Quality of life in dementia
From concept to practice

Carla Schölzel-Dorenbos

Colophon

I dedicate this thesis to Justien, my one and only!

Quality of life in dementia
From concept to practice

Een wetenschappelijke proeve op het gebied van de
Medische Wetenschappen

Proefschrift

ter verkrijging van de graad van doctor
aan de Radboud Universiteit Nijmegen
op gezag van de rector magnificus prof. mr. S.C.J.J. Kortmann,
volgens besluit van het college van decanen
in het openbaar te verdedigen op maandag 31 januari 2011
om 13.30 uur precies

door

Carolina Josina Maria Schölzel-Dorenbos
geboren op 12 maart 1951
te Amsterdam

Promotor: Prof. dr. M.G.M. Olde Rikkert

Copromotores: Dr. P.F.M. Krabbe (UMC Groningen)
                     Dr. R.J.F. Melis

Manuscriptcommissie: Prof. dr. M.J. Vernooij-Dassen
                     Prof. dr. R.M. Dröes (VUmc Amsterdam)
                     Dr. W.J.M. Dekkers

Quality of life in dementia
From concept to practice

An academic essay in
Medical Sciences

Doctoral Thesis

to obtain the degree of doctor
from Radboud University Nijmegen
on the authority of the Rector Magnificus prof. dr. S.C.J.J. Kortmann,
according to the decision of the Council of Deans
to be defended in public on Monday, January 31, 2011
at 13.30 hours

by

Carolina Josina Maria Schölzel-Dorenbos
born on March 12, 1951
in Amsterdam (The Netherlands)

Doctoral supervisor: Prof. dr. M.G.M. Olde Rikkert

Co-supervisors: Dr. P.F.M. Krabbe (UMC Groningen)
        Dr. R.J.F. Melis

Doctoral Thesis Committee: Prof. dr. M.J. Vernooij-Dassen
        Prof. dr. R.M. Dröes (VUmc Amsterdam)
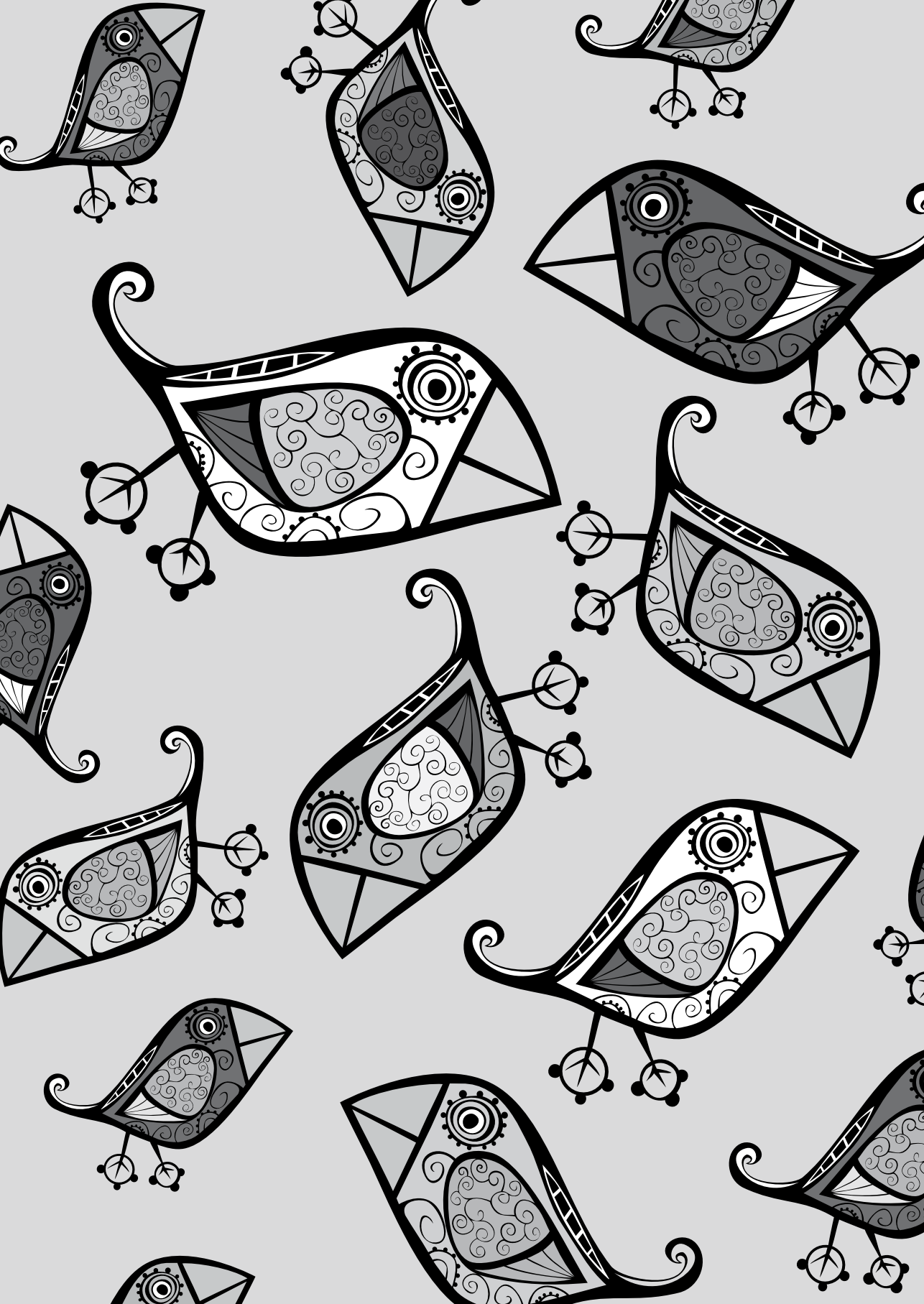   Dr. W.J.M. Dekkers

CONTENTS

CHAPTER 1

FOREWORD

This thesis addresses the concept and practice of quality of life in dementia. Quality of life in dementia is a rapidly growing field of research. We present an overview of theory, measurement and research. The thesis includes a theoretical and an empirical part. The first part addresses theoretical notions on quality of life in dementia. The empirical data consecutively address quality of life measurement in patients and informal caregivers, and application, understanding and development of quality of life measurement instruments. The general introduction will help to understand the complex scenery of quality of life research in dementia, and it will explain the relevance and the type of the research questions to be answered in this thesis. But for readers who are unfamiliar with dementia and quality of life research, we start with a glossary of basic definitions of key terms used in this thesis.

GLOSSARY OF KEYWORDS

A   Alzheimer's disease
Alzheimer's disease (AD) is a progressive neurological brain disorder leading to irreversible loss of neurons and dementia. The NINCDS-ADRDA Alzheimer's criteria were proposed in 1984 and are among the most used in the diagnosis of AD.[1] These criteria require that the presence of cognitive impairment and a suspected dementia syndrome be confirmed by neuropsychological testing for a clinical diagnosis of possible or probable AD, while they need histopathologic confirmation for the definitive diagnosis. The criteria specify eight cognitive domains that may be impaired: memory, orientation, language, perceptual skills, attention, constructive abilities and functional abilities, and problem solving. Since this proposal the advances in functional neuroimaging techniques and CSF biomarker profiles have led to proposals of revision into research criteria that take into account these techniques.[2] AD is the most common cause of dementia (60% of all cases) and usually arises in late middle age or in elderly people, but there is a rare familial subtype that occurs earlier.

A   Anosognosia
Unawareness of cognitive, emotional, and functional deficits. Condition in which persons who suffer disability seem unaware of or deny the existence of their disability. There is no strong consistent relationship between degree of anosognosia and severity of dementia. Frontotemporal dementia often starts with anosognosia. The word comes from the Greek words nosos (disease) and gnosis (knowledge).

B   Behavior
Actions or reactions of persons, usually in relation to their environment. Behavioral symptoms include disturbed perception, thought content, mood or behavior.

C   Caregiver (informal)
Person who provides unpaid care by looking after family members, friends or partners with disabilities. A big chunk of all costs of dementia (more than 40% globally) is attributed to informal care. It is therefore worrisome that, while the cost of formal care in high-income countries continues to escalate to unsustainable levels, the availability of informal support is predicted to decline in all regions.

C   Care-related quality of life
Care-related quality of life reflects and values the impact of informal caregiving on the caregiver's overall quality of life.

C   Cognition
Mental processes characterized by attention, knowing, thinking, learning, remembering, language, planning action, and judging.

C   Coping
Process of managing demanding circumstances and employment of behavioral and psychological efforts to deal with stressful events.

C   Cost utility analysis
Cost utility analysis (CUA) estimates the ratio between the cost of an intervention and the benefit it produces. Cost is measured in monetary units, benefit is expressed in QALYs (see Quality-adjusted life years) or the related DALYs (disability-adjusted life years). Both equal 1 for each year of full-health life, and less than 1 for various degrees of illness or disability. Thus the cost-effectiveness of a treatment can be assessed by the cost per QALY or DALY it produces.

D   Dementia
Progressive brain syndrome with significant loss of or decline in intellectual abilities such as memory, intellectual functions like reasoning and planning, and eventual loss of physical functions and personality, severe enough to interfere with a person's daily social or occupational functioning. The symptoms may also include changes in mood and behavior. Dementia mainly affects older people, although there is a growing awareness of cases that start before the age of 65. After age 65,

the likelihood of developing dementia roughly doubles every five years. Dementia affects 1 in 20 people above 65, 1 in 5 over 80 and 1 in 3 over 90 years of age. Alzheimer's disease (AD) is the most common cause of dementia and accounts for 60% of all cases. Other causes are vascular dementia (VD; 15%), mixed dementia (AD and VD; 13%) and remaining (12%), such as frontotemporal dementia, dementia with Lewy bodies and Parkinson dementia. Different types of dementia have been associated with different symptom patterns and distinguishing microscopic brain abnormalities. The symptoms of different types of dementia however may overlap and can be further complicated by coexisting medical conditions. Dementia is still an incurable disease, stressing the necessity of palliative care (see Palliative care).

D   Dementia Personalized Care Planning

Dementia Personalized Care Planning (DPCP) is a protocol we propose to guide dementia care. DPCP will be based on personal needs and goals of both patients and caregivers. DPCP is derived from the choices and choosing (C-C) model, a process that features the personal management of accessing choices and choosing among them.[3] The C-C model introduces a science base for understanding and guiding interventions that can assist people to achieve their quality of life goals. The C-C model is supplemented with structured eliciting of realistic most urgent problems and needs. The result of this process is converted into concrete goals for care planning, treatment and evaluation during follow-up visits.

D   Descriptive quality of life instruments

Descriptive quality of life instruments (health profiles) comprise multiple dimensions of health status. A small set of related items covers the content of various health domains and a score for each dimension is generated based on classical test theory.[4] The domains are regarded independently and their relative separate ratings are not intended to be aggregated into one score. Thus, these instruments are not appropriate to measure the overall level of health states. The SF-36 (Medical Outcomes Study 36-item Short-Form Health Survey) instrument is a frequently used descriptive generic quality of life measure worldwide.[5]

D   Disability paradox

It is often assumed that living with a chronic disease means a reduced quality of life. Disability paradox is the phenomenon that persons with serious disabilities against all odds report a relatively high health-related quality of life, while observers judge their life to be undesirable. The difference may be explained because patients first often fight, neglect or avoid losses, while adapting to their disease later in life.

D   Disease-specific index instruments for quality of life

This type of instrument combines disease-specificity and quantification of perceived quality in several health domains into one single figure. These instruments have been developed for some diseases, but not for dementia. We designed the prototype of a disease-specific index instrument for dementia, the Dementia Quality of life Instrument (DQI). The DQI is a classification system with five selected dementia domains to describe dementia status.

D   Disease-specific quality of life instruments

Disease-specific measures target individual diseases (or domains). They aim at emphasizing problems specific to patients with a specific disease such as dementia. Compared with generic measures, disease-specific measures normally are more sensitive and responsive to the changes in the assessment of quality of life of specific patient groups. Disease-specific scales only include items relevant for the disease in question and thus contain less 'noise' than generic instruments which also contain less appropriate items. However, the cost of greater specificity is less generalizability.

G   Generic quality of life instruments

Generic quality of life instruments are universal and cover general health aspects, which makes them relevant for multiple patient groups and allows comparison across different diseases. They rate quality of life in terms that are relevant for everybody, regardless of the presence or absence of a specific disease. Generic measures may include domains not relevant for patients with a specific disease and underestimate more relevant areas. This may result in a lower responsiveness. Typically a generic measure in clinical research is combined with one or more disease-specific measures.

H   Health-related quality of life (HRQoL)

Health-related quality of life is a more narrow concept than quality of life and reflects the individual's perception of the impact of a health status, e.g. dementia, on the ability to perform usual tasks and effects on everyday life, and physical, social and emotional well-being. HRQoL primarily looks at quality of life through the perspective of a person's health status and/or impact of a person's health condition or disability.

H   Health status

Health (status) according to the World Health Organization definition: a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity. Self-rated health status has been shown to be mostly related to physical health and function.

I   Index quality of life instruments

Index (preference or value-based) quality of life instruments evaluate the value that persons place on a particular health state and not directly the impact of a disease or treatment on their ability to function in life. Index measures quantify multiple health domains into one single figure. In the case of HRQoL, index measures quantify the desirability of a certain health state.[6] The generated values (variously called utilities, preferences, strength of preference, or weights) are often unambiguous; e.g., a value of 1.0 stands for 'perfect health' and 0.0 for 'death' (see Utilities). HRQoL values with metric characteristics are especially useful because they provide vital information for health outcome research and economic evaluations. The EuroQol-5 D (EQ-5D) is the most widely used HRQoL index instrument.[7;8] Applicable to a wide range of health conditions and treatments, it provides a simple descriptive profile and a single index value (utility) for health status.

M   Measurement of HRQoL

There are two fundamentally different approaches to HRQoL measurement. The first is the standard 'questionnaire' approach, using descriptive or profile instruments (see Descriptive quality of life instruments).[9] The second is the 'index' approach, using preference-based instruments (see Index quality of life instruments).[10;11] Based on the extent to which illnesses are covered, both types of HRQoL measures can be categorized into disease-specific instruments (see Disease-specific quality of life instruments) and generic instruments (see Generic quality of life instruments). The first target individual diseases or specific health problems, while generic instruments are more universal and cover general health aspects. In sum, there are 4 types of quality of life measurement instruments: disease-specific index instruments (i.e. the Dementia Quality of life Instrument (DQI), disease-specific descriptive instruments (i.e. Quality of Life-Alzheimer's Disease Scale (QOL-AD), generic index instruments (i.e. EQ-5D), and generic descriptive instruments (i.e. SF-36).

M   Mild cognitive impairment

Forgetfulness that is worse than normal for one's age but is not (yet) associated with certain cognitive problems common in dementia, such as disorientation or confusion. Persons with Mild Cognitive Impairment (MCI) are able to function in everyday activities without more assistance from others than previously needed, but have difficulty with memory or other cognitive functions. A variable part of the subjects with MCI convert to dementia patients.

M   Mini-Mental State Examination

The Mini-Mental State Examination (MMSE) is a screening test of cognitive function involving orientation, registration, attention and calculation, recall, language and praxis. The MMSE is widely used as a research tool, and has been extensively validated, translated, and modified.

O   Outcome measures

Assessing meaningful treatment benefits is complex. Many researchers state that cognitive response no longer suffices in anti-dementia trials.[12] There is little consensus on which domains are best suited to evaluate clinically meaningful results of treatment. Nevertheless European consensus to improve comparability of psychosocial intervention studies in dementia was reached. Recommended outcome measures were for patients: quality of life, mood, global function, behavior and daily living skills. For informal caregivers the preferred outcomes were mood, burden, coping with behavior and quality of life.[13] There is increasing recognition that adding patient-reported outcomes such as HRQoL is warranted.[14]

P   Palliative care

Definition of the World Health Organisation (WHO): an approach that improves the quality of life of patients and their families facing the problems associated with life threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and physical, psychosocial and spiritual problems. Palliative care provides relief from distressing symptoms, offers a support system to help patients live as actively as possible until death, offers a support system to help the family cope during the patients illness and in their own bereavement, uses a team approach to address the needs of patients and their families, will enhance quality of life and is applicable early in the course of illness.

Q   Quality-adjusted life years

Quality-adjusted life years (QALYs) assess the extent of benefits gained from interventions. It combines gained life time and quality of the gained time and it is defined that there exists the possibility of trade-off between these two aspects. When QALYs are used in different interventions, cross-comparisons can be made to describe the relative benefit. When combined with the costs of providing these interventions, decision makers can understand their relative cost-effectiveness. In case of scarce resources interventions should be reimbursed which provide the best incremental cost-effectiveness ratio.

Q   Quality of life

Definition according to the WHO: the perception of individuals of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns (WHOQOL 1995). Quality of life is a multidimensional construct of physical, material, social and emotional well-being, development and activity, and the ability to function in daily life. It is a broad ranging concept affected by the person's physical health, psychological state, level of independence, personal beliefs, social relationships, relationship to salient features of the environment, such as financial resources, accessibility and quality of professional care, opportunities for acquiring new information, skills and recreation. But, facets like transport, spirituality and religion are also involved. In this thesis the term 'quality of life' can refer to both quality of life and health-related quality of life.

R   Response shift

Response shift is the change in self-evaluation of quality of life as a result of recalibration (changes in internal measurement standards in assessing quality of life), reprioritization (changes in values or importance of domains constituting quality of life), or reconceptualization (redefinition of quality of life). According to response shift theory people rate their health in reference to a relative instead of an absolute standard, namely their current health. However, health state, and thus standards, change over time in case of progressive diseases. Response shift is often seen in patients with chronic disease who adapt to disease progression (see also Disability paradox).

S   Sense of competence

Sense of competence is the concept that denotes informal caregivers' feeling of being capable to care for their care recipients. It includes satisfaction with the care recipient, satisfaction with the person's own performance, and (adverse) consequences of caregiving for the personal life of the caregiver.

U   Utility

Utilities are values for health states: numeric measurements (0=death, 1=best possible health state) that reflect a person's beliefs about the quality of life weight of a health state. Utilities are derived by either direct or indirect index (utility) instruments. Direct measures include visual analogue scales (VAS), standard gamble (SG), and time trade-off (TTO) techniques. Health state utilities are used to calculate QALYs (see also Quality-adjusted life years) which are applied in cost-utility or cost-effectiveness analysis.

W   Well-being

State of being healthy, happy. Expression often used interchangeable with quality of life, but as quality of life is defined broader, well-being is best considered as associated with quality of life. At the individual level, well-being is influenced by factors such as family and social relationships, health and work. At the societal level, well-being consists of the collective well-being of individuals, social institutions, and the quality of their interactions. Choices and significant life events can alter the course of a person's life, and thus, his or her well-being.

INTRODUCTION

Quality of life

Quality of life is the perception of people of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns, irrespective of health status (WHOQOL 1995). Quality of life includes perceptions of overall quality of life, health, physical and material well-being, work, family, social relationships, community- and social activities, personal development, personal achievements, happiness, life satisfaction, personal experiences and values, active recreation, learning, education, and leisure.[15;16] Consequently, quality of life is a multidimensional concept that can be defined in terms of objectively measurable life conditions and the subjectively measurable satisfaction with these conditions. When quality of life is described three questions need to be answered. How well measure objective indicators the variance in quality of life of an individual? How important is a given quality of life domain for someone, and how satisfied is the person with this domain?

Quality of life has a multifaceted perspective. This requires a shift away from approaches that focus only on single areas of life (e.g. health, functioning, social support, life satisfaction, and well-being) towards an approach that also reveals the views of the persons with dementia. How quality of life is understood depends on which perspective one uses.[17;18] Quality of life is a dynamic construct with interactive domains and changing values resulting from processes such as aging, life experiences and diseases.

Thus, quality of life is on the one hand objective, external and quantitative, but on the other hand subjective, internal and qualitative. Objective information can be described with descriptive indicators, subjective information is described with evaluative indicators (e.g. satisfaction with a descriptive indicator). Both approaches are complementary and should not be treated as opposites.

Well-being

The expression 'well-being' is often used interchangeable with quality of life, but the latter has a broader definition. Well-being is a state of being healthy, happy. Well-being is best considered as associated with quality of life. At the individual level, well-being is influenced by factors such as family and social relationships, health and work. At the societal level, well-being consists of the collective well-being of individuals, social institutions, and the quality of their interactions. Choices and significant life events can alter the course of an individual's life, and thus, his or her well-being.

When considering quality of life as a global overarching concept it is also important to discern between what is a facet of quality of life and what determines quality of life. Determinants are factors that can influence quality of life but are not part of it. Treating or influencing major determinants has consequences for quality of life and thus therapeutic consequences.

