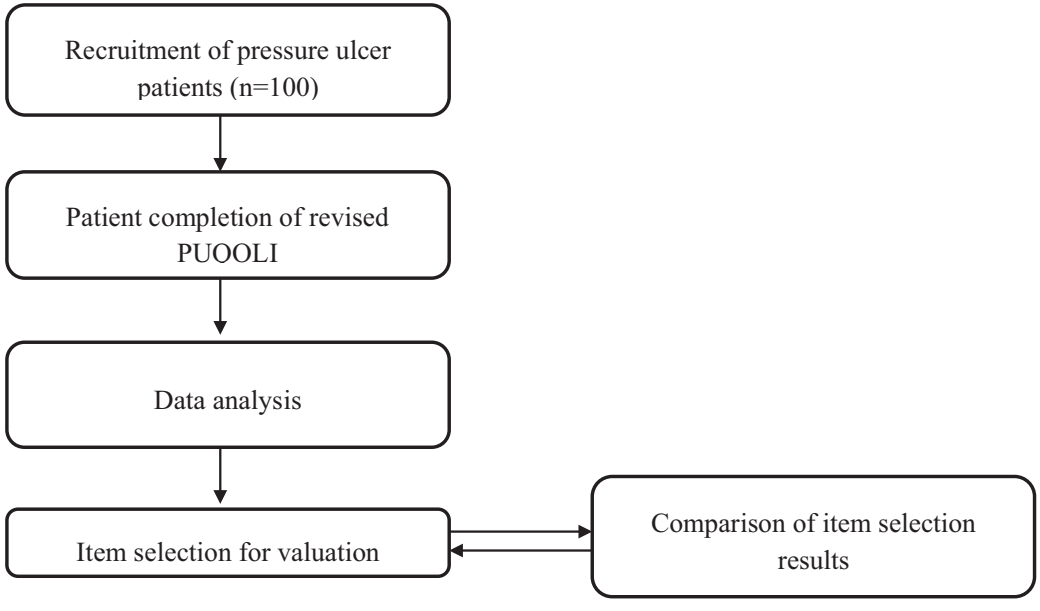
NB: This study protocol (version 6, dated 13 Jun 2013) is in a reduced format including only the study aims, methods and ethical considerations. Sections pertaining to study background have been removed as they are included as a chapter section. Information pertaining to data monitoring, quality assurance, confidentiality, archiving, statement of indemnity, study organisational structure, funding, and publication policy are available upon request.

Study Flow Diagram



Aims and Objectives

The overall aim of the project is to generate data using the revised version of the PUQoLI measure to enable item reduction analysis and a comparison of item selection methods.

1. To generate data on the new PUQoLI via a patient survey.
2. Conduct item selection analysis using the data.
3. Compare the items selected for the reduced PUQoLI from this and previous analyses.
4. Conduct additional methodological work such as mapping from the EQ-5D and from time-trade off values to the revised PUQoLI.

Methods

Item Selection and Health State Generation

A sample of patients with PUs will complete the interview administered measure either in hospital or in the community. In order that we are able to compare the item selection results across studies, the samples that provide the data have to be comparable in terms of PU severity, demographics (i.e. age and gender) and location of the participant (community or hospital). Sample size is not critical as it will be possible to randomly select a subsample from the original dataset (and rerun the analysis) to match the – likely - smaller dataset we will generate from this study.

The sample used for the original item selection are shown in the table below:

N = 229	N (%)
Gender	
Male	119 (52%)
Female	110 (48%)
Age	
Under 70 years	90 (39.5%)
70 years and over	138 (60.5%)
PU grade	
Superficial	115 (50%)
Severe	94 (41%)
Mixed	20 (9%)
Setting	
Hospital	141 (62%)
Community	88 (38%)

Sample size

The sample size is dependent on that required to obtain robust estimates from the Rasch analysis. Linacre (1994) proposed that for most purposes a sample size of 150 (n range, 108-243) will provide 99% confidence of item calibration of +/-0.5 logits and a sample size of 100 (n range, 64-144) will provide 95% confidence of item calibration within +/-0.5 logits. In this study we will aim for 95% confidence and therefore a sample of 100 patients.

Eligibility and Recruitment

Members of the tissue viability team (TVT) which includes the local Principal Investigator, tissue viability nurse specialists, nurse consultants, and other members of their local clinical team (i.e. tissue viability and clinical research nurses) at participating trusts will identify potential patients.

Eligibility

Patients from participating acute and community NHS Trusts, with existing PUs, will be included in the study if they are hospital in-patients or outpatients, intermediate care patients, or community patients under the care of community care nursing services, and they fulfil the criteria detailed below. We will ensure representation of patients from all PU categories (Categories 1-4/U) and treatment types. Consecutive patients will be identified from each PU category and approached to participate. Recruitment will continue on a rolling basis until a minimum of 10 patients from each PU group are recruited and interviewed.

