NB: This study protocol (version 5, dated 8 Mar 2010) 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 adverse events, confidentiality, archiving, statement of indemnity, study organisational structure, and publication policy are available upon request

4 AIMS AND OBJECTIVES

4.1 Study aim

The aim of this study is to develop a psychometrically rigorous, self-report patient-reported outcome (PRO) measure of health-related quality of life (HRQL) in pressure ulcer (PU) patients (PU-QOL) that is acceptable to patients, reliable, valid, and suitable for use in clinical trials, epidemiological studies and in the NHS. The perspective of persons with PUs will be central in all stages of questionnaire development and evaluation. Collaboration has been sought from members of the European Pressure Ulcer Advisory Panel (EPUAP) and from various acute and primary care NHS Trusts around the UK. Ethical approval is sought to undertake phases 2 and 3 of the development and evaluation of this measure.

5 STUDY DESIGN

5.1 Overview of project research design

This multi-centre study is designed to develop and evaluate the psychometric properties of a PU-specific HRQL instrument for patients with PUs. Guidance for developing and validating health outcome measures have been consulted to ensure high quality and standardisation for the development of the PU-QOL instrument [24-26]. The guidance recommends that collaboration and expert discussion is sought and utilised through all stages of instrument development and it proposes distinct phases for the development of a PRO measure.

The research design for the PUQ-OL instrument is based on the recommended guidance and will be developed in 3 phases: 1) conceptual framework; 2) generation of items for the PU-QOL instrument and pre-testing; and 3) PU-QOL evaluation in 2 parts, a preliminary field test 1 for item reduction and a final field test 2 for psychometric properties.

Phase 1 has been conducted. A conceptual framework has been developed by tapping into 3 sources. Firstly, a systematic review and narrative analysis of HRQL outcomes literature (i.e. symptomatic consequences such as pain, foul smell, comfort/discomfort) relevant to PU interventions and patient experiences of living with a PU has been undertaken. Secondly, in-depth qualitative interviews with a sample of PU patients, and thirdly, information obtained from the systematic review and qualitative interviews produced a conceptual framework.

Phase 2 of this project will be the development and pre-testing of the provisional PU-QOL instrument. Items will be generated from the conceptual framework and patient verbatim. The provisional instrument will then be reviewed for clarity and overlap by the project team and members of the collaborating expert group. Once expert consensus is achieved and the pre-test version of the instrument is developed, pre-testing will be undertaken by interviewing a small number of patients using cognitive interview techniques. This process will assist in clarifying any ambiguities in item wording and evaluate the appropriateness of the instruments' time-frame, question stem and response options. Based on information obtained from the cognitive interviews, the provisional PU-QOL will be revised to produce a preliminary version ready for field testing.

The evaluation of the PU-QOL instrument is phase 3 of this project. It will be undertaken in 2 parts: preliminary field test 1 (item reduction) including a mode of administration sub-study (refer to Appendix 1); and final field test 2 (psychometric properties). The preliminary field test will identify any items with poor psychometric performance for possible elimination. The final stage field test will be undertaken to evaluate the item-reduced version of the PU-QOL instrument for reliability, validity, and responsiveness. Gold standard psychometric methods [27-31] will be used to evaluate the PU-QOL to ensure rigour and scientific credibility.

6 PHASE 2: PRE-TESTING

6.1 Design for Pre-Test

Principles of Cognitive Aspects of Survey Methodology (CASM) [32] have been employed in the design of this phase. Cognitive pre-testing methods (interviews with patients) will be used to indicate how respondents interpret questions, response categories, and to prepare instructions for how to formulate their responses.

6.2 Eligibility

6.2.1 Inclusion criteria

Patients from participating acute and community NHS Trusts, with existing PUs (any grade, see Table 1), 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 following criteria:

- aged ≥18 years **and**
- with an existing PU of any grade, location, or duration **or**
- a PU that had healed within previous 3 months **and**
- able to provide written informed consent to participate **and**
- able to read and write in English

6.2.2 Exclusion criteria

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

- have only moisture lesions
- are unconscious or confused
- have cognitive impairment
- are unable to speak, read and/or write in English
- they do not have an existing PU or one that healed within previous 3 months
- are unable to provide informed consent

Table 1 EPUAP Pressure Ulcer Classification [5]

Grade 1	Non-blanchable erythema of intact skin. Discolouration of the skin, warmth, oedema, induration or hardness may also be used as indicators, particularly on individuals with darker skin.
Grade 2	Partial thickness skin loss involving epidermis, dermis, or both. The ulcer is superficial and presents clinically as an abrasion or blister.
Grade 3	Full thickness skin loss involving damage to or necrosis of subcutaneous tissue that may extend down to but not through underlying fascia.
Grade 4	Extensive destruction, tissue necrosis, or damage to muscle, bone, or supporting structures with or without full thickness skin loss.

Patients who are deemed ethically inappropriate to approach by members of the Tissue Viability Team (TVT) (see section 6.4), 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.

