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## Utility-Based Instruments for People with Dementia: A Systematic Review and Meta-Regression Analysis

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### ABSTRACT

**Background:** Several utility-based instruments have been applied in cost-utility analysis to assess health state values for people with dementia. Nevertheless, concerns and uncertainty regarding their performance for people with dementia have been raised. **Objectives:** To assess the performance of available utility-based instruments for people with dementia by comparing their psychometric properties and to explore factors that cause variations in the reported health state values generated from those instruments by conducting meta-regression analyses. **Methods:** A literature search was conducted and psychometric properties were synthesized to demonstrate the overall performance of each instrument. When available, health state values and variables such as the type of instrument and cognitive impairment levels were extracted from each article. A meta-regression analysis was undertaken and available covariates were included in the models. **Results:** A total of 64 studies providing preference-based values were identified and included. The EuroQol five-dimension questionnaire demonstrated the best combination of feasibility,

reliability, and validity. Meta-regression analyses suggested that significant differences exist between instruments, type of respondents, and mode of administration and the variations in estimated utility values had influences on incremental quality-adjusted life-year calculation. **Conclusions:** This review finds that the EuroQol five-dimension questionnaire is the most valid utility-based instrument for people with dementia, but should be replaced by others under certain circumstances. Although no utility estimates were reported in the article, the meta-regression analyses that examined variations in utility estimates produced by different instruments impact on cost-utility analysis, potentially altering the decision-making process in some circumstances.

**Keywords:** Alzheimer's disease, preference-based measures, systematic review, utility assessment.

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### Introduction

Dementia has become one of the leading chronic disease contributors to disability and dependency among the elderly worldwide. The total number of people living with dementia was estimated globally to be 47.5 million in 2015 and has been predicted to reach 75.63 million in 2030 and 135.46 million in 2050 [1]. The estimated worldwide cost of dementia in 2010 was approximately \$604 billion, and has been conservatively predicted to increase by 85% by 2030 [1].

As the global population ages and the prevalence of dementia increases, the proportion of constrained health care resources required for dementia care is also likely to increase. Health care reimbursement authorities around the world have recommended the use of cost-utility analysis (CUA) to determine the cost-effectiveness of new health care interventions. Converting the effectiveness data to cost per quality-adjusted life-year (QALY) gain enables the CUA to simultaneously integrate the changes in both quantity (length) of life (mortality) and quality of life

(morbidity) [2]. The QALY weights can be obtained directly using elicitation methods or indirectly using questionnaire-type multi-attribute utility instruments.

A number of multi-attribute utility instruments such as the EuroQol five-dimension questionnaire (EQ-5D) [3–5] and recently developed dementia-specific utility-based instruments such as the DEMQOL-U [6,7] have been applied in CUA to assess preference weights for people with dementia. Nevertheless, significant variations were observed in the literature and concerns have been raised regarding the performance of those instruments [8,9]. For instance, generic instruments such as the EQ-5D are widely used because they facilitate comparisons across disparate diseases and interventions in standard economic evaluations. Nevertheless, the classification systems of generic instruments may lack sensitivity to important differences in health status for specific conditions and diseases, such as dementia. Consequently, dementia-specific instruments may be more attractive to both researchers and funding authorities. Furthermore, assessing utility values is a complex and challenging issue for people

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with dementia, who suffer from constraints in judgment, thinking processes, and communicative abilities, resulting in high rates of nonresponders. In this case, it is likely that neither generic nor disease-specific utility-based instruments are able to capture every aspect of quality of life for people with dementia.

People with dementia also consistently have higher self-reported utility scores than those reported by a proxy [10–12]. Considering the loss of insight that has been found to be common in dementia, the higher ratings of patients may reflect a lack of insight into their impairments. Hence, proxy ratings may be more reliable and accurate for people with dementia and, thus, may be more reliable in CUA for policy decisions. On the contrary, studies have shown that caregivers may emphasize the negative aspects and overlook all positive aspects of a patient's quality of life, resulting in relatively low utility ratings, whereas the meaningful information that can be transmitted by people with dementia is overlooked, rather than interpreted by others [13]. No consensus has been reached in the literature as to whether the patient-reported or proxy-reported scores are more appropriate to be used in QALY calculation.