Inclusion criteria

- aged ≥18 years **and**
- with an existing PU of any grade, location, or duration **and**
  Give their written informed consent/verbal witnessed consent Exclusion criteria

Patients will be excluded from the study if any of the following criteria apply. They:

- have only moisture lesions
- are unconscious or confused
- have cognitive impairment
- do not speak or understand English
- they do not have an existing PU **or**
- are unable to provide informed consent

Patients who are deemed ethically inappropriate to approach by members of the TVT, for example, those where death is imminent (any patient who is on or meets the criteria of the Liverpool Care Pathway for the dying) will not be approached.

To clarify, those not deemed ethically appropriate is a clinical judgement about the appropriateness of approaching patients who are very seriously ill or distraught. For example,

patients where death is imminent (any patient who is on or meets the criteria of the Liverpool Care Pathway for the dying) will not be approached or in other circumstances (personal to that patient) where it is considered inappropriate (for example, distraught due to a recent bereavement).

In addition the assessment of capacity will relate specifically to decisions pertaining to this particular research project. Each patient will be assumed to have capacity unless it is established that they lack capacity. Ward/community based nurses identifying patients for study participation, will be asked to consider aspects of capacity before any approach to patients is made and during the information giving stage prior to consent. The TVT member will assess the patient's ability to understand what decisions they need to make and why; the consequences of the decision to participate; their ability to understand, use and retain the information related to the decision to participate and be able to communicate their decisions effectively (as specified in the Mental Capacity Act 2005) If there is any concern about capacity the TVT member will consult with other members of the attending clinical team and/or relative/carer/friend (as appropriate) and a decision will be made with the attending clinical team/relative/carer/friend as to whether the patient is able to provide written consent.

Recruitment and consent procedures

Potential participants will be identified by the direct care team from their local area of practice. A record of those identified as eligible, approached to participate, refusals, consenting patients and questionnaire returns will be made. A verbal explanation of the study and Patient Information Leaflet will be provided by the TVT member for the patient to consider. This will include details about the rationale, design, and personal implications of the study.

Following information provision, patients will have as long as they need to consider participation and will be given the opportunity to discuss the study with their family and other healthcare professionals before they decide whether they would be willing to take part in the study. Assenting patients will then be invited to provide informed, written consent. Should the patient be capable of giving consent but are physically unable to complete the written aspects of the consent form, witnessed consent should be obtained using the Witnessed Consent Form. An appropriate witness would be a family member or friend of the

patient, or another member of the patient's healthcare team who is not directly involved in the research study.

The researcher is required to utilise all possible methods to ensure that no patient feels pressurised to take part in the study. This will include emphasising that participation is entirely voluntary and that participants are free to withdraw consent at any point up to, during or following the survey. The right of the patient to refuse consent without giving reasons will be respected. Further, the patient will remain free to withdraw from the study at any time, without giving reasons and without prejudicing any further treatment. After signing the consent form patients will be handed the questionnaire schedule to complete.

To clarify, potential participants will be identified by the direct care team from their local area of practice. The direct care team includes ward and community staff. For some patients the direct care team also includes members of the Tissue Viability Team (i.e. if the patient is under the care of the Nurse Consultant/Nurse Specialist, they are part of the direct care team).

Where the patient is not under the care of the Tissue Viability Team, ward/community staff will identify potential participants, and obtain verbal assent for a visit by the Tissue Viability Team (Nurse Consultant/Specialist/Research Nurse) to discuss the possibility of study participation and flag the patient to the Tissue Viability Team.

Where the patient is under the care of the Tissue Viability Team (Nurse Consultant/Specialist) they will either discuss study participation with the patient (providing a full verbal explanation of the study and Patient Information Leaflet) or obtain verbal assent for a visit by the Research Nurse.

Registration

Patients will be registered with the CTRU following informed consent and confirmation of eligibility. The CTRU will issue a study identification number which includes centre code. Registration will include centre, confirmation of eligibility, confirmation of consent, date of birth, gender, PU grade and patient location (community or hospital). The data will be used for central monitoring of recruitment. CTRU will also be responsible for accrual recording with the NIHR.

Screening

The TVT member will complete a log of all patients screened for eligibility who are not registered either because they are ineligible or because they declined participation. All anonymised screening logs will be returned to the AUHE.

Anonymised information will be collected including:

- The reason not eligible for study participation or
- Eligible but declined
- Date of Birth
- Gender
- Ethnicity
- Pressure ulcer grade and location

Survey

The survey will be administered by a research nurse. The surveys will be completed in the out-patient clinic, in-patient ward or in the community as determined by the patient's circumstances and preferences at the time.

Study participants will complete the revised PUQoLI, the EQ-5D (a five-item health-related quality of life questionnaire) and EQ-VAS (a 0-100 health rating scale) (EuroQoL, 1990) and a set of socio-demographic and PU-related questions. They will also complete a paper version (Robinson, 2010) of the time trade off (TTO) task (Torrance, 1972). The TTO asks about how much time the patient would be willing to trade off in exchanging their current health status for full health. This will provide additional useful information in valuing the PUQoLI.

It is anticipated that the survey will take approximately 25 minutes to complete. A user manual for the PUQoLI is available and should be used with any queries relating to completion of that measure.

