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## Development of the Adult Vulvar Lichen Sclerosus Severity Scale—A Delphi Consensus Exercise for Item Generation

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**Objective:** To generate a list of items through international expert consensus consisting of both symptoms and clinical signs for inclusion in an adult vulvar lichen sclerosus severity scale.

**Methods:** This study was carried out as a three-stage Delphi consensus exercise. After an extensive literature review, any items used to determine disease severity in previous clinical trials were compiled into a survey. The Delphi participants were recruited from the International Society for the Study of Vulvovaginal Disease most of whom were gynecologists and in practice for more than 20 years. Participants were asked to rate the importance of these items. Consensus was defined as 75% agreeing that an item was very important or essential toward determining disease severity. Participants were also asked to indicate preferred method of measurement for these items.

**Results:** Of approximately 400 members of the International Society for the Study of Vulvovaginal Disease, 66 participated in the study. Of the 14 symptoms presented, 7 reached consensus for inclusion. Of the 23 signs presented, 11 reached consensus for inclusion and 1 reached consensus for exclusion. Of the six architectural changes presented, all six reached consensus for inclusion. No consensus was reached regarding method of measurement for any of the symptoms and signs that reached consensus for inclusion.

**Conclusion:** International consensus was reached for a variety of items for use in an adult vulvar lichen sclerosus severity scale that will be further developed and tested. Ideally, this scale will be used in clinical practice and in research to allow for high-quality trials.

**Key Words:** lichen sclerosus et atrophicus, lichen sclerosus, lichen sclerosis, severity scale, Delphi Consensus

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Lichen sclerosus is a chronic inflammatory skin condition that most commonly affects the anogenital region in women. Lichen sclerosus can be asymptomatic in some patients; however, in others, it can result in severe itch, burning, dyspareunia, and irreversible anatomical changes with the potential to interfere with voiding and sexual function.<sup>1</sup>

Over the past few decades, there have been many clinical trials testing treatments of vulvar lichen sclerosus. To date, there is

no agreed-on standard way to measure lichen sclerosus disease severity. Researchers have tried measuring disease severity using differing combinations of patients' symptoms, physical examination findings, quality of life, sexual functioning measures, histological characteristics, and immunohistochemical staining. Researchers conducting multiple trials in this field have used many of the same measures for disease severity,<sup>2–9</sup> yet there is still variation among individual research groups spanning different projects and even greater variation between research groups.

A major issue with the measurement tools used in previous studies is their lack of objective definitions for various levels of severity of signs and symptoms. Furthermore, these scales have not been tested for reliability and validity prior to being used in treatment trials. To perform high-quality treatment trials, a high-quality scale is required.

Owing to the wide variation in measurement of lichen sclerosus severity among clinical studies, it is very difficult to directly compare between studies. Creation of a standard severity scale would provide a tool for the clinical and research communities to describe lichen sclerosus, and a common language to test different treatments in future randomized controlled trials.

This study is the first step in creating an adult vulvar lichen sclerosus severity scale, and it sought to generate a list of items for inclusion in a vulvar lichen sclerosis severity scale with the combination of an extensive literature review, patient input, and expert consensus.

## METHODS

## Literature Review for Preliminary Item Generation

An extensive literature review was conducted with the use of MEDLINE and EMBASE databases. These databases were searched with a combination of medical subject headings (MeSH) as well as keywords to include every variation on spelling for lichen sclerosus along with a search for known lichen sclerosus treatments (Appendix A shows complete search strategy).

All clinical trials studying vulvar lichen sclerosus treatment were reviewed, and the measures of severity that were used to determine impact of treatment were extracted manually. This list was reviewed by the principal investigator, and items that were more frequently discussed in the literature were compiled; whereas those that were unfeasible to measure in a clinical setting for all patients (e.g., histological and immunohistochemical characteristics) and terms not using standard medical language were removed.

