

# Proactive against reactive treatment for lichen sclerosis

<b>Submission date</b> 09/01/2024	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 08/03/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 15/01/2026	<b>Condition category</b> Skin and Connective Tissue Diseases	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Lichen sclerosis (LS) is a long-term, itchy and distressing condition affecting vulval skin (the skin around the outside of the vagina). It needs ongoing treatment with steroid creams to manage flares of symptoms. If untreated, it may lead to scarring causing the labia minora (inner lips) to fuse together or the entrance to the vagina to narrow. People with LS are at higher risk of developing vulval cancer. Vulval LS can affect everyone, but most commonly children and women of any age, particularly women who have gone through the menopause and children before puberty. This study will try to find out what is the best way to manage future flares of LS: using a steroid treatment regularly (e.g. twice a week), even when symptoms are controlled OR using a steroid cream only during a flare.

### Who can participate?

Female patients with LS aged 5 years and over

### What does the study involve?

Participants are randomly allocated to either use their steroid cream twice a week or to only use it if they experience symptoms. The researchers will compare how many people in each group develop LS flares. With the optional consent of the participant/parent/guardian, photographs will be taken at baseline to check if scarring worsens during the trial. The researchers will follow patients for 2 years to gather data. With participants' consent (optional), the researchers will check their medical records at a later stage (after the trial ends) to see how many patients in each treatment group develop cancer. They will conduct an optional qualitative study and interview patients (those who consented to participate in qualitative sub-study) to explore how they feel about the trial and the different ways of treating LS that we are testing. The researchers will also compare the costs and outcomes of the two treatments used in the trial to see if one is better value for money for the NHS. If successful, the study results will be used to change clinical practice for the treatment of patients with LS.

### What are the possible benefits and risks of participating?

The study treatment involves topical steroid ointment/cream, which is normally prescribed to patients as their routine care for LS. The only difference between the study treatment and the routine care may be the treatment regimen. It is, therefore, believed that the risk associated

with the study due to the intervention is negligible. Participants will be asked to attend research appointments. Every effort will be made to coincide these appointments with participants' clinical appointments.

Safety data will be collected for the duration of participation and will be reported as per sponsor guidelines. Although the steroid treatment can be safely applied to the whole body in a single dose with minimal risk of adverse reactions, there is however a risk of adverse reactions following long-term use of topical corticosteroid on localised areas of skin (e.g. skin thinning, telangiectasia). These will be monitored during clinical examination at follow-up visits (or at an unscheduled trial visit, as necessary).

Where is the study run from?

Nottingham Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?

March 2023 to March 2028

Who is funding the study?

NIHR Health Technology Assessment Programme (UK)

Who is the main contact?

PEARLS study team, PEARLS@nottingham.ac.uk

## Contact information

### Type(s)

Scientific, Principal investigator

### Contact name

Dr Rosalind Simpson

### Contact details

Centre of Evidence-Based Dermatology

Applied Health Research Building

University Park

Nottingham

United Kingdom

NG7 2RD

-

rosalind.simpson@nottingham.ac.uk

### Type(s)

Public

### Contact name

Dr PEARLS Study Team

### Contact details

NCTU

University of Nottingham

University Park

Nottingham

United Kingdom  
NG7 2RD  
-  
PEARLS@nottingham.ac.uk

## **Additional identifiers**

### **Clinical Trials Information System (CTIS)**

Nil known

### **Integrated Research Application System (IRAS)**

1008267

### **ClinicalTrials.gov (NCT)**

Nil known

### **Protocol serial number**

23055, CPMS 61122

## **Study information**

### **Scientific Title**

Proactive against reactive therapy for the prevention of lichen sclerosis exacerbation and progression of disease – a pragmatic, parallel group randomised controlled trial with embedded economic evaluation and process evaluation

### **Acronym**

PEARLS

### **Study objectives**

Primary objective:

Compare the clinical and cost-effectiveness of a twice-weekly topical corticosteroid maintenance strategy (proactive therapy) with as-required treatment (reactive therapy) in the management of vulval lichen sclerosis (LS)

Secondary objectives:

1. Assess the effectiveness of proactive versus reactive use of topical corticosteroids (TCSs) over 24 months in reducing disease progression
2. Assess the clinical effectiveness of proactive versus reactive strategies for the management of vulval LS for up to 24 months
3. Assess the safety of using potent and superpotent TCSs in the vulval area over 24 months
4. Assess the cost-effectiveness of the two treatment strategies
5. Understand the acceptability of reactive and proactive long-term treatment strategies and the barriers and facilitators to continuing with prescribed treatment

### **Ethics approval required**

Ethics approval required

### **Ethics approval(s)**

approved 27/02/2024, South West – Central Bristol Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8197, +44 (0)207 104 8269, +44 (0) 207 104 8061; centralbristol.rec@hra.nhs.uk), ref: 24/SW/0016

## **Study design**

Open randomized controlled parallel-group trial

## **Primary study design**

Interventional

## **Study type(s)**

Efficacy, Safety

## **Health condition(s) or problem(s) studied**

Vulval lichen sclerosis

## **Interventions**

In the intervention group participants will be asked to apply potent or superpotent topical corticosteroid (TCS) on two non-consecutive days per week even in the absence of symptoms (proactive treatment). In the comparator group participants will be asked to apply potent or superpotent TCS as required to treat a LS flare (reactive treatment).