Health-related quality of life (HRQoL)

HRQoL is quality of life from the medical and health perspective. HRQoL primarily looks at quality of life through the perspective of a person's health status and/or impact of a person's health condition or disability. By definition HRQoL is a narrower concept than quality of life. The term HRQoL originated to distinguish outcomes relevant to health research from earlier sociological research on subjective well-being and life satisfaction in healthy populations. HRQoL can be defined as the value assigned to length of life as modified by the impairments, functional states, perceptions, and social opportunities that are influenced by disease, injury, treatment, or policy.[19] HRQoL reflects the individual's perception of the impact of a health condition on the ability to perform usual tasks and the effects on everyday life, physical, social and emotional well-being.[20] HRQoL can be distinguished from quality of life in that it concerns itself primarily with those factors that fall under the purview of health care providers and systems. However, because health is not just the absence of disease, HRQoL measures often also incorporate perceptions, role functions, social health, and general well-being. Carr et al. assumed HRQoL to be those aspects of an individual's subjective experience that relate both directly and indirectly to health, disease, disability, and impairment.[21] However, there is no consensus on the definition of HRQoL.

Health status

Quality of life and health status are separate constructs. Health status is comparable to HRQoL. However, in contrast tot HRQoL, health status is more clinically oriented and therefore does not include domains such as social activities. When rating quality of life, patients give greater emphasis to mental health than to physical functioning. This pattern is reversed for the appraisal of health status, for which physical functioning is a more important determinant than mental health. Thus, evaluations of effectiveness of interventions may differ depending on whether quality of life, HRQoL or health status is the study outcome.[22] Instruments to measure health status, including utility-based questionnaires, may not be suitable for measuring overall (HR)QoL, because most respondents will refer primarily to their physical condition.[22]

In sum, quality of life, well-being, HRQoL and health status are overlapping, but distinct concepts. The interrelationship between these concepts is presented in Figure 1. In this thesis the term 'quality of life' is used as the overarching concept covering quality of life, well-being, health-related quality of life (HRQoL) and health status. 'Quality of life' can refer to any of these concepts.

Figure 1. Overarching concept of quality of life in dementia

Dementia is a complex neurodegenerative syndrome characterized by decline in cognitive, social and physical functioning. The burden of dementia is not only or primarily reflected by decrease in cognition, but also by a variety of non-cognitive symptoms such as behavioral problems and physical handicaps. As the population ages more people will be faced with dementia. The number of dementia patients in the Netherlands is about 250,000, including 175,000 patients with Alzheimer's disease. Prevalence is 1-2% in people aged 65-70 years (www.RIVM.nl) and rises steeply with aging, up to 30-55% in people aged 90-94 years. The number of newly diagnosed dementia patients is about 30,000 per year. Dementia places a substantial medical, social and psychological burden on patients and their families and caregivers. The detrimental impact upon quality of life of all persons involved is well established. Most people regard dementia as a devastating end of life. Available medications for Alzheimer's disease temporarily reduce symptoms for some, but cannot change the underlying course of the disease. Given the complexity of dementia, there is emerging consensus that besides discrete areas of function, broad patient-reported outcome measures such as quality of life are warranted for com-

prehensive outcome measurement in clinical treatment, research and economical decision making. As such, quality of life can be regarded as one of the health outcomes of dementia, which in turn is related to and influenced by other outcomes. Measurement of quality of life provides a subjective evaluation that captures the benefits and harms of interventions and elements of health not detected by standard clinical outcomes.[23] Next to survival and clinical outcome parameters (such as cognition, behavior, instrumental and basic activities of daily living) quality of life has become an established outcome measure in evaluating clinical interventions, and for dementia patients and caregivers.[13;24;25]
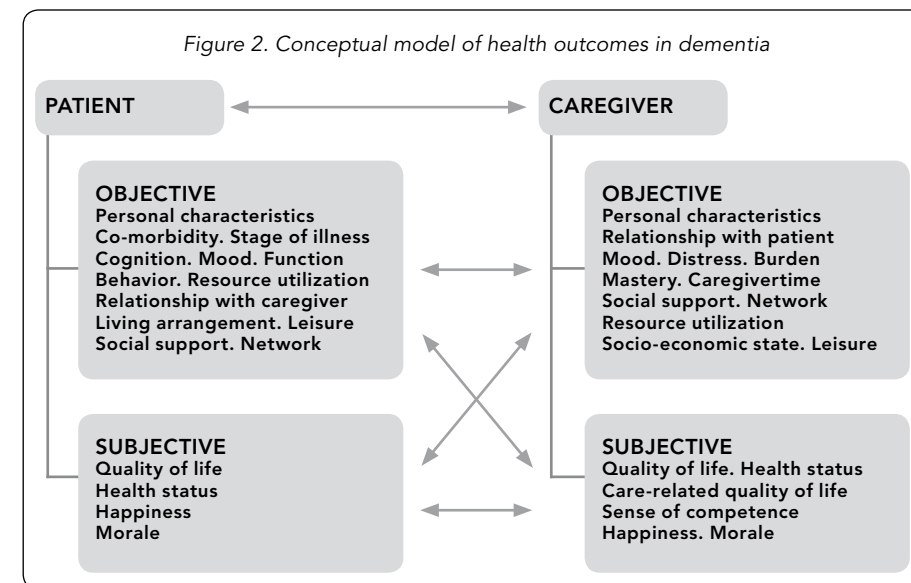
The impact of dementia, both in terms of cost of care and of lives affected, is staggering. Dementia places a massive strain on an already overburdened health care budget. In the absence of disease-modifying treatments dementia is a chronic and still incurable disease, implying the need of palliative treatment. The primary aim of palliative treatment should be to maintain or improve quality of life. Medical models of quality of life traditionally assume that the more symptoms present, and the more advanced the disease, the poorer the quality of life. Nevertheless, many people with serious and persistent disabilities report a high quality of life against all odds.[26] This phenomenon is called disability paradox. Disability paradox explains why many people with serious disabilities report that they experience a good or even excellent quality of life when to most external observers they seem to live an undesirable daily existence. People often overestimate the emotional impact that chronic illnesses and disability will have on their lives. There is a discrepancy between the happiness reports of patients with chronic illness or disability versus the happiness predictions of healthy people asked to imagine the same illnesses and disabilities. The available evidence suggests that, whereas patients misreport their well-being, healthy people also mispredict the emotional impact that chronic illness and disability will have on their lives.[27] The difference may be explained because patients first often fight, neglect or avoid losses, while adapting to their disease later in life. If we assume that intellectual capacities, judgment and insight are intact, disability paradox may be explained by the dynamics of coping and adaptations to disease states. First patients may fight, neglect or avoid losses, and later they may adapt themselves.[28] Thus, quality of life does not necessarily decrease during the course of dementia,[29;30] and is preserved in some people with advanced dementia despite disease progression.[31] Apparently the relationship between severity of dementia and quality of life is neither simple nor direct. Quality of life is dependent upon finding a balance between body, mind and spirit and on establishing and maintaining harmonious relationships within the person's social context and external environment.

Changes in individual quality of life measurements often do not only reflect changes in health status, but also changes in the psychological adaptation of perception of quality of life following a change in health status, e.g. by adaptation to progress of the disease. This phenomenon is called response shift. Response shift needs to be considered when interpreting serially measured patient reported outcomes.[32] Response shift is inextricably bound up with the quality of life concept and should be taken into account in the design and interpretation of clinical research. However, in the absence of gold standards for both quality of life and response shift, it is not yet clear which methods best quantify response shift.

Dementia is a hope-hindering life experience for patients as well as their informal caregivers and hope is important to maintain quality of life. But there are also many factors outside the dementia that influence quality of life. Quality of life is primarily defined by the person and his or her circumstances and not just by the dementia. It is therefore important to develop methodologies that include both generic and dementia-specific quality of life indicators, because domains that feature generic quality of life measures may be of just as much relevance to people with dementia as the more dementia-specific domains in disease-related quality of life measures.

Quality of life measurement can demonstrate whether benefits of treatments are perceived as meaningful by patients and caregivers.[33] If two different treatment options equally affect cognitive or functional domains, but one improved quality of life and the other did not, the therapy that would improve quality of life should probably be the therapy of choice (also depending on side effects, safety issues and costs). The International Working Group for the Harmonization of Dementia Guidelines has recommended that quality of life should be included as outcome parameter in dementia trials.[34] Empirical results of quality of life research will lead to identification of the relevant treatment goals for both patients and caregivers.

Figure 2 provides an overview of the relevant outcomes associated with quality of life in dementia. The objective domain includes dementia-related personal factors that are strongly influenced by the disease (e.g. physical health, function, cognition), general personal factors (e.g. age, sex, income) and objective external environmental influences (e.g. social support, living situation). The subjective domain consists of the individuals' personal values, defining the importance of certain objective life conditions, their subjective feeling of well-being (i.e. degree of satisfaction of persons with their objective life conditions) and finally the subjective evaluation of a person's life in general. All these domains and factors are intricately linked with each other. Individual quality of life is probably determined by multiple objective and subjective factors. This thesis will try to clarify some of these complex relationships.

Figure 2. Conceptual model of health outcomes in dementia

PATIENT ←→ **CAREGIVER**

OBJECTIVE
Personal characteristics
Co-morbidity. Stage of illness
Cognition. Mood. Function
Behavior. Resource utilization
Relationship with caregiver
Living arrangement. Leisure
Social support. Network

OBJECTIVE
Personal characteristics
Relationship with patient
Mood. Distress. Burden
Mastery. Caregivertime
Social support. Network
Resource utilization
Socio-economic state. Leisure

SUBJECTIVE
Quality of life
Health status
Happiness
Morale

SUBJECTIVE
Quality of life. Health status
Care-related quality of life
Sense of competence
Happiness. Morale

What are the pitfalls of measuring quality of life in dementia?

Dementia may interfere with understanding, the ability to remember relevant events, making comparisons across complex domains, and communicating. This raises doubt on validity and reliability of patient reported outcomes, especially on reflective measures such as quality of life. The impact of declining intellectual capacities, semantic knowledge and episodic memory, as well as varying deficits of judgment and insight, may compromise judgment and add to inter- and intra-individual variation in quality of life rating. Anosognosia (unawareness of deficits) is frequently reported as a cause for less reliable repeated self-reports and discrepancies between self-rating and proxy-rating. Also, judgments about what is important to quality of life may change as the dementia progresses: what seems important in early stages (e.g., preservation of intellectual capacity) may seem unimportant in late stages, when safety and comfort may take on primary importance. In the first section of this thesis we will discuss theoretical concepts that position quality of life in the broader perspective of patient related outcomes and needs, and discuss which criteria may guide in selecting specific types of quality of life measures for specific goals.

Who should rate quality of life in dementia?

The question who should rate quality of life is especially crucial in dementia. Discrepancy between objective and subjective assessments is common. Patients with the

same condition respond differently and even the same patient can respond differently at different time points, as a result of unawareness and variance or decrease in self-report accuracy. The objective approach of quality of life measurement reflects the traditional biomedical approach with the emphasis on objective measurement by e.g. professionals. However, there is no linear correlation between poor health and poor quality of life. The subjective approach values quality of life by definition as a subjective phenomenon that therefore can only be meaningful evaluated through self-report by the person concerned. Dementia patients are the persons with the actual experience of living with dementia, but the reliability of their quality of life rating may be(come) influenced by cognitive limitations. Reliable self-report is probably feasible until late dementia stages, also depending on the type of dementia, if scales are well chosen. Probably, the best approach is to combine self-report, observations and other evidence.[35] However, there is no consensus whether patients suffering from the impact of a certain disease, or persons naïve to this disease, provide more appropriate and representative valuation of health states from a societal perspective.

The subjective nature of quality of life limits the value of proxy-reports. The major advantage of proxy-rating, by someone closely related to the patient, is that it resolves the problem of missing data in longitudinal investigations in dementia research when patients in late disease stages are no longer possible to rate their own quality of life. A crucial question is whether proxy-rating offers a reliable alternative for self-report. Informal caregivers generally rate patients' quality of life lower than dementia patients themselves.[36-38] However, they are neither experiencing dementia, nor have prior knowledge of dementia, and often underestimate or neglect the capacity of patients to adapt to their illness. Confronted with a particular health state, people who are not in that state will report lower quality of life scores than patients who are actually experiencing that state. Furthermore, caregivers have their own health and mood problems, burden, changed relationship with the care recipient and altered perspectives. Also, they usually have not received professional training and are often isolated. Their quality of life depends on the balance between caregiving-related stressors and caregiving uplifts. Imbalance can lead to caregiver burn-out. Caring for people with dementia is associated with increases in distress and decreases in mental health, well-being and quality of life. All these issues influence proxy-rating. Also, the impact of dementia remains hypothetical and theoretical for formal and informal caregivers. It is hard to imagine how valuable life can be for people in later stages of dementia. Discrepancies may arise if patients adapt to illness and proxies (as well as the patients themselves beforehand) do not predict or appreciate this adaptation. Conventional quality of life measures will always be influenced by factors above and beyond the disease process. That is their strength, and at the same time

their weakness.

In sum, the patient's own opinion should remain the reference standard as long as possible when it comes to the subjective evaluation of quality of life. Use of parallel proxy-measures from the start of a longitudinal study prevents the necessity for substituting patient-rating by proxy-rating when patients are no longer able to judge their own quality of life. This reduces bias over time and prevents missing data. In the second section of this thesis we will address several questions concerning patient and proxy measurements of quality of life.

Which measures are available and should be used?

First we present an overview of how often quality of life is used as endpoint in pharmacological and non-pharmacological intervention randomized controlled trials in patients with MCI and dementia and their caregivers. Better understanding of the key determinants of quality of life of dementia patients and informal caregivers can help to improve dementia care. We therefore assessed how quality of life of patients and caregivers were associated. We have also attempted to identify the determinants of their individual quality of life. And finally we report on the validity and feasibility of the Dementia Quality of life Instrument (DQI) prototype. The DQI will become the first dementia-specific index measure allowing overall quantification of relevant health domains into one single metric figure. This figure will enable unequivocal interpretation of subjective dementia HRQoL states and provide the field with an outcome measure of added value for evaluation research in dementia.

OUTLINE OF THE THESIS

Quality of life in dementia. Theoretical part

Chapter 2 is a narrative review of the concept of quality of life and of the available measurement scales. Chapter 3 presents an overview of available measurement instruments and guidance for selection of the appropriate scale. Chapter 4 explores the interaction between quality of life in dementia in relationship to unmet needs. Chapter 5 describes the challenges and problems of accurate measurement of quality of life in dementia.

Quality of life in dementia. Empirical part

Chapter 6 presents the results of measurement of quality of life of Alzheimer's patients and their caregivers with the Schedule for the Evaluation of Individual Quality of Life (SEIQoL). In Chapter 7 associations between quality of life and burden of spouses of dementia patients are investigated. Chapter 8 provides a systematic review of how often quality of life is used as outcome in clinical trials. Chapter 9 investigates associations and determinants of quality of life in dementia patients and informal caregivers, and the implications for treatment. Chapter 10 presents the results of a cross-sectional study of dementia patient-caregiver pairs and a survey of dementia professionals about the construct validity of the prototype of the DQI (Dementia Quality of life Instrument), a novel disease-specific index instrument.

Chapter 11 summarizes the main findings of this thesis and provides conclusions and future perspectives.

QUALITY OF LIFE IN DEMENTIA

THEORETICAL PART

CHAPTER 2

QUALITY OF LIFE IN DEMENTIA
PATIENTS AND THEIR CAREGIVERS
A NARRATIVE REVIEW OF THE CONCEPT
AND MEASUREMENT SCALES

C.J.M. Schölzel-Dorenbos
P.F.M. Krabbe
M.G.M. Olde Rikkert

ABSTRACT

Dementia profoundly affects quality of life of patients as well as family and care-givers. Quality of life (QoL) refers to people's emotional, social and physical well-being, and their ability to function in daily life. QoL measures attempt to evaluate directly the impact of dementia or interventions on people's ability to function in life. Besides this global conceptualisation of QoL there is a growing field of research on QoL measures focused on the measurement of health-related quality of life (HRQoL), i.e. a person's satisfaction or happiness with domains of life insofar as they affect or are affected by the dementia. HRQoL can be distinguished from QoL in that it concerns itself primarily with those factors that fall under the purview of health care providers and health care systems. QoL measurement provides a subjective evaluation that captures benefits and harms of interventions not detected by standard clinical outcomes. Three methods of QoL assessment are available: self-report, proxy-report and rating by direct observation of behavior assumed to be related to QoL. Acknowledging the problem of potential bias of proxy-reports, self-report methods are preferable if possible. If not, observational methods by an uninvolved professional are an acceptable alternative.

By content, QoL measurement scales also can be categorized into three groups: generic, domain-specific or disease-specific. Generic scales can be divided in health profiles and utility measurements. Health profiles classify subjects with respect to a broad spectrum of QoL domains, thus producing a descriptive profile from several health domains. Generic utility measures enable cost-utility analysis. Cost is measured in monetary units. Benefit is usually expressed in quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs). Domain-specific questionnaires rate QoL on circumscript areas, such as mobility, physical restrictions, autonomy or mastery. Dementia-specific measures probably have a higher grade of responsiveness, i.e. a higher ability to identify changes that relate to the natural course of dementia or treatment interventions.

QoL measurement methods in dementia are still facing important challenges. Measurement properties encompass reliability, validity and responsiveness. Responsiveness, the ability to detect relevant change over time in health status, is an essential property of outcome measures for intervention studies and still largely unclear in dementia research. Another important item is response shift, referring to the psychological adaptation of perception of QoL following a change in health status (e.g. progress of the dementia), which should also be addressed adequately.

Next to the differential effects of dementia on the patients themselves, caring for people with dementia is often associated with increase in distress and decrease

in mental health and well-being, thus affecting QoL of proxies as well. Therefore, despite the remaining scientific challenges in the field, it is highly recommendable to include QoL assessment of patients and proxies as endpoints in all dementia and MCI intervention trials.

Introduction

Dementia is placing a substantial medical, social and psychological burden on patients and their families and profoundly affects quality of life (QoL) of all persons involved. QoL refers to people's emotional, social and physical well-being, and their ability to function in daily life. QoL measures attempt to evaluate directly the impact of dementia or interventions on people's ability to function in life. Besides this global conceptualisation of QoL there is a growing field of research on QoL measures focused on the measurement of health-related quality of life (HRQoL), i.e. a person's satisfaction or happiness with domains of life insofar as they affect or are affected by the dementia. HRQoL can be distinguished from QoL in that it concerns itself primarily with those factors that fall under the purview of health care providers and health care systems. HRQoL is a multidimensional concept that reflects the individual's perception of the impact of a health condition, such as dementia, on everyday life.[1] Instruments aimed at measuring subjects' health status outlook enable us to quantify the loss of QoL caused by disease and the improvement that can be achieved by interventions. HRQoL measurement provides a subjective evaluation that captures the benefits and harms of an intervention and elements of health not detected by standard clinical outcomes.[2] HRQoL measures are part of the class of patient reported outcome (PRO) measures. Improvement of QoL should have high priority in care and treatment, and become a focus of research of a chronic and as yet incurable disease like dementia. The international Working Group for the Harmonization of Dementia Guidelines has recommended that HRQoL should be included as outcome parameter in dementia trials.[3] Systematic reviews however proof that QoL has been used only in a very limited way in pharmacological and non-pharmacological randomized controlled trials (RCTs) in dementia and Mild Cognitive Impairment (MCI),[4-6] and that HRQoL measures are not used on a regular basis in drug clinical trials in general.[7]

Both dementia and dementia caregiving are processes that by face value profoundly affect QoL. Quality of life of caregivers depends on the balance between caregiving-related stressors and caregiving uplifts. Therefore, it is generally accepted that QoL assessment may provide a format for patients and (in)formal caregivers to express whether an intervention has made an important difference to the patient's and caregiver's life. Severity of dementia, care type, setting, and the

specific QoL domains an intervention focuses on, probably are important determinants in defining which QoL instrument is most appropriate in a specific situation.[8] The different approaches to QoL assessment in dementia are summarized in Table 1. In this chapter we review the concept of QoL in dementia and the optional modes to assess HRQoL, present an overview of available measurement scales, including an overview of their psychometric characteristics, and highlight issues for further study.