## Further Item Generation

The principal investigator posted on the International Society for the Study of Vulvovaginal Disease (ISSVD) Facebook page and sent messages through member newsletters and message boards to request suggestions of further categories to include (e.g., symptoms, signs, quality of life measures) as well as specific items to include (e.g., under symptoms: pruritus). Patient input was solicited through the international online support group for lichen sclerosus via an e-mail to its director (The Association for Lichen Sclerosus & Vulval Health).<sup>10</sup>

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### Delphi Consensus Exercise

Upon completion of the category and item generation phase, a questionnaire was created. A Delphi consensus exercise was embarked on to elicit expert consensus with a series of three online surveys. The experts selected in this case were members and fellows of the ISSVD who actively care for patients with vulvar lichen sclerosis. The individuals who participated were the most appropriate to provide expert consensus given their clinical experience in treating the disease. These were also the individuals who would be the most likely users of the severity scale after its establishment.

Research ethics board approval was attained through the Mount Sinai Hospital, Toronto, Ontario, Canada board (REB 16-0065-E). The ISSVD members were invited to participate via an e-mail invitation, which included a consent form. Consent was assumed if participants chose to move forward with the survey as indicated in the invitation letter and the introductory page of the survey. The survey was distributed using the online tool "SurveyMonkey".<sup>11</sup>

Each round of three surveys was conducted over a 2-week period. In the first round of the e-Delphi exercise (<http://links.lww.com/LGT/A77>), basic demographic information was collected about participants including specialty of practice, number of years in practice, and country of practice. Participants were asked to rate a series of symptoms and signs to assess disease severity on a five-point Likert scale from 1: not important at all, to 5: essential for assessing disease severity. An opportunity was provided for participants to add additional categories or items they felt to be important as well as to indicate which method they felt to be appropriate for measuring signs and symptoms (i.e., categorical distinction [presence or absence of that sign/symptom] or severity scale [e.g., a Likert scale]).

After all rounds, medians, interquartile ranges, and percentages were calculated, and these data were provided to participants. Items that did not reach consensus for inclusion or exclusion were carried forward to the next round. Participants were also notified with regard to which questions had been amended, added, or excluded after analysis.

Upon completion of the first round, items which 75% of participants had agreed on were "very important" (4 on the Likert scale) or "essential" (5 on the Likert scale) were considered to have reached consensus for inclusion. Items for which consensus of 75% was reached as "not important at all" (1 on the Likert scale) or "not very important" (2 on the Likert scale) were determined to have reached consensus for exclusion. The 75% cutoffs used were in accordance with similar studies using the Delphi technique.<sup>12,13</sup>

In the second round (<http://links.lww.com/LGT/A78>), the survey was repeated with a few amendments. Questions that were determined to be confusing or unhelpful were removed. Additional items suggested by participants in the first round were incorporated into the second round. The scale was shifted after review of the results of the first round, as the study investigators were concerned that the group would not be able to move toward a consensus with the neutral response ("somewhat important": 3 on the Likert scale) available to respondents with a five-point scale. In the second round, a four-point Likert scale was used, where 75% of participants had to agree that the item was "very important" (3 on the Likert scale) or "essential" (4 on the Likert scale) for the item to reach consensus for inclusion and to agree that the item was "not important at all" (1 on the Likert scale) or "not very important" (2 on the Likert scale) for the item to reach consensus for exclusion. After the third round (<http://links.lww.com/LGT/A79>), this process was repeated a final time. The scale was again shifted to allow participants the option to either

**TABLE 1.** Summary of Literature Review Findings

	Most common items	Methods of measurement
Symptoms	Pruritus [14] Burning [14] Dyspareunia [14] Pain [14]	Individual symptoms: Continuous scales (0–10) [2] Discrete scales (4- to 10 point scales) [2] Combination of symptoms: Mild, moderate, severe [6] Symptoms and quality of life: 3-point scale [40] Qualitative: Mild, moderate, severe [26]
Signs	Hyperkeratosis [14] Erosion [14] Atrophy [14] Erythema [2] Purpuric lesions and/or itching-related excoriations [2]	Individual signs: Continuous scales [13] Discrete scales [7] Lesion size [40] Lesion duration [43] Qualitative: Mild, moderate, severe [47] Early, mid, end stage [45] Symptoms and signs [40]
Symptoms with pre-existing validated scales	Quality of life [47] Sexual function interference [17]	Female Sexual Function Index [17], Dermatology Life Quality Index [47])
Histological	Epidermal atrophy [47] Hyperkeratosis [47] Dermal inflammation [47]	Discrete scales (4-point scale) [47]
Immunohistochemical	H&E staining for lymphocytic infiltrates [19]	Discrete scales (4- to 6-point scales) [19]

H&E indicates hemotoxylin and eosin.

