

Quality of Life in Dementia

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ABSTRACT: There is a growing consensus that quality of life (QOL) is an important outcome for assessing the effectiveness of interventions for dementia, but there is no agreement about how to best measure it. Various approaches to QOL assessment have been employed to measure the QOL of persons with dementia, including patient self-report, caregiver proxy report and observational assessment by trained observers. Furthermore, several dementia-specific measures of QOL have been developed, and several generic measures of QOL have been used to assess QOL in dementia. However, to date, QOL has rarely been included as an outcome measure in clinical trials of pharmacotherapy for dementia. This manuscript reviews the current state of knowledge about QOL assessment in dementia.

RÉSUMÉ: Qualité de vie et démence. La qualité de vie (QDV) est de plus en plus reconnue comme étant importante dans l'évaluation de l'efficacité des interventions dans la démence. Cependant il n'existe pas de consensus sur la meilleure façon de la mesurer. Différentes approches ont été utilisées pour l'évaluer chez des patients déments, dont l'auto-évaluation, l'évaluation indirecte par le soignant et l'évaluation par des observateurs entraînés. De plus, plusieurs instruments de mesure de la QDV spécifiques de la démence ont été développés et plusieurs mesures génériques de la QDV ont été utilisées pour évaluer la QDV dans la démence. Cependant, la QDV a rarement été incluse comme critère d'évaluation dans les essais cliniques en pharmacothérapie de la démence jusqu'à maintenant. Ce manuscrit revoit les connaissances actuelles sur l'évaluation de la QDV dans la démence.

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Quality of life (QOL) measurement provides a subjective evaluation that captures the benefits and harms of a treatment and elements of health not detected by standard clinical outcomes.¹ Quality of life has become increasingly recognized as an important outcome for assessing the effectiveness of dementia interventions. The International Working Group for the Harmonization of Dementia Guidelines has recommended that QOL be included as an outcome measure in dementia trials.² Despite the growing consensus about the need to measure QOL in dementia trials, there is a lack of agreement about how to define and measure QOL.²⁻⁴ In keeping with the World Health Organization's definition of health,⁵ health-related QOL is generally considered to be a multidimensional construct that includes physical health, mental health, social function and general well-being. Numerous different quality of life measures have been developed, which can be categorized into disease-specific or generic measures.⁶

DISEASE-SPECIFIC VERSUS GENERIC QOL MEASURES

Disease-specific QOL measures focus only on dimensions relevant to a specific disease, which tends to increase their responsiveness (i.e. their ability to identify changes that relate to the natural history of the disease or to treatment interventions).⁶ Generic measures allow for comparisons across different

diseases or their treatments and can be helpful in health policy decisions.⁶ However, generic measures often exhibit less responsiveness than disease-specific measures, which may limit their usefulness in clinical trials.⁶ Generic measures can be classified as health profiles or utility measures. Health profiles, such as the Short Form-36 (SF-36) and the Sickness Impact Profile, classify an individual with respect to a broad spectrum of QOL domains.⁶ Utility measures provide a global measure of an individual's preference for a health state in a single number from 0 (death) to 1 (full health).⁶ Utility measures have the specific advantage of being readily incorporable into cost-effectiveness analyses that assess interventions in terms of their cost per

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quality-adjusted life year.^{6,7} Utilities can be directly elicited from individuals using standard techniques, or can be obtained from health indexes that incorporate both a health state classification system and a set of population-derived weights that yield a utility score. The three most commonly used health indexes are the Health Utilities Index (HUI), the European QOL scale (EQ-5D) and the Quality of Well-Being scale (QWB).⁸

APPROACHES TO QOL ASSESSMENT IN DEMENTIA PATIENTS

Three approaches have been used for assessing QOL in dementia patients: 1) direct observation of behaviours and activities assumed to be related to QOL; 2) proxy reports by a family member or caregiver; and 3) self-reports by the individual with dementia.^{9,10} Until quite recently dementia patients were assumed not to be able to provide meaningful information about their QOL because of their cognitive impairments, leading to the proliferation of observational and proxy QOL measures.^{1,11} However, both these approaches exclude consideration of the patient's subjectively appraised experiences, which many believe to be an inherent feature of QOL.^{1,9,11} Central to the question of whether patients or caregivers should be asked to assess the patients' QOL is whether patients can reliably rate their own QOL and whether there is agreement between patients and caregivers regarding their ratings of patients' QOL.