Quality of life as outcome measure in dementia research
Current symptomatic treatments for dementia have only modest efficacy and dementia is still an incurable disease. Assessing meaningful benefits in this variably progressive syndrome is complex and difficult. Many authors state that cognitive symptom response no longer suffices in anti-dementia trials.[9] QoL is mentioned as one of the primary outcomes of interest in dementia drug trials in a Cochrane update on cholinesterase inhibitors for Alzheimer's disease (AD).[10] However, in a recent systematic review we showed that the use of QoL as outcome measure is limited to 4,4% of all dementia and MCI related RCTs. In case QoL measures were applied, most papers included insufficient details to quantify responsiveness, i.e. sensitivity to clinically relevant changes, and to define clinical relevance. In non-pharmacological trials QoL was measured more often and resulted more often in positive outcome than in pharmacological intervention studies (5 out of 7 vs 0 out of 3 trials reporting QoL, respectively).[6] These results confirm the literature described in a systematic review published in 2004 of RCTs of pharmacologic treatment, which also showed that QoL was rarely included as an outcome measure.[5]

Quality of life measurements: by patient, proxy or observation
Subjective evaluation of QoL by dementia patients may be influenced by their cognitive limitations and may reflect reduced insight. Yet, they represent the best way of understanding the experience of life with dementia.[11] However, dementia may interfere with understanding, ability to remember relevant events, making comparisons across complex domains and communicating.[12] This features potentially jeopardize both reliability and validity of self-rating of QoL. The way out seems to be to have proxies rate the QoL of the patients with dementia they care for. Unfortunately, proxy QoL ratings generally do not accurately reflect patients' ratings.[2] For this reason often both modes of assessment are used, depending on the aim of QoL measurements, recognizing their advantages and limitations. In longitudinal studies in dementia it may have advantages to simultaneously use proxy-rating, because of the progressive global deterioration of dementia patients. Furthermore,

the use of proxy reports throughout the course of a longitudinal study, rather than substituting them only when the person with dementia becomes unable to report his or her own HRQoL, reduces bias over time.[13] In case of (very) severe dementia independent professionals can use qualitative observation of behavior assumed to be related to QoL to assess QoL and to investigate the effects of an intervention. Also qualitative observations however are subjective.

In sum, three methods of QoL assessment are available: self-report by patient, proxy-report and direct observation. Two types of proxies can be distinguished: informal and formal, the latter referring to professional proxies. Logsdon et al. showed that patients can rate their own QoL until late stages of dementia, and that caregiver ratings do not substitute for patient ratings.[14] Sands et al. found that caregivers rated patients' QoL lower than patients, associated with increased caregiver burden and depressive symptoms of the patient.[15] Boyer et al. found poor patient/family proxy concordance for the dimension emotional reaction of the Nottingham Health Profile.[16] The disadvantage of proxy-ratings is that they filter a subjective measure through the opinion of another person. Moreover, this rating can be biased because of perceived caregiver burden or depression. Acknowledging the problem of potential bias of proxy-reports, self-rating methods are preferable if possible. If not, observational methods by an uninvolved professional are an acceptable alternative. We agree with Brod et al. that the patient's subjective ratings should be the gold standard, but that independent observational ratings are of benefit for patients with (very) severe dementia.[17]

Quality of life of proxies of dementia patients
Outcomes should also appropriately encompass effects on caregivers. Caring for people with dementia is associated with well-documented increases in distress and decrease in mental health and well-being.[18] Caregivers of dementia patients experience higher levels of stress and psychological morbidity compared to caregivers of non-demented elderly persons. Especially behavioral symptoms and impairments in instrumental activities of daily living activities cause caregiver strain.[19] Quality of life assessment so far largely focuses on QoL of dementia patients. However, assessment of QoL of the proxy is equally important, especially if the patient still lives in the community. To our knowledge, three disease-specific methods are available that can validly assess QoL in patients as well as their carers: the SEIQoL, QOL-AD and the QoL scale developed in the PIXEL studies.[8;14;20] Also, generic instruments can be applied. More often QoL of caregivers is measured indirectly with mood/depression scales or caregiver burden scales. Theoretically, a direct and detailed measurement of subjective proxy QoL, however, is a better tool, be-

cause positive factors and stressors affecting the personal QoL are probably highly variable among caregivers.[21] It is highly recommendable to include QoL assessment of proxies as effectiveness endpoint in all dementia and MCI intervention trials.

Quality of life measurements: dementia-specific, domain-specific or generic

Based on their content, QoL measures can be categorized into three groups: disease-specific, domain-specific and generic measures.[22] Disease-specific instruments measure the consequences of a specific disease such as dementia. Domain-specific questionnaires rate QoL on circumscript areas of life, such as mobility, physical restrictions, autonomy or mastery. Generic measures can be divided in health profiles and utility measures. Generic measures rate QoL in terms that are relevant for everybody, regardless of the presence or absence of a specific disease. Utility measures enable cost-utility analysis (CUA), a form of economic analysis used to guide procurement decisions, applied in pharmacoeconomics, especially health technology assessment (HTA). The purpose of CUA is to estimate the ratio between the cost of a health-related intervention and the benefit it produces in terms of the number of years lived in full health. Hence it can be considered a special case of cost-effectiveness analysis (CEA), and the two terms are often used interchangeably. Cost is measured in monetary units. Benefit is expressed in quality-adjusted life years (QALYs) or the related disability-adjusted life years (DALYs). Both equal 1 for each year of full-health life, and less than 1 for various degrees of illness or disability. Thus the cost-effectiveness of a treatment can be assessed by the cost per QALY or DALY it produces. We will subsequently discuss the most important disease-specific and generic measurement scales we are aware of.

Disease-specific quality of life measurement

Disease-specific measurements are devised to assess the impact of a specific disease across a spectrum of important domains of life. They evaluate the domains relevant for a specific disease. Thus, dementia-specific HRQoL measurements intend to focus on dimensions relevant to dementia. This enables a higher grade of responsiveness, i.e. a higher ability to identify changes that relate to the natural course of dementia or to treatment interventions.[22] An advantage of disease-specific scales is that they contain less inappropriate and irrelevant items and thus contain less 'noise'. However, the cost of greater specificity is less generalizability. A large number of disease-specific scale for dementia are available. In Table 2 an overview of the dementia-specific rating scales and their references is presented. In summary: ADR-QL: Alzheimer's Disease health-Related Quality of Life scale, CBS: Cornell-Brown Scale for QoL in dementia, QOLAS: Quality of Life Assessment

Schedule, DCM: Dementia Care Mapping, DEMQOL, DQoL: Dementia Quality of Life scale, DSDAT: Discomfort Scale-Dementia of Alzheimer Type, QOL-D: Quality of Life for Dementia, QOL-AD: Quality of Life-Alzheimer's Disease scale, PDS: Progressive Deterioration Scale, AAI: Activity and Affect Indicators of QoL, PWB-CIP: Psychological Well-Being in Cognitively Impaired Persons, QUALID: Quality of Life in Late-Stage Dementia scale, Qualidem, Vienna List and BASQID: Bath Assessment of Subjective Quality of Life in Dementia. Because of this large number of measurement scales it is very relevant to define selection criteria, and consequently select the appropriate QoL rating scale. On the one hand, recommendation of specific measures depends on the type of research question, severity of dementia, care type, setting and the specific QoL domains an intervention focuses on. On the other hand, the psychometric qualities of QoL measurement scales also guide the selection process. No instrument can be used in all stages of dementia, or in all types of care and settings. The QOL-AD probably is the most promising and most widely used dementia-specific questionnaire, consisting of a 13-item self-report scale, which remains applicable up to very low Mini-Mental State Examination scores. This measurement scale has separate versions both for patients (Participant self-reported QoL) and informal caregivers (Caregiver report of the Participant's QoL). Besides this, caregivers can report on their own QoL with the CQOL (Caregiver QoL). Recently a new self-reporting measure, the BASQID, proved to provide valid, reliable and useful information at a group level in people with mild to moderate dementia.[11] The Qualidem is a 40-item behavior observation-scale for patients up to severe dementia in institutions. The DSDAT is an objective scale for trained observers to measure discomfort in non-communicative patients with severe dementia.[8] Pros and cons of the various measures have been discussed in detail earlier.[8;23]

Generic quality of life measures

Generic measures generally are the measures of choice in case of economic health care research and in case external validity is of primary importance. These instruments enable comparisons across different (severity of) diseases or interventions, measurement of the burden of illness of groups of patients with chronic diseases as compared with normals and can also be of use in health policy decision making.[4;22] They encompass a broad scope of QoL domains, are applicable for every disease, and thus produce results that are externally valid and can be compared to other studies. Because generic scales are usually more frequently used, there are more data available regarding validity and reliability. However, generic measures also include domains not relevant for patients with a specific disease and underesti-

mate more relevant areas. This may result in a lower responsiveness. In general, patient's impairments are better reflected in disability measures, than in HRQoL instruments.[24]

For the measurement of HRQoL two different approaches exist: health profile and utility measurements. For extensive details on their theoretic background, validity, reliability and applicability, we refer to numerous excellent reviews comparing these instruments (see other chapters in this book). Here we will limit ourselves to some general findings and to results of validation studies using these generic QoL measures in populations of patients suffering from dementia, and we only give a few examples of this type of measurements.

Generic quality of life measures, subcategory health profiles

Health profiles classify subjects with respect to a broad spectrum of QoL domains, thus producing a descriptive profile from several health domains. These health domains are considered independently and are not intended to be commensurable or aggregated. The scores on these domains are relative and for that reason such figures are not appropriate to measure the overall level of health states. Examples are the SF-36: Medical Outcomes Study 36-item Short Form Health Survey, SF-12: Medical Outcomes Study 12-Item Short Form Health Survey, SIP: Sickness Impact Profile, NHP: Nottingham Health Profile, DHP: Duke Health Profile, QOLAS: Quality of Life Assessment Schedule, WHOQOL 100: World Health Organization Quality of Life 100, HSQ: Health Status Questionnaire and SEIQoL: Schedule for the Evaluation of Individual Quality of Life. The health profiles and their references are summarized in Table 3.

The SEIQoL measurement scale is a good example of a generic QoL instrument covering multiple domains. It measures the level of functioning in five self-nominated facets of life (qualitative information) and the relative weight or importance attached to these areas. Thus, the SEIQoL allows quantitative measurement of individualized QoL and probably can be used to monitor changes in QoL.[25] It is a generic instrument validated in dementia, and is applicable until mild dementia stages.[26;27] For later stages the more simple SEIQoL-DW (Direct Weighting; replacing weighting procedure with a pie chart format) version offers an alternative. The SEIQoL provides an overall score of QoL of both patient and proxy.

Generic quality of life measures, subcategory utility measures

Unlike QoL measures, utility measures attempt to evaluate the value that persons place on a particular health state and not directly the impact of a disease or treatment on their ability to function in life. Cost-utility analysis (CUA) quantifies the re-

lationships between intervention and outcomes in terms of money. CUA is enabled by utility measures: economical evaluations express health effects in quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs). Typically, health-state values based on the HRQoL concept are combined with duration spent in these states, thus generating QALYs. QALYs are global summary measures of health and are very attractive because they enable medical specialists to express different diseases into one single comparable measure. Another benefit of QALYs is that these measures not only inform physicians, but are also easily understood by policy makers and patients.

Thus, utility measures produce a descriptive profile on multiple health domains, but in addition are specifically designed to aggregate the scores into one overall score expressing the quality of health states. Utility-based QoL measures often place levels of wellness on a continuum anchored by death (0.00) and optimum function or perfect health (1.00). Preference measurement studies are used to define the meaning of points along that continuum. This approach is also referred to as a preference-based or value-based methodology and produces overall scores from 0.00-1.00 with a fixed meaning and interpretation. Such scores have metric properties, allowing comparison of the severity of various diseases and to perform basic computational procedures. The many methods to quantify health states and continuous scales are described in Table 4a and b. Health states are valued using techniques such as standard gamble (SG), time trade-off (TTO),[28] or person trade-off (PTO). PTO differs from TTO in that subjects are required to trade-off person years lived healthy against person years lived with some defined disability, thus making choices in the context of a decision involving other people rather than themselves. Whether PTO reflects actual preferences is still unclear.[29] These valuations are used to generate a scoring algorithm, by which a single utility score for each health state can be deduced.

An overview of utility measures is presented in Table 5. The European Quality of life-5 Dimensions (EQ-5D) questionnaire describes health status according to the dimensions mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has three levels, which were valued using the TTO method. Based on these valuations, utility scores can be deduced by means of an additive function. These are now widely used in cost-utility analyses.[30] Besides the five dimensions, the EQ-5D consists of a visual analogue scale (VAS) ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). The EQ-5D+C or EQ-6D is an extended version of the EQ-5D that also includes the domain cognitive functioning.[31] At this moment utilities are only available for the EQ-5D. It is still unclear whether addition of a cognitive dimension to the EQ-5D has a

separate and significant effect on utility values.[32] The EQ-5D is commonly used to measure HRQoL and has been shown to be responsive, internally consistent and reliable in the normal population and other patient groups,[33] as well as in patients with dementia.[34]

Other preference based measures are the SF-6D,[35] Health Utilities Index Mark 2 (HUI2),[36] Health Utilities Index Mark 3 (HUI3),[37] and Quality of Well-Being scale (QWB),[38] all standardized multi-dimensional health state classifications. The SF-6D was derived from the SF-36 by revision into a six-dimensional health state classification, for use in economic evaluations. The health states were valued using Standard Gamble.[39] Among studies that compared preference-based systems, the EQ-5D tended to provide larger change scores and more favourable cost-effectiveness ratios than the HUI2 and -3, while the SF-6D provided smaller change scores and less favourable ratios than the other systems.[40] In a systematic literature review the EQ-5D proved to be the most frequently used utility measure (47,5%). Other instruments used were HUI, QWB, SF-6D, Rosser-Kind Index, and 15D. The rest (23.8%) used a direct valuation method: TTO, SG, VAS or rating scale.[41] Using different preference-based HRQoL instruments may yield different utility scores, which could have a great impact on QALY estimates. This highlights the importance of selecting appropriate instruments for economic evaluations.[42] Others however state that although clinically important differences in utility measurements were present for different preference-based instruments, the impact of these differences on CUA appeared relatively minor.[43] Here we conclude that the various utility measurement tools measure a similar underlying construct, but are not interchangeable because they are scaled differently and produce varying results. Apart from this, utility measurements in dementia have methodological problems similar to the other QoL measurements in dementia (described earlier). These findings all have potential implications for the interpretation and comparability of health outcome studies and economic analyses.[44]

Generic quality of life measures and their use and relevance in dementia
The EQ-5D, QWB and HUI were all administered to dementia patients and their proxies. The EQ-5D is a valid but easy to administer measure with a short completion time. One of the criticisms of the QWB is that it is in general more difficult to administer than competing measures, such as the SF-36. This can be a disadvantage in dementia. The Quality of Well-Being scale, Self-Administered (QWB-SA) addresses this criticism. The QWB-SA was acceptable to older respondents and correlated with other measures of HRQoL (SIP and SF-36).[45] For the SF-6D there are concerns with inconsistent estimates and over prediction of the value of the poorest health states, which is especially of interest in a discussion on applicability in dementia.[39] Councill et al. expressed concerns regarding the validity of patient self-rated HRQoL data obtained with the EQ-5D.[46] Others however concluded that dementia patients are capable of expressing their HRQoL through a brief instrument as the EQ-5D.[32;34] Naglie et al. compared the EQ-5D, QWB and HUI in patients with mild dementia and their proxies. They found that for patient and proxy ratings, the EQ-5D had the best combination of measurement properties, although it had a substantial ceiling effect for patient ratings. In this study proxy QoL ratings did not accurately reflect patients' ratings.[2] Others however found that proxies can reliably assess the QoL of dementia patients with the EQ-5D,[2;32] HUI,[48] and QWB.[38] Until now, health utility measures are not validated satisfactorily in dementia, thereby questioning the results of previous health economic analyses in dementia.[49] In mental health patients with mood and/or anxiety disorders both EQ-5D and SF-6D discriminated between severity subgroups and captured improvements in health over time. However, the use of EQ-5D resulted in larger health gains and consequent lower cost-utility ratios, especially for the subgroup with the highest severity of problems.[50] These findings may also have consequences for outcome studies in dementia.

Clinical relevance of QoL measurements: responsiveness and minimal important difference
To fulfil it's promise of high(er) clinical relevance, QoL measurements should not only be valid and reliable (over time and between raters), but also sensitive to change (responsive) and it should be possible to reach agreement on scale differences reflecting clinically relevant changes. Information on validity and reliability of the dementia specific measures is summarized in Table 6. Patients, proxies, clinicians, investigators and drug companies all have different interests, resulting in different definitions of a positive response to treatments. Furthermore, small changes on responsive psychometric cognitive tests, even if statistically significant by including large numbers of patients, may not be clinically relevant. Registration authorities already require that outcome measures' response criteria are defined unambiguously in registered trial designs, which requires to define the changes in the outcome variables considered to be clinically relevant. Here we will shortly describe the concepts of responsiveness and minimal important difference as relevant in comparing and selecting QoL measurements scales in dementia.

Responsiveness
Measurement properties encompass reliability, validity and responsiveness. Res-

ponsiveness represents an instrument's ability to detect relevant change over time in health status and is a critical property of outcome measures in clinical trial settings. Responsiveness has three important aspects: 1. type of change (within persons, between persons, or both; investigated with anchor- and distribution-based procedures), 2. type of setting (group or individual) and 3. magnitude of change: minimal or substantial. Responsiveness of QoL measures used in dementia drug trials has had little formal analysis,[14] and still lacks a firm empirical base. Dementia-specific measures may be hypothesized to have a higher responsiveness, because they focus only on dimensions relevant to dementia. Generic QoL measures often demonstrate low responsiveness, but a firm comparison has not been made for QoL ratings in dementia.[22]

Responsiveness is determined by evaluating the relationship between changes in clinical and patient-based endpoints and changes in scores over time, or based on the application of a treatment of known and demonstrated efficacy (anchor-based responsiveness). Longitudinal studies are needed to determine whether a PRO instrument is responsive.[51] Responsiveness can be assessed using measures of internal responsiveness (standardized effect size, standardized response mean) and external responsiveness (receiver operator curve analysis, mixed model regression).

Minimal important difference

The minimal important difference (MID) is a related concept to responsiveness and denotes the smallest difference in scores of a PRO measure that signifies a clinically significant change, rather than a trivial change in symptoms.[52] In validation studies MID can serve as the anchor for validation. Anchor-based methods applying relevant patient- or clinician-rated and disease-specific variables provide meaningful estimates of an instrument's MID. Distribution-based methods can support estimates from anchor-based approaches and can be used in situations where anchor-based estimates are unavailable. MID is best be based primarily on relevant patient-based and clinical anchors, with clinical trial experience used to further inform understanding of MID. When MID is connected to clinical anchors, it is referred to as the minimal clinically important difference (MCID).[51] The responsiveness index (RI) as developed by Guyatt is one way of quantifying sensitivity to change in clinimetrics.[53] The RI reflects the ratio between the magnitude of the minimally or other standardized important difference that can be detected and the noise level (the differences measured in a population in which QoL may be assumed not to have changed, according to anchor-based comparisons). In other words, the RI is based on the magnitude of meaningful change related to the distribution of change by chance in a stable population, which is important in defining the sample size needed for clinical trials to detect a meaningful difference.[52] Because responsiveness and MID depend on population and contextual characteristics, there is not necessarily a single MID value for a PRO instrument across all applications and patient samples.[51]

Quality of life measurement and response shift

When applying QoL measures in patients and proxies the phenomenon of response shift should always be taken into account. Medical models of QoL traditionally assume that QoL decreases when more symptoms are present, and disease progresses.[11] However, persons with chronically invalidating diseases often keep reporting a high QoL,[54] while caregivers initially rate patients' QoL lower than dementia patients themselves and caregivers also rate QoL lower than patients during disease progression.[15;16] In these ratings, the phenomenon that patients or caregivers may rate their QoL differently during the course of a disease is referred to as response shift. In general terms, response shift is a change in valuation of QoL over time and over disease severity, which may result from a change in internal standards of QoL.[55] Response shift is the psychological change in perception of QoL following a change in health status and thus can affect results of QoL outcome measurements. If significant response shift is likely to occur, one should take this into account in designing future clinical research. Response shift may also have biased the results of previous studies, in which this problem was not considered beforehand. Adaptation to illness provides a reasonable explanation for the occurrence of response shift.

