

# Development of DEMQOL-U and DEMQOL-PROXY-U: generation of preference-based indices from DEMQOL and DEMQOL-PROXY for use in economic evaluation

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## Executive summary

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# Executive summary

## Background

### *The challenge of dementia*

Dementia is one of the most common and serious disorders in later life with a prevalence of 5% and an incidence of 2% per year in the over-65s. In the UK there are currently 750,000 people with dementia and 200,000 new cases every year. It causes irreversible decline in global intellectual, social and physical functioning. Abnormalities in behaviour, insight and judgement are part of the disorder, as are neuropsychiatric symptoms such as psychosis, anxiety and depression. The economic cost of caring for people with dementia is immense. In the UK, the cost of dementia is around £17B per year, greater than the costs of stroke (£3B), heart disease (£4B) and cancer (£2B). More importantly, the negative impacts of dementia on those with the disorder, in terms of deteriorating function, and on carers are profound. Worldwide there are 35 million people with dementia and this costs \$600B per year; these numbers are set to double and the costs to at least triple in the next 20 years. The need to improve care for people with dementia is a policy priority.

### *Evaluation of clinical effectiveness in dementia*

Given its importance in public health terms and its devastating effects, it is understandable that there is a large and growing volume of basic, translational and applied research under way investigating the effectiveness of interventions to help people with dementia. This includes evaluations of psychological, educational and social interventions as well as trials of pharmacological treatments. Given the complexity of the syndrome of dementia, there has been discussion about how best to measure the impact of interventions. There is an emerging consensus that we need to measure broad patient-reported outcomes such as health-related quality of life (HRQL) in dementia as well as discrete areas such as cognition or behaviour. A variety of instruments are available to measure discrete areas of function across many of the major domains including cognition, behavioural problems and psychological symptoms, activities of daily living and depression in dementia, often using proxy reports of observable behaviour.

Measuring quality of life in dementia is more challenging, not least because of poor recall, time perception, insight and communication. However, recent studies indicate that meaningful measurements can be made using condition-specific measures, using both subjective and proxy instruments.

Funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme, we developed the DEMQOL system, a condition-specific measure of HRQL in dementia. The DEMQOL system consists of two interviewer-administered tools: DEMQOL (28 items), which is completed by the person with dementia (score range 28–112, with a higher score indicating better HRQL); and DEMQOL-Proxy (31 items), a proxy report of the HRQL of the person with dementia, completed by the main carer (score range 31–124). A global quality-of-life item is also included in both instruments but does not contribute to the overall score. The system was designed according to best psychometric practice, and there is some evidence for the validity of the scale. DEMQOL has good psychometric properties for people with mild to moderate dementia [defined as a Mini Mental State Examination (MMSE) score of 10+]. DEMQOL-Proxy can be used across dementia severity, from mild to severe.

### *Economic evaluation in dementia*

The last two decades have seen the increased use of economics to inform the allocation of resources between competing health-care interventions around the world and particularly the use of cost-effectiveness, in which interventions are often assessed in terms of their cost per quality-adjusted life-year (QALY). The QALY provides a way of measuring the benefits of health-care interventions, including improvements in HRQL. Brief generic (i.e. not condition-specific) measures of HRQL are most commonly

used to put the 'Q' into the QALY. Such measures include the European Quality of Life-5 Dimensions (EQ-5D) and Short Form questionnaire-6 Dimensions (SF-6D); it is suggested that these are applicable to all interventions and patient groups. This claim has support across certain conditions, for example rheumatoid arthritis, for which it has passed conventional psychometric tests of reliability and validity, but is more questionable for others, such as visual impairment, hearing loss and schizophrenia.

There is reason to believe that the available brief generic measures of HRQL do not work well in dementia. The inherent impairments in dementia of recall, time perception, insight and expressive and receptive communication mean that it is not possible to assume that what works for a general non-cognitively impaired population will work for those with dementia. This means that instruments to be used in dementia need to be psychometrically tested in populations of people with dementia. When this has been done, the results have suggested that there are major potential difficulties in using such generic measures in dementia, with considerable error likely.

