

Outcome measures in vulval disease – A systematic review

1. Background

Description of the problem/issue

Summarising knowledge on therapeutic interventions through systematic reviews and meta-analyses can only be conducted when standardised and valid outcome measurements are consistently applied in all randomised controlled trials (Schmitt 2007).

Health-related quality of life (QoL) measures are of increasing importance in clinical practice for therapeutic decision-making and developing service provision. Numerous disease specific severity scores exist within dermatology, as do quality of life indices. However, none have been specifically designed to holistically cover all aspects of vulval disease.

We believe that a generic validated questionnaire dedicated to vulval disease is lacking and wish to review the evidence to highlight the current gaps in this domain. If the systematic review confirms our suspicion, areas for future research will be identified.

Description of the methods being investigated

Treatment of vulval skin conditions can be challenging and there is current lack of consensus in methods of assessment, particularly inflammatory disorders. We will therefore investigate which outcomes have been used in interventional randomised controlled trials in the vulval literature to date. We will explicitly look for vulval specific scales, but in the likelihood of their absence, will also comprise a list of outcome measures that have been utilised by researchers.

Why it is important to do this review

The prevalence and impact of vulval skin conditions (both benign and malignant) is likely to be underestimated. Exact figures are not known as many women delay in seeking medical advice due to embarrassment or concerns about a possible infectious or malignant cause for their condition. This delay is often compounded by women self-medicating with over the counter preparations, including anti-itch and anti-thrush treatments (Lawton and Littlewood 2006). Vulval skin conditions can affect women's physical functioning, restrict physical activities, and affect everyday activities such as walking, sitting, relaxing, and sleeping as well as causing pain with a range of sexual and non-sexual contact (e.g. use of tampons, friction with clothing, urination, and defecation). They can also impact on social, psychosexual, and psychological well-being (Bellman 1998, Sargeant 2007, Hickey 2010). Little has been published on the subject of common benign gynaecological conditions and their effect on QoL (Jones 2002).

There is a lack of laboratory or bedside tests that measure the severity of vulval disease. Therefore methods of evaluating severity are often crude, subjective and not reproducible, which can create discrepancy in results and inter-individual variations. This

means that performing clinical trials and collating results from previously published studies to form an evidence-based opinion on treatments for vulval diseases is difficult.

In recent years there has been a growing recognition of the importance of measuring disease severity and the impact of treatment from the patient's perspective. Patient-based outcome measures addressing aspects such as symptoms, functional ability, satisfaction with care, and QoL are increasingly being used as primary and secondary endpoints both in clinical trials and clinical practice within dermatology (Charman et al 2004). There are specific dermatology QoL and disease measures which have been validated and used widely both in clinical trials and clinical practice such as the Dermatology Life Quality Index (DLQI, Finlay 2005) but none have been specifically designed for vulval skin conditions. Dermatology QoL questionnaires have been used alongside other sexual function scales in disease specific vulval QoL papers (Van de Nieuwenhof 2010), Other studies have looked specifically at QoL and vulval pain (Sargeant 2007, Marriot 2008).

Through personal communication with members of the UK Lichen Planus support group, we found that patients with vulval erosive lichen planus (ELPV) did not feel that the DLQI accurately reflects the true effect of their disease as its scope is too general (Simpson 2012). The outcomes most important to patients in this ELPV group were improvement of pain, physical appearance, scarring and sexual functioning. Many patients found their treatments were ineffective at reducing distressing symptoms and did not enable them to lead a normal lifestyle.

Although previously published studies looking at vulval conditions (vulval pain, (Sargeant 2007), lichen sclerosus (Hedwig 2010), genital psoriasis (Meeuwiss 2011)) have utilised a variety of validated scores incorporating sexual function and QoL, we believe that, a generic vulval disease validated questionnaire which can be used in clinical practice is lacking.

2. Objectives

To map which outcome measures have been utilised in randomised controlled trials that investigate the treatment of vulval skin conditions.

