi (e-Delphi) survey.

The protocol was developed in line with CS-COUSIN (Cochrane Skin Core Outcomes Initiative, now known as C3) guidance and followed Core Outcome Set-STAndards for Development (COS-STAD) recommendations[18] and accepted methodology.[19] It was prospectively made publicly available.[20] The intention to develop a COS in LS was also registered on the COMET, CROWN and C3 websites. The scope of this COS was all patients with LS, all treatments and all settings.

Development of domains took a three-stage process:

1 Identification of possible domains using key documents in the literature;
2 Provisional agreement of the most important domains via a three-stage e-Delphi consensus study;
3 Final agreement of domains: international virtual consensus meetings.

Identification of potential domains

A long list of possible outcome domains was identified through RCTs included in key guideline and systematic review documents,[10,16,21] as well as qualitative published studies.[22–24]

Domains were extracted from these documents independently by three steering group members (R.C.S., G.K. and A.S.). These were then reviewed by the whole steering group and any domains perceived to be missing were added. Similar domains were grouped together and summarized to create a list of meaningful concepts and definitions, based on agreed taxonomy.[25] Patient representatives advised on wording of domains to be understandable by members of the public.

Provisional agreement of the most important domains

The long list of domains was entered into a three-stage e-Delphi consensus study using DelphiManager software from the COMET group.[26] Although the main e-Delphi survey was in English, to increase accessibility, participant

information sheets and the survey welcome page were available in nine different languages. Support for participants with translation of the survey was offered although this was not taken up.

Stakeholders included healthcare professionals, patients, patient representatives/carers, researchers and systematic reviewers in the field of LS, industry representatives and journal editors. Stakeholders were identified through the International Society for the Study of Vulvovaginal Disease (ISSVD), the British Society for the Study of Vulval Disease (BSSVD), the Australian and New Zealand Vulvovaginal Society (ANZVS), the European College for the Study of Vulvar Disease (ECSVD) and the Indian and the North American chapters of the ISSVD. Editors of journals signed up to the CROWN and COMET initiatives were invited. Patients were identified through international LS patient support groups. Invitations were sent via a range of methods including advertisements on social media, mailshots to members of the relevant societies and direct email invitations to people recognized as key figures in the field of LS. Those stakeholders who expressed interest via an online form were subsequently provided with the survey links once available.

Delphi Round 1 asked participants to score the importance of each outcome domain on a nine-point Likert scale (1–3, not important; 4–6, important but not critical; 7–9, critical) and an 'unable to score' option. Each domain had a plain English description of its definition available by 'hovering' over the domain. Participants were allowed to provide feedback on individual domains and suggest additional domains if they felt any were missing. Feedback was collated and discussed with the steering group with plans to reword domains if necessary. Additional items were categorized and assessed against the long list of domains to check whether any were missing. Outcome domains that were missed were added for voting on in the second round of the e-Delphi survey.

Definition of consensus was determined a priori. The criteria for a domain to be considered as part of the COS was at least 70% of participants scoring an outcome as 'critical' with 15% or fewer participants voting as 'not important'. Analysis was undertaken by downloading DelphiManager scores to a Microsoft Excel spreadsheet and calculating for each of the domains the percentage of respondents who voted 1–3 (not important), 4–6 (important but not critical) and 7–9 (critical).

Domains that did not meet consensus as 'critical' after two rounds were removed. Subsequently, Round 3 used a SurveyMonkey[27] questionnaire to present the outcome domains that had reached consensus as being 'critical' and asked participants to rank them in terms of their importance (1, most important; 11, least important). Items were presented to participants in a randomized order to minimize bias when ranking. SurveyMonkey automated analysis was used to calculate the average ranking for each answer choice to determine which answer choice was most preferred overall; i.e. the answer choice with the largest average ranking represents the most preferred choice. We calculated ranking for each stakeholder group, as well as overall rankings.

Reminder emails were sent to participants at key stages of the process to ensure maximum return of the e-Delphi survey questionnaire.

