

## Outcome domains in Lichen Sclerosus

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Dear Editor,

Lichen Sclerosus (LS) is a chronic inflammatory dermatosis predominantly affecting the genitals. It can affect men, women and children. LS affecting female genitalia typically presents with itchy patches that impact on physical and psychosocial-sexual functioning<sup>1,2</sup>. Symptoms in men include difficulty urinating due to urethral narrowing, difficulty in foreskin retraction due to scarring, and dyspareunia. Complications include loss of anatomy and malignant transformation.

Clinical trials are vital for evidence-based practice by providing current supportive evidence to inform clinical decision-making. When results of multiple clinical studies are pooled, a stronger evidence base is obtained than with a single study. However, there is inconsistency in outcomes measured in trials of vulval skin conditions; one systematic review found 28 vulval randomised controlled trials, measuring 25 outcomes using 49 different scales<sup>3</sup>. The heterogeneity of these outcomes/scales means they cannot be effectively compared or combined in meta-analyses, which is a source of research wastage<sup>4</sup>.

Minimising differences in outcomes collected during trials by developing and using Core Outcome Sets can reduce this research 'waste'. A Core Outcome Set is an agreed standardised minimum collection of outcomes that should be measured and reported across all clinical trials of a specific condition<sup>5</sup>.

The aim of this study was to inform development of a Core Outcome Set for genital LS by establishing outcome domains of importance to patients and healthcare professionals.

An online survey was disseminated to international stakeholders from September-October 2017 during a James Lind Alliance LS Priority Setting Partnership<sup>6</sup>. As this was patient and public involvement into research, ethical approval was not required.

Anonymised free-text responses about 'important symptoms or aspects of LS' were collected. Data were analysed using NVivo12 software through an iterative sequence of qualitative analyses<sup>7</sup>. First, keywords were identified using word frequency counts. They were subsequently analysed in the wider context of the data in a 'keyword-in-context' analysis. This informed a thematic analysis, where each response was summarised/characterised using a 'code' (a simple label of content). Similar 'codes' were grouped within broader 'themes', with review of themes (and data captured therein) informing the generation of outcome domains.

The survey was completed by 653 respondents submitting 1953 responses in total. 404 participants were patients/carers (92% female, 5% male) of whom 5% were children/representatives of children. 222 participants were healthcare

professionals (64 gynaecologists, 58 dermatologists, 35 sexual health physicians) and 27 'other'.

Word counts identified that itch was the most commonly used 'keyword' (used 395 times); contextual review identified variation in how 'keywords' were used (e.g. 'presence of itch' or 'itch ceasing'). Consistent use of keywords informed the creation of 37 distinct 'codes', each code capturing a commonly reported experience/opinion. Codes were organised within 6 broader 'themes', which drew together closely related or connected codes (Table 1).

Each theme points to an outcome domain of importance for LS, the thematic analysis therein provides insight about how to potentially operationalise that domain.

Symptoms of LS, such as itching and pain, and their persistent nature cause significant discomfort and psychological distress (*Symptoms*). As such LS impacts on daily activities and normal functioning (*Quality of Life*). People with LS reported problems with dyspareunia, physical inability to engage in intercourse due to narrowing of the vaginal opening, and lack of sexual drive from loss of sensation. They referred to the emotional impact on relationships as well as their own psychosocial-sexual wellbeing (*Sexual Dysfunction*). Responses placed greater significance on the changes related to anatomical structure (229 responses) than on variations in cosmetic appearance (70 responses) (*Appearance*).

Many participants described fear of potential progression to malignancy and irreversible stenosis (*Progression of the Condition*). The importance of better awareness of LS among the general public and doctors was highlighted to aid earlier diagnosis and prevention of scarring. Many patients called for treatment that quickly resolves symptoms, reduces flare ups and is easier to use than the standard first-line therapy of topical steroids (*Management of Condition*).

The six key themes/domains identified above will inform the first stage of development for a LS Core Outcome Set through the CORALS (Core Outcomes for ReseArch in LS) initiative<sup>8</sup>. The first stage will obtain international consensus on core outcome domains via an electronic-Delphi exercise. Subsequent work to identify appropriate outcome measurement instruments will then be needed to use in the final Core Outcome Set.

Although CORALS is intended for use in randomised trials, we believe understanding these outcomes of importance is valuable for managing LS in the outpatient clinic. Ensuring that these issues are addressed during the consultation will benefit patient experience and overall quality of care.

<b>Theme/Domain</b>	<b>Codes</b>	<b>Example of data</b>
<b>Quality of Life</b>	Impact on daily activities/ normal function	"It takes a lot of everyday life...when you have to pee, you want to have sex, go swimming, go cycling, etc... I miss being spontaneous."
	Psychological distress	"The psychological impact it has on your relationship to your partner"
<b>Sexual dysfunction</b>	Physically unable to have sex	"Being able to have a normal sex life with vaginal intercourse (without risk of damages or pain from scratches, skin growing together, thin skin and other anatomical changes)"
	Dyspareunia	"Able to have intercourse without the pain during and after"
	Emotional impact on relationships	"Fusing, anything to stop the fusing, my partner asked why I had been circumcised, I'm white British female, I haven't been circumcised."
<b>Symptoms</b>	Itching	"Flare ups of agonizing unceasing itching"
	Pain	"Cracking of the skin in the vulva area, which is rather painful"
<b>Appearance</b>	Anatomical Change	"Architecture. I no longer have external labia, neither a noticeable clitoris and my vulva looks like a pair of white bicycle inner tubes...I very much miss feeling like a complete woman"
	Cosmetic Appearance	"Scarring / ugly red patches on the genitals"
<b>Progression of the condition</b>	Cancer risk	"Anxiety about the possible development of cancer."
<b>Management of the condition</b>	Better awareness	"The tendency for GPs and other practitioners to wrongly diagnose LS...and dismiss women presenting with repeated problems"
	Earlier diagnosis	"Develop an easier way to diagnose the disease so more women will be able to be tested early enough."
	Better treatment	"Clearer and consistent guidance on treatment...what works best, when, how and how much/frequently"

*Table 1 Summary of the thematic analysis showing 6 key themes identified and the codes and examples of raw data that contributed to these.*

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