Response shift can be determined and estimated with several approaches, for instance the Then-test, Ideal scale approach, anchor-recalibration, structural equation modelling (SEM) and Rating of vignettes. The Then-test is a retrospective judgment of pre-intervention QoL and is used in combination with the pretest-posttest design. Results of interventions are usually measured by comparing pre- and post-treatment scores, assuming that the observed change represents a treatment effect. However, in case of response shift the person's rating is changed and this may confound interpretation of the results. The Then-test is one of the least complicated methods to measure response shift.[55] An important drawback of the Then-test is that it's validity depends on the correct recall of the pre-intervention health state. In the Ideal scale approach current and ideal QoL are rated on the same scale. Persons rate their current and their ideal QoL on the same scale on different points of time. The assumption is that response shift influences the current score to the same extent as the ideal score. With this method shifts in the ideal scores, indicative of response shift, can be detected.[56] In the Anchor-recalibration

approach shifts in patients' individual definitions of the scale-anchors (worst and best imaginable QoL) over time are assessed.[57] In the SEM approach response shift is deduced from mathematically defined changes in confirmatory factor analysis' results and variance-covariance matrices over time. The claim is that SEM can detect reconceptualization, reprioritization, and recalibration.[55] Finally, rating of vignettes, a novel method, is a promising additional technique to assess response shift.[58] It has not been established so far if a dementia diagnosis induces response shift, but longitudinal QoL measurements of dementia patients not resulting in significant QoL changes over time make response shift in dementia highly likely.[59] For studies this is a problem, for patients it is profitable to be able to adapt to newly occurring disease stages and not perceiving a gradual decrease in QoL. In proxies, response shift probably is different from response shift in patients, which may have implications when using proxy-rating.

Available scales for quality of life measurement in dementia: which one and why?
The selection of appropriate outcome measures in dementia research first depends on the type of intervention and the study aim. Often it is important to relate outcomes directly to healthcare utilization, QoL, caregiver burden and to be able to allow pharmacoeconomic analyses.[60] Providing meaningful outcomes will improve acceptance of therapeutic strategies. Thus, selection of appropriate outcome measures is very important. In Table 7 the selection criteria for QoL measurements in dementia research are presented. No instrument can be used in all stages of dementia, types of care, settings and research questions. In our view, four measurement scales best represent the domains of QoL that are important for patients and that professionals focus on: QOL-AD, SEIQoL, Qualidem and DSDAT. The first two are self-rating quantitative instruments that can assess QoL of patients as well as proxies. If self-report is no longer possible observational instruments like Qualidem (for mild to severe dementia) and Discomfort scale-Dementia of Alzheimer Type (DSDAT; for severe dementia) by uninvolved professionals can be used. Utility measures are a central component of economic evaluations in health care. To calculate utility values the EQ-5D performs well for evaluating HRQoL in patients aged 55 and older with cognitive impairments, also by using proxy-ratings.[32] However, until now, health utility measures are not validated satisfactorily in dementia, thus calling into question previous health economic analyses.[49]

References

1. Anderson RT, Aaronson NK, Bullinger M et al. A review of the progress towards developing health-related quality-of-life instruments for international clinical studies and outcomes research. Pharmacoeconomics 1996;10:336-55.
2. Naglie G, Tomlinson G, Tansey C et al. Utility-based Quality of Life measures in Alzheimer's disease. Qual Life Res 2006;15:631-43.
3. Mack JL, Whitehouse PJ. Quality of Life in Dementia: state of the art--report of the International Working Group for Harmonization of Dementia Drug Guidelines and the Alzheimer's Society satellite meeting. Alzheimer Dis Assoc Disord 2001;15:69-71.
4. Naglie G. Quality of life in dementia. Can J Neurol Sci 2007;34:S57-61.
5. Santaguida PS, Raina P, Booker L et al. Pharmacological treatment of dementia: evidence report/technology assessment no. 97 (Prepared by McMaster University Evidence-based Practice Center under contract no. 290-02-0020). Evid Rep Technol Assess (Summ) 2004;1-16.
6. Schölzel-Dorenbos CJM, van der Steen MJ, Engels LK, Olde Rikkert MG. Assessment of quality of life as outcome in dementia and MCI intervention trials: a systematic review. Alzheimer Dis Assoc Disord 2007;21:172-8.
7. Miguel RS, Lopez-Gonzalez AM, Sanchez-Iriso E et al. Measuring health-related quality of life in drug clinical trials: is it given due importance? Pharm World Sci 2007.
8. Schölzel-Dorenbos CJM, Ettema TP, Bos J et al. Evaluating the outcome of interventions on quality of life in dementia: selection of the appropriate scale. Int J Geriatr Psychiatry 2007;22:511-9.
9. Trial Designs and Outcomes in Dementia Therapeutic Research. London and New York: Taylor & Francis Group, 2006.
10. Birks J. Cholinesterase inhibitors for Alzheimer's disease. Cochrane Database Syst Rev 2006;CD005593.
11. Trigg R, Jones RW, Skevington SM. Can people with mild to moderate dementia provide reliable answers about their quality of life? Age Ageing 2007;36:663-9.
12. Rabins PV. Measuring Quality of Life in Persons With Dementia. Intern Psychogeriatr 2000;12:47-9.
13. Smith SC, Lamping DL, Banerjee S 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 Technol Assess 2005;9:1-iv.
14. Logsdon RG, Gibbons LE, McCurry SM et al. Assessing quality of life in older adults with cognitive impairment. Psychosom Med 2002;64:510-9.
15. Sands LP, Ferreira P, Stewart AL et al. What explains differences between dementia patients' and their caregivers' ratings of patients' quality of life? Am J Geriatr Psychiatry 2004;12:272-80.

16. Boyer F, Novella JL, Morrone I et al. Agreement between dementia patient report and proxy reports using the Nottingham Health Profile. Int J Geriatr Psychiatry 2004;19:1026-34.

17. Brod M, Stewart AL, Sands L. Conceptualization of quality of life in dementia. Journal of Mental Health and Aging 1999;5:7-20.

18. Sörensen S, Duberstein P, Gill D et al. Dementia care: mental health effects, intervention strategies, and clinical implications. Lancet Neurol 2006;5:961-73.

19. Gonzalez-Salvador MT, Arango C, Lyketsos CG et al. The stress and psychological morbidity of the Alzheimer patient caregiver. Int J Geriatr Psychiatry 1999;14:701-10.

20. Thomas P, Lalloue F, Preux PM et al. Dementia patients caregivers quality of life: the PIXEL study. Int J Geriatr Psychiatry 2006;21:50-6.

21. Joyce CR. Health status and quality of life: which matters to the patient? J Cardiovasc Pharmacol 1994;23:S26-33.

22. Guyatt GH, Feeny DH, Patrick DL. Measuring health-related quality of life. Ann Intern Med 1993;118:622-9.

23. Ettema TP, Dröes RM, de Lange J et al. A review of quality of life instruments used in dementia. Qual Life Res 2005;14:675-86.

24. Weisscher N, de Haan RJ, Vermeulen M. The impact of disease-related impairments on disability and health-related quality of life: a systematic review. BMC Med Res Methodol 2007;7:24.

25. O'Boyle CA, McGee H, Hickey A et al. Individual quality of life in patients undergoing hip replacement. Lancet 1992;339:1088-91.

26. Coen R, O'Mahony D, O'Boyle C et al. Measuring the quality of life of dementia patients using the Schedule for the Evaluation of Individual Quality of Life. Irish J Psychology 1993;14:154-63.

27. Schölzel-Dorenbos CJM. Measurement of quality of life in patients with dementia of Alzheimer type and their caregivers: Schedule for the Evaluation of Individual Quality of Life (SEIQoL). Tijdschr Gerontol Geriatr 2000;31:23-6.

28. Brazier J, Deverill M, Green C et al. A review of the use of health status measures in economic evaluation. Health Technol Assess 1999;3:i-164.

29. Green C. On the societal value of health care: what do we know about the person trade-off technique? Health Econ 2001;10:233-43.

30. Kind P. Guidelines for value sets in economic and on-economic studies using EQ-5D. In: Brooks R, Rabin R, Charro Fd, eds. The measurement and evaluation of health status using EQ-5D: A European perspective. Kluwer Academic Publishers, 2003.

31. Krabbe PF, Stouthard ME, Essink-Bot ML et al. The effect of adding a cognitive dimension to the EuroQol multiattribute health-status classification system. J Clin Epidemiol 1999;52:293-301.

32. Wolfs CA, Dirksen CD, Kessels A et al. Performance of the EQ-5D and the EQ-5D+C in elderly patients with cognitive impairments. Health Qual Life Outcomes 2007;5:33.

33. Nowels D, McGloin J, Westfall JM et al. Validation of the EQ-5D quality of life instrument in patients after myocardial infarction. Qual Life Res 2005;14:95-105.

34. Ankri J, Beaufils B, Novella JL et al. Use of the EQ-5D among patients suffering from dementia. J Clin Epidemiol 2003;56:1055-63.

35. Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. J Health Econ 2002;21:271-92.

36. Feeny D, Furlong W, Boyle M et al. Multi-attribute health status classification systems. Health Utilities Index. Pharmacoeconomics 1995;7:490-502.

37. Furlong WJ, Feeny DH, Torrance GW et al. The Health Utilities Index (HUI) system for assessing health-related quality of life in clinical studies. Ann Med 2001;33:375-84.

38. Kerner DN, Patterson TL, Grant I et al. Validity of the Quality of Well-Being Scale for patients with Alzheimer's disease. J Aging Health 1998;10:44-61.

39. Brazier J, Roberts J, Tsuchiya A et al. A comparison of the EQ-5D and SF-6D across seven patient groups. Health Econ 2004;13:873-84.

40. McDonough CM, Tosteson AN. Measuring preferences for cost-utility analysis: how choice of method may influence decision-making. Pharmacoeconomics 2007;25:93-106.

41. Räsänen P, Roine E, Sintonen H et al. Use of quality-adjusted life years for the estimation of effectiveness of health care: A systematic literature review. Int J Technol Assess Health Care 2006;22:235-41.

42. Marra CA, Marion SA, Guh DP et al. Not all "quality-adjusted life years" are equal. J Clin Epidemiol 2007;60:616-24.

43. Wee HL, Machin D, Loke WC et al. Assessing differences in utility scores: a comparison of four widely used preference-based instruments. Value Health 2007;10:256-65.

44. Conner-Spady B, Suarez-Almazor ME. Variation in the estimation of quality-adjusted life-years by different preference-based instruments. Med Care 2003;41:791-801.

45. Andresen EM, Rothenberg BM, Kaplan RM. Performance of a self-administered mailed version of the Quality of Well-Being (QWB-SA) questionnaire among older adults. Med Care 1998;36:1349-60.

46. Coucill W, Bryan S, Bentham P et al. EQ-5D in patients with dementia: an investigation of inter-rater agreement. Med Care 2001;39:760-71.

47. Jonsson L, Andreasen N, Kilander L et al. Patient- and proxy-reported utility in Alzheimer disease using the EuroQoL. Alzheimer Dis Assoc Disord 2006;20:49-55.

48. Neumann PJ, Kuntz KM, Leon J et al. Health utilities in Alzheimer's disease: a cross-sectional study of patients and caregivers. Med Care 1999;37:27-32.

49. Katona C, Livingston G, Cooper C et al. International Psychogeriatric Association consensus statement on defining and measuring treatment benefits in dementia. Int Psychogeriatr 2007;19:345-54.

50. Lamers LM, Bouwmans CA, van Straten A, Donker MC, Hakkaart L. Comparison of EQ-5D and SF-6D utilities in mental health patients. Health Econ 2006;15:1229-36.

51. Revicki D, Hays RD, Cella D et al. Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. J Clin Epidemiol 2008;61:102-9.

52. Guyatt G, Walter S, Norman G. Measuring change over time: assessing the usefulness of evaluative instruments. J Chronic Dis 1987;40:171-8.

53. Guyatt GH, Kirshner B, Jaeschke R. Measuring health status: what are the necessary measurement properties? J Clin Epidemiol 1992;45:1341-5.

54. Albrecht GL, Devlieger PJ. The disability paradox: high quality of life against all odds. Soc Sci Med 1999;48:977-88.

55. Visser MR, Oort FJ, Sprangers MA. Methods to detect response shift in quality of life data: a convergent validity study. Qual Life Res 2005;14:629-39.

56. Zmud R, Armenakis AA. Understanding the measurement of change. Acad Manage Rev 1978;3:661-9.

57. Sprangers MA, Schwartz CE. Integrating response shift into health-related quality of life research: a theoretical model. Soc Sci Med 1999;48:1507-15.

58. Korfage IJ, de Koning HJ, Essink-Bot ML. Response shift due to diagnosis and primary treatment of localized prostate cancer: a then-test and a vignette study. Qual Life Res 2007;16:1627-34.

59. Missotten P, Ylieff M, Di Notte D et al. Quality of life in dementia: a 2-year follow-up study. Int J Geriatr Psychiatry 2007;22:1201-7.

60. Schwam EM, Abu-Shakra S, del Valle M et al. Health economics and the value of therapy in Alzheimer's disease. Alzheimer's & Dementia: The Journal of the Alzheimer's Association 2007;3:143-51.

Table 1. Different approaches to quality of life assessment in dementia

Type of measure	Dementia specific	Generic-health profile	Generic-utility
Administration	Self report	Proxy report	Observational report
Target	Mild dementia	Moderate dementia	Advanced dementia
Longitudinal validity	Responsive	Nonresponsive	
Respondent	Patient	Proxy	Both
Domains	Broad scope	Narrow scope	
Change over time	Stable	Response shift	

Table 2. Examples of disease-specific quality of life measurements in dementia

Acronym	Measurement scale	References
ADR-QL	Alzheimer's Disease health-Related Quality of Life scale	Rabins et al. J Ment Health Aging 199;5:33
CBS	Cornell-Brown Scale for quality of life in dementia	Ready et al. Alzh Dis Assoc Disord 2002;16:109
QOLAS	Quality of Life Assessment Schedule	Selai et al. Neuropsych Rehabilitation 2001;11:219
DCM	Dementia Care Mapping	Kitwood et al. J Adv Health Nurs Care 1992;1:41
DEMQOL	-	Smith et al. Int J Geriatr Psych 2005;20:889. Smith Health Technol Assess 2005;9:1
DQoL	Dementia Quality of Life scale	Brod et al. Gerontologist 1999;39:25
DSDAT	Discomfort Scale-Dementia of Alzheimer Type	Hurley et al. Res Nurs Health 1992;369 Volicer. J Mental Health Aging 1999;5:83
QOL-D	Quality of Life for Dementia	Terada et al. Int J Geriatr Psychiatry 2002;17:851
QOL-AD	Quality of Life-Alzheimer's Disease scale	Logsdon et al. Psychosom Med 2002; 64:510
PDS	Progressive Deterioration Scale	De Jong et al. Clin Ther 1989;11:545
AAI	Activity and Affect Indicators of quality of life	Albert et al. J Am Geriatr Soc 1996; 44:1342
PWB-CIP	Psychological Well-Being in Cognitively Impaired Persons	Burgener et al. Alzh Dis Assoc Disord 2002;16:88
QUALID	Quality of Life in Late-Stage Dementia scale	Weiner et al. J Am Med Dir Assoc 2000;1:114
Qualidem	-	Ettema et al. Int J Geriatr Psych 2007; 22:424&549
Vienna List	-	Porzsolt et al. Health Qual Life Outcome 2004;2:10
BASQID	Bath Assessment of Subjective Quality of Life in Dementia	Trigg et al. Age Ageing 2007;36:663 Trigg et al. Gerontologist, 47:789-97

Table 3. Examples of generic health profile measurements applicable in dementia

Acronym	Measurement scale	References
SEIQoL	Schedule for the Evaluation of Individual Quality of Life	McGee. Psychol Med 1991; 21:749. Schölzel. T Ger Geriatr 2000;31:23
SF-36	Medical Outcomes Study 36-item Short Form Health Survey	Ware et al. Med Care 1992;30:473
SF-12	Medical Outcomes Study 12-Item Short Form Health Survey	Ware et al. Med Care 1995; 33:AS264
SIP	Sickness Impact Profile	Bergner et al. Med Care 1981; 19:787
NHP	Nottingham Health Profile	Bureau-Chalot et al. Gerontology 2002;48:220
DHP	Duke Health Profile	Novella et al. Dement Geriatr Cogn Disord 2001;12:158
QOLAS	Quality of Life Assessment Schedule	Selai et al. Neuropsychol Rehab 2001;11:219
WHOQOL 100	World Health Organization Quality of Life 100	WHOQOL Group. Psychol Med 1998;28:551
HSQ	Health Status Questionnaire	Pettit et al. Int J Geriatr Psychiatry 2001;16:1061

Table 4a. Methods to quantify health states

Valuation technique	Based on
Utility measurement	SG (Standard Gamble) TTO (Time Trade-Off)
Ordinal judgment	Ranking Category rating Paired comparisons
Cardinal judgment	Magnitude estimation PTO (Person Trade-Off) VAS (visual analogue scale)

Table 4b. Methods of quantification of various continuous scales

One dimensional	One dimensional	One dimensional	Separate dimensions
Direct estimation	Comparative methods	Econometric methods	Similarities of objects
VAS	Thurstone's method	SG	
Adjectival scales	Guttman scaling	TTO	MDS (Multi-dimensional scaling)
Likert scale	Paired-comparisons		

Table 5. Examples of generic utility measurements applicable in dementia

Acronym	Measurement scale	References
EQ-5D	European Quality of life - 5 Dimensions	EuroQol Group. Health Policy 1990;16:199. Brooks. Health Policy 1996;37:53
EQ-6D	European Quality of life - 6 Dimensions	Krabbe et al. J Clin Epidemiol 1999;52:293
QWB	Quality of Well-Being scale	Kerner et al. J Aging Health 1998; 10:44
QWB-SA	Quality of Well-Being scale, Self-Administered	Andresen et al. Med Care 1998; 36:1349
HUI2	Health Utilities Index Mark 2	Feeny et al. Pharmacoecon 1995; 7:490
HUI3	Health Utilities Index Mark 3	Furlong et al. Ann Med 2001; 33:375
SF-6D	SF-36 revised into a six-dimensional health state classification	Brazier et al. J Health Econ 2002; 21:271
Other	Activities Limitations Index. Rosser-Kind Index. 15D	Räsänen et al. Int J Technol Assess Health Care 2006;22:235
Direct valuation	Time Trade-Off, Person Trade-Off, Standard Gamble, Visual Analogue Scale, Rating Scale	Pinto Prades. Health Econ 1997; 6:71. Green. Health Econ 2001; 10:233. Räsänen et al. Int J Techn Assess Health Care 2006; 22:235

Table 6. Validity and reliability of quality of life measures in dementia								
Measure	SEIQoL McGee 1991	DQoL Brod 1999	ADRQL Rabins 1999	QOL-AD Logsdon 1999	DSDAT Volicer 1999	CBS Ready 2002	QOLAS Selai 2001	PDS De Jong 1989
Reliability								
Internal consistency	0,60-0,75	0,67-0,89	0,80	0,81-0,90	0,86-0,89	0,81	0,78	+
Inter-rater reliability	+	n.a.	n.a.	>0,70	0,74-0,98	0,90		+
Test-retest reliability	0,88	0,64-0,90	n.a.	0,76 / 0,92	0,97	n.a.		+
Validity								
Criterion related	-	-	-	-	-	-	+	
Construct validity	+	+	+	+	+	+	+	+
Responsiveness								
Sensit. to interventions	+	n.a.	+	n.a.	+	n.a.		
Longitudinal change	+	+	+	+	+	n.a.		+
Sample size							n=22	
Measure	AAI Albert 1996	PWB-CIP Burgener 2002	QUALID Weiner 2000	DEMQOL Smith 2005	Qualidem Ettema 2006	Basqid 24 Trigg 2007	Vienna List Porzsolt 2004	
Reliability								
Internal consistency		0,66-0,79	0,77	0,87	0,60-0,90	0,91	0,81-0,94	
Inter-rater reliability			0,83	n.a.	0,66-0,88		0,35-0,81	
Test-retest reliability			0,81	0,76-0,84	0,74-0,88	0,82	n.a.	
Validity								
Criterion related				-	-	n.a.	-	
Construct validity				+	+	+	+	
Responsiveness								
Sensit. to interventions	n.a.		+	n.a.	n.a.	n.a.	n.a.	
Longitudinal change	n.a.	±	±	n.a.	n.a.	+	n.a.	
Sample size	n=130	n=96	n=42		n=60/150			

n.a.= not available

Table 7. Selection criteria for quality of life measurements in dementia research			
Type of measure	Generic	Domain specific	Disease specific
Type of rating	By patient	By proxy	By observation
Type of rating	Quantitative	Qualitative	
Validity	Criterion related	Construct validity	
Reliability	Internal consistency	Inter-rater reliability	Test-retest reliability
Responsiveness	Sensitive to intervention	Longitudinal change	
Feasibility	Time to completion	Difficulty of scale	

EVALUATING THE OUTCOME OF INTERVENTIONS ON QUALITY OF LIFE IN DEMENTIA: SELECTION OF THE APPROPRIATE SCALE

C.J.M. Schölzel-Dorenbos
T.P. Ettema, J. Bos
E. Boelens-van der Knoop
D.L. Gerritsen, F. Hoogeveen
J. de Lange, L. Meihuizen
R-M. Dröes

ABSTRACT

Background: A literature study was conducted to contribute to an adequate use of quality of life (QoL) instruments for the evaluation of interventions in dementia care by providing an overview of properties of QoL measures that acknowledge domains important to dementia patients.