6.3 Methods

The provisional questionnaire will be pre-tested with a sample of patients. We estimate that approximately 40 patients will be needed to reach saturation (no new issues arising). This process is intended to clarify ambiguities in item wording and to evaluate questionnaire length, time-frame, question stem and response options, and to address any additional queries that participants may raise. Standard one-to-one cognitive interviewing techniques will be used by the researcher Claudia Gorecki (CG), who has training and experience in conducting patient interviews, to gain a better understanding of how respondents interpret questions and whether questions are understood in the way that they are intended.

This involves the researcher (CG) asking respondents to complete the questionnaire on their own but throughout completion they will be required to flag/mark any items that they find are annoying, upsetting or intrusive, or confussing/difficult to understand. After completion of the questionnaire, de-briefing questionning will be used by CG which include the use of general and specific questions and probes to: i) clarify ambiguities and/or misunderstandings in item wording; ii) identify items judged by the respondent to be either irrelevant or relevant but not included; and iii) questions relating to time-to-complete, ease of response, and whether any questions were confusing or upsetting to patients to determine instrument acceptability. De-briefing questioning will be guided by an interviewers' manual to ensure standardisation across administration.

In addition to the cognitive interviews, we will use a computerised appraisal tool, the Questionnaire Understanding Aid (QUAID) [33], to identify problems with question comprehension, including unfamiliar technical terms, vague or imprecise relative terms, vague or ambiguous noun phrases, complex syntax, and working memory overload. Results of pre-testing will be used to revise the provisional questionnaire to produce a long version of the PU-QOL for field testing. The qualitative comments made will be recorded and

reviewed. Expert opinion will be sought and appropriate revisions and modifications to the provisional questionnaire will be made based on the patient and professional recommendations.

6.4 Recruitment and consent procedure

Patients will be purposively sampled (up to 40 patients) ensuring representation of patients from all PU categories (grades 1-4, Table 1) 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 5 patients from each PU group are recruited and interviewed. A sample size of up to 40 patients will allow for any initial changes to the interview schedule should they be required following the first few interviews and will ensure that saturation is met with no new major issues emerging.

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. A record of those identified as eligible, approached to participate, refusals, and consenting patients will be made (see section 6.4.1).

Patients that meet the eligibility criteria will be approached, informed about the study, and provided with a project information leaflet which includes details about the rationale, design, and personal implications of the study, and an 'agree to be contacted by the researcher' form to be either contacted by telephone or visited at the ward.

Following information provision, patients will have as much time as they need to complete the 'agree to researcher contact' form, which will be either faxed or posted back to the Clinical Trials Research Unit (CTRU). Members of the TVT, the researcher, and the project Chief Investigator (CI) will be available to answer any questions that patients might have about the study. After receiving a signed agreement to be contacted form from the patient, the researcher will telephone the patient to arrange a time for the interview. The researcher will provide information about the study and interview process, will answer any questions about the research, and remind the patient that participation is completely voluntary and that they are free to withdraw taking part at any time, before gaining verbal consent and arranging

an interview at a mutually convenient time. For in-patients who cannot be contacted by telephone and who are expected to be in the hospital during the interview, the TVT member will (with the patient's permission) liaise with the researcher and patient to arrange a mutually convenient time for the researcher to see the patient on the ward to discuss the study further.

The researcher (CG) will interview patients in their own home (following standard safe practice SOP), in the out-patient clinic, or in-patient ward as determined by the patient's circumstances and preferences at the time of the interview. It is anticipated that a similar number of community and hospitalised patients will be interviewed.

Before the interview, each participant will be given a further verbal explanation of the study by the researcher; informed that the interview will be recorded but that all identifiable information will remain anonymous; reminded that participation is completely voluntary and that they can withdraw from the study at any time without it affecting their care; and invited formally to participate. They will be given an opportunity to ask any questions and then if they agree to take part, the participant will be asked to sign the consent form. A copy of the consent form will be given to the patient to keep, one filed in the patients' health care record, and the original copy kept by the researcher to take back to the CTRU.

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 interview. 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, again, without giving reasons and without prejudicing any further treatment.

6.4.1 Non-registration

The TVT member will complete a log of all patients screened for potential participation. Anonymised information will be collected including:

- The reason not eligible for study particpation
- Eligible but declined
- Date of birth

- Gender
- Ethnicity
- Pressure ulcer grade and location

6.5 Data collection

Participants will complete the provisional questionnaire on their own but will be asked to flag/mark any items that are annoying, upsetting or intrusive, or confusing. Following completion, the researcher, guided by a standard set of questions and probes, will seek to elicit the cognitive processes employed by the participant while completing the provisional questionnaire. Data collected will relate to feedback on participants' understanding of each question and associated response category and instructions, and to verbalise how they had gone about producing their answers, with particular emphasis on retrieval from memory and subsequent judgements and decisions [32].

Questionnaire completion and follow-up interview may take around 40-60 minutes and will be discontinued at any time if participants are unable to go on or wish to discontinue. The interviews will be conducted, recorded, and analysed by CG with supervison from experienced researchers (AEN, DL), who will undertake quality assurance.

