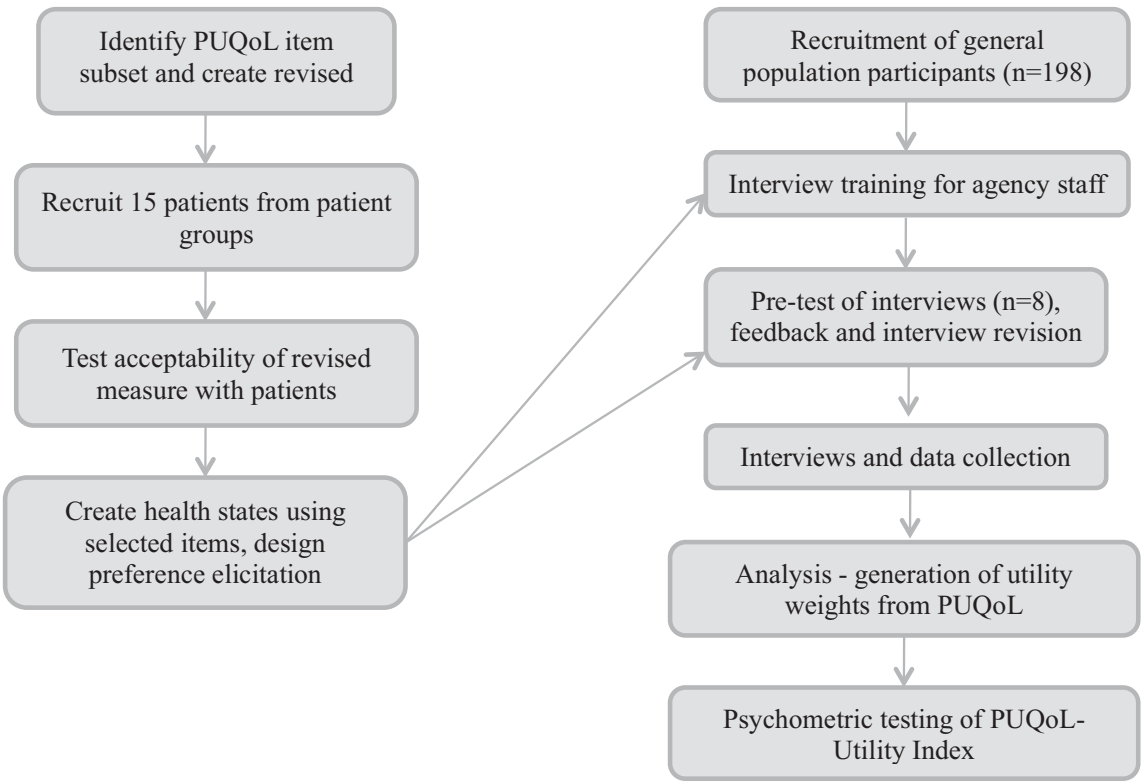
NB: This study protocol (version 5, dated 7 Feb 2013) is in a reduced format including only the study aims, methods and ethical considerations. Sections pertaining to study background have been removed as they are included as a chapter section. Information pertaining to data monitoring, quality assurance, 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 derive a preference-based utility index from the PUQoLI (the PUQoL-UI), enabling the collection of utility values from the PUQoLI and, therefore, the calculation of QALYs for the purpose of economic evaluation. Specific objectives include:

1. To check the acceptability of the revised PUQoLI with people with experience of PUs.
2. To generate PU-specific health state descriptions comprising responsive and valid PUQoLI items.
3. To conduct a preference elicitation exercise with the general population.
4. To conduct analyses establishing an algorithm and utility index scores associated with the PUQoLI item subset.

Methods

The derivation of the PUQoL-UI will follow best practice (Brazier et al, 2011). It will involve: health state generation from the reduced PUQoLI, health state valuation interviews with the general population and modelling of the health state valuations to derive the PUQoL-UI scoring tariff.

Item Selection

Prior to the start of this study it was necessary to revise and reduce the number of items in the PUQoLI. This was done using a previously collected dataset and by employing a range of statistical techniques in line with best practices (Brazier et al, 2011). A brief report describing this process is available on request.