What then is needed to enable cost-effectiveness evaluation in dementia? If the use of the currently available brief generic measures is problematic because of the error inherent in their use, might it be possible to use instruments that can measure HRQL in dementia, such as DEMQOL and DEMQOL-Proxy? These instruments cannot directly be used in economic evaluation in their current form because they do not incorporate preference information. They therefore cannot yet be used to calculate QALYs for use in incremental cost-effectiveness analysis. This is a major limitation in the currently available measurement technology. To meet this need, this study aims to generate a preference-based single index for the two instruments that comprise the DEMQOL system (DEMQOL and DEMQOL-Proxy) for use in economic evaluation using general population values. In addition, we set out to generate patient and carer values for a sample of states to compare with the general population values and to test the new system using a trial data set.

## Objectives

1. To derive health-state classification systems that are amenable to valuation from DEMQOL and DEMQOL-Proxy which can be used to categorise all patients with responses to the measures.
2. To generate utility values for every health state defined by the health-state classification systems developed from DEMQOL and DEMQOL-Proxy.
3. To examine whether or not utility values elicited from the general population differ from utility values elicited from patients and carers for dementia health states generated by the classification system.
4. To examine the psychometric performance of the dementia-specific preference-based measures using trial data.

## Method and results

The overall aim was to develop two preference-based measures, one from DEMQOL and one from DEMQOL-Proxy. These measures use a subset of items from DEMQOL and DEMQOL-Proxy, respectively, to form classification systems so that utility scores can be produced for any study that has used the existing DEMQOL and/or DEMQOL-Proxy instruments. We have named the new measures DEMQOL-U and DEMQOL-Proxy-U, with the 'U' referring to the utility scores generated in this project. This was a complex multiphase study. The project had four linked phases:

- phase 1 – derivation of the health-state classification system
- phase 2 – general population valuation survey and modelling to produce values for every health state
- phase 3 – patient/carer valuation survey
- phase 4 – application of measures to trial data.

### ***Phase 1a: derivation of the health-state classification system – quantitative evaluation of DEMQOL and DEMQOL-Proxy dimension structure***

The analysis used DEMQOL ( $n = 1189$ ) and DEMQOL-Proxy ( $n = 1223$ ) data drawn from two sources: routine data collected from a memory service and data collected from a study assessing HRQL in dementia.

#### **Method**

We evaluated rates of missing data, maximum endorsement frequencies, adjacent endorsement frequencies and redundancy to evaluate the factor structure of DEMQOL and DEMQOL-Proxy and to determine the extent to which the conceptual domains are supported.

#### **Results**

We identified two separate five-factor models for DEMQOL and DEMQOL-Proxy. Both models reflect aspects of the original conceptual framework but also highlight important differences between self- and proxy reports. The factor structures were robust enough to provide the basis for the development of dementia-specific preference-based measures for patient self-report and proxy report by carers.

### ***Phase 1b: derivation of the health-state classification system – development of a health-state classification system for DEMQOL AND DEMQOL-Proxy***

The aim of this stage was to identify one item for each of the dimensions identified in DEMQOL and DEMQOL-Proxy.

#### **Method**

To identify the most robust items for use in the health-state classification system, five separate Rasch models were generated for both DEMQOL and DEMQOL-Proxy.

#### **Results: final health-state classification systems**

The five items selected to reflect the DEMQOL dimension structure form the basis for the DEMQOL classification system. This was named DEMQOL-U. Each dimension has four response levels that correspond to the options included on the original DEMQOL instrument. Therefore, the DEMQOL-U descriptive system generates a possible 1024 (i.e.  $4^5$ ) health states. The four items selected to reflect the DEMQOL-Proxy dimension structure form the basis of the DEMQOL-Proxy classification system. This was named DEMQOL-Proxy-U. It contains four dimensions each with four levels corresponding to those included in the original measure. Therefore, DEMQOL-Proxy-U generates 256 (i.e.  $4^4$ ) health states.