6.5.1 Baseline data

Following questionnaire completion and specific probing, the researcher will record the following information as provided by the patient:

- Patient initials and date of birth
- Gender
- Ethnicity
- Pressure ulcer grade, location and number of pressure ulcers
- Duration of pressure ulcer
- Treatment plan (information about which treatment interventions the patient is currently receiving)
- Co-morbidity and/or speciality (i.e. spinal cord injured, trauma, vascular, care of the elderly ward)

6.6 Data analysis

Review and analysis of information collected from cognitive interviews will be conducted as soon as possible after the interview, but at minimum after every 3 interviews. This will enable any major flaws in the provisional questionnaire to be identified and revised prior to subsequent testing with the revised version. This form of multiple rounds of testing will determine whether the problem identified has indeed been rectified and no new problems introduced.

A systematic way of evaluating questionnaires will be developed to ensure that each questionnaire item was assessed systematically. An appropriate tool, the Question Appraisal System (QAS-99) [34] will be used to categorise item problems identified during the cognitive interview process. The QAS-99 consists of eight major categories that focus on question characteristics that are likely to present problems when completing and forming responses to questionnaires.

Review and analysis will involve the researcher listening to the recorded interview and making structured contemporaneous notes of specific problems identified based on the categories of the QAS-99 appraisal tool. Specifically, focus will be on identifying dominant trends (problems occurring repeatedly) across interviews, and key findings (problems that may only be identified in a single interview, but have the potential to cause serious problems). Comments made, both within and across interviews, will be aggregated so that they can be used to review the provisional questionnaire. In addition to cognitive pre-testing, expert appraisal of the provisional questionnaire will inform revisions.

7 PHASE 3: FIELD TESTING

The psychometric properties of the PU-QOL will be evaluated through two-stage field testing including a preliminary field test (item reduction) to identify items with poor psychometric properties for possible elimination and identify subscales, and a final field test (psychometric evaluation) to evaluate the reliability and validity of the item-reduced version of the PU-QOL. The overall strategy and methods for the psychometric evaluation of PU-QOL are based on the methods used to develop and validate PROs in several other areas of medicine and surgery [27,28,31,35].

7.1 Design for preliminary field test 1 (item reduction)

The purpose of the preliminary field test 1 is to produce a short (item-reduced) version of the PU-QOL from the provisional version and to undertake an initial psychometric evaluation of the item-reduced questionnaire.

An item reduction strategy developed for evaluation of PROs in other medical areas [27-31] will be used to: i) identify items on the provisional version of the PU-QOL with poor psychometric properties for possible elimination; ii) conduct a preliminary evaluation of PU-QOLs' subscales; and iii) undertake a preliminary evaluation of the acceptability, reliability and validity of the item reduced PU-QOL. Results of the item reduction analyses will be used to develop a shorter version of PU-QOL for final psychometric field testing.

In addition, to address methodological issues identified from the pre-test phase relating to patient difficulties in self–completion, a mode of administartion sub-study will be undertaken to determine the mode of administration in which the questionnaire will be developed and validated (ie both self-complete and interview-administered modes or interview-administered only) (see Appendix 1 for details of the sub-study).

There are two possible outcomes from the sub-study:

1) One questionnaire can be developed and psychometrically evaluated for use with either of the two modes of administration (i.e. self-complete and interview-administered modes) or;
2) Two mode-specific questionnaires are required.

If the analysis of the sub-study finds that one questionnaire can be developed for use with either mode of administration, all of the following sections of the protocol will apply. If the analysis finds that two mode-specific questionnaires are required, only the interview-administered sections of the subsequent protocol will apply.

7.2 Eligibility

Patients from participating acute and community NHS Trusts, with existing PUs (any grade, see Table 1), will be included in the study if they are hospital in-patients or outpatients, intermediate care patients, nursing home patients or community patients under the care of community care nursing services, and they fulfil the criteria detailed below in section 7.2.1.

Patients who took part in pre-testing will not be approached to take part in the field testing phase.

7.2.1 Inclusion criteria

- aged ≥18 years **and**
- with an existing PU of any grade, location, or duration **and**
- able to provide informed consent to participate

7.2.2 Exclusion criteria

Patients will also 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 Tissue Viability Team (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.

7.3 Methods

An approximate sample of 150-250 PU patients will be purposively sampled ensuring representation of patients with all PU categories (grades 1-4, Table 1) and treatment types. There are no formal sample size estimation methods for evaluation of PRO measures, so the 'rule of thumb' recommendation of 5-10 patients for every item in the questionnaire has been used to estimate the sample size of 150-250 patients [24]. Consecutive patients will be identified and approached to participate. Accrual will be reviewed to ensure that there is balanced representation of patients in all PU categories. If we are validating the questionnaire for both modes of administration (i.e. self-complete and interview-administered modes) then accrual will be monitored to ensure equal numbers of patients are recruited into both mode groups. Where possible patient recruitment will be piggy-backed onto local audit and Quality Assurance (QA) activity (prevalence surveys, incidence monitoring, critical

incidence reporting) to maximise the identification of patients with PUs whilst minimising disruption and demand on the local clinical team.

7.4 Recruitment and consent procedures

Members of the TVTs at participating trusts will identify eligible patients. A record of those identified as eligible, approached to participate, refusals, consenting patients and questionnaire returns will be made (see section 7.4.1 and 7.5).