Checking the acceptability of the revised PUQoLI

Before the health states are generated for the valuation interviews it will be necessary to check the acceptability of the revised PUQoLI with a small group of people who have experience of PUs. This will involve conducting a small number of semi-structure, face-to-face interviews with people who have (or who have had) a PU. Participants will be interviewed by an experience qualitative researcher. They will be asked to complete the revised PUQoLI and asked general questions about whether or not the questionnaire was easy to understand and complete and whether or not there were aspects or questions that were confusing. Participants will be asked specifically whether or not the new question lead-in (after the removal of the PU attribution) makes sense in each dimension. An information sheet given to people interested in the study is included in the appendix along with a consent form and an interview schedule. People with be offered £20 worth of high street vouchers for taking part in the study.

Members of the project team will review the interview responses and agree on whether or not revisions to the questionnaire are required.

Health State Generation

After any revisions to the PUQoLI have been incorporated, health state scenarios (incorporating the selected items from the revised measure) will be developed for inclusion in the preference elicitation (valuation) exercise. Health states would be generated with checks in place to ensure face validity and a range of severity is represented. An example of a hypothetical health state based on PUQoLI items is given below. The items and wording included in the final scenarios will be determined after health state sampling has been conducted and be based on the results of the interview responses.

Example pressure ulcer health state based on PUQoLI items:

Please imagine you are in the following health state:

You have a pressure ulcer and…..

You are a little bothered by throbbing pain it causes
Being kept awake by it causes you a little bother
It causes you a little bother as it limits your ability to walk
It causes a little bother as it makes it difficult for you to do your regular daily activities
You have not been bothered by fatigue from it
The concern or worry over it causes you a little bother
Having to plan going out around caring for it causes a lot of bother

Given respondent burden, it is likely that some PUQoLI constructs will have to be collapsed or will not be represented in the final valuation exercise. It is anticipated that between 25 and 50 health states will be required for the preference elicitation exercise. It is also assumed that each health state will be valued at least 20 times to ensure a robust valuation is obtained. The

selection of the health states will be based on statistical design, employing an orthogonal array.

Preference Elicitation

The preference elicitation exercise will follow NICE recommendations (NICE, 2008) and thus will mirror the methodology employed to value the EQ-5D measure. Namely, we will ask members of the UK general population to complete a series of time trade off (TTO) exercises to value the PUQoLI health states.

Valuation interviews

The interviews will be conducted by a private research organisation who are experienced in this line of work. An information sheet for the general population is included in Appendix E. Interview resources will be developed by the research team, including questionnaires, laminated cards incorporating the health state descriptions and a time-trade-off prop to aid understanding of the elicitation exercise. The draft interview schedule is included in. Interviews will be conducted face-to-face either in the person's own home, at the offices of the research agency. Respondents will also be given information regarding pressure ulcers in order that they base their interview responses on informed preferences.

The time trade-off (TTO) technique is a standard economic technique to elicit individuals' strength of preferences for various health states (Torrance et al. 1972). In the TTO, individuals choose between two certain options: full length of life (assume 20 years) in the health state to be valued, or a shorter period in 'full health' (after which they die). The amount of time (months, years) to be spent in full health is varied until the respondent can no longer easily decide which option they prefer (the point of indifference) signalling the end of the exercise. The final utility value assigned to the health state being valued is given by time spent in full health, divided by the time spent in the health state (in this case 20 years). So if the respondent was indifferent between living for 5 years in full health and 20 years in the health state being presented, the utility of that health state would be (5/20) = 0.25. The 'ping-pong' technique will be used whereby the amount of time in good health is varied until the participant reaches a point of indifference between the two choices.

The utility value of health state *i* is $h_i = 1 - (1 - h_j)x/t$ where *t* is the time in state *i* and *x* is the time of indifference.

Respondents will complete between 8-10 TTO exercises each. They will be presented with a laminated card describing a pressure-ulcer-related health state (such as the example given above) and a TTO board. The TTO board is a prop with a slide mechanism to help respondents understand the exercise and to make it easier for them to respond. The interviewer is present to make sure the respondent understands the task, to answer any queries and to record responses.

As there is a concern that the elderly may have problems in understanding and completing the TTO, we will also include a ranking exercise. In this exercise, participants will be asked to rank the PU scenario cards they considered for the TTO in order of 'severity' (the order from best-to-worst). After that they will be asked to assign a number from 0-100 to each card denoting its position on the 'health thermometer' visual analogue scale (VAS) shown in Appendix F, with 0 representing 'dead' and 100 representing 'full health'. Participants will be informed that scenarios can have equal values.