International consensus meetings

The aim of the consensus meeting was to agree on core domains for the future LS COS. As a result of the COVID-19 pandemic, it was not felt appropriate to hold 'in-person' consensus meetings as described from previously published COSs. Therefore, using Microsoft Teams, we held two sets of virtual consensus meetings. Each meeting set had two dates at different times where the content and processes were repeated. This provided the opportunity for stakeholders from different time zones to participate. To encourage as wide international engagement as possible, the meetings were opened to CORALS' wider contact network as well as those who participated in the e-Delphi surveys. Pre-meeting information was circulated detailing the process to date and results from the e-Delphi surveys. Tasks were set to encourage participants to consider in advance which domains meant most to them.

The sessions comprised a mixture of presentations, whole-group discussion and smaller moderated breakout groups. Moderators were instructed to remain impartial and facilitate discussion but not voice their opinion. There was a moderator guide (Appendix S1; see Supporting information) to support standardization of the breakout groups.

In the whole-group session, outcome domains were presented in detail. Then, to prioritize domains down to the core minimum, the smaller groups were asked to determine their 'top three' domains. Breakout group results were presented to the main group and after further discussion participants were asked to vote anonymously, using Microsoft Forms, for each of the domains by asking the question 'Should the domain be in the final core outcome set? Yes/no/not sure'. A backup questionnaire was prepared to send immediately after the meeting had ended to participants who identified as being unable to vote during the live sessions. To avoid bias, results from the consensus meetings were not shown to participants until both meetings were complete and those who could not vote live had been given the opportunity to complete the questionnaire.

Definition of consensus was that if 70% or more agreed, then the domain would be in the COS. If more than 30% disagreed, the domain was not added into the COS. In the situation where fewer than 70% agreed, but fewer than 30% disagreed, the domain was considered as 'provisionally in the COS', pending further discussion and voting. Any dissenting views were discussed with the whole group to allow others to consider and gather wider opinion.

Results

Apart from the decision to conduct two online consensus meetings instead of face-to-face meetings, there were no deviations from the protocol.

The initial literature review identified a list of 11 broad outcome domains (Table 1). Demographics of participants in the e-Delphi consensus process and the virtual consensus meetings are reported in Table 2.

Delphi consensus survey

During Round 1 (26 April – 4 June 2021), 64 additional items to be included were suggested by participants. Of these,

Table 1 Long list of lichen sclerosus outcome domains identified from the literature review (domains are presented in alphabetical order)

Domain	Explanation of domain
Clinical (visible) signs	Examples include skin colour change, skin texture change, damage to surface of the skin, changes in the anatomy of the genital area
Control of disease	Includes length of time without flares, frequency of flares, progression of the disease
Development of vulval/penile cancer	Development of cancer
Extent of disease	Which parts of the genitals or anus are affected?
Histological changes	Changes seen when skin sample taken and specimen reviewed under the microscope by specialist doctor
Impact on important relationships	For example, relationships with partners, family relationships, interactions with friends, forming new relationships
Quality of life – general health	A more general measure looking at overall quality of life (i.e. someone's overall health and wellbeing both physical and psychological)
Quality of life – lichen sclerosus-specific	Activities of daily living specific to genital lichen sclerosus
Sexual functioning	Including ability to enjoy closeness/tenderness, sexual desire or sexual interest, arousal during sexual activity or intercourse, ability to have an orgasm, satisfaction with sexual life and sexual relationships, pain/soreness (related to sexual activity), inability to tolerate or enjoy sex play or penetrative sex
Societal/resource use	Costs related to healthcare use and overall cost to society
Symptoms	Examples include itch, burning, irritation, pain/soreness (unrelated to sexual activity), feeling of dryness, fragile skin/splitting of skin (loss of elasticity of skin), bleeding, constipation, difficulty passing urine/pain when passing urine