A verbal explanation of the study and Patient Information Leaflet will be provided by the TVT member or the researcher* (CG) for the patient to consider. These will include detailed information about the rationale, design and personal implications of the study. Following information provision, patients will have as much time as they need to consider participation and will be given the opportunity to discuss the study with their family and healthcare professionals before they are asked whether they would be willing to take part. The right of the patient to refuse consent without giving reasons will be respected.

Should the patient be capable of giving consent but 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, career or friend or another member of the patient's healthcare team who is not directly involved in the research study.

**Where the researcher is involved in the recruitment and consent process, the patient will be asked to give verbal permission to be approached by the researcher*

Assenting patients will then be invited to provide informed, written consent to collect baseline assessment data and to complete the questionnaire. Formal eligibility assessment and informed consent will be undertaken by the TVT member or researcher. The patient will remain free to withdraw from the study at any time without giving reasons and without prejudicing any further treatment. The original consent form will be filed within the PURPOSE Investigator Site File or designated secure location. One copy of the consent form will be given to the patient and one will be filed with the patients medical file.

7.4.1 Registration

Patients will be registered with the CTRU following informed consent and confirmation of eligibility. When eligibility has been confirmed, registration and baseline data (section 7.5.1) will be collected and a questionnaire pack containing the final provisional PU-QOL will either be provided to the patient to self-complete or be administered. Registration and baseline information and completed questionnaire packs will be collected from the patient by the attending TVT member, recognising the potential for completion bias this may incur. However, in this patient population and in order to maximise questionnaire return rates, collection of the questionnaires by the attending TVT member is considered essential.

7.4.2 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 CTRU.

Anonymised information will be collected including:

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

7.5 Data collection/assessment

Study data will be recorded by members of the TVTs or the researcher on the case record forms (CRFs) and by patients, members of the TVTs or the researcher on questionnaire booklets. Anonymised data will be returned to the CTRU.

Assessments will be undertaken as follows:

- Registration and Baseline data
- PU-QOL Questionnaire booklet

7.5.1 Registration and Baseline Data

Patients who meet the inclusion criteria and provide informed written consent (for baseline assessment and questionnaire completion) will be registered to this study. Registration and baseline information will be recorded by the TVT member or researcher including:

- Patient initials and date of birth
- Gender
- Ethnicity
- Marital status
- Education
- Presence of PU symptoms
- Pressure ulcer grade, location and number of pressure ulcers
- Duration of pressure ulcer
- Treatment plan (information about which treatment interventions the patient is currently receiving)
- Co-morbidity and/or speciality (i.e. spinal cord injured, trauma, vascular, care of the elderly ward)
- Centre code
- Name of the TVT/clinical research staff member conducting registration
- Confirmation of eligibility and written informed consent
- Braden scale

7.5.2 PU-QOL questionnaire booklet

Self-complete version

The patients will self-complete the PU-QOL questionnaire booklet, which will be provided to them by the person obtaining consent (i.e. member of the TVT or the researcher (CG)). It is anticipated that completion of the questionnaire may take up to 40 minutes.

Interview-administered version

A questionnaire pack will be administered to patients by either a member of the TVT or the researcher, following an interview manual. It is anticipated that administration of the questionnaire may take up to 40 minutes. Training in administering the questionnaire will be provided by the CTRU.

7.6 Item reduction analysis

The purpose of the item reduction analysis is to produce a psychometrically robust short version of the PU-QOL questionnaire. Standard psychometric tests and criteria for acceptability, reliability and validity will be performed to identify and retain items with strong psychometric properties and eliminate items with poor psychometric properties to produce a shorter, item-reduced version of the PU-QOL questionnaire. These analyses will also evaluate the hypothesised subscales of the questionnaire

Item reduction analysis will include item analysis and principal component factor analyses, including missing data <5%, maximum endorsement frequencies <80% (floor/ceiling effects <80%), aggregate adjacent endorsement frequencies >10%, item redundancy (inter-item correlations <0.75), internal consistency (item-total correlations <0.25), evidence of item responsiveness, and tests of scaling assumptions (item convergent/discriminant validity). A preliminary psychometric evaluation of the short, item-reduced version will be carried out using standard psychometric tests for acceptability, reliability (internal consistency), and validity (factor analysis, item convergent/discriminant validity).

In addition to standard psychometric tests, methods from modern measurement theory will be used to evaluate the psychometric properties of the PU-QOL questionnaires' scales and items [36]. This is proposed in order to strengthen methodological rigour.

8 FIELD TEST 2: PSYCHOMETRIC EVALUATION

8.1 Design for field test 2

In order to establish the PU-QOL as a valid measure of PU HRQL and to determine whether the instrument meets gold-standard criteria, scientific psychometric tests of acceptability, reliability, and validity will be performed.

A questionnaire pack will be provided to patients to self-complete or be administered to them. The pack will include the PU-QOL instrument and additonal measures selected for validation purposes (section 8.5.1). In addition, a sub-sample of the patients who complete and return the questionnaire packs at baseline will be asked to self-complete or have administered to them a second (re-test) questionnaire pack 2-7 days after the initial questionnaire completion.

8.2 Eligibility

Patients from participating acute and community trusts, with existing PUs (any grade, see Table 1), will be included in the study if they are hospital in-patients or hospital outpatient, or intermediate out-patient, nursing home patients or community patients under the care of community care nursing services, and they fulfil the criteria detailed in section 7.2.