Methods: Domains important to patients, and domains that professional caregivers in different settings focus on, are compared to domains represented in nine QoL instruments. Data on psychometrics and applicability are generated.

Results: Four instruments best represent domains of QoL important to patients and domains professional caregivers in 24-hour care and daytime activities focus on. Two are self-rating instruments: Schedule for the Evaluation of Individual Quality of Life, applicable in mild dementia, measuring individual QoL of patient and informal caregiver, and Quality of Life-Alzheimer's Disease scale, which can be applied up to moderately severe dementia. For patients with advanced dementia receiving residential care, the observational instruments Qualidem and Discomfort scale-Dementia of Alzheimer Type are recommended. The first is easily administered by nurse assistants or occupational therapists and covers several QoL domains on which they focus in daily practice. The second can be used by various professionals.

Conclusions: QoL assessment provides a format for patients and (in)formal caregivers to express whether an intervention has made an important difference to the patient's life. Improvement of QoL in dementia should have high priority in care, treatment and research. This study shows that severity of dementia, care type, setting, and the specific QoL domains an intervention focuses on, determine which QoL instrument is most appropriate in a specific situation.

Introduction

Quality of life (QoL) is a multi-dimensional concept that includes well-being and has objective and subjective aspects (Logsdon et al., 2004; Sprangers, 2005). Domains in QoL measures vary considerably (Albert et al., 2001). Examples are: affect, self-esteem/awareness of self, social contact and physical/mental health. The QoL in dementia working group of the Leo Cahn Foundation investigated which domains patients and professional caregivers in nursing homes and meeting centres consider important. Most domains mentioned by patients were acknowledged by caregivers and represented in QoL scales, although each instrument contains only a selection of the domains. Some were not mentioned by caregivers (being useful/giving meaning to life) and not represented in the scales (security/privacy, selfdetermination/freedom, being useful). Apparently there are differences in views on QoL between patients, caregivers and theoretical models (Dröes et al., 2006). The working group also investigated on which domains professional caregivers actually focus in daily practice (Gerritsen et al., submitted). Caregivers focus on most of the domains that patients consider important. However, financial situation, self-determination/freedom, and being useful/giving meaning to life are focused on least, the latter domain being particularly important to patients with dementia (Rabins, 2000).

QoL scales must encompass the domains considered important by patients and the domains an intervention focuses on. Because cognitive decline may interfere with the ability to understand a complex topic such as QoL, the selection of the instrument is also influenced by the severity of dementia (Rabins, 2000). To contribute to an optimal use of QoL instruments in intervention studies, we reviewed their properties and the domains indicated as relevant by patients and focused on by professional caregivers. We propose which scales are best used to evaluate the outcome of care at different stages of dementia and for a specific research question/setting.

Methods

Nine QoL instruments were selected: Dementia QoL scale (DQoL) (Brod et al., 1999b); Alzheimer's Disease Health-Related QoL (ADRQL) (Rabins et al., 1999); Quality of Life-Alzheimer's Disease scale (QOL-AD) (Logsdon et al., 2002); Discomfort scale- Dementia of Alzheimer Type (DSDAT) (Hurley et al., 1992; Volicer et al., 1999); Cornell-Brown Scale for QoL in Dementia (CBS) (Ready et al., 2002); Vienna List (Porzsolt et al., 2004); DEMQOL (Smith et al., 2005a,b); Qualidem (Ettema et al., 2006) and Schedule for the Evaluation of Individual QoL (SEIQoL), a non-dementia specific instrument validated in dementia (McGee et al., 1991).

We investigated to what extent domains patients consider important are represented, if the scales measure the domains on which professional caregivers focus in daily practice and for which patients they are intended. For each scale we reviewed psychometric properties, setting, expertise necessary for application, method of data collection, sensitivity to change, and validated languages.

Because QoL of the caregiver/proxy is of major influence on coping with the patient (Logsdon et al., 2004), we investigated whether the instrument also provides for measurement of their QoL. Finally, based on the earlier studies of the working group, we selected the scales best used to evaluate daytime activities/institutional 24-hour care at different stages of dementia.

Results

Domains of QoL

Table 1 summarizes domains considered important by patients, domains that profes-

sional caregivers focus on and representation of these domains in the nine scales. Caregivers providing daytime activities/24-hour care focus especially on affect, social contact, attachment, general health, security/privacy; to some degree on self-determination/freedom and spirituality; and to a limited degree on financial situation. Differences between daytime activities/24-hour care exist mainly in the degree of focusing on enjoyment of activities, sense of aesthetics and being useful/giving meaning to life (Gerritsen et al., submitted).

The domain affect is represented in all scales, except for the DEMQOL. Self-esteem/social contact are often included. Only four instruments include attachment and physical/mental health (SEIQoL, DQOL, DSDAT, Qualidem), and two include enjoyment of activities/sense of aesthetics (ADR-QL, SEIQoL). Security/privacy, self-determination/freedom, being useful/giving meaning to life and spirituality can only be assessed with the SEIQoL. Yet all these domains are explicitly mentioned by patients as important aspects of their QoL.

Description and properties of QoL scales
Characteristics and practical applicability of the scales are presented in Table 2.

SEIQoL
The SEIQoL uses a technique derived from judgment analysis that enables respondents to nominate five areas most important to their QoL (McGee et al., 1991; Schölzel-Dorenbos and Jellesma-Eggenkamp, 2001). The technique is applicable in mild dementia (Coen et al., 1993; Schölzel-Dorenbos, 2000). For later stages the SEIQoL-DW (Direct Weighting; replacing weighting procedure with a pie chart format) offers an alternative (Hickey et al., 1996). The SEIQoL provides an overall score of QoL of both patient and proxy.

DQoL
29-item interview of patients with mild-moderate dementia (Mini-Mental State Examination (MMSE; 0-30)>12) (Brod et al., 1999b). Ten domains on five subscales (self-esteem/positive-negative affect/feelings of belonging/sense of aesthetics) are assessed with a 5-point Likert-scale, providing a profile of scores. Subjects with a MMSE≥13 understood the questions (Suzuki et al., 2005). 60% of people with a MMSE of 10 could complete the DQoL (Selwood et al., 2005).

ADRQL
Dementia-specific scale applicable regardless of disease severity (Rabins et al., 1999). The proxy-rated measure focuses on observable behavior during the past

2-4 weeks. An overall QoL score is obtained by a trained interviewer summarizing the scores of 47 items in five domains: social interaction/awareness of self/enjoyment of activities/feeling-mood/response to surroundings. The ADRQL-score is associated with disease severity. It measures efficacy of interventions/settings and is sensitive to change (Lyketsos et al., 2003).

QOL-AD
Dementia-specific 13-item self-report scale covering physical health/energy/mood/ living situation/memory/family/marriage/friends/chores/fun/money/self and life as a whole, scored on a 4-point Likert-scale (Logsdon et al., 2002). The QOL-AD can be used by patients (Participant self-reported QoL) and informal caregivers (Caregiver report of the Participant's QoL), yielding a single score, weighing the patient's score twice as heavily as the caregiver's. Caregivers can report on their own QoL with the CQOL (Caregiver QoL). Interrater-reliability, content and criterion-concurrent validity (DQoL, EQ-5D) are good (Thorgrimsen et al., 2003). Subjects with mild-moderate dementia (MMSE≥11) could complete the QOL-AD, including 3% of people with a MMSE of 11 (Selwood et al., 2005). There is evidence for reliability in severe dementia (MMSE 3; Hoe et al., 2005; Thorgrimsen et al., 2003). QoL did not decrease as cognition deteriorated. The level of agreement between patient/ caregiver ratings was modest, caregivers consistently rate the patient's QoL lower (Thorgrimsen et al., 2003). This was not explained by cognitive ability of the patient and probably reflects a real difference in the way they perceive the patient's QoL. Caregiver reports correlated strongly with both caregiver depression and burden.

DSDAT
Objective scale for trained observers to measure discomfort in non-communicative patients with severe dementia (MMSE 0-2), by observing their behavior during five minutes (Hurley et al., 1992; Volicer et al., 1999). It encompasses nine behavioral indicators, 7 negative (noisy breathing/negative vocalization/sad/frightened facial expression/frowning/tense bodylanguage/fidgeting) and 2 positive (content facial expression/relaxed bodylanguage). The Dutch version of the DSDAT showed good inter-observer reliability (Hoogendoorn et al., 2001).

CBS
Modification of Cornell Scale for Depression in Dementia, based on the conceptualization that high QoL is indicated by presence of positive affect, satisfactions and self-esteem, and relative absence of negative affect (Ready et al., 2002); completed by a clinician after brief interview with patient and caregiver. The CBS is composed

of 19 bipolar items, rated on a 5-point scale, yielding a single QoL score. Domains are mood, ideational/behavioral disturbances, physical signs and cyclic functions. The scale demonstrated adequate interrater/internal consistency reliability and criterion-validity (visual analogue positive mood ratings) in 50 patients (mean MMSE 22) (Ready et al., 2002).

Vienna List
Description of well-being in severe dementia, based on observations of professionals. Containing five factors encompassing most of the behavioral repertoire in severe dementia: communication/negative affect/bodily contact/aggression/mobility. The psychometric properties have to be proved in further studies (Porzsolt et al., 2004).

DEMQOL
Self-report questionnaire administered by interviewer (Smith et al., 2005a,b). It has a patient (DEMQOL; 28 items) and carer (DEMQOL-Proxy; 31 items) version and assesses dementia-specific QoL from the patient's perspective. The two versions give different but complementary perspectives on QoL and it is recommended that both are used together. Five domains are covered: daily activities/looking after yourself/health/well-being/cognitive functioning/social relationships/self-concept. In severe dementia (MMSE<10), only DEMQOL-Proxy should be used.

Qualidem
40-item behavior observation-scale for patients up to severe dementia in institutions (Ettema et al, 2006; Ettema et al, submitted). Nine subscales (care relationship/ positive and negative affect/restless/tense behavior/positive self image/ social relations/social isolation/feeling at home/having something to do) provide a QoL profile. It can be used for longitudinal investigation, and to evaluate effects of interventions and changes in daily care.

Selection of QoL instruments for application in practice
Selection of the appropriate instrument should take into account, apart from its psychometric properties, the following. Firstly, instruments that allow patients to rate their own QoL are preferred, if their judgment permits. Secondly, for what stage of dementia and setting is the instrument to be used? Thirdly, does the instrument measure the QoL domains that the professional or intervention focuses on? Finally, in case of community-dwelling patients, it is preferable if the scale provides for QoL measurement of the caregiver as well.

Based on these criteria four scales (Table 3) are recommended. For those offering daytime activities to people with mild dementia the SEIQoL seems the best choice, for 24-hour care the QOL-AD is advised. The SEIQoL offers both patient and caregiver QoL measurement. In moderately severe dementia, the SEIQoL-DW can be used. The QOL-AD contains most of the domains nurse assistants focus on in 24-hour care, and remains applicable during disease progression, an advantage in longitudinal studies. With the CQOL-AD the QoL of the caregiver can be assessed. ADRQL (all stages of dementia) and DQoL (mild-moderately severe dementia) are appropriate choices for professionals offering daytime activities focusing specifically on affect, self esteem, sense of aesthetics, social contact (DQoL) and enjoyment of activities (ADRQL). For general evaluation of daytime activities these measures are less appropriate, because both instruments only represent a selection of the domains that professionals offering daytime activities focus on. A relative disadvantage of the ADRQL is that the (in)formal caregiver reports on the patient, as it is known that informant and self-perception of QoL differ substantially. To date, neither source of information is superior (Ready et al., 2004). Professional caregivers could assess the well-being of patients more positively if they are also the care-provider (Porsolt et al., 2004). To measure QoL in mild-moderate dementia in 24-hour institutional care the observational instrument Qualidem seems most appropriate, supplemented with the self-report QOL-AD instrument, which is also applicable in day-care. In severe dementia the Qualidem together with the DSDAT seem adequate to evaluate the influence of daytime activities and 24-hour care on QoL. The selected instruments obviously do not cover all stages of dementia. Two instruments can assess QoL of both patient and caregiver: SEIQoL and QOL-AD (CQOL version).

Discussion
Measuring cognitive and functional response in dementia is no longer enough (Bannerjee et al., 2006). QoL measures should be applied more often as currently no disease modifying therapy is available. Our aim was to operationalize QoL criteria that are most important for patients and help professionals select the best scale, taking into account the relevant domains they focus on in daily practice.
Our overview shows three methods of QoL assessment: self-report by patient, proxy-report by proxy or professional, and direct observation of behavior assumed to be related to QoL. Dementia may interfere with understanding, ability to remember relevant events, making comparisons across complex domains and communicating (Rabins, 2000). Logsdon et al. (2002), however, showed that patients can rate their own QoL until late stages of dementia and that caregiver-ratings do

not substitute for patient-ratings. Sands et al. (2004) found that caregivers rated patients' QoL lower than patients, associated with increased caregiver burden and depressive symptoms of the patient. Boyer et al. (2004) found poor patient/family proxy concordance for the dimension emotional reaction of the Nottingham Health Profile. The disadvantage of proxy-ratings is that they filter a subjective measure through the opinion of another person.

Acknowledging the problem of potential bias of proxy-reports, self-rating methods are preferable if possible. If not, observational methods by an uninvolved professional are an acceptable alternative. We agree with Brod et al. (1999a) that the patient's subjective ratings should be the gold standard, but that independent observational ratings are of benefit for patients with (very) severe dementia.

In this paper we specifically focused on QoL scales appropriate for professional caregivers providing daytime activities/24-hour care. We found no instruments that can be used in all stages of dementia, types of care/settings. Four measures best represent the domains of QoL that are important for patients and that professionals focus on in the mentioned care settings. The first two are self-rating instruments. For people living in the community who are offered daytime activities, and their proxies, we advise assessment of QoL with the SEIQoL (mild dementia) or SEIQoL-DW (mild-moderate dementia). The QOL-AD remains applicable up to MMSE scores of 3. Though the QOL-AD encompasses only 4/13 domains mentioned as relevant for QoL by dementia-patients, this is sufficient if the intervention deals primarily with these domains, as is often the case in 24-hour care. The CQOL-AD version assesses caregiver's QoL. If self-report is not possible we recommend the observational instruments Qualidem (for mild to severe dementia) and DSDAT (for severe dementia) by uninvolved professionals, both for evaluation of daytime activities and 24-hour care. The other QoL instruments are less appropriate, but could be useful in the evaluation of interventions that focus specifically on domains included in those instruments.

In conclusion, QoL instruments must, if possible, acknowledge the opinion of patients with dementia. Interventions must take into account the domains they consider most important and the applied instrument should encompass the relevant domains for the care type/setting in question. If necessary more instruments could be used together to compensate for omissions in the application of one isolated scale. Investigators must select the scale(s) appropriate for the user, research question and care-type/setting. Rating of QoL of the caregiver is equally important, especially in community-dwelling patients. Improvement of QoL of dementia-patients and their caregivers should have a high priority in dementia care. QoL assessment provides a format to express whether an intervention has made an important difference to the patient's life (Selwood et al., 2005). The measures we recommend are tools to contribute to this goal. One should not assume that any instrument for QoL is automatically suitable to evaluate the effect of every intervention in all care-settings and stages of dementia. If the main focus in daily practice is on aspects that are not measured with the applied instrument, the effectiveness of the intervention cannot be assessed adequately. This study shows that severity of dementia, care-type/setting, and the specific QoL domains an intervention focuses on, are important factors to decide which QoL instrument would be best to use in a specific situation.

References

– Albert SM, Jacobs DM, Sano M et al. Longitudinal study of quality of life in people with advanced Alzheimer's disease. Am J Geriatr Psychiatry 2001;9:160-8.
– Banerjee S, Smith SC, Lamping DL et al. Quality of life in dementia: more than just cognition. An analysis of associations with quality of life in dementia. J Neurol Neurosurg Psychiatry 2006;77:146-8.
– Boyer F, Novella JL, Morrone I et al. Agreement between dementia patient report and proxy reports using the Nottingham Health Profile. Int J Geriatr Psychiatry 2004;19:1026-34.
– Brod M, Stewart AL, Sands L. Conceptualization of quality of life in dementia. Journal of Mental Health and Aging 1999a;5:7-20.
– Brod M, Stewart AL, Sands L et al. Conceptualization and measurement of quality of life in dementia: the dementia quality of life instrument (DQoL). Gerontologist 1999b;39:25-35.
– Coen R, O'Mahony D, O'Boyle C et al. Measuring the quality of life of dementia patients using the Schedule for the Evaluation of Individual Quality of Life. Irish J Psychology 1993;14:154-63.
– Dröes RM, Boelens-van der Knoop ECC, Bos J et al. Quality of life in dementia in perspective; an explorative study of variations in opinions among people with dementia and their professional caregivers, and in literature. Dementia: The International Journal of Social Research and Practice 2006;5:533-58.
– Ettema TP, Dröes RM, de Lange J et al. QUALIDEM: Development and evaluation of a Dementia Specific Quality of Life Instrument. Scalability, Reliability and Internal Structure. Int J Geriatr Psychiatry 2007;22:549-56.
– Ettema TP, Dröes RM, Lange Jd et al. QUALIDEM: Development and evaluation of a Dementia Specific Quality of Life Instrument-Validation. Int J Geriatr Psychiatry 2007;22:424-30.
– Gerritsen DL, Ettema TP, Boelens E et al. Do professional carers focus on the domains of quality of life that persons with dementia consider important? Am.J Alzh Dis Other Demen 2007;22:176-83.

- Hickey AM, Bury G, O'Boyle CA et al. A new short form individual quality of life measure (SEIQoL-DW): application in a cohort of individuals with HIV/AIDS. BMJ 1996;313:29-33.
- Hoe J, Katona C, Roch B et al. Use of the QOL-AD for measuring quality of life in people with severe dementia-the LASER-AD study. Age Ageing 2005;34:130-5.
- Hoogendoorn LI, Kamp S, Mahomed CA et al. The role of observer for the reliability of Dutch version of the Discomfort Scale-Dementia of Alzheimer Type (DSDAT). Tijdschr Gerontol Geriatr 2001;32:117-21.
- Hurley AC, Volicer BJ, Hanrahan PA et al. Assessment of discomfort in advanced Alzheimer patients. Res Nurs Health 1992;15:369-77.
- Logsdon RG, Gibbons LE, McCurry SM et al. Quality of Life in Alzheimer's Disease: Patient and caregiver reports. J Ment Health Aging 1999;5:21-32.
- Logsdon RG, Gibbons LE, McCurry SM et al. Assessing Changes in Quality of Life in Alzheimer's Disease. Proceedings of the 9th International Conference on Alzheimer's Disease and related disorders. Philadelphia, USA. 2004.
- Logsdon RG, Gibbons LE, McCurry SM et al. Assessing quality of life in older adults with cognitive impairment. Psychosom Med 2002;64:510-9.
- Lyketsos CG, Gonzales-Salvador T, Chin JJ et al. A follow-up study of change in quality of life among persons with dementia residing in a long-term care facility. Int J Geriatr Psychiatry 2003;18:275-81.
- McGee HM, O'Boyle CA, Hickey A et al. Assessing the quality of life of the individual: the SEIQoL with a healthy and a gastroenterology unit population. Psychol Med 1991;21:749-59.
- Porzsolt F, Kojer M, Schmidl M et al. A new instrument to describe indicators of well-being in old-old patients with severe dementia-the Vienna List. Health Qual Life Outcomes 2004;2:10-8.
- Rabins PV, Kasper JD, Kleinman L et al. Concepts and methods in the development of the ADRQL: An instrument for assessing health-related quality of life in persons with Alzheimer's disease. J Ment Health Aging 1999;5:33-48.
- Rabins PV. Measuring Quality of Life in Persons With Dementia. Intern Psychogeriatr 2000;12:47-9.
- Ready RE, Ott BR, Grace J. Patient versus informant perspectives of Quality of Life in Mild Cognitive Impairment and Alzheimer's disease. Int J Geriatr Psychiatry 2004;19:256-65.
- Ready RE, Ott BR, Grace J et al. The Cornell-Brown Scale for Quality of Life in dementia. Alzheimer Dis Assoc Disord 2002;16:109-15.
- Sands LP, Ferreira P, Stewart AL et al. What explains differences between dementia patients' and their caregivers' ratings of patients' quality of life? Am J Geriatr Psychiatry 2004;12:272-80.
- Schölzel-Dorenbos C, Jellesma-Eggenkamp M. Een meetmethode voor individuele kwaliteit van leven bij Nederlandse ouderen. Nederlands Tijdschr voor de Psychologie 2001;56:16-8.
- Schölzel-Dorenbos CJM. Measurement of quality of life in patients with dementia of the Alzheimer type and their caregivers: Schedule for the Evaluation of Individual Quality of Life (SEIQoL). Tijdschr Gerontol Geriatr 2000;31:23-6.
- Selwood A, Thorgrimsen L, Orrell M. Quality of life in dementia-a one-year follow-up study. Int J Geriatr Psychiatry 2005;20:232-7.
- Smith SC, Lamping DL, Banerjee S 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 Technol Assess 2005a;9:193,III-IV.
- Smith SC, Murray J, Banerjee S et al. What constitutes health-related quality of life in dementia? Development of a conceptual framework for people with dementia and their carers. Int J Geriatr Psychiatry 2005b;20:889-95.
- Sprangers MAG. Levenskwaliteit telt. 2005. www.aup.nl. Spui 2005;3:20-2.
- Arcares. Zicht op eigen leven. Meetinstrument voor de kwaliteit van leven. 2005. www.arcares.nl. Publicatienummer 05.007.
- Suzuki M, Uchida A, Kanamori M et al. Development of the Dementia Quality of Life Instrument-Japanese version. Nippon Ronen Igakkai Zasshi 2005;42:423-31.
- Thorgrimsen L, Selwood A, Spector A, et al. Whose quality of life is it anyway? The validity and reliability of the Quality of Life-Alzheimer's Disease (QoL-AD) scale. Alzheimer Dis Assoc Disord 2003;17:201-8.
- Volicer L, Hurley AC, Camberg L. A model of psychological well-being in advanced dementia. Journal of Mental Health and Aging 1999;5:83-9.