46 were not outcomes (treatments, $n=14$; LS causes, $n=8$; disease course, $n=7$; LS clinical follow-up, $n=4$; LS education, $n=4$; LS treatment regimen, $n=2$; other, $n=7$). The 18 suggested outcomes were categorized into three overarching domains (adverse events, emotional/psychological impact, treatment acceptability). These three domains were added into Round 2 (8–31 August 2021), so participants voted on a total of 14 outcomes in this round. Of these, 11 were voted as 'critical' by at least one stakeholder group (Table 3) and went through to Round 3 for ranking. The three

Table 2 Demographics of participants during three rounds of e-Delphi surveys and virtual consensus meetings

Demographic	Delphi Round 1, *n* (%)	Delphi Round 2, *n* (%)	Delphi Round 3, *n* (%)	Consensus meetings 1+2, *n* (%)	Consensus meetings 3+4, *n* (%)
Total participants	199	141	123	42	29
Stakeholder group					
Healthcare professionals	71 (36)	54 (38)	44 (35)	21 (50)	14 (48)
Patients/patient representatives	126 (63)	85 (60)	77 (63)	15 (36)	9 (31)
Researchers	2 (1)	2 (1)	2 (2)	6 (14)	6 (21)
Minority group representation					
Representatives of children	41 (21)			19 (45)	10 (34)
Representatives of male patients	17 (9)			14 (33)	9 (31)
Geographical representation – country of origin of participants					
Australia	9				1
Austria	2				
Brazil	2				
Canada	26			4	1
Chile	0			1	
Czech Republic	1				
Denmark	27			2	5
Germany	26			6	2
Finland	1				
France	2			1	1
Israel	3				
Italy	3			4	
Jersey	1				
Lithuania	1			1	1
Luxembourg	1			1	1
Mexico	1				
Netherlands	6			2	1
Northern Ireland	1				
New Zealand	3				1
Portugal	1				
Russia	1				
Scotland	1			1	1
Spain	1				
Switzerland	8				
Taiwan	1				
UK	35			11	8
USA	35			8	6

outcome domains removed were 'impact on important relationships', 'histological changes' and 'societal/resource use'.

Following the ranking round, the top three domains for healthcare professionals/researchers ($n=45$) were: symptoms; control of disease; development of cancer. The top three domains for patients/patient representatives ($n=77$) were: control of disease; symptoms; sexual functioning. Combined ranking results for all stakeholder groups are shown in Figure 1.

Virtual consensus meetings

Meetings held on 26 and 28 January 2022 had 42 participants (21 health professionals, 15 patients/patient representatives, 6 researchers) from 12 different countries. Representation from all stakeholder groups, including minority groups (men and representatives of children), was present. Due to technical difficulties, not all participants voted despite having the opportunity to do so during the meeting. A follow-up questionnaire was available for those who could not vote in real time. Overall, each of the outcome domains received votes from at least 90% (38 of 42) of participants (Table 4).

Of those who voted, 100% voted 'yes' for the 'symptoms' domain to be in the COS. Overall, 92% (36/39) voted for 'QoL – LS-specific' to be in the final COS. 'Control of disease' and 'clinical (visible) signs' were close to consensus (65% and 64% voted 'yes', respectively). A further meeting was arranged for further discussion and voting of these latter two domains. The remaining seven outcome domains were not voted into the final COS.

The second set of consensus meetings (25 May and 9 June 2022) focused on 'control of disease' and 'clinical (visible) signs' only (Table 5). There were 29 participants overall (14 healthcare professionals, 9 patients/patient representatives, 6 researchers) from 12 countries. Discussion centred around the definition of 'control of disease' and whether it represented a standalone outcome or incorporated repeated measures of other markers of control (e.g. signs, symptoms, QoL) over time. There was also discussion about 'clinical signs' being an objective measure as it is measured by the clinician rather than being patient-reported.

The domain 'clinical (visible) signs' was voted to be included in the final COS (28/29, 97% of votes), whereas 'control of disease' did not receive sufficient votes to be included in the final COS (5/29, 17% of votes).