8.3 Methods

An approximate sample of 150-250 PU patients (5-10 patients for each item on the PU-QOL instrument) will be purposively sampled ensuring representation of patients with all PU categories (grades 1-4, Table 1) and treatment types. Consecutive patients will be identified and approached to participate. Accrual will be reviewed to ensure that there is balanced representation of patients in all PU categories. If we are validating the questionnaire for both modes of administration (i.e. self-complete and interview-administered modes) then accrual will be monitored to ensure equal numbers of patients are recruited into both mode groups. Where possible, patient recruitment will be piggy-backed onto local audit and QA activity (prevalence surveys, incidence monitoring, critical incidence reporting) to maximise the identification of patients with PUs by the local clinical team.

Test-Retest

A test-retest will be undertaken with a sub-sample of participants recruited for the final field test. Consenting participants will complete a second questionnaire pack 2-7 days after the first questionnaire pack (approximately 75 patients for each mode of administration group). The length of the test-retest interval must be short enough to ensure that clinical change in the PU is unlikely to occur, but sufficiently long to ensure that respondents do not recall their responses from the first assessment. A short test-retest interval is necessary to ensure that stability per se is being evaluated, rather than clinical change in the PU during the test-retest interval, which will underestimate reliability.

8.4 Recruitment and consent procedure

Members of the TVTs at participating trusts will identify eligible patients. A record of those identified as eligible, approached to participate, refusals, consenting patients and questionnaire returns will be made (see section 7.4.1 and 7.5). The recruitment and consent methods described above in the preliminary field test will be used (section 7.4).

In addition to the information described in section 7.4, the patient information leaflet for the final field test indicates that participants can take part in 2 ways: 1) self-complete or administered questionnaire booklet at baseline, and if they agree, 2) complete a second self-complete or administered questionnaire booklet 2-7 days later. There will be an option on the consent form where participants can indicate whether they agree to take part in a second questionnaire. In addition to the original consent form being filed within the PURPOSE Investigator Site File or designated secure location, one copy for the patient, and one for the patient's medical notes, a copy of the consent form will be sent to the CTRU.

Self-complete version

If patients who self-complete a questionnaire at baseline agree, they will provide home address details so that a second questionnaire booklet can be given to them when the first booklet is collected or sent out to them with a return stamped, self-addressed envelope. Where patients are still hospital in-patients, they will complete the second questionnaire on the ward and return it to the researcher or TVT member that provided it to them.

Interview-administered version

If patients who were administered a questionnaire at baseline agree, they will provide home address details so that a second questionnaire booklet can be administered to them at a time agreed by the patient and the person administering the questionnaire (must be between 2-7 days after baseline administration). Where patients are still hospital in-patients, they will have a second questionnaire pack administered to them on the ward. The researcher or TVT member that administered the questionnaire pack will be responsible for returning completed questionnaires to CTRU.

8.5 Data collection/assessments

Study data will be recorded by members of the TVTs on the CRFs and by patients on questionnaire packs. Data will be returned to the CTRU.

Assessments will be undertaken as follows:

- Registration and Baseline
- PU-QOL Questionnaire booklet

- 2-7 day follow-up questionnaire pack (approx. 75 patients from baseline sample)

8.5.1 Registration and baseline Data

Baseline information will be recorded by the TVT member including:

- Patient initials and date of birth
- Gender
- Ethnicity
- Marital status
- Education
- Presence of PU symptoms
- Pressure ulcer grade, location and number of pressure ulcers
- Duration of pressure ulcer
- Treatment plan (information about which treatment interventions the patient is currently receiving)
- Co-morbidity and/or speciality (i.e. spinal cord injured, trauma, vascular, care of the elderly ward)
- Centre code
- Name of the TVT/clinical research staff member conducting registration
- Confirmation of eligibility and written informed consent
- Braden scale

8.5.2 PU-QOL questionnaire pack

Baseline questionnaire pack will include:

- The Provisional PU-QOL
- SF-12 (rather than SF36 to reduce respondent burden)
- Additional questionnaires selected for validation purposes (ethics will be notified about which questionnaires are selected, section 8.5.3)

Test-retest questionnaire pack will include:

- The Provisional PU-QOL
- SF-12 (rather than SF36 to reduce respondent burden)
- Additional questionnaires selected for validation purposes (ethics will be notified about which questionnaires are selected, section 8.5.3)

8.5.3 Assessment instruments

The Short Form-12 Health Survey Questionnaire

Use of the SF-36 was considered however it was decided by the project team that it was too long for use with PU patients. Instead, the SF-12 will be used to reduce respondent burden. The SF-12 is a generic instrument that assesses HRQL in eight domains of physical functioning, role-physical, body pain, general health, energy/fatigue, social functioning, role-emotional and mental health. These are the same domains as the SF-36. Even though this instrument has not been validated for use with PU patients, it has been used with other related chronic-skin wound conditions to validate their corresponding disease-specific HRQL instruments.