“include” or “exclude” items that had not reached consensus in the first or second rounds.

After the final analysis, the results were circulated for formal feedback and comments from the participants.

## Statistical Analysis

Data were analyzed with Microsoft Excel 2013 for measures of central tendency (i.e., mean, mode, and median) as well as level of dispersion (standard deviation and interquartile range).

## RESULTS

### Literature Search

A literature search conducted with the use of MEDLINE and EMBASE databases yielded 359 and 638 results, respectively (Appendix A shows full description of the literature search). When duplicated articles were removed and irrelevant articles screened out with the use of titles and abstracts, 338 articles remained. In total, an exhaustive list of items was generated including 103 items spanning the categories of symptoms, signs, histological findings, immunohistochemical markers, quality of life, and sexual functioning. The various scales used to measure the severity of the items within these categories were also compiled. Results of this search are summarized in Table 1. Although input was elicited from members and fellows of the ISSVD and patient members of the Association of Lichen Sclerosus & Vulval Health, no items were suggested by either of these groups.

With regard to symptoms, scales for measurement included continuous<sup>14</sup> and discrete<sup>2,4-9,15-34</sup> scales varying between 4 and 10 points. These scales focused on specific symptoms with itching, burning, and dyspareunia being the most common. Qualitative measures of minimal, moderate, or severe were also used without any associated numerical values or definitions of the labels used.<sup>35</sup>

Clinical appearance was measured in much the same way as symptoms. The most common signs measured were hyperkeratosis, erosion, atrophy, erythema, and purpuric lesions and/or itching-related excoriations. Both discrete<sup>15</sup> and continuous scales<sup>4-9,18,20,21,23,27,29,32,36-42</sup> were used to measure these signs. In addition to determining the specific sign, some studies added measurements of lesion size<sup>28,29,38,41,43</sup> as well as the duration of the lesion.<sup>44,45</sup> As with measurement of symptoms, there were also those who measured signs within qualitative categories of mild, moderate, and severe or early-, mid-, and end-stage disease, with some providing definitions of two of these labels (early and end stage,<sup>46</sup> and moderate, and severe<sup>47</sup>), and others not defining these labels at all.<sup>48</sup> Some studies combined symptomatic complaint scores with clinical signs scores.<sup>41,42</sup>

Less commonly used measures of disease severity included the description of histological features such as epidermal atrophy, hyperkeratosis, and dermal inflammation<sup>14,25,48-53</sup> and the measurement of various inflammatory marks with immunohistochemical staining.<sup>14,20,21,26,46,48,51,54-58</sup> Finally, some studies focused on the quality-of-life effects of this disease as well as interference with sexual functioning.<sup>18,22,35,48,59,60</sup>

### Delphi Consensus Exercise

Of approximately 400 members and fellows of the ISSVD, 66 participated in the three rounds of the survey. Retention of participants was 100% from the first round to the third round of the survey. Most participants were practicing gynecologists (67%), practitioners from the United States (45%), and practitioners with more than 20 years in practice (52%), although there was also good representation from dermatologists; the exercise included participants from 15 countries across the world (Table 2). Over the three rounds of the survey, 24 items reached consensus for

inclusion including 7 symptoms, 11 signs, and 6 architectural changes (Table 3). Upon completion of the last round of the survey, 18 items remained for which no consensus had been reached (Table 4). With regard to methods of measurement, 72% of the participants wished to measure symptoms with a five-point severity scale (Table 4). When asked whether to measure frequency of symptoms (described in items 4 and 5 in Table 4), 82% of the participants agreed that this should be done. With regard to measuring special symptoms (including quality of life and changes in sexual functioning), most participants (52%) preferred to measure these with a five-point severity scale rather than a pre-existing validated scale (Table 5). There was a fairly even distribution of how practitioners preferred to measure signs and architectural changes (Table 4), although most agreed that these items must be measured to determine disease severity. With regard to architectural changes, most participants (87%) felt that either a photo or a colored-in diagram were to be used to record architectural changes in the context of determining disease severity.