Analysis

Item selection

In the first instance, one item representing each of the ten PUQoL instrument constructs will be chosen. Items will be selected on the basis of traditional psychometric analyses and Rasch analyses.

Rasch analysis (Rasch, 1961) is now seen as the method of choice for the development and improvement of questionnaires as it has several advantages over Classical Test Theory approaches such as factor analysis (Wright, 1996; Wright and Tennant, 1996; Luquet et al., Prieto et al., 2003; Tennant et al., 2004; Waugh and Chapman, 2005; Nijsten et al., 2006a). Rasch is often the method employed to identify reduced forms of measures that will be used in preference valuation studies. (e.g. Brazier et al 2012; Kowalski et al, 2012; Mulhern et al, 2012) The Rasch model is a simple logistic latent trait Item Response Theory model. Rasch analysis places response data for each individual and each item on the same spectrum of severity (logit scale). According to the model, the probability that an individual will respond in a certain way to a particular item is a logistic function of the relative distance between the item location (parameter) and the person location (parameter), and only a function of these two factors. Persons and items are plotted on the same logit scale on the basis of the difference in their location on the underlying spectrum. This difference governs the probability of the expected response for a person, of a given severity, on a question of a given severity. If the observed data do not deviate significantly from the expected responses, then the items fit the Rasch model.

Criteria for item selection:

Rasch measurement method analyses –

- Degree of fit to the Rasch model (Rasch, 1961) – Chi^2 probability and fit residual (items with non-significant Chi^2 and residuals $<\pm 2.5$ are candidates)
- Differential item functioning (DIF) based on age and gender such that bias by these factors is minimised (items with no DIF are candidates)
- Item logit position on each construct's measurement continuum such that items with a range of severity (spanning the entire measurement range) can be identified (items that collectively represent a wide spread of the latent trait are candidates)
- Disordered response category thresholds (items with correctly functioning response categories are candidates)

Traditional psychometric analyses –

- Distribution of scores and presence of floor/ceiling effects (items with no floor/ceiling effect are candidates)
- Item-to-total correlation (items with ITC 0.2-0.8 are candidates)
- Principal components factor analyses (items having a moderate-high factor loading within a subscale being candidates)
- Ability to discriminate between pressure ulcer severity groups – T-tests for superficial vs severe PU patient scores (highly discriminatory items are candidates)
- Pearson correlations with EQ-5D and global PUQoL-I item ("How would you rate your overall QoL because of your pressure sore(s)") (items with moderate-high correlations are candidates)

The final selection of items will be compared with those selected from earlier analyses (and based on the PU-attributable data). The performance of each in terms of the above criteria will be described and compared across analyses.

Mapping analysis

In addition to the item selection analysis we will also conduct a mapping analysis (Brazier et al, 2010) whereby regression techniques are employed to predict the EQ-5D scores and TTO responses using responses on the PUQoLI (and other factors such as age and gender).

This would generate an algorithm that would allow the indirect estimation of utility values from the PUQoLI.

Data Monitoring

Data will be monitored for quality and completeness by the project team (PT). The PT will liaise with nurses to ensure that the sample recruited matches as far possible that used for the original analyses. The proportion of males/females, different PU grade and location (hospital/community) of recruited patients will be monitored to enable this.

Ethical considerations

This study will include elderly and highly dependent patients considered as vulnerable. Ethical issues are largely related to the involvement of vulnerable adults/elderly patients with

high levels of co-morbidity including acute and chronic illness. Clinically, older patients are treated in the same way as younger patients and it is therefore important to ensure that the study is representative of the clinical population. In addition, the survey requires the patient to reflect on their experience of having a PU and for some people this may raise topics considered to be sensitive, embarrassing or upsetting, and possibly emotionally distressing.

Ethical issues are largely related to the involvement of vulnerable adults/elderly patients with high levels of co-morbidity including acute and chronic illness. The ethical issues surrounding these potentially vulnerable patients have been addressed through the design of the recruitment process which uses local staff and includes experienced clinical nurses to help with recruitment and we will provide a caring and supportive environment in which to discuss any sensitive issues that may arise. If the patient becomes distressed during survey completion, then the nurse will immediately stop the interview/survey. It will be stressed to all patients that they are able to withdraw from participation at any time without giving reason, and without any effect on their care. They will be referred back to their treating nurse specialist if required.

No treatments or procedures are incorporated into the PUQALY study design so there is minimal risk to the patient sample. Participants will be made aware that they free to leave the study or discontinue at any time without their future care being affected.

The study will be performed in accordance with the recommendations guiding physicians in biomedical research involving human subjects adopted by the 18th World Medical Assembly, Helsinki, Finland, 1964, amended at the 52nd World Medical Association General Assembly, Edinburgh, Scotland, October 2000. Informed written consent will be obtained prior to involvement into the study. The right of a patient to refuse participation without giving reasons will be respected. The study will be submitted to and approved by a main Research Ethics Committee (main REC) and the appropriate Site Specific Assessor for each participating centre prior to entering patients into the study. The PT will provide the main REC with a copy of the final protocol, patient information sheets, consent forms and all other relevant study documentation.

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