Additional questionnaires

Participants will complete the short version of the PU-QOL, the SF-12, and additional measures to assess construct validity (convergent, discriminant, known groups). The guiding principle in selecting the validating measures will be to include measures that will allow a comparison of PU-QOL subscales with measures of similar constructs (convergent validity) and with measures of different constructs (discriminant validity), and to compare PU-QOL scores in clinically defined known groups whose HRQL would be expected to differ. At this stage it is not possible to anticipate the subscales and item stem of the PU-QOL until it has been developed (pre-testing, section 6). As such, selection of validating measures is not possible. However, where available, short versions of measures selected for validation purposes and only measures deemed essential for validation testing will be included in the questionnaire packs. All measures will be administered in the same order. It is anticipated that completion of questionnaire packs may take up to an hour.

8.6 Psychometric evaluation analysis

Analyses will include examination of:

Item-level performance will determine missing data (<5%), maximum endorsement frequencies (<80%), and item redundancy (inter-item correlations <0.75).

Acceptability will be assessed by completeness of data (e.g. missing data for summary scores <5%) and score distributions (e.g. distribution of endorsement frequencies across response categories, skew and floor/ceiling effects for summary scores <10%).

Reliability will be assessed on the basis of internal consistency (Cronbach's alpha for summary scores ≥0.70 and item-total correlations ≥ 0.30) and test-retest reliability (correlations for summary scores ≥0.70).

Validity will include a within-scale analyses to determine whether a single entity (construct) is being measured and that items on the measure can be combined to form a summary score (Cronbach's alpha ≥0.70), and analysis against external criteria (convergent, discriminant and known groups differences validity). To evaluate convergent validity we will compare PU-QOL with the SF-12, and additional relevant measures as determined once the PU-QOL questionnaire is developed. Discriminant validity will be assessed by examining PU-QOL scores by age, gender and medical specialty. PU-QOL scores for patients by PU severity (superficial vs severe), site of PU (heel vs elsewhere), and sensitivity impaired vs. no sensitivity impaired will be compared to evaluate known group differences. Factor analysis, together with the results of other item-level analyses described in table 2, will be used to investigate hypothesised subscales.

Evaluation of subscales will be determined by factor analysis and item convergent/ discriminant validity

In addition to standard psychometric tests, modern psychometric methods will be used to strengthen methodological rigour [36].

12 ETHICAL CONSIDERATIONS

This project will recruit patients with PUs and therefore 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, questionnaire completion/interview requires the patient to reflect on their experience of having a PU and how interventions received have impacted on their QOL. For some people this may raise topics considered to be sensitive, embarrassing or upsetting, and possibly emotionally distressing.

The ethical issues surrounding these potentially vulnerable patients have been addressed through the study design and include a thought out consent process, the use of one-to-one

semi-structured interviews using de-briefing questioning for data collection at the development pre-testing stage to provide a caring and supportive environment in which to discuss any sensitive issues that may arise, and the use of only essential measures required for validation purposes (short version where available) to reduce respondent burden. If the patient becomes distressed during the interview or from completing the questionnaire, then the interview will be immediately stopped. It will be stressed to all patients that they are able to withdrawn 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.

This study will be conducted in accordance with the Declaration of Helsinki in its latest form. The study will be submitted to and approved by a REC prior to identifying eligible patients. The CTRU will provide the REC with a copy of the final protocol, patient information leaflets, consent forms, and all other relevant study documentation.

16 REFERENCES

5. EPUAP. Pressure Ulcer Treatment Guidelines. http://www.epuap.org/gltreatment.html 1999. Oxford, European Pressure Ulcer Advisory Panel.
24. Blazeby J, Sprangers M, Cull A, Groenvold M, Bottomley A. EORTC Quality of Life Group: Guidelines for Developing Questionnaire Modules. 3rd edition revised. 2002.
25. FDA. Patient reported outcome measures: Use in medical product development to support labelling claims (draft guidance). 2006. MD, US Department of Health & Human Support Food & Drug Administration.
26. Streiner D, Norman G: *Health Measurement Scales: A Practical Guide to Their Development and Use*, 3rd edn. Oxford University Press; 2003.
27. Hilari K, Byng S, Lamping DL, Smith SC: **Stroke and Aphasia Quality of Life Scale-39 (SAQOL-39): evaluation of acceptability, reliability, and validity.** *Stroke* 2003, **34:** 1944-50.
28. Lamping DL, Schroter S, Marquis P, Marrel A, Duprat-Lomon I, Sagnier PP: **The community-acquired pneumonia symptom questionnaire: a new, patient-based outcome measure to evaluate symptoms in patients with community-acquired pneumonia.** *Chest* 2002, **122:** 920-9.