## DISCUSSION

Although there have been many studies in the past to propose methods for measurement of lichen sclerosus severity,<sup>2-9,14-61</sup> this

**TABLE 2.** Demographic Characteristics of Participants (n = 66)

	n (%)
Sex	
Female	51 (77%)
Male	15 (23%)
Field of practice	
Gynecology	44 (67%)
Dermatology	16 (24%)
Sexual medicine	4 (6%)
Nurse practitioner	1 (2%)
Family doctor/General practitioner	1 (2%)
Country	
USA	30 (45%)
Australia	6 (9%)
UK	5 (8%)
Canada	5 (8%)
Portugal	4 (6%)
Netherlands	3 (5%)
Italy	3 (5%)
New Zealand	2 (3%)
England	2 (3%)
Norway	1 (2%)
France	1 (2%)
Uruguay	1 (2%)
Mexico	1 (2%)
India	1 (2%)
Spain	1 (2%)
Years in practice	
Less than 5 years	6 (9%)
6–10 years	13 (20%)
11–15 years	6 (9%)
16–20 years	7 (11%)
Greater than 20 years	34 (52%)
ISSVD member or fellow	
Member	40 (61%)
Fellow	26 (39%)

**TABLE 3.** Items That Reached Consensus for Inclusion ( $\geq 75\%$  Agreeing Item Is “Very Important” or “Essential”) and Exclusion ( $\geq 75\%$  Agreeing Item Is “Not Important at All”, or “Not Very Important”) Along With Round in Which Consensus Was Reached and % of Participants Supporting Inclusion/Exclusion

Category item	Include?	Exclude?	Round of survey	% of participants
<b>Symptoms</b>				
Itch	Yes		Round 1	77%
Pain unrelated to intercourse (burning, soreness, discomfort, etc.) at rest or during activity	Yes		Round 2	77%
Pain with intercourse	Yes		Round 2	91%
Bleeding and pain with intercourse	Yes		Round 2	85%
Skin tearing with intercourse	Yes		Round 2	88%
Quality of life	Yes		Round 1	79%
Changes/decrease in sexual function	Yes		Round 2	83%
<b>Signs</b>				
Fissures	Yes		Round 1	76%
Whitening	Yes		Round 1	77%
Crinkly/fine wrinkling of skin/parchment-like skin	Yes		Round 1	77%
Extent of disease (figure of eight vs localized to labia, localized to clitoris, localized to perineum or combined)	Yes		Round 1	89%
Erosions	Yes		Round 2	92%
Ulcerations	Yes		Round 2	82%
Hyperkeratosis	Yes		Round 2	89%
Excoriations	Yes		Round 2	77%
Lichenification	Yes		Round 2	79%
Elasticity (or loss of elasticity)	Yes		Round 2	77%
Sclerosis	Yes		Round 2	92%
Telangiectasia		Yes	Round 3	76%
<b>Architectural changes</b>				
Clitoral hood fusion	Yes		Round 1	89%
Labial fusion/resorption	Yes		Round 1	88%
Narrowing of the introitus	Yes		Round 1	89%
Anterior changes (fusion anteriorly below the clitoris, causing urethral occlusion at its extreme)	Yes		Round 2	95%
Perianal involvement	Yes		Round 2	85%
Formation of posterior commissure bands/fourchette webs	Yes		Round 3	80%

is the first study to present a list of items for inclusion in a scale based on an international expert consensus using the iterative Delphi consensus protocol.

Lichen sclerosis treatment varies widely especially with regard to maintenance therapy.<sup>62</sup> A meta-analysis in 2012 concluded that the limited evidence available supports clobetasol propionate, mometasone furoate, and pimecrolimus for treating adult vulvar lichen sclerosis.<sup>63</sup> Since then, many additional randomized controlled trials have been completed studying treatments including clobetasol propionate, mometasone furoate, fibroblast lysate cream, and topical tacrolimus<sup>5,18,20,37,63–66</sup>; however, as trials between different research groups have been completed with individual nonstandardized severity scales, comparison of results is challenging and imprecise.