3. Methods

Vulval conditions to include

Vulval skin conditions where assessment of clinical severity and/or patient reported outcomes are documented. These may include:

- Inflammatory disease – e.g. eczema/dermatitis, psoriasis, lichen sclerosus, lichen planus;
- Non inflammatory disease – Vulval intraepithelial neoplasia, vulval cancer, extramammary paget's disease;
- Vulval pain syndromes – vulvodynia, vestibulodynia.

N.B. These lists of conditions are not exhaustive and if other vulval skin conditions are identified in trials, these too will be considered.

Exclusions

- Papers where the **primary** outcomes are:
 - Determined by laboratory tests (e.g. histopathological specimens, microbiological tests);
 - Determined by survival rates;
 - Pertaining to cervical disease;
 - Pertaining to menopausal symptoms;
 - Pertaining to infective conditions.
- Papers which do not have clinically assessed or patient-reported outcomes in the title/abstract

Types of studies

Randomised controlled trials that evaluate the effectiveness of any intervention for vulval/vaginal skin conditions will be considered. Non-randomised studies will be excluded.

Types of participants

Any female with a vulval skin condition (as outlined above), who has been diagnosed by a health care professional.

Types of Interventions

We will include all types of topical, intralesional, systemic and surgical treatments that have been used in trials of the above mentioned vulval conditions.

Types of outcome measures

The purpose of this systematic review is to summarise to date which outcome measures have been used in randomised clinical trials of interventions for vulval skin conditions. As we are practitioners of clinical dermatology, we will look at all outcome measures that have been used in trials to assess response to treatment. However, trials which report the **primary** outcome measure as survival rates (as these relate to the management and cure of malignancy, which is treated by related surgical specialties), histological confirmation of outcome (as this does not reflect usual dermatological practice) or resolution of infection (e.g. vulvovaginal candidiasis) as an outcome will be excluded.

Search methods for identification of studies

Electronic searches

We will search for relevant trials in:

The Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* (last update)

MEDLINE

EMBASE

No time limit will be placed on the searches.

Searching other resources

We will also search reference lists of relevant trials identified.

Language

Papers with full text not available in English will be excluded.

Data extraction and management

A paper data extraction form will be designed according to the pre-defined selection criteria. Two authors will independently extract data. Differences in opinion will be resolved by discussion with a third author until a consensus is met. Logs of excluded studies with reasons for exclusion will be kept.

Dealing with missing/unclear information

We shall contact the trial authors to try to obtain information that has not been fully reported and is therefore unclear.

Future work

We will go on to discuss the most commonly used outcome measures in focus groups with patients to assess which are most important (or relevant) from the patient perspective. Following future consensus work we hope to be able to recommend a core set of outcome measures that can be used in future trials of interventions for vulval conditions. If the measures that are currently available are considered unsuitable, we will work on developing and validating our own scale.

References

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Other relevant references:

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Data Abstraction Form

Trial I.D:

First Author	
Year	
Country	
Vulval condition being investigated	
Study interventions	
Is the trial blinded (description of blinding)	
Duration of trial	
Primary outcome(s) specified?	Y/N (if NO assume the first reported outcome in results is the designated primary outcome)
Primary outcome (put as outcome A)	
Number of participants randomised	
Primary outcome	
Outcome A	
Scales or categories used for outcome A	
Has it been used previously?	Y/N/Unclear
Outcome assessed by Patient?	Y/N/Unclear
Outcome assessed by Clinician?	Y/N/Unclear
Outcome assessed by digital image?	Y/N/Unclear
Comments on outcome A	
What time point(s) was outcome A assessed?	weeks
Secondary outcomes	
Outcome B	

Scales or categories used for outcome B	
Has it been used previously?	Y/N/Unclear
Outcome assessed by Patient?	Y/N/Unclear
Outcome assessed by Clinician?	Y/N/Unclear
Outcome assessed by digital image?	Y/N/Unclear
Comments on outcome B	
What time point(s) was outcome B assessed?	weeks

Continue form to include *all secondary outcome measures*

Paper Screening Form for articles reviewed in full text

Paper I.D.	Author	Article Title	Journal/ Reference	Outcome of full text review		Data abstraction	
				Included	Excluded (reason)	Reviewer 1	Reviewer 2