29. Lamping DL, Hobart JC, Schroter S, Smith SC: **Developing short-form outcome measures: Methodological approaches to item reduction.** Edited by Edited by International Society for Quality of Life Research: Orlando; 2002.
30. Lamping DL, Schroter S, Kurz X, Kahn SR, Abenhaim L: **Evaluation of outcomes in chronic venous disorders of the leg: development of a scientifically rigorous, patient-reported measure of symptoms and quality of life.[see comment].** *Journal of Vascular Surgery* 2003, **37:** 410-9.
31. Smith S, Lamping D, Banerjee S, Harwood R, Foley B, Smith P *et al.*: **Measurement of health-related quality of life for people with dementia: development of a new instrument (DEMQOL) and an evaluation of current methodology.** *Health Technology Assessment* 2005, **9**.
32. McColl E: **Developing questionnaires.** In *Assessing quality of life in clinical trials*. 2nd edition. Edited by Fayers P, Hays R. New York: Oxford University Press; 2005:9-23.
33. Graesser AC, Wiemer-Hastings K, Kreuz R, Wiemer-Hastings P, Marquis K. QUAID: a questionnaire evaluation aid for survey methodologists. Behaviour Research Methods, Instruments and Computers 32, 254-262. 2000.
34. Willis G, Lessler J. Question appraisal system: QAS-99. National Cancer Institute . 1999.
35. Stead ML, Brown JM, Velikova G, Kaasa S, Wisloff F, Child JA *et al.*: **Development of an EORTC questionnaire module to be used in health-related quality-of-life assessment for patients with multiple myeloma. European Organization for Research and Treatment of Cancer Study Group on Quality of Life.** *British Journal of Haematology* 1999, **104:** 605-11.
36. Edelen MO, Reeve BB: **Applying item response theory (IRT) modeling to questionnaire development, evaluation, and refinement.** *Quality of Life Research* 2007, **16:** Suppl-18.
37. Zumbo BD. A Handbook on the Theory and Methods of Differential Item Functioning (DIF): Logistic Regression Modeling as a Unitary Framework for Binary and Likert-Type (Ordinal) Item Scores. 1999. Ottawa, ON: Directorate of Human Resources Research and Evaluation, Department of National Defense.

APPENDIX 1 – MODE OF ADMINISTRATION SUBSTUDY

BACKGROUND TO SUB-STUDY

Initially, the purpose of the PU-QOL study was to develop and psychometrically evaluate a HRQL questionnaire for patients with pressure ulcers as a self-complete mode of administration questionnaire. However, preliminary analysis of the pre-test data has identified problems with completion rate, posing a question about the appropriateness of a self-complete measure for patients with pressure ulcers, particularly elderly patients aged over 80 years. To address these methodological issues identified from the pre-test, we are proposing to undertake a mode of administration sub-study. The sub-study will determine the mode of administration for which the questionnaire will be developed and validated.

Aim and objectives

The purpose of the sub-study is to determine whether one questionnaire can be developed and validated for use with both modes of administration or whether two mode-specific questionnaires are required.

METHODS

Design

A mode of administration sub-study including a differential item functioning (DIF) analysis [37] will be undertaken to establish measurement equivalence across two mode of administration groups (self-complete and interview-administered modes). A DIF analysis will investigate the equivalence of the PU-QOLs' questionnaire items by comparison of these two groups.

A sample of 60-100 patients are required for the sub-study. Consecutive patients will be approached to take part. Eligible patients who provide written informed consent will be randomised to either the self-complete or interview-administered groups (see section 2.2).

We plan to develop one PU-QOL questionaire – the results of the sub-study will determine whether PU-QOL should be developed as interview-administered only OR both self-complete and interview-administered (see section 5 for more details).

Eligibility

To ensure an equivalent or representative sample in both mode of administration groups (i.e. both groups need to have the same clinical presentation to perform a differential item

functioning analysis, see section 6), the eligibility criteria has been adapted from the main study to include only patients who are able to read and write in English (i.e. patients able to self-complete a questionnaire will be randomised to both mode of administration groups).

Patients from participating acute and community NHS Trusts, with existing PUs (any grade, see Table 1), will be included in the sub-study if they are hospital in-patients or outpatients, intermediate care patients, nursing home patients or community patients under the care of community care nursing services, and they fulfil the criteria detailed below in section 2.2.1. Patients who took part in pre-testing will not be approached to take part in the sub-study.

Inclusion criteria

- aged ≥18 years **and**
- with an existing PU of any grade, location, or duration **and**
- able to provide informed consent to participate **and**
- able to read and write in English (i.e. able to self-complete a questionnaire)

Exclusion criteria

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

- have only moisture lesions
- are unconscious or confused
- have cognitive impairment
- are unable to read or write in 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 Tissue Viability Team (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.

Recruitment and consent

Members of the TVTs at participating trusts will identify eligible patients for the sub-study. A record of those identified as eligible, approached to participate, refusals, consenting patients and questionnaire returns will be made (see section 3.1).

A verbal explanation of the study and patient information leaflet will be provided by the TVT member or the researcher* (CG) for the patient to consider. These will include detailed information about the rationale, design and personal implications of the study. Following information provision, patients will have as much time as they need to consider participation and will be given the opportunity to discuss the study with their family and healthcare professionals before they are asked whether they would be willing to take part. The right of the patient to refuse consent without giving reasons will be respected.

Should the patient be capable of giving consent but 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.

**Where the researcher is involved in the recruitment and consent process, the patient will be asked to give verbal permission to be approached by the researcher*

Assenting patients will then be invited to provide informed, written consent to collect baseline assessment data and to complete the questionnaire. Formal eligibility assessment and informed consent will be undertaken by the TVT member or researcher. The patient will remain free to withdraw from the study at any time without giving reasons and without prejudicing any further treatment. The original consent form will be filed within the PURPOSE Investigator Site File or designated secure location. One copy of the consent form will be given to the patient and one will be filed with the patients medical file.