Disease severity scales feature prominently in dermatological research with scales for diseases such as leprosy, hyperhidrosis, and psoriasis.<sup>67–69</sup> However, in the subspecialized field of gynecological dermatology, such scales are lacking; and for conditions that affect the other regions apart from the vulva, such as lichen planus, a scale exists for oral lichen planus alone.<sup>70</sup>

To produce higher-quality research in a randomized controlled fashion, to improve observational research, and to compare data between different populations across the world, the creation and implementation of a standardized adult lichen sclerosis severity scale is essential. This study proposes 24 items for inclusion in

a future lichen sclerosis severity scale. The categories of items proposed included symptoms, signs, and architectural changes. Although previous studies had considered the use of histological and immunohistochemical markers,<sup>14,20,21,25,26,46,48–58</sup> these categories were not used in the initial survey because including them would require a biopsy at every patient visit. The fact that these categories were not proposed by any of the experts throughout the consensus exercise indicates that this feeling was upheld by experts worldwide. It may be objective to look at biopsy changes to treatment, but it is unclear whether this outcome is important to patients and likely should be used as an adjunct to other measures.

Most of the participants in this study were practitioners having more than 20 years of experience in the field. The participants were also those who actively see patients with vulvar lichen sclerosis as part of their clinical practice, which lends greater credibility to the results. The 100% retention rate through the three rounds of the survey demonstrates a commitment on behalf of the participants to advancing the field.

Despite its strengths, this study has several limitations. First, although this study sought to include patients' input, unfortunately, this endeavor was unsuccessful; this removes a very important voice from the development of the scale. However, as the list of items included in the scale was based on an extensive literature review, it was thought that most if not all the items that would have been suggested by patients would likely have already been

**TABLE 4.** Items Which Did Not Reach Consensus for Inclusion or Exclusion Along With % of Participants Supporting Inclusion by Round 3

Category item	% of participants
<b>Symptoms</b>	
Irritation	58%
Dryness	36%
Difficulty urinating (dribbling, having to stand up to void)	58%
Difficulty with bowel movements (constipation)	30%
Bleeding with scratching	50%
“I don’t have any symptoms”	64%
Change or decrease in mood	38%
<b>Signs</b>	
Petechiae	42%
Ecchymosis	55%
Color (normal vs abnormal)	65%
Pallor	42%
Hypopigmentation	70%
Hyperpigmentation	47%
Erythema	56%
Induration	56%
Edema	44%
Atrophy (thinning or depression of skin due to reduction of underlying tissue)	67%
Whether the disease is symmetrical versus asymmetrical	42%

considered when generating the first survey. The type of scale used to rate the items was changed between rounds of the survey (from a five-point Likert, to a four-point Likert, to a choice between two options) for the purpose of moving the group toward consensus. The change of the scale may have affected the quality of the data collected. The expert group consisted mostly of gynecologists, which may have skewed the results toward one specialty. However, given that gynecologists are more likely to encounter the more severe cases of lichen sclerosus, it was thought that this would not affect the tool’s use too heavily, but future testing is required to see if this is true. Furthermore, although this study was conducted in English, for some of the international experts, English was not their first language. This could have affected the understanding of some questions and affected the answers provided. Despite three rounds, consensus was not reached on several items, and there was an even split into three groups over the ideal way to measure anatomical changes. It is a matter of concern that participants did not want to use already validated scales to measure things like sexual function and quality of life and speaks to a lack of understanding of the difficulty in creating high-quality measurement tools. Finally, the principal investigator and research coordinator were responsible for determining which items to incorporate into the survey based on the literature review, which allowed for personal bias.