In the advanced stages of dementia, patients are too cognitively impaired to rate their own QOL so we must rely on proxy reports or direct observation of QOL of patients. However, mounting evidence suggests that the majority of patients with mild-moderate dementia can meaningfully rate their own QOL.¹²⁻¹⁴ Mozley et al¹² found that in a nursing home population, over 80% with MMSE scores ≥ 11 could provide meaningful answers to a generic QOL questionnaire. Brod et al¹⁴ found that 96% of patients with MMSE scores ≥ 13 were able to reliably and validly rate their own QOL using the Dementia QOL (DQOL) scale. Logsdon et al¹³ found that 88% of Alzheimer's patients were able to reliably and validly rate their QOL on the QOL-Alzheimer's Disease (QOL-AD) scale, and that all patients with MMSE scores ≥ 11 were able to do so. Novella and colleagues^{15,16} found that patient self-ratings could be reliably carried out in dementia patients with MMSE scores ≥ 15 using the SF-36 and the Duke Health Profile using a facilitated interview process.

Several recent studies have compared the agreement between dementia patient and caregiver proxy ratings using disease-specific and generic QOL instruments.^{13,17-21} These studies have shown that patients tend to rate their QOL significantly higher than their caregivers do and that there are significant differences between QOL ratings by different proxy sources. Various patient and caregiver factors can influence QOL ratings, thus contributing to discrepancies between raters. Such factors may include patient factors such as adaptation to their illness, as has been shown with other chronic illnesses,²³ and loss of insight into their impairments, and caregiver factors such as caregiver burden and depression.^{19,22-25} These results suggest that although caregiver proxy ratings provide important QOL information from the perspective of persons without dementia, they do not accurately reflect the patients' subjective view of their own QOL. Therefore, whenever possible, studies should include both patient ratings (in those with mild-moderate dementia) and proxy

ratings, since they provide distinct information reflecting different perspectives.

QUALITY OF LIFE MEASURES USED TO ASSESS QOL IN DEMENTIA PATIENTS

In the late 1980's, the Progressive Deterioration Scale (PDS) was developed as the first disease-specific measure to assess QOL in Alzheimer's disease.²⁶ This 27-item proxy measure was based primarily on daily activities, and current consensus is that the PDS is more a measure of function than a multidimensional measure of QOL.²⁷ In the past ten years, several new QOL measures have been developed for dementia populations. Lawton²⁸ provided a theoretical model that has served as the basis for many dementia QOL measures. The model includes four dimensions: (1) behavioural competence (e.g. physical health, functional and cognitive abilities, and social behaviour); (2) psychological well being; (3) objective environment (e.g. social support, living situation); and (4) perceived overall QOL. Some of the new QOL measures have incorporated items from all four dimensions, while others have included items from only one or two.⁴

Two recent review articles and a recent book summarize disease-specific QOL measures that have been developed for dementia populations.^{3,4,29} These measures vary in many ways:

1. **Content:** some of the measures include a broad scope of QOL domains including function and cognition. Others have specifically excluded items about function and/or cognition with the rationale that these items are determinants rather than features of QOL, and others still have limited their focus to only one or two domains (e.g. activities, affect, behaviour).^{14,30-34}
2. **Respondent:** some of the measures have been developed exclusively for patient or proxy (i.e. informal or formal caregiver) ratings, while some have been developed for either patient or proxy ratings.
3. **Method of Administration:** most patient and proxy rated measures are interviewer-administered, although some measures are self-administered, and direct observational measures require a trained assessor to observe specific behaviours and/or activities for a fixed period of time.
4. **Target Population:** many of the measures were developed mainly for use in patients with mild-moderate dementia,^{13,14,30,31,35,36} although others were developed primarily for use in severely demented or institutionalized patients,^{32,33} or for use across the spectrum of disease severity.^{37,38}

Three disease-specific measures that have been used in several dementia studies and that have some data supporting their reliability and validity are the QOL-AD, the DQOL and the Alzheimer's Disease Related Quality of Life (ADRQL).⁴ The QOL-AD is a 13-item measure (physical health, energy, mood, living situation, memory, family, marriage, friends, chores, fun, money, self, and life as a whole) that was developed for either patient or proxy ratings.^{13,24,39,40} The DQOL is a 30-item measure with five subscales (self-esteem, positive affect, negative affect, feelings of belonging and sense of aesthetics) and a single item to assess overall QOL that was developed initially exclusively for patient ratings, but that has subsequently also been used for proxy ratings.^{11,14,19,39} The ADRQL is a 47-item measure of

positive and negative behaviours across five domains (social interactions, awareness of self, feelings and mood, enjoyment of activities and response to surroundings) that was developed for caregiver proxy ratings.^{37,39,41}