During the consensus meetings, the 'development of cancer' and 'sexual function' domains were also discussed at length. It is acknowledged that while these are significantly important outcomes, they are not relevant to all trials of genital LS in all people. For example, development of cancer is a rare and long-term outcome. To include it as a core outcome, all LS trials would need to continue for sufficient duration to identify cancer development. Sexual function is not relevant to children or adults who are not sexually active and is likely to be captured when measuring QoL.

Discussion

CORALS followed methodology in line with accepted best practice for COS development and as such, used a robust and accepted process to obtain international consensus.[19] After three rounds of e-Delphi surveys and two online consensus meetings, there was international agreement for three core domains to be included in all future LS clinical trials: symptoms, clinical (visible) signs and QoL – LS-specific. Using bespoke software to manage the e-Delphi consensus process was beneficial in tracking participants and individualizing communications to maximize participation. However, as DelphiManager was unable to allow ranking, different software was needed for Round 3. An attrition of 38% of participants was seen between e-Delphi Round 1 and Round 3. This is higher than experienced in other similar COS projects

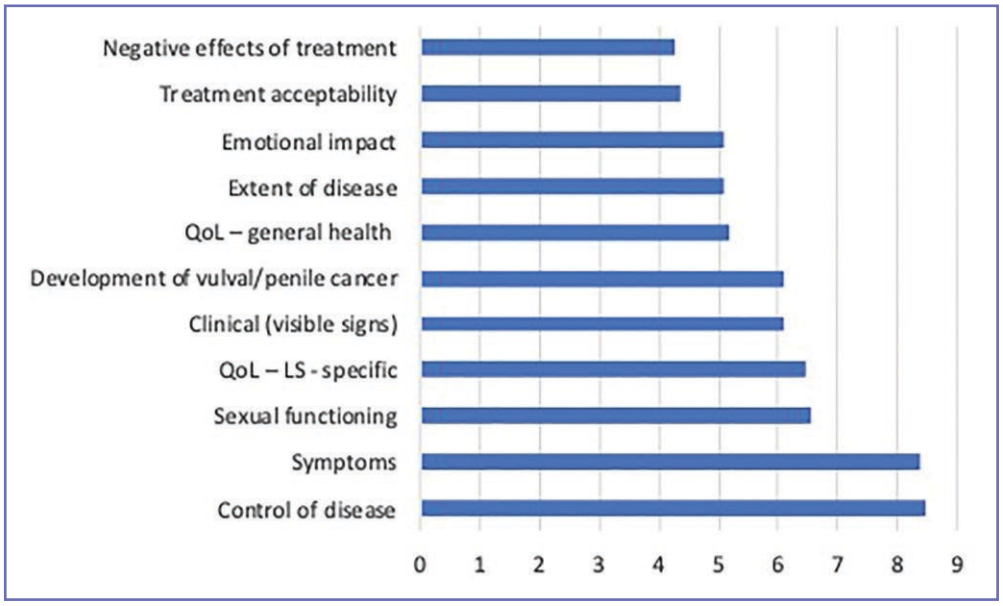

Figure 1 Electronic Delphi (e-Delphi) survey Round 3 – ranking results. Bars demonstrate the ranking for the 11 outcome domains (y-axis) that met consensus by at least one stakeholder group in the first two e-Delphi rounds. The answer choice with the largest average ranking (x-axis: 0, low; 9, high ranking) represents the most preferred choice. QoL, quality of life.

Table 3 Proportion of voters rating outcomes as 'critical' on nine-point Likert scale after two rounds of voting in the e-Delphi surveys

Domain	Patients	Healthcare professionals/researchers
Met consensus across all stakeholder groups as being critical		
Quality of life – lichen sclerosus-specific	93%	96%
Control of disease	95%	89%
Symptoms	94%	88%
Development of vulval/penile cancer	84%	91%
Sexual functioning	84%	84%
Extent of disease	84%	77%
Emotional impact	86%	73%
Clinical (visible) signs	78%	75%
Met consensus with one stakeholder group as being critical		
Quality of life – general health	84%	50%
Negative events of treatment	79%	61%
Treatment acceptability	71%	59%
Not voted as critical by any stakeholder groups		
Impact on important relationships	67%	68%
Histological changes	43%	32%
Societal/resource use	17%	10%