This study is only the first step of many subsequent steps that must be undertaken for the completion of a lichen sclerosus severity scale. Before testing the items generated through this study, patient focus groups will need to be conducted for their crucial input on relevant symptoms, and the symptom list will subsequently be expanded before testing the symptom section with patients. Future steps include testing the scale for inter-rater and intrarater reliability, examining ratings by dermatologists versus gynecologists, completing a factor analysis to combine similar items, removing

redundant and unhelpful items, and ensuring feasibility of use in a clinical setting. Currently, there are too many items and there is overlap in items that will be reduced through testing the scale. The various ways to measure anatomical changes will need to be tested to see which method gives the most reliable reproducible results. Upon completion of these steps, further studies will be undertaken to determine whether the scale is useful for assisting with medication selection and determining prognosis. The ultimate goal of these further studies will be to

**TABLE 5.** Various Methods of Measuring Symptoms, Signs, and Architectural Changes Presented With Percentage of Participants Favouring Each Method

Category method of measurement	% of participants
<b>Symptoms</b>	
Presence or absence of symptoms (e.g., Yes/No)	18%
If screen positive then... 5-point severity scale (e.g., 1, absent/never; 2, sometimes/occasionally; 3, often; 4, most of the time; 5, all the time)	36%
If screen positive then... 10-point visual analog scale (e.g., 1, no itch at all; 10, worse itch imaginable)	0%
If screen positive then... 5-point severity scale (as above) + scale for frequency (e.g., every day, $\geq$ once per week, $\geq$ once every 2 weeks, $\geq$ once per month)	36%
If screen positive then... 10-point visual analog scale (as above) + scale for frequency (e.g., every day, $\geq$ once per week, $\geq$ once every 2 weeks, $\geq$ once per month)	8%
Other	2%
<b>Special symptoms (including change/decrease in quality of life, change/decrease in sexual function)</b>	
Presence or absence of symptoms (e.g., yes/no)	20%
If patient screens positive then... 5-point severity scale (e.g., 1, no impact; 2, barely affected; 3, slightly affected; 4, moderately affected; 5, strongly affected)	52%
If patient screens positive then... use previously validated scale for severity (e.g., female sexual function index, dermatology quality-of-life index or a variation of it, etc.)	29%
<b>Signs</b>	
Presence or absence of signs (e.g., yes/no)	35%
If patient screens positive then... classify sign subjectively as mild, moderate, or severe	38%
If patient screens positive then... classify sign as mild, moderate, or severe depending on percentage of vulva affected (mild, <30%; moderate, 30–50%; severe, >50%)	27%
<b>Architectural changes</b>	
Presence or absence of that change (e.g., yes/no)	29%
If patient screens positive then... classify subjectively as mild, moderate, or severe	32%
If patient screens positive then... classify extent of change as slight, partial, or complete (e.g., slight, partial, or complete labial fusion)	29%
If patient screens positive then... classify according to percentage of architecture affected (e.g., <30% labial fusion, 30–50% labial fusion, >50% labial fusion)	11%

produce a severity scale that is high enough in quality for use in research and, concurrently, sufficiently user-friendly that it will have high uptake clinically.

It was felt that the results thus far would be helpful to clinicians and researchers involved in the care of women with vulvar lichen sclerosis. In a recent editorial, Foster et al. (2017) highlighted the absence of core outcome sets, which they define as “a minimum set of outcomes that is used in clinical trials and observational studies... that will enable trials or studies to be compared in meta-analyses”, within the field of vulvovaginal disease, making the production of high-quality research trials next to impossible.<sup>71</sup> Although there is a long way to go toward the completion of a validated scale for measuring adult vulvar lichen sclerosis severity and creating an internationally accepted core outcome set for adult vulvar lichen sclerosis, this study brings us one step closer toward achieving this goal.

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## APPENDIX

Database search strategy for both MEDLINE and EMBASE MeSH heading “Lichen Sclerosus et Atrophicus” was searched with subclassifications of “therapy”, “classification”, and “drug therapy”. This term was combined with “lichen sclerosus et atrophicus” as a keyword with a subclassification of “disease” with OR as well as keyword “lichen scleros?s” to include all spellings of the term and MeSH heading “Lichen Sclerosus et Atrophicus” without any subclassifications. These two terms were further combined with the MeSH heading “Clobetasol”, keyword “Clobetasol propionate”, MeSH heading “Tacrolimus”, keyword “tacrolimus”, MeSH heading “glucocorticoids” in exploded form, keyword “topical steroid\*”, and keyword “glucocorticoid\*” with an OR term.

The results were then limited to “female”.

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