Screening and registration

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

Anonymised information will be collected including:

- The reason not eligible for study particpation **or**
- Eligible but declined
- Date of Birth
- Gender

- Ethnicity
- Pressure ulcer grade and location

Registration and randomisation

Screened patients who are both eligible for sub-study participation and provide written informed consent will be registered and randomised to the sub-study. Informed consent for entry into the sub-study must be obtained prior to randomisation. Following confirmation of written informed consent and eligibility, registration and baseline data will be collected (see section 7.5), and patients will be randomised into the study by an authorised member of staff at the study research site.

Randomisation will be carried out by the Clinical Trials Research Unit (CTRU), at the University of Leeds, using a telephone randomisation service that will ensure allocation concealment. Randomisation will be performed using the CTRU 9.00–17.00 telephone randomisation service (9:00 to 17:00 Monday to Friday excluding public/bank holidays, the period between Christmas and New Year and all Tuesdays following a bank holiday except for Mayday).

The following information will be submitted prior to randomisation:

- Patients details including initials, gender, date of birth
- confirmation of eligibility
- confirmation of written informed consent
- date of written informed consent
- details relating to the stratification factors

Patients who fulfil the eligibility criteria, and have given written informed consent, will be randomised on a 2:1 basis to receive either self-complete or interview-administered mode of administration. The 2:1 ratio will be used to account for the likelihood of increased missing data from self-completed questionnaires; a minimum of 30 fully completed questionnaires are required for the DIF analysis. Randomisation will be stratified by: age (≤ 70, >70 years), and PU severity (superficial vs. severe PU).

Direct line for randomisation: 0113 343 xxxx

Assessments and data collection

Study data will be recorded by members of the TVTs or the researcher on the case record forms (CRFs) and by patients, members of the TVTs or the researcher on questionnaire booklets. Data will be returned to the CTRU.

Assessments will be undertaken as follows:

- Registration and Baseline data
- Randomisation
- PU-QOL Questionnaire booklet

Baseline assessment

Patients who meet the inclusion criteria and provide informed written consent (for baseline assessment and questionnaire completion) will be registered to this sub-study. Registration and baseline information will be recorded by the TVT member or researcher including:

- Patient initials and date of birth
- Gender
- Ethnicity
- Marital status
- Education
- Presence of PU symptoms
- Pressure ulcer grade, location and number of pressure ulcers
- Duration of pressure ulcer
- Treatment plan (information about which treatment interventions the patient is currently receiving)
- Co-morbidity and/or speciality (i.e. spinal cord injured, trauma, vascular, care of the elderly ward)
- Centre code
- Name of the TVT/clinical research staff member conducting registration
- Confirmation of eligibility and written informed consent
- Braden scale

PU-QOL questionnaire booklet

Self-complete version

The patients will self-complete the PU-QOL questionnaire booklet, which will be provided to them by the person obtaining consent (i.e. member of the TVT or the researcher (CG)). It is anticipated that completion of the questionnaire may take up to 40 minutes.

Interview-administered version

A questionnaire pack will be administered to patients by either a member of the TVT or the researcher following and interview manual. Training in administering the questionnaire will be provided by the CTRU. It is anticipated that administration of the questionnaire may take up to 40 minutes.

Sample size

To perform a differential item functioning (DIF) analysis, a minimum of 30 fully completed questionnaires (i.e. no missing data) are required for each mode of administration group. Consecutive patients will be randomised until a minimum of 30 fully completed questionnaires are collected from each mode of administration group (30 self-completed and 30 interview-administered questionnaires). We anticipate approximately 100 patients are required for the sub-study to meet the data requirement for the DIF analysis.

DIF analysis

The purpose of the sub-study analysis is to determine whether the PU-QOL questionnaire can be used with either self-complete or interview-administered modes or whether there is the need to develop and validate two mode-specific versions of the questionnaire (i.e. a self-complete version and an interview-administered version).

The DIF analysis will determine whether scores are directly comparable between both modes of administration (i.e. whether scores from both modes of administration are similar enough to continue developing and validating one version of the questionnaire, or whether scores are divergent and there is a requirement to develop two mode-specific questionnaires).

DIF techniques match scores on questionnaires from different groups according to their total questionnaire scores and then investigate how the different groups performed on individual questionnaire items to determine whether the questionnaire items are creating problems for a

particular group [37] (i.e. specific mode of administration group). DIF is based on the assumption that test takers who have similar knowledge (based on total test scores) should perform in similar ways on individual test questions regardless of various demographics. To ensure that the DIF analysis is a valid interpretation of group differences dependent on mode of administration and not an artefact of differences within the groups; differences that could present if for example younger, healthier patients were assigned to the self-complete group and older, more frail patients were assigned to the interview-administered group, only patients who meet the inclusion criteria (section 2.2) will be included in the sub-study. This will ensure that both group's participants are matched on clinical presentation and relevant underlying ability before determining whether participants of the two groups differ in their probability for success [37].

There are 2 possible outcomes of the analysis:

1. One questionnaire can be developed and validated for use with either mode of administration or
2. Two mode-specific questionnaires are required.

The outcome of the sub-study will determine the mode of administration in which the questionnaire will be developed and validated (ie both self-complete and interview-administered modes or interview-administered only).