Table 1. Domains important for quality of life according to patients with dementia, focused on by professional caregivers and their representation in measuring instruments for quality of life in dementia

Domain of quality of life	Affect	Self-esteem/self-image	Social contact	Attachment	Physical and mental health	Enjoyment of activities	Sense of aesthetics in living environment	Financial situation	Security and privacy	Self-determination and freedom	Being useful/giving meaning to life	Spirituality
Important to patients in NH/MC*	+/+†	+/+	+/+	+/+	+/+	+/+	+/-	+/+	+/+	+/+	+/+	-/+
Focused on by NA in 24-hour care in NH*	4‡	4	3,5	4	4	3	3	2	4	3	2	3
Focused on by NA/OT in NH and MC*	4‡	4	3,5	4	4	4	4	2	4	3	3	3
SEIQoL McGee et al. 1991	+	+	+	+	+	+	+	+	+	+	+	+
DQoL Brod et al. 1999a	+	+		+			+					
ADR-QL Rabins et al. 1999	+	+	+			+	+					
QoL-AD Logsdon et al. 1999	+	+	+		+			+				
DSDAT Volicer et al. 1999	+	+		+	+							
CBS Ready et al. 2002	+	+			+							
Vienna List Porzsolt et al. 2004	+		+		±							
DEMQOL Smith et al. 2005		+	+		+							
Qualidem Ettema et al. 2006	+	+	+	+		+						

* NH = nursing home; MC = meeting and day-care centre; NA = nurse assistant; OT = occupational therapist. † + = present; - = absent. ‡ 5 = daily practice focused on the domain to a very high degree; 4 = a high degree; 3 = some degree; 2 = a limited degree; 1 = a very limited degree.

Table 2. Psychometric and practical properties of quality of life measures in dementia

	SEIQoL McGee et al.	DQoL Brod et al.	ADRQL Rabins et al.	QOL-AD Logsdon et al.	DS-DAT Volicer et al.	CBS Ready et al.	Vienna List Porzsolt et al.	DEMQOL Smith et al.	Qualidem Ettema et al.
Reliability									
Internal consistency	0,60-0,75	0,67-0,89	0,80	0,81-0,90	0,86-0,89	0,81	0,81-0,94	0,87	0,60-0,90
Inter-rater reliability	+	n.a.*	n.a.	>0,70	0,74-0,98	0,90	0,35-0,81	n.a.	0,66-0,88
Test-retest reliability	0,88	0,64-0,90	n.a.	P0,76, C0,92	0,97	n.a.	n.a.	0,76-0,84	0,74-0,88†
Validity									
Criterion related‡	-	-	-	-	-	-	-	-	-
Construct validity	+	+	+	+	+	+	+	+	+
Responsiveness									
Sensitive to intervention	+	n.a.	+	n.a.	+	n.a.	n.a.	n.a.	n.a.
Longitudinal change	+	+	+	+	n.a.	n.a.	n.a.	n.a.	n.a.
Applicability									
Stage of dementia	Mild	Mild-moderate	All stages	Mild-moderate	Severe	Mild-moderate	Severe	Mild-moderate§	Mild-severe
Data collection	Interview	Interview	Observation	Interview	Observation	Interview	Observation	Interview	Observation
Rating by	Patient	Patient	Proxy	Professional	Professional	Professional	Professional	Patient; Proxy	Professional
Assessment QoL proxy	+	-	-	+ (CQOL)	-	-	-	-	-
Setting	Community, institution	Community, institution	Institution	Community, institution	Institution	Community, institution	Institution	Community, institution	Institution
Inclusion environmental factors	+	-	+	+	-	-	-	-	+
Rating by#	O	O	O	O	O, N	O	NA, O	Ph, N	2 NA
Difficulty of application	Trained interviewer	Easily administered	Trained interviewer	Easily administered	Trained interviewer	Easily administered	Easily administered	Easily administered	Easily administered
Validated in	E/D‖	E	E	E	E/D	E	E	E	D

*n.a.: not available. † By 2 nurse assistants. 1 nurse assistant: 0,49-0,79. ‡ There is no gold standard, because Quality of Life is by definition subject to individual interpretations.
§ Severe dementia: only DEMQOL-Proxy. # O=other investigators/researchers. N=nurse. NA=nurse assistant. Ph=physician. ‖ E = English D = Dutch.

Table 3.   Four measures to evaluate the outcome of daytime activities and 24-hour care on quality of life (QoL) in dementia

	SEIQoL(-DW)	QOL-AD/CQOL-AD	Qualidem	DSDAT
Stage of dementia	Mild dementia (DW: moderate)	Mild-moderate severe dementia	Mild-moderate severe dementia	Severe dementia
Setting	Community and institution	Community and institution	Institution	Institution
Type of care	Daytime activities	24-hour care	Daytime activities/24-hour care	24-hour care
Domains of QoL	All relevant domains	Sufficient	Attuned to institutional care	Attuned to institutional care
Rating QoL proxy	+	+	-	-
Difficulty of application	Trained interviewer, difficult	Easy after simple training	Easy after simple training	Easy after simple training
Rating by	Investigator	Investigator	Two nurse assistants	Nurse assistant/Investigator
Dutch validation	+	-	+	+
English validation	+	+	-	+

CHAPTER 4

INTEGRATING UNMET NEEDS INTO DEMENTIA HEALTH-RELATED QUALITY OF LIFE RESEARCH AND CARE INTRODUCTION OF THE HIERARCHY MODEL OF NEEDS IN DEMENTIA (HMND)

C.J.M. Schölzel-Dorenbos
E.J. Meeuwsen
M.G.M. Olde Rikkert

ABSTRACT

Objectives: To make an inventory of needs assessment instruments in dementia, explore the interaction between unmet needs and health-related quality of life (HRQoL), and relate these to the conceptual model of Maslow's Hierarchy of needs in order to design a dementia-specific model.

Methods: Narrative review of literature on (measures of) needs of patients and caregivers and HRQoL determinants important in dementia. Relating these needs to individual goal setting instruments and Maslow's Hierarchy of needs model.

Results: The Camberwell Assessment of Needs for the Elderly (CANE) turns out to be a valid tool to assess needs of dementia patients, suitable for research and clinical use. The Carers' Needs Assessment for Dementia (CNA-D) is a valid instrument to assess needs of caregivers. Patients identified significantly fewer needs than (in)formal caregivers. The most important needs, that also determine large part of HRQoL, are need for information; support with regard to symptoms of dementia; social contact and company; and for health monitoring and safety. Goal Attainment Scaling in dementia is an important but not yet valid outcome measure, with only few data on feasibility in dementia patients.

Conclusions: There are several instruments to assess needs of dementia patients and caregivers. Domains of unmet needs and HRQoL overlap. The Hierarchy Model of Needs in Dementia (HMND) offers a new theoretical framework to address the interplay between meeting of needs and improvement of HRQoL in dementia. By identifying unmet needs in dementia-research, and focussing on unmet needs in dementia-care, much can be done to improve HRQoL.

Introduction

Health-related quality of life (HRQoL) studies have limited influence on clinical decision making,[1] and HRQoL is rarely used as primary outcome measure in dementia trials.[2,3] One of the main reasons is the difficulty clinicians and researchers experience in unequivocal interpretation of HRQoL findings.[4] The lack of a definition of minimal clinically important differences connected to clinical anchors (MCIDs) in HRQoL measures is a major barrier for application in trials. Nevertheless HRQoL assessment provides an ideal domain for patients and (in)formal caregivers to express whether an intervention has made a meaningful difference to their life. Conceptually MCIDs in HRQoL are related to needs and especially unmet needs. Dementia patients as well as their informal caregivers probably have more health needs than the general population, many of which are unrecognised and unmet by professionals and informal carers. However so far, both in clinical practice and research, the connection between HRQoL and needs assessment is not further elaborated on. Unmet needs can be divided in subjective, objective, personal and societal needs. Subjective needs are the needs experienced by patients and caregivers, for example the need for comfort and compassion. Objective needs are objectively diagnosed needs, for example in patients with clear signs of neglect. Needs can also be distinguished on a personal and societal level, with the latter pointing for example at the opportunity of having day care services for the patient and/or volunteer services to help the informal caregiver. In this review we concentrate on subjective unmet needs of dementia patients and their caregivers, experienced in domains of psychological distress, company, information and daytime activities. Reliance solely on assessment of needs by professional caregivers may lead to under recognition of personal unmet needs.[5] A patient-centred approach is a precondition to be sensitive for tracing unmet needs. However, the issue of determination of needs and HRQoL in dementia and older patients in general is complex, also because of atypical illness and complaint presentation. In case of dementia, the influence of cognitive impairment on reliability and validity of self-reporting capability and unawareness of deficits also plays a role. Many dementia patients experience unmet needs with regard to available care, which results in under use of services and support. Moreover, they frequently experience needs with regard to information on the consequences of dementia. Literature on met and unmet needs is often limited to practical issues and organisation of care.

Goal Attainment Scaling (GAS) may offer patients and caregivers the opportunity to discuss their needs and to choose and prioritize important aspects of their HRQoL.[6] GAS enables inclusion of care recipients' views in the intervention and thus potentially enhances the effectiveness of interventions and ultimately the HRQoL in dementia.

We designed the Hierarchy Model of Needs in Dementia (HMND) based on the humanistic psychology of Maslow, especially his theory of motivation and hierarchy of needs. Maslow's model presents a global framework for quality of life and perceived needs but has not yet been discussed in dementia care literature. The relationship between needs and HRQoL in dementia can be visualized by two parallel pyramids: one depicting the levels of needs in dementia and the other showing the consequences when those needs remain unmet. This perspective could serve as a new model and a theoretical framework to study the interplay between needs and HRQoL. Ideally this could generate a new decision model for future research and appropriate allocation of finances and care for the increasing societal problem of dementia. Our study aims to present an overview of (unmet) needs assessment instruments, of dementia-related HRQoL determinants, GAS and Maslow's Hierarchy of needs Model, and to introduce the HMND.

Methods

According to the methodology of narrative reviews,[7] we searched the literature with the PubMed search terms 'Unmet needs AND Dementia', 'Unmet needs AND Dementia AND Quality of life' and 'Unmet needs OR Maslow's hierarchy of needs OR Goal Attainment Scaling AND dementia AND quality of life', and the references of the articles retrieved. Based on this information we present an overview of measurement instruments for needs of dementia patients and caregivers: the Camberwell Assessment of Needs for the Elderly (CANE),[8] Care Needs Assessment Pack for Dementia (CareNap-D),[9] and Carers' Needs Assessment for Dementia (CNA-D).[10] Differences in needs according to patients and caregivers were analysed as well as HRQoL determinants in dementia, by incorporating data from two of our earlier studies. In the first study spouses of AD patients were assessed for their relevant individual domains of HRQoL with the Schedule for the Evaluation of Individual Quality of Life (SEIQoL).[11] In a recent review we identified the domains most relevant for HRQoL according to dementia patients.[12] Next, we summarized the information about the use of GAS in dementia. Finally we related these findings to the concept of Maslow's Hierarchy model of (unmet) needs and designed a new theoretical framework of consequences of (unmet) needs and HRQoL.

Results

Measurement instruments for needs of dementia patients

Two measurements instruments were found: CANE and CareNap-D.[8;9] Mild or moderately severe dementia patients are able to assess their own met and unmet needs with the CANE. Reynolds et al. developed the CANE on the basis of the Camberwell Assessment of Need (CAN), a widely used needs assessment for people with severe mental illness. Needs were assessed in 24 areas of life and cover a broad range of health, social and psychological domains.[8] The CANE turned out to be suitable for both research and clinical use and applicable in various settings and populations. It has good content, construct and consensual validity and demonstrates appropriate criterion validity. Reliability is high: kappa>0.85 for inter-rater reliability. Correlations of inter-rater and test-retest reliability of total numbers of needs identified by professionals were 0.99 and 0.93, respectively. The CANE proved to have good feasibility, as it easily could be used by a wide range of professionals without formal training.

The CareNap-D consists of 57 activity and behavioral items and is used to evaluate the status of care needs as 'No-Met-Unmet needs' in seven domains of functioning.[9] The CareNap-D is a reliable and valid multidisciplinary assessment of needs for people with dementia living in the community and their carers. Inter-rater reliability was good and kappa statistic demonstrated that agreement for 76.2% of items in the CareNap-D was good. There was low intra-item variance and high agreement on the items.[13]

Measurement instruments for needs of caregivers

One instrument was identified for assessing carer's needs: CNA-D. This semi-structured research interview includes 18 problem areas with several possible interventions. Inter-rater and test-retest reliability, concurrent and content validity were investigated among dementia caregivers and professionals. Significant positive associations were found between Zarit Burden Inventory, number of problems and number of unmet needs according to the CNA-D. Kappa statistic demonstrated that agreement between interviewers was good. The CNA-D is a valid and reliable instrument for comprehensively assessing the needs of dementia caregivers.[10]

Needs in dementia

The most frequently mentioned unmet needs by dementia patients and their informal caregivers can be summarized as the unmet need for information, for support with regard to symptoms of dementia, for social contact and company; and for health monitoring and perceived safety.[14] Table 1 provides an overview of domains of personal needs of dementia patients and informal caregivers.

Needs according to patients

Hancock et al. identified the unmet needs of dementia patients in care homes, using the CANE. They had a mean of 4.4 unmet and 12.1 met needs. Environmental and physical health needs were usually met. However, sensory or disability (including mobility problems and incontinence) needs, mental health needs, and social needs, such as company and daytime activities, were often unmet. Unmet needs were associated with psychological problems (anxiety and depression).[15] Patients reported a relatively higher number of unmet needs than caregivers and professionals, especially for psychological distress, company and information, daytime activities and eyesight/hearing problems.[5] In community dwelling dementia patients, assessed on the CareNap-D, 13 of 33 needs were unmet. High levels of unmet needs were identified in the domains behavior, mental state, and social interaction. Increasing age, lower Mini-Mental State Examination score, and living alone were associated with greater total levels of unmet needs.[16]

Needs according to caregivers

Carer needs include support with (daily) activities and supervision. Care giving can

result in social isolation, psychological stress and depression. Caregivers of Alzheimer's disease patients living at home most often needed physiotherapy for the patient, financial support, house-cleaning and home respite care during holidays. Official services poorly met caregivers' needs for support and help.[17]

Differences between needs according to patients and caregivers
Hancock et al. compared rating by (in)formal caregivers on how older people with mental health problems perceived their own needs, using the CANE.[18] Patients identified significantly fewer of their needs (5.5) than either staff (8.1) or carers (8.3) did. The kappa's indicating level of agreement between professional/care user, care user/caregiver and caregiver/care user were low, indicating that patient-reported outcomes should be given a high priority. Orrell et al. compared the ratings of needs of dementia patients in care homes with the CANE.[5] They concluded that patients' views on their needs should be sought and that assessment by informal caregiver and professionals may lead to under recognition of unmet needs.

Quality of life determinants in dementia
Spouses of AD patients were assessed for the relevant individual domains of their quality of life by means of the SEIQoL.[11] The most frequently mentioned determinants were physical fitness of patient, and state of their marriage and family. In another explorative study we identified the domains most relevant for HRQoL according to dementia patients, professional caregivers and the literature.[12] Patients and professionals have different perspectives. Some domains were not mentioned by professionals (i.e. 'sense of aesthetics in living environment', 'financial situation' and 'being of use/ giving meaning to life'), and not selected in the measuring instruments ('security and privacy', and 'self-determination and freedom'). We summarized these domains in Table 2, and also expressed which items were perceived as domains for unmet needs as well. The results suggest considerable overlap between the two paradigms of HRQoL and needs assessment.

Goal Attainment Scaling in dementia
Goal Attainment Scaling (GAS) offers patients and (in)formal caregivers the opportunity to select the relevant domains of HRQoL and has been used as an outcome measure in clinical dementia trials.[6;19;20] GAS can be considered as an operationalization of the unmet need with highest priority. In long-term care GAS is a feasible and responsive measure.[21] In a systematic review empirical support was found for the validity of goal setting for use in physical rehabilitation settings, but research demonstrating its reliability, sensitivity and feasibility seems limited.[22] In this review

on clinimetric aspects and feasibility of GAS in dementia, we found mixed results for responsiveness, content validity, inter-rater reliability and construct/convergent validity. GAS proved to be useful on important aspects of an outcome measure, but the evidence is not strong enough yet to state that GAS is an applicable outcome measure in this population.[23]

Maslow's Hierarchy Model of Needs
Maslow's Hierarchy Model of Needs (MHMN) is based of the humanistic psychology of Maslow, especially his theory of motivation and hierarchy of needs. When related to the enumeration of HRQoL domains and the unmet needs, it enables understanding of these objectives in view of more universal human needs.[24] The MHMN is often depicted as a pyramid consisting of different levels, comprising five fundamental human needs. The lower level deals with physiological basic needs (food, drinks, shelter, and warmth), while the top levels are associated with psychological needs: safety, love and belongingness, self-esteem and needs of self-actualization (the desire to become everything that one is capable of becoming). The lower four layers of the pyramid, i.e. physiological, safety and security, love and belonging, and esteem, are what Maslow called 'deficiency needs'. Deficiency needs must be met first.

Hierarchy Model of Needs in Dementia
Maslow's model has not yet been discussed in dementia care literature.[24] We related the theoretical and general perspective of the MHMN (unmet) needs to the needs and HRQoL in dementia. We visualized this relationship by means of two parallel pyramids, one depicting the levels of needs in dementia and the other showing the consequences on f.i. HRQoL when needs remain unmet (see Figure 1). The Hierarchy Model of Needs in Dementia (HMND) provides a comprehensive approach for needs assessment and the design of interventions to achieve goals that meet the wishes of patients and caregivers. The physiological basic needs include maintaining personal hygiene, housing and feeding. Safety-needs deal with prevention of harm caused by wandering, apraxia, agnosia, disturbance in executive functioning or decreased judgment capacities. Love and belonging-needs deal with affection, love and acceptance in the face of a progressive neurodegenerative illness, which hinders patients to have social contacts that may result in receiving signs of love, acceptance and affection. Self-esteem-needs concern fears for loss of mastery and independency; esteem, respect, and appreciation for the patient, who experiences rapid loss of societal roles. And on top of all these needs we position self-actualization, a 'being'-need, which motivates or drives behavior.

Discussion

The striving for completion of unmet needs is, similar to learning theory and altered stress thresholds theory, one of the relevant psychologically oriented paradigms in dementia care.[25] Quality of life refers to the needs that are considered most important. Goal attainment scoring is the concrete next goal on a very or the most important unmet need. These needs can be related to each other using a hierarchical model.

Needs can be assessed in one of two ways: either by adopting an epidemiological approach and performing a survey, or by examining health service usage. Despite many provisions of care directed at improving HRQoL, there still remain a high number of unmet needs in dementia patients,[26] and little understanding of why these needs remain unmet.[27] Interventions should be tailor-made, to fulfil needs in a manner that matches a person's cognitive, physical, and sensory abilities, and their lifelong habits and roles. Sometimes people with dementia are unable to clearly or consistently verbalize symptoms or complaints. Thus, in patients with severe dementia it may be difficult to know the content and extent of their needs. The consequences of need-driven, dementia-compromised behavior (C-NDB) theory shows the effects of behavioral symptoms and results of unmet needs.[28] Behavioral symptoms may be expressions of unmet (non-)physiologic needs or goals. Unmet needs analysis can guide the treatment of behavioral problems in dementia. Open ended discussion can also produce unexpected information that is outside the goals of the researcher, but relevant to the people being studied, reflecting the unique nature of each person's experience with dementia.