### ***Phase 2: general population valuation survey and modelling to produce values for every health state***

Preference-based measures have two components: first, a health-state classification system that can be used to categorise all patients with the condition of interest; and second, a means of obtaining a utility score for all states defined by the system. In this phase of the development we generated a preference-based single index for each classification system.

#### **Method**

The first stage of generating the preference-based single index involved a valuation study in which a representative sample of the general population valued a sample of health states derived from each classification system. The sample of states that was valued was derived using simulation. The time trade-off (TTO) technique, which asks respondents to trade off years in full health to avoid living in a particular health state, and ranking, in which respondents order health states from best to worst, were used for the valuation study. The analysis used a range of multivariate regression models including ordinary least squares and random-effects generalised least squares to produce a single-index measure from each classification system anchored on a full health–dead 1–0 scale, in which a value of 1 is equal to full health and a value of 0 is equal to being dead.

## Results

The data generated were subjected to multiple multivariate regression and preference weights were generated. These enable a health-state utility value to be estimated for every health state defined by each classification system. These preference weights can be used to generate a utility score for a person with dementia each time they complete the DEMQOL questionnaire or their carer completes the DEMQOL-Proxy questionnaire.

### *Phase 3: patient/carer valuation survey*

In the previous stage of the study we estimated a preference-based single index for each classification system using values obtained from the general population. However, such values can be obtained from other sources; here, we investigated patients and carers.

## Method

Health states matched with a selection of those valued by the general population were valued using TTO by samples of people with dementia and carers. The elicited values were compared with the general population values.

## Results

People with dementia and carers of people with dementia gave systematically lower utility values than members of the general population. These results suggest that the population used to produce dementia health-state utility values may well impact on the results of cost-effectiveness analysis and potentially affect resource allocation decisions, and no systematic adjustment between values is possible.

### *Phase 4: application of measures to trial data*

If the DEMQOL-U and DEMQOL-Proxy-U are to be used alongside or instead of generic preference-based measures it is important to assess their psychometric validity, responsiveness and level of agreement between patient and carer report. This can be assessed by applying psychometric methods to data sets containing responses to the DEMQOL system alongside generic preference-based and non preference-based measures.

## Method

We compared the validity, patient/proxy agreement and responsiveness of the EQ-5D and the DEMQOL-U and DEMQOL-Proxy-U utility measures. The data for these analyses were obtained from the HTA Study of Antidepressants for Depression in Dementia (HTA-SADD), a multicentre placebo-controlled pragmatic randomised controlled trial of the clinical effectiveness of sertraline and mirtazapine.

## Results

There is some evidence for the acceptability of the DEMQOL system, in particular the DEMQOL-Proxy-U, which displays low missing data rates. There is no clear pattern regarding agreement between patients and carers. In terms of responsiveness, there is evidence that the DEMQOL utility measures and EQ-5D are less sensitive to change than the original DEMQOL and DEMQOL-Proxy. The psychometric performance of the DEMQOL utility measures may be impacted by the sample used, which focused on those with depression in dementia and so may not be representative of all those with dementia. The inconclusive nature of the results means that further testing on a range of samples is required.

## Conclusions

We have detailed the development and application of two dementia-specific preference-based measures, one for self-completion (DEMQOL-U) and the other to be completed by carers (DEMQOL-Proxy-U). These measures can be used to generate health-state utility values on the QALY scale for use in economic evaluation of interventions in this group of patients. These are the first condition-specific preference-based measures in dementia. The results of the psychometric analysis are encouraging but the validity and

responsiveness of the instruments require further investigation; therefore, until more evidence is available, we would recommend that the DEMQOL instruments are used alongside a generic measure such as the EQ-5D in future evaluations of interventions for dementia.

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