Table 4 Results of virtual consensus meetings January 2022

Domain (total number of voters for that domain)	Yes, *n* (%)	No, *n* (%)	Not sure, *n* (%)	Did not vote
Consensus met for domain to be in the final core outcome set				
Symptoms ($n=39$)	39 (100)	0	0	3
QoL – lichen sclerosus-specific ($n=39$)	36 (92)	2 (5)	1 (3)	3
Consensus close and for further voting				
Control of disease ($n=40$)	26 (65)	6 (15)	8 (20)	2
Clinical (visible) signs ($n=39$)	25 (64)	7 (18)	7 (18)	3
Consensus not met				
Sexual functioning ($n=39$)	12 (31)	22 (56)	5 (13)	3
Extent of disease ($n=39$)	6 (15)	30 (77)	3 (8)	3
Treatment acceptability ($n=39$)	5 (13)	30 (77)	4 (10)	3
Negative effects of treatment ($n=40$)	4 (10)	30 (75)	6 (15)	2
Development of vulval/penile cancer ($n=39$)	3 (8)	29 (74)	7 (18)	3
Emotional impact ($n=40$)	3 (8)	30 (75)	7 (17)	2
QoL – general health ($n=38$)	2 (5)	36 (95)	0	4

QoL, quality of life.

Table 5 Results of virtual consensus meetings May and June 2022

Domain (total number of voters for that domain)	Yes, *n* (%)	No, *n* (%)	Not sure, *n* (%)	Did not vote
Consensus met				
Clinical (visible) signs ($n=29$)	28 (97)	0 (0)	1 (3)	0
Consensus not met				
Control of disease ($n=29$)	5 (17)	13 (45)	11 (38)	0

which report between 9% and 20% dropout[28–30] but lower than in a recently published COS development project.[31] The cause is likely to be multifactorial but is particularly attributable to workplace and life pressures faced during the COVID-19 pandemic.

Face-to-face consensus meetings, as traditionally used for previously published COSs, were not feasible due to challenges faced during and after the COVID-19 pandemic. Guidance issued through the COMET initiative was consulted to support the smooth running of the meetings and give the greatest chance of success.[32] We found that engagement from international stakeholders across the four virtual meetings was strong and potentially led to better attendance than an in-person event. Earlier meetings reported for other COS groups had fewer participants overall despite the disease areas being more common.[33–36]

Preparing participant resources that were circulated 2 weeks in advance was beneficial in meeting preparation. Test voting at the beginning of the meetings helped to identify technical issues that some participants were experiencing and most of these could be resolved prior to the real voting. Having a backup questionnaire to send out immediately to participants who could not vote live was also helpful in maximizing votes.

There was good geographical representation overall, but participants from the Far East and Africa/India were not represented. CORALS must work to engage participants from these locations in the future. In the e-Delphi surveys, there

was also minimal representation from researchers and none from histopathologists. This led to concern at the consensus meetings that the domain 'histological changes' was voted out too early as a result. However, a greater number of researchers were present at the virtual meetings and this concern was not shared. To agree that histological changes should be a core outcome would mean that ALL clinical trials in LS would need to take serial biopsies, e.g. from the genital site (vulva/penis), as part of their protocol. This is not practical to implement and would be likely to limit uptake of the COS.

Representation of minority groups (male patients and representatives of children) was relatively low during the e-Delphi surveys. A similar pattern of under-representation has been reported previously and reasons cited are that males are less willing than women to engage with health-related surveys and that LS is less common in children.[17] The numbers of these groups were proportionately higher in the virtual consensus meetings, suggesting greater motivation to attend a meeting rather than enter a survey, or that CORALS had succeeded in promoting the initiative more widely.

