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| Host department: Nottingham |
| Project Title: |
| Identifying core instruments for inclusion in the core outcome set for research in lichen sclerosus (CORALS) |
| Proposed supervisory team:  Professor Kim Thomas: Professor of Applied Dermatology Research, Co-Director of Centre of Evidence Based Dermatology. Expertise includes research methodology, clinical trials prioritisation and development, diagnostic test accuracy studies, outcome measurement generation and assessment.  Dr Rosalind Simpson : Associate Professor and Consultant Dermatologist. Expertise includes women’s health, clinical dermatology, outcome measurement, disease definition, designing clinical trials. |
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| Potential for cross consortium networking and educational opportunities: |
| Links to dermatology clinical department and the educational programme that takes place twice monthly at Nottingham University Hospital.  Links to multidisciplinary societies passionate in women’s health including clinically relevant conferences and meetings.  Networking through the Centre of Evidence Based Dermatology (CEBD) with opportunity to link with primary care collaborators both in Nottingham and nationally. This includes the Primary Care Dermatology Society and Society of Academic Primary Care Specialist Interest Group (SAP SIG). The CEBD has experts in community pharmacy, statistics and qualitative research and citizen science where the student will have opportunity to understand ongoing projects in these different areas of dermatology.  Educational opportunities through the UK Dermatology Clinical Trials Network and CEBD research clubs. |
| Project description:  Background  Lichen sclerosus (LS) is a chronic inflammatory condition which predominantly affects genital skin. It causes distressing symptoms as well as having a significant impact on quality of life. Inflammation can cause scarring with irreversible anatomical changes and approximately 5% of cases progress to develop cancer. Several types of treatment are available for LS and they are aimed at symptom relief, reducing progression of scarring, minimising cancer risk and maintaining normal daily function. One of the main limiting factors in pooling data from multiple RCTs and conducting meta-analyses is the variation in outcome measures selected to capture treatment effects, and differences in how and when these outcomes are measured. CORALS (Core Outcomes for Research in Lichen Sclerosus) is a global collaborative network to agree a core outcome set for LS. The collaboration includes patients, clinicians, pharmaceutical industry representatives and regulators. For more information about CORALS please see: [CORALS - The University of Nottingham](https://www.findaphd.com/common/clickCount.aspx?theid=145665&type=184&DID=7004&url=https%3a%2f%2fwww.nottingham.ac.uk%2fresearch%2fgroups%2fcebd%2fprojects%2f5rareandother%2fcorals.aspx).  CORALS has identified, by international consensus, three core outcome domains (‘what’ to measure in LS clinical trials). These core domains are symptoms, clinical signs and quality of life. The next stage is to identify outcome instruments which will be used to measure the domains (‘how’ to measure). The proposed series of linked studies, which make up this PhD, will finalise the core instrument for a chosen domain.  Aims and objectives  Aim: To finalise the core instrument for one of the CORALS agreed outcome domains  Objectives: This project will follow established methodology for core outcome set development:   1. Identification of all possible outcome instruments via systematic literature review. 2. Quality assessment of the identified instruments’ psychometric properties using the COSMIN critical appraisal tool checklist. 3. Qualitative study to establish the identified instruments’ validity and feasibility via patient discussion groups. Narrow the long list of potential instruments down to short list. 4. Address validation gaps in the short list of potential instruments via multicentre longitudinal observational clinical study. 5. If no suitable instruments are identified, the student will consider the development of a novel outcome scale for LS   Method(s)  Stage 1: Through a systematic review the student will identify all outcome measurement instruments that are available to assess the chosen domain. The systematic review protocol will be prospectively registered with PROSPERO. The review will include assessment of previous randomised controlled trials for LS as well as performing a systematic review of published scales for vulval skin conditions. To run the search strategy, COSMIN guidance and a Patient-Reported Outcome Measure filter (University of Oxford) will be implemented in at least three databases with assistance from an Information Specialist. Data will be extracted by two researchers who will independently complete a standardized proforma. Any difference in opinion will be adjudicated by a third researcher.  Stage 2: For each outcome measurement instrument identified in stage 1, the extent and quality of testing of the measurement properties will be determined. To accurately assess the instruments’ psychometric properties, the COSMIN critical appraisal tool checklist will be used. Measurement properties that will be assessed in the following order of importance: Content/face validity (the degree to which the instrument measures what it is meant to), feasibility (can the instrument be applied easily in the clinical setting), internal structure (structural validity and internal consistency). The remaining psychometric measurement properties (reliability, measurement error, hypothesis testing, cross-cultural validity, construct validity and responsiveness). If content validity is not clear, the assessment of other measurement properties will not be undertaken. For those where content validity is clear, if the instrument is not feasible as part of a core outcome set, or internal structure is poor then further evaluation will not take place. It is possible that gaps of validation will be identified during this stage and will need to be later addressed (stage 4).  Stage 3: Whole and small group discussions with patients will take place, with support of additional facilitators experienced in running discussion groups. Participants will be encouraged to think about the feasibility of identified the outcome measure instruments from stage 1, followed by whole group feedback and discussion. Each small group will be asked to evaluate and rank the instruments according to content/face validity and feasibility, prior to whole group feedback and discussion. Results will allow shortlisting of instruments to be tested further in a longitudinal clinical study.  Stage 4: In a UK based, potentially multicentre, observational longitudinal study, involving up to 100 patients, the short list of outcome measure instruments from stage 3 will be applied over a 6 month period to establish missing validation criteria. Psychometric properties such as content validity, construct validity, responsiveness to change will be collected during patient’s usual clinical visits at baseline, 3 and 6 months.  Stage 5: Instruments from stages 1-4 that meet essential validity criteria will be discussed and voted upon at international consensus meetings. Participants in the meetings will be multidisciplinary stakeholders, including patients. This will determine which outcome measure instrument will be agreed to be included in the final LS core outcome set. If no instruments in stages 1-4 meet essentially validity criteria, the student will be supported to consider how to develop a new instrument in the specific outcome domain.  Impact  By engaging with the international community of multidisciplinary stakeholders, the student will promote their work and the CORALS core outcome set globally. The outcome instrument identified through the PhD will be recommended for use in all future LS trials. By defining a core outcome set in LS, results from different trials will be compared more easily and the quality of trials will be improved, translating to better evidence based care in this field. |

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| Training and development provision by host: |
| **Formal training:**   * BEES (Better Evaluation of Evidence and Statistics) course – 3 day course held by the CEBD * Nottingham Systematic review course * COSMIN (COnsensus-based Standards for the selection of health Measurement Instruments) clinimetrics 3-day online course |
| **Informal training:**  This project would give the successful applicant the opportunity to learn skills in:   * Conducting systematic reviews * Development of outcome scales for use in clinical research * Testing psychometric properties of scales * Designing and conducting studies to evaluate psychometric properties (including qualitative and quantitative studies) * Statistical techniques * Consensus methodology * Patient and public involvement |
| **PPIE:**  Patients are a key stakeholder in the COS development process. The CORALS steering group has 3 engaged patient members whom the PhD student will liaise with during the course of the project. All CORALS consensus meetings will have patient involvement and the student will be involved in organising these meetings and therefore ensuring good patient participation.  The CEBD has a strong and active Patient Panel, led by Dr Carron Layfield. The student will have opportunity to engage with this group and attend Patient Panel meetings. In addition, the COMET group (Core Outcome Measures for Effectiveness Trials) have a PPIE group in which the student can engage for support. |