Furthermore, research has shown that differences exist within utility values obtained using various preference-based instruments from the same samples. For example, reported mean utility scores were the highest for the EQ-5D, followed by the Quality of Well-Being (QWB) and the Health Utilities Index (HUI), in studies in which these three instruments were administered to the same patients [12,14]. Studies suggested that both preference measurement technique to weight instrument items (time trade-off vs. standard gamble) and the utility combination rule (additive, multiplicative, and regression) may internally lead to differences across different utility-based instruments [15,16]. Nevertheless, wide variations in reported utility values were also found for the same instrument across different samples. For instance, the reported HUI scores for people with moderate dementia varied between 0.53 and 0.87 [14,17]. Such differences may indicate that not only the instrument itself but also the study-level covariates such as patients' characteristics and methodology could have impacts on reported utility values.

The need for greater understanding of utility weights for people with dementia has been highlighted in the most recent literature [18,19]. It is particularly important to ensure that the values of the measured health states obtained from utility-based instruments are reliable and robust and enable accurate and consistent calculation of QALYs for economic evaluations. To our knowledge, one study has reviewed preference weights for people with dementia obtained from the EQ-5D between 1990 and 2009 [9]. Another study reviewed all relevant utility-based instruments, but only for people with Alzheimer disease (AD) and on the basis of data collected during the period from 2000 to 2011 [8]. Consequently, this study aimed to fill the literature gap by 1) providing a comprehensive comparison of performance (feasibility, precision, reliability, validity, and responsiveness) of all utility-based instruments for people with dementia through a systematic review of published evidence and 2) investigating the factors contributing to the variations in utility values obtained from different utility-based instruments through meta-regression analyses.

## Methods

### Literature Search and Inclusion Criteria

This systematic review was conducted in line with the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines [20]. A database search was performed in April 2016. The

search included the electronic databases of EuroQol, MEDLINE, CINAHL, Cochrane Library, Embase, PsycINFO, Econlit, and PubMed, using the search terms listed in [Appendix Table A1 in Supplemental Materials](#) found at <http://dx.doi.org/10.1016/j.jval.2017.09.005>. Additional articles were found through citations and an updated database search in January 2017. The study selection process was performed by two independent reviewers who initially screened the titles and abstracts for eligibility. The full-text versions of all included studies were then obtained and reviewed for eligibility using the same inclusion and exclusion criteria. Differences between the results of the two reviewers were resolved by discussion with a third reviewer.

Articles were included in this review if they 1) were published in English; 2) involved any type and stage of dementia, including AD, vascular dementia, or dementia with Lewy bodies; and 3) were studies in which health state values or preference weights were presented as outcome measures. Working papers, protocols, editorials or letters, systematic reviews, abstracts, and studies that lacked reported health state values were excluded.

### Systematic Review and Analysis of Utility-Based Instrument Performance

From the studies that satisfied the inclusion criteria, information or data relevant to the instruments' psychometric properties were extracted to investigate their performance for people with dementia. An instrument's measurement performance can be assessed by its feasibility, precision, reliability, validity, and responsiveness. *Feasibility* represents the willingness or ability of participants to complete an instrument [21]. Although difficult to evaluate directly, this is most readily assessed through time taken to complete the instrument, response rates, and number of missing items [9]. *Precision* is the ability of an instrument to distinguish changes in relation to the reported health states [21]. When more than 20% of respondents have maximum good or bad health scores, this indicates ceiling or floor effects, respectively [21]. *Reliability* is defined as the ability to provide stable instrument scores when repeated on an unchanged population, which can be assessed by measuring the test-retest correlation over two points in time [22]. In addition, reliability in instruments refers to the comparability of responses across different assessors (such as patient and proxy report), which can be measured by the inter-rater agreement [23]. Instruments are considered to be strongly reliable and recommended if correlation coefficient estimates are greater than 0.70 [21,24]. *Validity* is the ability of the dimensions of an instrument to adequately cover the core determinants of health-related utility. Applied to health state preferences, content validity refers to the adequacy of the health state description (classification system) in representing health status [25]. Construct validity is assessed by either convergence validity (correlation between targeted instrument and other quality-of-life measures) or known-group validity (correlation of utility values obtained from groups that are expected to differ in cognitive impairment levels) [21,23]. The strength of correlation is considered to be weak if estimates are less than 0.3, moderate if less than 0.5, and strong if more than 0.50 [23]. *Responsiveness* is defined as the ability of an instrument to measure changes in health-related utility over time [21]. It is difficult to assess responsiveness because no criterion standard is available for comparison. Nevertheless, effect size can be viewed as the most common indicator for assessing responsiveness for instruments. Instruments are considered to be the most responsive if the effect size score is more than 0.80, moderately responsive if the score is between 0.5 and 0.8, and mildly responsive if the score is only larger than 0.2 [21].

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