Although disease-specific measures have received a lot of attention, many studies have also evaluated the use of generic health profile measures, including the SF-36, the Sickness Impact Profile, and the Nottingham and Duke Health Profiles,^{15,16,42} and utility measures, including the time-tradeoff, EQ-5D, QWB and HUI,^{17,21,40,43-47} for patient and/or proxy ratings in dementia populations. These studies provide evidence that various generic health profiles and the EQ-5D are reliable for patient ratings in patients with mild-moderate dementia, and that the EQ-5D, the QWB, the HUI and the time-tradeoff are reliable and valid for proxy ratings.^{17,40,44-47}

QUALITY OF LIFE MEASURES IN DEMENTIA CLINICAL TRIALS

Quality of life instruments selected for use in clinical trials must have established reliability and validity in the specific population being studied, as well as proven responsiveness to detect clinically relevant change.⁶ Although there are increasing data on the reliability and validity of several measures for assessing QOL in dementia, there are minimal data on their responsiveness, and there is no consensus on what change in QOL on any given measure constitutes a clinically significant change.⁴ In addition, little is known about the impact of various potential confounders (e.g. comorbidity, patient's living circumstance) on patient and proxy QOL ratings.

A recent systematic review of published randomized controlled trials (RCTs) of pharmacologic treatments for dementia, including tacrine (8 RCTs), donepezil (11 RCTs), rivastigmine (6 RCTs), galantamine (6 RCTs), metrifonate (9 RCTs), memantine (3 RCTs), selegiline (6 RCTs), estrogens (5 RCTs) and *Gingko biloba* (3 RCTs), showed that QOL was rarely included as an outcome measure.⁴⁸ Four donepezil trials included the Blau QOL measure as a secondary outcome,⁴⁹ assessing patient ratings in three trials, and patient and proxy ratings in one trial.⁵⁰⁻⁵³ The Blau⁴⁹ QOL is a generic measure covering 10 domains, with no data supporting its reliability or validity for patient or proxy ratings in dementia.^{3,27} The Blau QOL ratings in the donepezil trials exhibited marked variability within subjects and did not show any consistent treatment effects across the trials.^{52,53} One tacrine RCT,⁵⁴ one donepezil RCT,⁵⁵ two rivastigmine RCTs,^{56,57} and one galantamine RCT⁵⁸ included the PDS as a secondary outcome measure. As mentioned earlier, most consider the PDS to be a measure of function rather than QOL. In fact, in three of the five RCTs in which it was used, it is referred to as a measure of daily activities. The PDS results were inconsistent across the trials.²⁷

None of the newer dementia-specific QOL measures have been included in the published RCTs of pharmacologic treatments. However, a recent randomized trial of a cognitive stimulation therapy program included the QOL-AD as a secondary outcome measure and showed that the treatment group had a statistically significant improvement in the QOL-AD.⁵⁹ However, the effect size (0.28) was small.⁶⁰ Another recent clinical trial of the effects of a cognitive communication program plus a cholinesterase inhibitor in AD patients used the QOL-AD as a secondary outcome measure.⁶¹ This study showed

no significant differences between the treatment and control groups.

QUALITY OF LIFE OF CAREGIVERS

Although this review has focused primarily on the assessment of the QOL of patients with dementia, assessing the QOL of their caregivers is also important because it may be affected by antidementia treatments.⁶²⁻⁶⁶ Studies of caregiver outcomes have tended to focus more on constructs such as burden, affect and physical health than on QOL.⁶⁷ Nevertheless, some studies have included QOL measures and have demonstrated that caregiving for patients with dementia has detrimental effects on caregiver QOL.^{64,68} The systematic review of RCTs of drug treatments for dementia⁴⁸ documented only one trial that included a measure of caregiver QOL (the SF-36) as a secondary outcome measure, but the results for this outcome were not reported.⁶⁹ If one of the goals of treatments for dementia is to improve caregiver outcomes, then it is imperative that caregiver QOL be included as an outcome measure.

CONCLUSIONS

Patient and caregiver QOL outcome measures should be included in studies of antidementia therapies. At this time no specific measures can be recommended. Disease-specific measures will likely be more responsive to treatment effects, while generic measures may be necessary to address policy issues such as cost-effectiveness. For patients with mild-moderate dementia, both patient and proxy rated QOL measures are encouraged, as they appear to provide different information. For patients with severe dementia, proxy and/or observational QOL measures are recommended. Future studies are needed to clarify the criteria for inclusion of patients for self-rating and for identifying the most appropriate proxy informants, to identify the characteristics of patients and proxies that influence their QOL ratings over time, and to determine which QOL measures are the most reliable, valid and responsive for specific dementia populations.

DECLARATION

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