Older people apparently tolerate unmet needs.[29] However, in dementia cascading effects occur, in which not meeting too many original needs results in new needs and behavioral symptoms.[28] Unmet needs will affect HRQoL with consequences for care and caregivers and increasing risks for institutionalization. It has been shown that determining unmet needs may be useful in identifying dementia patients at risk for nursing home placement and death.[30] In residential care environmental and physical health needs were usually met. However, sensory or physical disability (f.i. mobility problems, incontinence) needs, mental health needs, and social needs (f.i. company, daytime activities), were often unmet. Unmet needs were associated with psychological problems, such as anxiety and depression which may decrease HRQoL.[15] Care services have been developed with little evaluation as to how needs have been met by these services. Professionals should be aware that in dementia care often only the basic levels of needs are partially met, that many needs remain unmet and that much can be done to improve HRQoL.[15] The first goal is to address the most simple goals, but the ultimate goal is to also meet more complex (e.g. emotional and social) unmet needs in such a way that this improves HRQoL.

The aim of interventions should be to move the care from basic to more complex levels. Behaviors associated with dementia may be expressions of unmet needs or goals. Despite many provisions, there still remains a high degree of unmet need.[26] Identification of these needs provides a conceptual framework and local, regional and national overviews of most important problems for frail elderly subjects. The higher the pyramid level of HNMD a patient can reach, the higher his or her HRQoL, and probably the less disturbing behavioral and neuropsychological symptoms occur. Assistance to caregivers can reduce the severity of patients' symptoms and delay institutionalization. Because this assistance requires provision of multiple health care and social services, a coordinated system of care, guided by need and HRQoL is warranted. Patient-based assessment will assist healthcare providers to prioritize needs according to what the users themselves consider to be most important, beneficial, and acceptable.[18]

Thus, we propose a new theoretical framework by combining GAS and HNMD to address the needs and HRQoL of dementia patients and their caregivers at the highest achievable level. We strongly recommend to address needs and HRQoL simultaneously in research and clinical practice. Dementia is a still incurable chronic disease, but patients and caregivers probably will benefit from a coordinated system of care and psychosocial and community-based intervention protocols, guided by (unmet) needs and HRQoL assessment, carried out by a case manager. Besides improvement of HRQoL, prioritizing of needs also helps to achieve the most efficient allocation of health and social care resources.

References

1. King MT, Fayers PM. Making quality-of-life results more meaningful for clinicians. Lancet 2008;371:709-10.

2. Santaguida PS, Raina P, Booker L et al. Pharmacological treatment of dementia: evidence report/technology assessment no. 97 (Prepared by McMaster University Evidence-based Practice Center under contract no. 290-02-0020). Evid Rep Technol Assess (Summ) 2004;(97):1-16.

3. Schölzel-Dorenbos CJM, van der Steen MJ, Engels LK, Olde Rikkert MG. Assessment of quality of life as outcome in dementia and MCI intervention trials: a systematic review. Alzheimer Dis Assoc Disord 2007;21:172-8.

4. Guyatt G, Schunemann H. How can quality of life researchers make their work more useful to health workers and their patients? Qual Life Res 2007;16:1097-105.

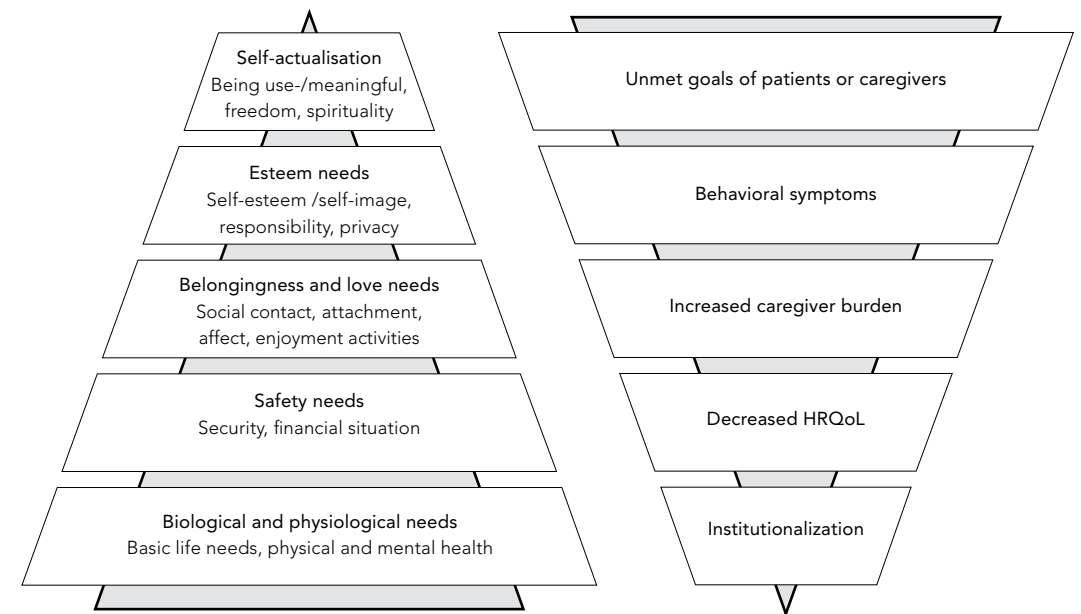5. Orrell M, Hancock GA, Liyanage KC et al. The needs of people with dementia in care homes: the perspectives of users, staff and family caregivers. Int Psychogeriatr 2008;20:941-51.

6. Rockwood K, Stolee P, Fox RA. Use of goal attainment scaling in measuring clinically important change in the frail elderly. J Clin Epidemiol 1993;46:1113-8.

7. Overcash JA. Narrative research: a review of methodology and relevance to clinical practice. Crit Rev Oncol Hematol 2003;48:179-84.

8. Reynolds T, Thornicroft G, Abas M et al. Camberwell Assessment of Need for the Elderly (CANE). Development, validity and reliability. Br J Psychiatry 2000;176:444-52.

9. Chung JC. Care needs assessment of older Chinese individuals with dementia of Hong Kong. Aging Ment Health 2006;10:631-7.

10. Wancata J, Krautgartner M, Berner J et al. The Carers' Needs Assessment for Dementia (CNA-D): development, validity and reliability. Int Psychogeriatr 2005;17:393-406.

11. Schölzel-Dorenbos CJM, Draskovic I, Vernooij-Dassen MJ, Olde Rikkert MJM. Quality of life and burden of spouses of Alzheimer's disease patients. Alzheimer Disease & Associated Disorders 2009;23:171-7.

12. Dröes R-M, Boelens ECC, Bos J et al. Quality of life in dementia in perspective; an explorative study of variations in opinions among people with dementia and their professional caregivers, and in literature. Dementia: Int J Social Research and Practice 2006;5:533-58.

13. McWalter G, Toner H, McWalter A et al. A community needs assessment: the care needs assessment pack for dementia (CarenapD)-its development, reliability and validity. Int J Geriatr Psychiatry 1998;13:16-22.

14. Lauriks S, Reinersmann A, Van der Roest HG et al. Review of ICT-based services for identified unmet needs in people with dementia. Ageing Res Rev 2007;6:223-46.

15. Hancock GA, Woods B, Challis D et al. The needs of older people with dementia in residential care. Int J Geriatr Psychiatry 2006;21:43-9.

16. Meaney AM, Croke M, Kirby M. Needs assessment in dementia. Int J Geriatr Psychiatry 2005;20:322-9.

17. Raivio M, Eloniemi-Sulkava U, Laakkonen ML et al. How do officially organized services meet the needs of elderly caregivers and their spouses with Alzheimer's disease? Am J Alzheimers Dis Other Demen 2007;22:360-8.

18. Hancock GA, Reynolds T, Woods B et al. The needs of older people with mental health problems according to the user, the carer, and the staff. Int J Geriatr Psychiatry 2003;18:803-11.

19. Rockwood K, Howlett S, Stadnyk K et al. Responsiveness of goal attainment scaling in a randomized controlled trial of comprehensive geriatric assessment. J Clin Epidemiol 2003;56:736-43.

20. Rockwood K, Fay S, Song X et al. Attainment of treatment goals by people with Alzheimer's disease receiving galantamine: a randomized controlled trial. CMAJ 2006;174:1099-1105.

21. Gordon JE, Powell C, Rockwood K. Goal attainment scaling as a measure of clinically important change in nursing-home patients. Age Ageing 1999;28:275-81.

22. Hurn J, Kneebone I, Cropley M. Goal setting as an outcome measure: A systematic review. Clin Rehabil 2006;20:756-72.

23. Bouwens SF, van Heugten CM, Verhey FR. Review of Goal Attainment Scaling as a Useful Outcome Measure in Psychogeriatric Patients with Cognitive Disorders. Dement Geriatr Cogn Disord 2008;26:528-40.

24. Maslow AH. A Theory of Human Motivation. Psychological Review 1943;50:370-96.

25. O'Connor DW, Ames D, Gardner B, King M. Psychosocial treatments of behavior symptoms in dementia: a systematic review of reports meeting quality standards. Int Psychogeriatr 2008;1-16.

26. Franks PJ, Salisbury C, Bosanquet N et al. The level of need for palliative care: a systematic review of the literature. Palliat Med 2000;14:93-104.

27. Walters K, Iliffe S, Orrell M. An exploration of help-seeking behaviour in older people with unmet needs. Fam Pract 2001;18:277-82.

28. Kovach CR, Noonan PE, Schlidt AM et al. A model of consequences of need-driven, dementia-compromised behavior. J Nurs Scholarsh 2005;37:134-40.

29. Smith F, Orrell M. Does the patient-centred approach help identify the needs of older people attending primary care? Age Ageing 2007;36:628-31.

30. Gaugler JE, Kane RL, Kane RA et al. Unmet care needs and key outcomes in dementia. J Am Geriatr Soc 2005;53:2098-105.

31. Orrell M, Hancock G, Hoe J et al. A cluster randomised controlled trial to reduce the unmet needs of people with dementia living in residential care. Int J Geriatr Psychiatry 2007;22:1127-34.

32. Schölzel-Dorenbos CJM, Ettema TP, Bos J et al. Evaluating the outcome of interventions on quality of life in dementia: selection of the appropriate scale. Int J Geriatr Psychiatry 2007;22:511-9.

Table 1. Domains of personal needs of dementia patients (P) and informal caregivers (C)

Psychosocial needs	Physical and practical needs
Information on dementia (P,C)	Physical health (P,C)
Cognition (P)	Senses (vision and hearing) (P)
Behavior and mental state (P,C)	Physical ability (mobility and falls) (P)
Emotional support (P,C)	Self-care (P)
Emotional distress (depression and anxiety) (P,C)	Toileting (P)
Social interactions, company (P,C)	Incontinence (P)
Marriage, family (C)	Accommodation (P,C)
Community living; institutionalization (P)	House-care (P,C)
Safety (P)	Food preparation (P)
Respite care (C)	Help with supervision (C)
Day-time activities (P)	

Table 2. Domains of quality of life judged by patients as most important in dementia

Psychosocial domains	Physical and practical domains
Mental health	Physical health*
Affect	Security and privacy*
Attachment*	Financial situation*
Self-esteem /self-image	
Being useful/ giving meaning to life*	
Enjoyment of activities*	
Self-determination and freedom*	
Social contact*	
Sense of aesthetics in living environment	
Spirituality	

*Domains judged as relevant for quality of life and also directly or indirectly mentioned as (unmet) needs, according to own research and literature.[5;12;14-18;29;31;32]

Figure 1. New model of levels of needs, and consequences of unmet needs in dementia

Self-actualisation
Being use-/meaningful, freedom, spirituality

Esteem needs
Self-esteem /self-image, responsibility, privacy

Belongingness and love needs
Social contact, attachment, affect, enjoyment activities

Safety needs
Security, financial situation

Biological and physiological needs
Basic life needs, physical and mental health

Unmet goals of patients or caregivers

Behavioral symptoms

Increased caregiver burden

Decreased HRQoL

Institutionalization

CHAPTER 5

THE CHALLENGES OF ACCURATE MEASUREMENT OF HEALTH-RELATED QUALITY OF LIFE IN FRAIL ELDERLY AND DEMENTIA

C.J.M. Schölzel-Dorenbos
M.G.M. Olde Rikkert
E.M.M. Adang
P.F.M. Krabbe

Given the complexity of dementia, there is emerging consensus that patient-reported outcomes such as health-related quality of life (HRQoL) are warranted for comprehensive outcome measurement. HRQoL measurement demonstrates whether interventions are perceived as meaningful by patients and caregivers,[1] and will play a key role in assessing outcome of disease-modifying interventions once they become available. However, several issues threaten accuracy of HRQoL assessment in frail elderly. These issues are under recognized, especially in dementia. In this letter we want to highlight relevant issues in measurement procedure and choice of instrument.

The impact of declining intellectual capacities, semantic knowledge and episodic memory, as well as varying deficits of judgment and insight, may compromise dementia patients' judgment and add to inter- and intra-individual variation in HRQoL rating. Behavioral and noncognitive symptoms are also of influence.[2] Judgments about what is important to HRQoL may change as dementia progresses: what seems important in early stages (e.g., preservation of intellectual capacity) may seem unimportant in late stages (when safety and comfort may take on primary importance).[3] Furthermore, anosognosia (unawareness of deficits), is frequently reported as cause for less reliable repeated self-reports and discrepancies between self- and proxy-rating.[4]

Quality of life, health status and HRQoL represent three distinct constructs. In quality of life rating patients give greater emphasis to mental health. In health status rating, physical functioning is more important.[5] HRQoL is a more narrow concept than quality of life and reflects individuals' perception of the impact of a health status, e.g. dementia, on the ability to perform usual tasks and effects on everyday life, physical, social and emotional well-being.[6]

The first question to be answered is which HRQoL measures are preferable. HRQoL measures can be categorized into disease-specific and generic instruments. Disease-specific instruments target to measure consequences of specific diseases, whereas generic instruments can be used in all health areas but lack the sensitivity of disease-specific instruments. Furthermore, most – if not all – of present dementia HRQoL instruments are constructed within a measurement framework that precludes expressing the measures as single overall metric measure. Summary values are important because they can be compared with effects of other diseases/interventions and facilitate economical decision-making.

Second, several factors should be taken into account in interpreting HRQoL outcomes in dementia. In general, persons with chronic diseases often report a relatively high HRQoL, when observers judge their life to be undesirable. This is known as disability paradox.[7] Response shift may contribute to this phenomenon. Response shift is change in self-evaluation due to recalibration (changes in internal measurement standards), reprioritization (changes in values or importance of domains constituting HRQoL), or reconceptualization (redefinition of HRQoL). Altogether the relation between (severity of) dementia and HRQoL is neither simple nor direct.

Third, the question who should rate HRQoL is especially crucial in dementia. Can caregivers express patients' perceptions?[8] On the one hand caregivers rate patients' HRQoL lower.[9] This may be explained by their own health problems, mood, burden and by differences in perspectives. On the other hand the judgment of patients, who have the actual experience of living with dementia, may be(come) influenced by cognitive limitations. Nevertheless, reliable rating is probably feasible until late dementia-stages, if scales are well chosen. Patients' own opinion should remain the gold standard for as long as possible.[10] Use of parallel proxy-measures from the start of a longitudinal study prevents the necessity for substituting patient- by proxy-rating when patients are no longer able to judge their HRQoL. This reduces bias over time and prevents missing data.

As patient-reported outcomes become more established, these measurement issues need to be addressed. Until now HRQoL is infrequently used as outcome in dementia research.[11] An important reason is the subjective nature of the concept, which makes that this type of 'risky' outcomes are only applied if strictly obliged by regulatory bodies. Nevertheless, HRQoL should play a key role in assessing efficacy of new treatments in frail elderly, especially dementia patients. However, measurement remains cumbersome and the issues described should be addressed to arrive at valid and reliable outcomes. We plead for application of HRQoL measurement as important outcome measure in dementia intervention trials and intend to initiate an international working group 'HRQoL measurement in frail elderly and dementia'. The first aim is to design a HRQoL instrument with low cognitive burden combining advantages of disease-specific and value-based generic HRQoL instruments, covering the relevant domains. The instrument should be applicable for self- and caregiver-report, and produce a single metric figure expressing the overall HRQoL of individual patients. For this purpose novel measurement methods are available and will be applied.

References

1. Rabins PV, Black BS. Measuring quality of life in dementia: purposes, goals, challenges and progress. Int Psychogeriatr 2007;19:401-7.

2. Logsdon RG, Gibbons LE, McCurry SM et al. Assessing quality of life in older adults with cognitive impairment. Psychosom Med 2002;64:510-9.

3. Whitehouse PJ, Orgogozo JM, Becker RE et al. Quality-of-life assessment in dementia drug development. Position paper from the International Working Group on Harmonization of Dementia Drug Guidelines. Alzheimer Dis Assoc Disord 1997;S3:56-60.

4. Farias ST, Mungas D, Jagust W. Degree of discrepancy between self and other-reported everyday functioning by cognitive status: dementia, mild cognitive impairment, and healthy elders. Int J Geriatr Psychiatry 2005;20:827-34.

5. Smith KW, Avis NE, Assmann SF. Distinguishing between quality of life and health status in quality of life research: a meta-analysis. Qual Life Res 1999;8:447-59.

6. Anderson RT, Aaronson NK, Bullinger M et al. A review of the progress towards developing health-related quality-of-life instruments for international clinical studies and outcomes research. Pharmacoeconomics 1996;10:336-55.

7. Albrecht GL, Devlieger PJ. The disability paradox: high quality of life against all odds. Soc Sci Med 1999;48:977-88.

8. Schwartz CE, Andresen EM, Nosek MA et al. Response shift theory: important implications for measuring quality of life in people with disability. Arch Phys Med Rehabil 2007;88:529-36.

9. Boyer F, Novella JL, Morrone I et al. Agreement between dementia patient report and proxy reports using the Nottingham Health Profile. Int J Geriatr Psychiatry 2004;19:1026-34.

10. Logsdon RG, Gibbons LE, McCurry SM et al. Assessing quality of life in older adults with cognitive impairment. Psychosom Med 2002;64:510-9.

11. Schölzel-Dorenbos CJM, van der Steen MJ, Engels LK, Olde Rikkert MG. Assessment of quality of life as outcome in dementia and MCI intervention trials: a systematic review. Alzheimer Dis Assoc Disord 2007;21:172-8.

QUALITY OF LIFE IN DEMENTIA

EMPIRICAL PART

CHAPTER 6

QUALITY OF LIFE OF PATIENTS WITH ALZHEIMER'S DISEASE AND THEIR CAREGIVERS: SCHEDULE FOR THE EVALUATION ON THE INDIVIDUAL QUALITY OF LIFE (SEIQOL)

C.J.M. Schölzel-Dorenbos

ABSTRACT

Context: Twelve patients with mild to moderate Alzheimer's Disease (AD) and their caregivers were interviewed with the Schedule for the Evaluation of Individual Quality of Life (SEIQoL). The SEIQoL measures quality of life by taking into account the relevant determinants for a particular individual.

Methods: The subject rates five areas in life most important to the quality of life. The relative contribution of each area to the overall quality of life is then calculated with a multiple regression analysis programme developed for the purpose. Next the SEIQoL Index score, validity and reliability are computed.

Results: One patient was unable to complete the interview. The remaining (8 women, 3 men, mean age 71.3 years) had a mean SEIQoL Index score of 79.9 (median: 85.4), which is comparable to healthy Dutch elderly. The caregivers (10 spouses, 2 daughters, mean age 67.4 years), on the other hand, had a lower SEIQoL Index score: 62.2 (median: 63.8). Validity and reliability were good for both groups.

Conclusion: Caregivers in this pilot study experienced a lower quality of life than AD patients and healthy Dutch elderly. The SEIQoL allows quantitative measurement of completely individualized quality of life for AD patients and their caregivers.

Introduction

Quality of life is important for everyone, but no less for patients with dementia: 'not knowing where I am does not mean I do not know what I like'![1] The quantification of quality of life therefore receives more attention partly because there are so few good methods available.