Challenges to consider moving forward with the next stages of this COS are whether the different groups affected by LS – males, females and children – can be kept together when identifying COS instruments. A COS that is applicable to greater numbers of people is likely to generate more powerful evidence in the longer term than one that is used for groups separately; however, it may not be practicable or possible to agree on instruments that are applicable to all. For example, capturing QoL in different age groups is challenging as instruments designed for adults are not tailored for the needs of children. However, this has been overcome in other COS initiatives as certain QoL tools, such as the Dermatology Life Quality Index (DLQI), has versions validated in different age groups.[37]

CORALS has agreed on a small number of core domains which we hope will encourage researchers to adopt the final set more easily. Some COS groups have a larger number of domains, e.g. acne[38] (six core domains) or capillary malformations[39] (11 core domains), but CORALS is similar to eczema[30] (four core domains). There are similarities in the chosen domains with other initiatives: hidradenitis suppurativa,[29] eczema and acne have chosen general clinical signs, whereas vitiligo has specified repigmentation as the important clinical sign to measure. Condition-specific QoL was agreed in hidradenitis suppurativa (HS) and eczema. 'Symptoms' were agreed on for eczema but not for HS or vitiligo.

The domains 'clinical (visible) signs' and 'symptoms' are broad and may possibly need further breaking down. Further discussion on 'QoL – LS-specific' is also needed to ascertain whether an overall genital QoL tool is acceptable, as it would potentially have greater use across other genital disease COS in the long term. Other initiatives, such as the incontinence-associated dermatitis group,[40] have chosen domains that are specific to the disease state. There is no published guidance on how broad or specific to be.

Although outcome measure instruments for LS have not been identified as yet, we recommend that implementation of the core domains should start with immediate effect. Trialists and researchers should include these three domains in their protocols and systematic reviewers should report these domains in their work.

The next steps are to generate international working groups for each of the domains. The groups will identify existing outcome measurement instruments and evaluate the quality of evidence regarding their measurement properties. These will then be discussed at further international consensus meetings to form the final LS COS. CORALS should work to increase global participation, particularly from under-represented geographical regions and minority groups.

Acknowledgments

We thank all participants of the Delphi consensus process and the consensus meetings for their time and willingness to participate. We also acknowledge the support of the ISSVD and BSSVD in raising awareness of the CORALS through their membership. Thank you to C3 for provision of methodological support. Finally, thank you to our steering group patient representatives, both past and present, for their continued valuable input.

Funding sources

This study was developed with support from the UK Dermatology Clinical Trials Network (UK DCTN) via the 2018 'Themed Call' award. The UK DCTN is grateful to the British Association of Dermatologists and the University of Nottingham for financial support of the Network.

Conflicts of interest

There are no conflicts of interest to declare from any members of the Steering Group.

Data availability statement

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

Ethics statement

Not applicable.

Supporting Information

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

References

1 Williamson PR, Altman DG, Blazeby JM *et al.* Developing core outcome sets for clinical trials: issues to consider. *Trials* 2012; **13**:132. https://doi.org/10.1186/1745-6215-13-132.
2 Clarke M. Standardising outcomes for clinical trials and systematic reviews. *Trials* 2007; **8**:39. https://doi.org/10.1186/1745-6215-8-39.
3 Core Outcome Measures in Effectiveness Trials (COMET). Available at: http://www.comet-initiative.org/ (last accessed 14 October 2022).
4 Molloy EJ, Gale C, Marsh M *et al.* Developing core outcome set for women's, newborn, and child health: the CROWN Initiative.