Eligible patients will be individually allocated in a 1:1 ratio to either proactive or reactive use of TCS. Treatment will be assigned randomly using a minimisation algorithm with a random element, balancing across groups on the recruiting site, age, time since last flare and strength of prescribed TCS.

The choice of TCS will be according to the patient's usual care. PEARLS is a pragmatic trial, and the researchers will test the strategy of proactive vs reactive treatment using the potency of topical corticosteroid recommended by the treating clinician (potent or superpotent). There are several generic names available for these prescribed TCSs and all available brands and forms can be prescribed. The examples of the most commonly prescribed brands/products of the TCS class are:

1. Dermovate ointment - superpotent TCS
2. Elocon® 0.1% w/w ointment - potent TCS

The topical dosage of TCSs for both trial groups will be recommended in Fingertip Units (FTU) depending upon the area affected by LS (typically 0.5-1 FTU). FTU is the amount of topical steroid (ointment or cream) that is applied along an adult's fingertip to the first crease in the finger. One FTU is sufficient to treat an area of skin twice the size of the flat of an adult's hand with the fingers together (i.e. a 'handprint'). FTU is also used to treat an area of skin on a child. The treating physician will advise on the dosage for adults or children.

## **Intervention Type**

Drug

## **Phase**

Phase IV

## **Drug/device/biological/vaccine name(s)**

## Topical Corticosteroid (TCS)

### Primary outcome(s)

Number of flares over 12 months. Flare is defined as the worsening of symptoms requiring increased application of TCS, measured via text/app/email reminders every 2 weeks for 12 months.

### Key secondary outcome(s)

Clinical effectiveness:

1. Progression of scarring, assessed by a blinded assessor at 12 and 24 months by comparing the post-randomisation assessment to baseline photographs (if patients consented), or assessed clinically if consent has not been given for photographs:

1.1. Adults: scarring worsened (yes/no).

1.2. Children and adolescents: failure of normal vulval development (clinical assessment) and/or evidence of scarring (yes/no)

2. Vulval Architectural Severity Scale (VASS) at 12 and 24 months post-randomisation, assessed clinically

3. Time to first flare, measured via text/app/email reminders at the point of first flare

4. Clinician global severity assessment of LS using a 5-point ordinal scale at 3, 6, 12, 18 and 24 months. Also assessed by a blinded assessor at 12 and 24 months. This will be measured via clinical assessment.

5. Condition-specific quality of life (QoL) measured at 3, 6, 12, 18 and 24 months using:

5.1. Vulvar Quality Life Index (VQLI) (adults)

5.2. Children's Dermatology Life Quality Index (CDLQI) (adolescents and children)

5.3. Sexual function (adults only) assessed using the Female Sexual Function Index at 12 and 24 months

Safety:

1. Adverse reactions (e.g. stinging, skin thinning) measured throughout the trial by patient-reported symptoms and clinical examination from randomisation over 24 months

2. Development of vulval intraepithelial neoplasia or vulval squamous cell carcinoma at 24 months, measured by clinical assessment and/or medical notes

Treatment acceptability and potential barriers/facilitators to treatment:

1. Acceptability of treatment strategy measured using a Likert scale at 12 and 24 months

2. Adherence to treatment measured using a bespoke questionnaire completed by participants at 3, 6, 12, 18 and 24 months

3. Qualitative interview sub-study at 12 months

Cost-effectiveness:

1. Generic utility instrument to measure QoL at 3, 6, 12, 18 and 24 months with EQ-5D-5L

(adolescents and adults) and Child Health Utility Instrument - Nine Dimensions (CHU-9) (children)

2. Resource use including prescription, direct and indirect healthcare and out-of-pocket costs associated with vulval LS at 3, 6, 12, 18 and 24 months, measured via a bespoke questionnaire

### Completion date

01/03/2028

## Eligibility

### Key inclusion criteria

1. Clinical or biopsy confirmed diagnosis of vulval LS
2. Currently controlled disease (asymptomatic with minimal clinical evidence of active disease) at baseline
3. Age  $\geq 5$  years
4. Able to give consent/child assent plus parental consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Lower age limit**