The respondents will also complete a set of questions on their general health, a socio-demographic survey and the EQ-5D measure. Interviews should last between 30-50 minutes. The Agency will offer a small incentive to participants.

Sample

Checking the acceptability of the revised PUQoLI

A sample of around 15 people who have experienced (preferably who currently have) a pressure ulcer is thought sufficient to check the acceptability of the revised PUQoLI. These will be recruited via local groups (such as Leeds Carers UK) who have agreed to participate in the study. The groups will mention the study to their members (pass on the study information sheet) who will be instructed to contact a specified member of the research team if they wish to participate. People meeting the inclusion criteria will be asked to complete a consent form and will then be able to state a location and time convenient for an interview.

Valuation interviews

The NICE guidance (NICE, 2008) states that any valuation of condition-specific measures should follow the EQ-5D valuation methodology. For this reason the sample of participants will be a representative sample of the UK general population.

Sample size

The sample size for the valuation study depends on the number of dimensions chosen for the valuation exercise – the greater the number of dimensions, the greater the sample required. It is also dependent on the number of valuations required per health state, the number of TTO valuations conducted per person and the approach taken to modelling the data.

For the analysis assuming:

- We include 8 dimensions, each with 3 levels (response options)
  = 6561 potential health states.
- We only need to value 1% (based on published valuation studies) of these health states
  = 66 states
- We need to value each a minimum of 20 times = 1320 valuations
- Each respondent can complete 8 valuations
  - Gives a sample size of 165
  - Assuming an 80% completion rate means we will require a sample of 198

Eligibility

PU sample and recruitment

Inclusion criteria

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

Exclusion criteria

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

- are unconscious or confused
- have cognitive impairment
- do not speak or understand English
- are unable to provide informed consent

The researcher will interview participants in their own home (following standard safe practice SOP). Before the interview, each participant will be given a further verbal explanation of the study by the researcher; informed that the responses they provide are made 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 participant to keep and the original copy kept by the researcher to take back to Leeds Institute of Health Sciences.

The researcher is required to utilise all possible methods to ensure that no person 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 person to refuse consent without giving reasons will be respected. Further, participants will remain free to withdraw from the study at any time, again, without giving reasons and without prejudicing any further treatment.

General population:

An external market research agency will be responsible for the recruitment of the general population sample. They have a group of participants on their records who regularly participate in interviews. A sample representative of the UK general population will be chosen including a spread of age, gender, educational attainment and ethnicities.

To encourage participation in the general population group, a small incentive will be offered. The research agency will be responsible for the interviewing, data recording and checking and incentive payments.

As with the patient sample, in the unlikely event that an interviewee from the general population sample becomes distressed, the interview will be stopped immediately.

Analysis

Modelling the health state valuations

It is impractical to value every health state possible in the PUQoL-UI descriptive system. Therefore, it is likely that around 0.05%-1% of the potential health states from the PUQoL-UI would be valued given the sample proposed. Those health states not directly valued by the general population will be valued indirectly using regression modelling from values attributed to health states that were included in the elicitation exercise.

Analyses will explore the two main ways to model health states: multi-attribute utility theory (MAUT) and statistical modelling (Stevens et al, 2007). A number of statistical model specifications will be explored including ordinary least squares and random effects models. Model performance will be judged using standard error statistics such as mean absolute error and root mean squared error in predicting mean health state utility values. The model with the lowest prediction errors will be selected as that to value the remaining PUQoL-UI health states. From this algorithm a scoring tariff to obtain PUQoL-UI scores from the PUQoLI questionnaires will be generated.

Ethical considerations

This study will include both members of the general population and may include elderly and highly dependent participants considered as vulnerable. Clinically in the treatment of PUs, older people are treated in the same way as younger people and it is therefore important to ensure that the study is representative of the clinical population. In addition, the interview requires the participant 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 participants with high levels of co-morbidity including acute and chronic illness. The ethical issues surrounding these potentially vulnerable participants have been addressed through the design of the recruitment process which uses local groups 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 participant becomes distressed during the interview or from completing the questionnaire, then the interview will be immediately stopped. It will be stressed to all participants that they are able to withdrawn from participation at any time without giving reason.

No treatments or procedures are incorporated into the PUQALY study design so there is minimal risk to the participant sample. Participants will be made aware that they free to leave the study or discontinue the elicitation interviews at any time.

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 person to refuse participation without giving reasons will be respected. The participant will remain free to withdraw at any time from the study without giving reasons.

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