Pediatr Res 2018; **84**:316–17. https://doi.org/10.1038/s41390-018-0041-9.
5 The CHORD COUSIN Collaboration (C3). Available at: https://www.c3outcomes.org (last accessed 14 October 2022).
6 Veysey EC, Ingram JR, Apfelbacher CJ, Drucker AM. Core outcome set implementation supported by the *BJD*. *Br J Dermatol* 2021; **184**:987–9. https://doi.org/10.1111/bjd.20050.
7 Simpson RC, Thomas KS, Murphy R. Outcome measures for vulval skin conditions: a systematic review of randomized controlled trials. *Br J Dermatol* 2013; **169**:494–501. https://doi.org/10.1111/bjd.12391.
8 Goldstein AT, Marinoff SC, Christopher K, Srodon M. Prevalence of vulvar lichen sclerosus in a general gynecology practice. *J Reprod Med* 2005; **50**:477–80.
9 Lansdorp CA, van den Hondel KE, Korfage IJ *et al.* Quality of life in Dutch women with lichen sclerosus. *Br J Dermatol* 2013; **168**:787–93. https://doi.org/10.1111/bjd.12137.
10 Kirtschig G, Becker K, Günthert A *et al.* Evidence-based (S3) guideline on (anogenital) lichen sclerosus. *J Eur Acad Dermatol Venereol* 2015; **29**:e1–43. https://doi.org/10.1111/jdv.13136.
11 Halonen P, Jakobsson M, Heikinheimo O *et al.* Lichen sclerosus and risk of cancer. *Int J Cancer*. 2017; **140**:1998–2002. https://doi.org/10.1002/ijc.30621.
12 Bleeker MC, Visser PJ, Overbeek LI *et al.* Lichen sclerosus: incidence and risk of vulvar squamous cell carcinoma. *Cancer Epidemiol Biomarkers Prev* 2016; **25**:1224–30. https://doi.org/10.1158/1055–9965.EPI-16-0019.
13 Sargeant HA, O'Callaghan FV. The impact of chronic vulval pain on quality of life and psychosocial well-being. *Aust N Z J Obstet Gynaecol* 2007; **47**:235–9. https://doi.org/10.1111/j.1479-828X.2007.00725.x.
14 Sargeant HA, O'Callaghan F. Predictors of psychological well-being in a sample of women with vulval pain. *J Reprod Med* 2009; **54**:109–16.
15 Arnold S, Fernando S, Rees S. Living with vulval lichen sclerosus: a qualitative interview study. *Br J Dermatol* 2022; **187**:909–18. https://doi.org/10.1111/bjd.21777.
16 Chi CC, Kirtschig G, Baldo M *et al.* Topical interventions for genital lichen sclerosus. *Cochrane Database Syst Rev* 2011; **12**:CD008240.
17 Simpson RC, Cooper SM, Kirtschig G *et al.*; Lichen Sclerosus Priority Setting Partnership Steering Group. Future research priorities for lichen sclerosus – results of a James Lind Alliance Priority Setting Partnership. *Br J Dermatol* 2019; **180**:1236–7. https://doi.org/10.1111/bjd.17447.
18 Kirkham JJ, Davis K, Altman DG *et al.* Core Outcome Set-STAndards for Development: the COS-STAD recommendations. *PLoS Med* 2017; **14**:e1002447. https://doi.org/10.1371/journal.pmed.1002447.
19 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. https://doi.org/10.1038/jid.2014.320.
20 The Core Outcomes for Research in Lichen Sclerosus (CORALS) initiative. Available at: https://www.nottingham.ac.uk/research/groups/cebd/projects/5rareandother/corals.aspx (last accessed 14 October 2022).
21 Lewis FM, Tatnall FM, Velangi SS *et al.* British Association of Dermatologists guidelines for the management of lichen sclerosus, 2018. *Br J Dermatol* 2018; **178**:839–53.
22 Green N, Sheinis M, Selk A. Vulvar lichen sclerosus: outcomes important to patients in assessing disease severity. *J Low Genit Tract Dis* 2020; **24**:299–304. https://doi.org/10.1097/LGT.0000000000000547.
23 Goodrum CA, Leighton PA, Simpson RC. Outcome domains in lichen sclerosus. *Br J Dermatol* 2020; **183**:966–8. https://doi.org/10.1111/bjd.19253.
24 Rees S, Kirby L, Simpson RC. Living with vulval lichen sclerosus: a systematic review. *Br J Dermatol* 2019; **180**:1555–6. https://doi.org/10.1111/bjd.17790.