5 years

**Upper age limit**

100 years

**Sex**

Female

**Total final enrolment**

0

**Key exclusion criteria**

1. Previous vulval intraepithelial neoplasia (VIN) or vulval squamous cell carcinoma (SCC)
2. Contraindications to topical steroids
3. Concomitant use of other topical anti-inflammatory vulval treatments
4. Using systemic immunosuppressants (for any indication)
5. Using systemic treatment for LS
6. Patients with surgical alteration of vulval skin as part of gender reaffirming surgery, or patients not born with a vulva
7. Pregnant and breastfeeding women

**Date of first enrolment**

01/04/2024

**Date of final enrolment**

31/03/2026

**Locations****Countries of recruitment**

United Kingdom

England

Scotland

Wales

**Study participating centre**

**Axess Sexual Health, Royal Liverpool University Hospital**

Mount Vernon St

Liverpool

England

L7 8XP

**Study participating centre**

**Liverpool Women's Hospital**

Liverpool Womens Hospital

Crown Street

Liverpool

England

L8 7SS

**Study participating centre**

**Aberdeen Royal Infirmary**

Foresterhill Road

Aberdeen

Scotland

AB25 2ZN

**Study participating centre**

**Royal Blackburn Hospital**

Haslingden Road

Blackburn

England

BB2 3HH

**Study participating centre**

**The James Cook University Hospital**

Marton Road

Middlesbrough

England

TS4 3BW

**Study participating centre**

**St Mary's Hospital**

Oxford Road  
Manchester  
England  
M13 9WL

**Study participating centre**

**Market Street Health Centre, Oxleas**

16-20 Market Street  
Woolwich  
London  
England  
SE18 6QR

**Study participating centre**

**Whipps Cross University Hospital**

Whipps Cross Road  
Leytonstone  
London  
England  
E11 1NR

**Study participating centre**

**Queen Elizabeth Hospital**

Sheriff Hill  
Gateshead  
England  
NE9 6SX

**Study participating centre**

**Florence Nightingale Community Hospital**

London Road  
Derby  
England  
DE1 2QY

**Study participating centre**

**Royal Derby Hospital**

Uttoxeter Road  
Derby



England  
DE22 3NE

**Study participating centre**

**Churchill Hospital**

Churchill Hospital

Old Road

Headington

Oxford

England

OX3 7LE

**Study participating centre**

**Leicester Royal Infirmary**

Infirmary Square

Leicester

England

LE1 5WW

**Study participating centre**

**Nottingham City Hospital**

Hucknall Road

Nottingham

England

NG5 1PB

**Study participating centre**

**Princess Royal Hospital**

Apley Castle,

Grainger Drive

Apley

Telford

England

TF1 6TF

**Study participating centre**

**East Surrey Hospital**

Canada Avenue

Redhill

England

RH1 5RH

**Study participating centre**  
**Norfolk and Norwich University Hospital**  
Colney Lane  
Colney  
Norwich  
England  
NR4 7UY

**Study participating centre**  
**County Durham and Darlington NHS Foundation Trust**  
Darlington Memorial Hospital  
Hollyhurst Road  
Darlington  
England  
DL3 6HX

**Study participating centre**  
**Cumberland Infirmary**  
Newtown Road  
Carlisle  
England  
CA2 7HY

**Study participating centre**  
**Modality Community Gynaecology Service**  
Nishkam Pharmacy, 21 Soho Road  
Birmingham  
England  
B21 9SN

**Study participating centre**  
**Hull University Teaching Hospitals NHS Trust**  
Hull Royal Infirmary  
Anlaby Road  
Hull  
England  
HU3 2JZ

**Study participating centre**  
**Cardiff & Vale University Lhb**  
Woodland House  
Maes-y-coed Road  
Cardiff  
Wales  
CF14 4HH

## Sponsor information

**Organisation**  
Nottingham Clinical Trials Unit

## Funder(s)

**Funder type**  
Government

**Funder Name**  
Health Technology Assessment Programme

**Alternative Name(s)**  
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

**Funding Body Type**  
Government organisation

**Funding Body Subtype**  
National government

**Location**  
United Kingdom

## Results and Publications

### Individual participant data (IPD) sharing plan

The datasets analysed during the current trial will be available upon request from the NCTU (ctu@nottingham.ac.uk), a minimum of 6 months after publication of the main results paper. Access to the data will be subject to review of a data sharing and use request by a committee including the CI and sponsor and will only be granted upon receipt of a data sharing and use agreement. Any data shared will be anonymised which may impact on the reproducibility of published analyses.

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol file</a>	Old version, not in use version 2.0	05/02/2024	01/08/2024	No	No
<a href="#">Protocol file</a>	version 5.1	03/09/2025	15/01/2026	No	No