25 Dodd S, Clarke M, Becker L *et al.* A taxonomy has been developed for outcomes in medical research to help improve knowledge discovery. *J Clin Epidemiol* 2018; **96**:84–92. https://doi.org/10.1016/j.jclinepi.2017.12.020.
26 Crew R, Williamson P. *COMET Initiative DelphiManager brochure*. Available at: https://www.comet-initiative.org/delphimanager/docs/DelphiManagerBrochureV4.0.pdf (last accessed 14 October 2022).
27 SurveyMonkey software. Available at: https://www.surveymonkey.com (last accessed 14 October 2022).
28 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. https://doi.org/10.1111/pcmr.12354.
29 Thorlacius L, Ingram JR, Villumsen B *et al.* A core domain set for hidradenitis suppurativa trial outcomes: an international Delphi process. *Br J Dermatol* 2018; **179**:642–50. https://doi.org/10.1111/bjd.16672.
30 Schmitt J, Langan S, Stamm T, Williams HC; Harmonizing Outcome Measurements in Eczema (HOME) Delphi panel. Core outcome domains for controlled trials and clinical recordkeeping in eczema: international multiperspective Delphi consensus process. *J Invest Dermatol* 2011; **131**:623–30. https://doi.org/10.1038/jid.2010.303.
31 Lechner A, Coleman S, Balzer K *et al.* Core outcomes for pressure ulcer prevention trials: results of an international consensus study. *Br J Dermatol* 2022; **187**:743–52. https://doi.org/10.1111/bjd.21741.
32 Gorst SL, Barrington H, Brookes ST *et al.* COMET document: Online consensus meetings for COS development – issues to consider. Available at: https://www.comet-initiative.org/Downloads/Issues%20to%20consider%20for%20online%20consensus%20meetings.pdf (last accessed 14 October 2022).
33 Schmitt J, Williams H; HOME Development Group. Harmonising Outcome Measures for Eczema (HOME). Report from the First International Consensus Meeting (HOME 1), 24 July 2010, Munich, Germany. *Br J Dermatol* 2010; **163**:1166–8. https://doi.org/10.1111/j.1365-2133.2010.10054.x.
34 Schmitt J, Spuls P, Boers M *et al.* Towards global consensus on outcome measures for atopic eczema research: results of the HOME II meeting. *Allergy* 2012; **67**:1111–17. https://doi.org/10.1111/j.1398-9995.2012.02874.x.
35 Chalmers JR, Schmitt J, Apfelbacher C *et al.* Report from the third international consensus meeting to harmonise core outcome measures for atopic eczema/dermatitis clinical trials (HOME). *Br J Dermatol* 2014; **171**:1318–25. https://doi.org/13237.
36 Thorlacius L, Garg A, Ingram JR *et al.* Towards global consensus on core outcomes for hidradenitis suppurativa research: an update from the HISTORIC consensus meetings I and II. *Br J Dermatol* 2018; **178**:715–21. https://doi.org/10.1111/bjd.16093.
37 Thomas KS, Apfelbacher CA, Chalmers JR *et al.* Recommended core outcome instruments for health-related quality of life, long-term control and itch intensity in atopic eczema trials: results of the HOME VII consensus meeting. *Br J Dermatol* 2021; **185**:139–46. https://doi.org/10.1111/bjd.19751.
38 ACORN initiative. Available at: https://www.c3outcomes.org/acorn (last accessed 12 December 2022).
39 Langbroek GB, Wolkerstorfer A, Horbach SER *et al.*; COSCAM study group. A core outcome domain set for clinical research on capillary malformations (the COSCAM project): an e-Delphi process and consensus meeting. *Br J Dermatol* 2022; **187**:730–42. https://doi.org/10.1111/bjd.21723.
40 Van den Bussche K, Kottner J, Beele H *et al.* Core outcome domains in incontinence-associated dermatitis research. *J Adv Nurs* 2018; **74**:1605–17.