In the last few years, clinical and scientific interest in dementia has been increasing. Developments in the pharmacotherapeutic area have spurred more interest. The importance of making the diagnosis and determining the etiology of dementia are important factors leading to an increase in the number of Memory Clinics in the Netherlands.[2;3] Valid methods are available to measure the effects of interventions (e.g. dementia pharmacotherapy) on cognitive, behavioral and general functioning.[4-6] Yet, measuring impact on quality of life is a scarcely developed field.[7;8] To date, most assessments of quality of life of the patient are indirect, by the caregiver[9] Although the opinion of caregivers is important it should not replace the judgment of persons with dementia themselves. Many elderly people are able to answer questions about their quality of life despite the presence of significant cognitive deficits.[1]

The quality of life of dementia caregivers is equally important. They suffer from higher levels of stress and psychological morbidity than caregivers of non-demented chronically ill patients.[10] The quality of life of the caregiver is often indirectly estimated from the amount of burden he or she experiences. Obviously, a direct measurement is preferable.

This pilot study describes the individual quality of life of patients with mild to moderate dementia of the Alzheimer's type and their informal caregivers simultaneously and with the same method. A similar study, to our knowledge, has not been previously done in the Netherlands. For the measurement of quality of life we used the Schedule for the Evaluation of Individual Quality of Life (SEIQoL). The SEIQoL has been previously used in healthy elderly as well as patients with mild dementia. The method is useful and reliable as long as the patient's insight is still good and their cognitive impairment is still mild.[11] The SEIQoL measures fully individualized quality of life quantitatively on a continuous scale from 0 to 100. The method is based on Judgment Analysis, a technique derived from the Social Judgment Theory.[12-14] Judgment Analysis quantifies the contribution of different factors to the overall quality of life assessment. The SEIQoL has been extensively validated in both older and younger people.[13-15] The Dutch translation of this semistructured interview was recently validated with healthy Dutch elderly. Strong test-retest reliability makes it applicable for the evaluation of interventions.[16] The responsiveness in prospective intervention studies has previously been shown.[17] In this pilot study we present the results of the measurement of quality of life of patients and their caregivers with the SEIQoL and compare the results with the previous measurement of quality of life of healthy Dutch elderly.[16] We also present some of the results of the neuropsychological assessment of the patients to indicate the severity of their cognitive impairment.

Methods

Patients and caregivers

Twelve community-dwelling patients and their informal caregivers referred to the Outpatient Memory Clinic of the Slingeland Hospital between March and July of 1999 participated in the study. Patients were diagnosed with probable Alzheimer's Disease (AD) according to the DSM-IV and NINCDS-ADRDA criteria.[18] Participants gave informed consent and the Internal Review Board of the Slingeland Hospital approved this research.

Meaurements

SEIQoL

Participants were interviewed with the SEIQoL in a standardized semi-structured format. Standard instructions for possible problems are provided in conducting the interview. The first step in the SEIQoL is Cue Elicitation. Respondents are asked to

name five areas of life ('cues') considered most important in assessing their overall quality of life. Suitable cues are aspects of life, not individuals. If the participant mentions general cues very similar to quality of life (e.g. satisfaction, quality of life) the interviewer tries to elicit more specific cues. Sometimes it is necessary to provide suggestions from a standard list. When the interview is repeated in intervention studies, previously selected cues are used this second time.

The second step is to rate the current level for each cue (see Figure 1) on a vertical visual analogue scale (VAS) labeled on the lower and upper extremes respectively by the terms 'As bad as could possibly be' and 'As good as could possibly be.' The ratings were recorded in the form of a bar chart, each bar representing a cue nominated by the individual. Along the left hand side of the rectangle is a scale ranging from 'worst possible' (0) on the bottom to 'best possible' (100) on the top. The height of the bar indicates the value ('cue level'). Next the value of the overall quality of life at that moment is indicated by a cross on a horizontal VAS, which runs from the worst to the best life one can imagine (0-10). In order to quantify the relative importance of each cue, respondents are then asked to estimate the overall quality of life assigned to 30 hypothetical case profiles on a horizontal VAS (0-10) under the profile. The case profiles are randomly computer generated in advance and the five bars are labeled with the own five cues chosen by the respondent. This is illustrated in Figure 2. A total of 30 cases is necessary to reliably quantify the 5 cues, 20 of these being unique profiles and 10 of these being randomly interspersed repeat profiles, which are needed to determine judgment reliability. The 10 pairs of judgments are correlated to provide a reliability coefficient (Pearson r). Judgments on the 30 hypothetical cases were analyzed in the standard manner using Policy PC (1986), a program based on multiple regression analysis.[19] This program extracts the cue weights that indicate the relative importance of each area for the overall quality of life of the individual. Next, the SEIQoL Index score (0-100) is calculated by multiplying the five cue levels by the matching cue weights and summing up the products. Policy PC also directly estimates R^2, the variance in quality of life judgments explained by the set of cues used. R^2 values of 0.7 or above are considered as acceptable.[20]

Neuropsychological assessment

Neuropsychological assessment of the patients included the Mini-Mental State Examination (MMSE) and the Dutch adaptation of the Cambridge Cognitive Examination (CAMCOG).[21;22] The MMSE (0-30) is a widely used screening tool for identifying cognitive impairment. A score of 24/30 is often used as cut-off point for suggesting mild cognitive impairment.[23] CAMCOG (0-106) is the cognitive part of the Cambridge Examination of Mental Disorders of the Elderly: CAMDEX. The CAMDEX was developed to help in early diagnosis and determine the severity of dementia in the elderly.[24]

Results

A total of 24 individuals were examined, 12 patients and 12 caregivers. One patient (MMSE score 15/30, CAMCOG score 46/106) was excluded from the evaluation due to her insufficient understanding of the method. The other 11 patients, including 8 women (72.7%) had a mean age of 71.3 years (SD: 3.9). The mean MMSE score (0-30) was 22 (SD: 3.9) and the score on the CAMCOG (0-106) averaged 74.5 (SD: 10.4). The 12 caregivers (10 spouses, 2 daughters) had a mean age of 67.4 years (SD: 12.8). The results of assessment of quality of life are summarized in Table 1. Patients had an average SEIQoL Index score of 79.9 (median 85.4; range: 55.3-100). For caregivers the average score was 62.2 (median 63.8; range: 43.9-79). The average R^2 was 0.79 and 0.84 respectively. The average Pearson r was 0.74 for patients and 0.83 for caregivers.

One patient and one caregiver had a low Pearson r, 0.34 and 0.43 respectively. A low Pearson r value can indicate a lack of understanding, fatigue or boredom, or change of judgment during the interview.

The task took and average of 37 ± 11 minutes for patients and 23 ± 8 minutes for caregivers to complete. Both groups needed one or more suggestions in about 1/3 of the cases in choosing the cues. Commonly used cues in both groups were: marriage, health, children, entertainment, religion and finance. The patient group required more guidance to complete the interview. For example, forgetting the original task required intervention However, the judgments were performed independently.

Discussion

Eleven of the 12 patients examined in this study completed the interview without any problem. One patient had insufficient understanding of the method. Internal validity (R^2) and internal reliability (Pearson r), in both groups, were higher than in healthy Dutch elderly.[16] Browne et al. found that both R^2 and Pearson r had a low but significant correlation with height of the MMSE score.[25] The SEIQoL appears reliably applicable in patients with mild to moderate dementia of the Alzheimer type. Caregivers, mostly the partners, experienced a lower quality of life than AD patients and healthy Dutch elderly.
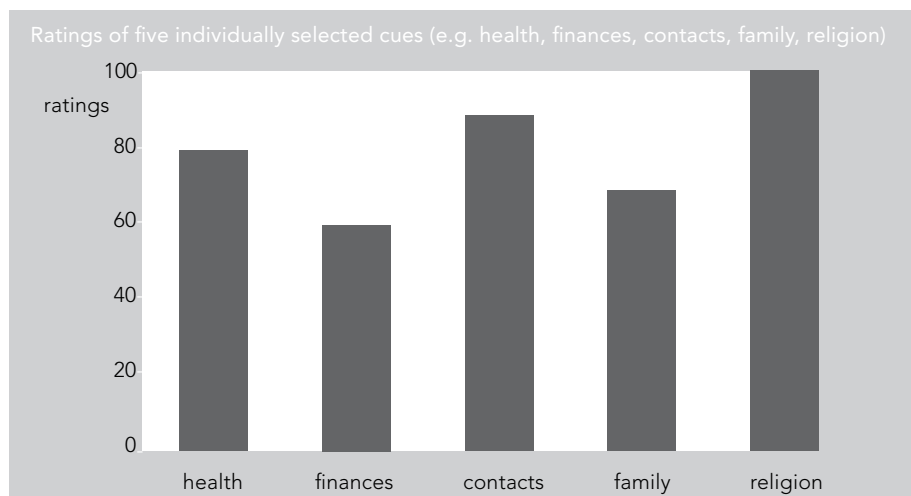
The literature also shows that the SEIQoL is a reliable measure of quantitative rating of the effect of interventions. Thus, the method may be used in the decision

on the continuation of a once established treatment. The SEIQoL also measures the effects of burden of care on quality of life of the caregiver. The uniqueness of the method, although complex and labor intensive, is the ability to evaluate quantitative and individual quality of life of both patients and caregivers simultaneously. This makes it a valuable tool in clinical research.

References

1. Mozley CG, Huxley P, Sutcliffe C et al. 'Not knowing where I am doesn't mean I don't know what I like': cognitive impairment and quality of life responses in elderly people. Int J Geriatr Psychiatry 1999; 14:776-83.
2. Verhey FRJ, Nods M, Ponds RWHM et al. Geheugenpoliklinieken in Nederland. Ned Tijdschr Neurol 1999;3:169-75.
3. Schölzel-Dorenbos CJM. De geheugenpolikliniek, een nieuwe polikliniek in het Slingeland Ziekenhuis. Ned Tijdschr Ziekenhuis Administratie 2000; in press.
4. Rosen WG, Mohs RC, Davis KL. A new rating scale for Alzheimer's disease. Am J Psychiatry 1984; 141:1356-64.
5. Teunisse S, Derix MM, van Crevel H. Assessing the severity of dementia: patient and caregiver. Arch Neurol 1991;48:274-7.
6. Verhey FR, Heeren TJ, Scheltens P et al. Cholinesterase inhibitors for Alzheimer disease: preliminary recommendations for treatment. Dutch Society for Psychiatry, Section of Geriatric Psychiatry. Ned Tijdschr Geneeskd 1998;142:2091-6.
7. Olde Rikkert MG, Jansen RW. Cholinesterase inhibitors in Alzheimer disease: preliminary recommendations for treatment. Ned Tijdschr Geneeskd 1998;142:2644.
8. Schölzel-Dorenbos CJM, Jellesma-Eggenkamp MJH. Cholinesterase inhibitors in Alzheimer disease: preliminary recommendations for treatment. Ned Tijdschr Geneesk 1999;143:122-3.
9. Albert SM, Castillo-Castaneda C, Sano M et al. Quality of life in patients with Alzheimer's disease as reported by patient proxies. J Am Geriatr Soc 1996;44:1342-7.
10. Gonzalez-Salvador MT, Arango C, Lyketsos CG et al. The stress and psychological morbidity of the Alzheimer patient caregiver. Int J Geriatr Psychiatry 1999;14:701-10.
11. Coen R, O'Mahony D, O'Boyle C et al. Measuring the quality of life of dementia patients using the Schedule for the Evaluation of Individual Quality of Life. Irish J Psychology 1993;14:154-63.
12. Stewart TR. Judgment analysis procedures. In: Bremer B, Joyce CRB, editors. Human judgment: the social judgment theory view. Amsterdam, North-Holland. 1998:41-75.
13. McGee HM, Hickey A, O'Boyle C et al. Judgment analysis (JA) as a technique for providing individualized assessments of quality of life (QoL). Br J Clin Pharmacol 1988;26:653-4.
14. O'Boyle CA, McGee H, Hickey A. Reliability and validity of judgment analysis as a method for assessing quality of life. Br J Clin Pharmacol 1989;27:155.
15. McGee HM, O'Boyle CA, Hickey A et al. Assessing the quality of life of the individual: the SEIQoL with a healthy and a gastroenterology unit population. Psychol Med 1991;21:749-59.
16. Schölzel-Dorenbos CJM, Jellesma-Eggenkamp MJH. SEIQoL: a measure for for individual quality of life. Validation in an elderly Dutch population. Ned Tijdschr Psychologie 2001;56:16-8.
17. O'Boyle CA, McGee H, Hickey A et al. Individual quality of life in patients undergoing hip replacement. Lancet 1992;339:1088-91.
18. American Psychiatric Association. DSM-IV. Diagnostic and Statistical Manual of Mental disorders, Fourth edition. 2000.
19. Policy PC Judgment Analysis software. Executive Decision Services, Inc. Albany, New York. Reference Manual, third edition 1986.
20. Joyce CRB, O'Boyle C, McGee H. Individual quality of life. Approaches to conceptualisation and assessment. Amsterdam: Harwood academic publishers, 1999.
21. Folstein MF, Folstein SE, McHugh PR. Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.
22. Derix MM, Hofstede AB, Teunisse S et al. CAMDEX-N: the Dutch version of the Cambridge Examination for Mental Disorders of the Elderly with automatic data processing. Tijdschr Gerontol Geriatr 1991;22:143-50.
23. Kempen GI, Brilman EI, Ormel J. The Mini-Mental Status Examination. Normative data and a comparison of a 12-item and 20-item version in a sample survey of community-based elderly. Tijdschr Gerontol Geriatr 1995;26:163-72.
24. Roth M, Tym E, Mountjoy CQ et al. CAMDEX. A standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. Br J Psychiatry 1986;149:698-709.
25. Browne JP, O'Boyle CA, McGee HM et al. Individual quality of life in the healthy elderly. Qual Life Res 1994;3:235-44.

*Figure 1. SEIQoL interview; elicited cues and current judgment of quality of life*

Ratings of five individually selected cues (e.g. health, finances, contacts, family, religion)

ratings

100
80
60
40
20
0

health   finances   contacts   family   religion

my life is:

as bad as it could possibly be ——————————— x ——— as good as it could possibly be

Figure 2. Judgment of 30 hypothetical case profiles and calculation of weights by Judgment Analysis

Judgment of 30 hypothetical case profiles

2
1

100
80
60
40
20
0

(labeled by individually 5 selected cues)
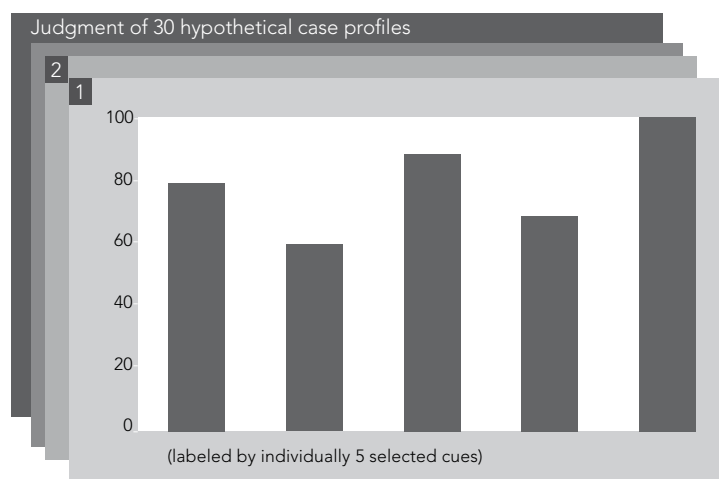
life (...) is:

as bad as it could possibly be ——————————— x ——— as good as it could possibly be

10   9   33   18   30

↓

=weights extracted by judgment analysis (scale 0-100: 0=not at all important, 100=very important; sum weights of 5 cues=100)

Table 1. SEIQoL interview results of Alzheimer's patients, caregivers and healthy Dutch elderly

	N	SEIQoL Index (SD)	R^2 (SD)	Pearson r (SD)
Patients	11	79.9 (14.8)	0.79 (0.08)	0.74 (0.17)
Caregivers	12	62.2 (10.5)	0.84 (0.10)	0.83 (0.14)
Healthy elderly[16]	32	76.3 (11.0)	0.73 (0.13)	0.68 (0.22)

CHAPTER 7

QUALITY OF LIFE AND BURDEN OF SPOUSES OF ALZHEIMER'S DISEASE PATIENTS

C.J.M. Schölzel-Dorenbos
I. Draskovic
M.J. Vernooij-Dassen
M.G.M. Olde Rikkert

ABSTRACT

Objectives: The objective of the study was to explore, in a sample of spouses of mild-moderate Alzheimer disease (AD) patients, predictors of quality of life (QoL) by rating QoL and burden.

Methods: The authors assessed 97 spouses in a cross-sectional study with the Schedule for the Evaluation of Individual Quality of Life (SEIQoL), Self-Rated Burden scale (SRB), perceived stress scale (EDIZ) and Zarit Burden Interview (ZBI). Patient cognition was rated with the Mini-Mental State Examination (MMSE). Factors best predicting QoL were analyzed with multiple regression analysis.

Results: 87 (53% male, mean 72 years) fulfilled the SEIQoL internal reliability criteria, and had a mean SEIQoL score of 68.6±14.8. Most important QoL domains were condition of patient (31%) and marriage (26%). Caregiver burden scores on SRB (0-100), EDIZ (0-9) and ZBI (0-48) were 44.1±23.5 (n=67) , 4.9±2.2 (n=53) and 13.1±6.2 (n=53) respectively. Mean patient MMSE score (0-30) was 20.3±4.2.

Conclusions: Spouses experienced lower QoL than AD patients and healthy elderly (historical controls), and perceived moderate levels of burden. Patient cognition is a significant predictor of caregiver QoL. Burden, measured by ZBI, is significantly negatively correlated with SEIQoL. The results underline the importance of implementing health services known to improve QoL and alleviate burden, and to explore new effective interventions.

Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by impairment of cognitive performance, disability in instrumental and basic activities of daily living and deterioration in global functioning, which is often accompanied by neuropsychiatric symptoms. Measuring quality of life (QoL) is an important, challenging, and growing area of dementia research.[1] Caring for people with dementia is associated with well-documented increases in distress and decrease in mental health and well-being.[2] Caregivers of demented patients experience higher levels of stress and psychological morbidity compared to caregivers of non-demented elderly persons. Particularly, the patients' behavioral symptoms, and impairments in instrumental activities of daily living, cause caregiver strain. The degree of this strain is referred to as caregiver burden, which is higher in early onset dementia.[3] QoL measures so far largely focused on QoL in the patients. However, assessment of QoL and perceived burden in the caregiver is equally important, especially if the patient still lives in the community.

Walker et al. carried out systematic reviews on measures for assessment of the impact of disease, and instruments that claim to measure QoL in drug trials. They found no validated methods of assessing the QoL of both dementia patients and their carers at the same time.[4] To our knowledge, three methods are available that can validly assess QoL in dementia patients as well as their caregivers: the Schedule for the Evaluation of Individual Quality of Life (SEIQoL), the patient and caregiver version of the Quality of Life-Alzheimer's Disease scale (QOL-AD) and the QoL scale developed in the PIXEL studies.[5-7] More often QoL of caregivers is measured indirectly with mood or depression scales. Theoretically, a direct measurement of subjective QoL, however, is a better tool, because positive factors and stressors affecting the personal QoL are probably highly variable among caregivers. Also, in addition to qualitative data, the measurement should best be quantitative, permitting evaluation of effects of interventions on QoL. The SEIQoL, which is devised from a technique known as Judgment Analysis, originating in Social Judgment theory, fulfills these criteria.[8] It measures the level of functioning in five self-nominated aspects of life (qualitative information) and the relative weight or importance attached to these areas. Thus, the SEIQoL allows quantitative measurement of individualized QoL and can be used to monitor changes in QoL. According to Joyce et al., the advantages of SEIQoL are that: 1. cues and weights are evaluated by each individual in his own preferred language, so no translation is needed for the respondent, and a problem characteristic of conventional methods is thus avoided; 2. the SEIQoL score is probably no more culture-bound than systolic blood pressure or body temperature; 3. there is sufficient commonality in the numerical estimates for the observations to be entered into statistical analyses of the kind performed by WHO and other organisations.[9] Being a highly individualized measure of QoL as well as being language- and culturefree makes SEIQoL appear suitable for use in dementia patients and caregivers, allowing for comparison between the two groups.

The SEIQoL has been applied in dementia patients,[10;11] but hardly any data are available for spousal caregivers. Also, for this population there are no data on the relationship between QoL and their perception of burden. It seems plausible to expect that perceived QoL and burden will be inversely related, and that both will depend on the severity of cognitive impairment of the patient. Coen et al did measure carer individually perceived QoL (IQoL), rated with the SEIQoL-DW, and burden in 28 carers of AD patients. Increased patient behavior disturbance appeared to be a major factor when the carer's situation worsened over time.[12] In 2002 these investigators studied caregiver characteristics and IQoL factors distinguishing low- and high-burden caregivers. In the high-burden caregiver group daughters were over-represented, QoL was lower and the patients were more behaviorally disturbed. Of the many QoL factors elicited from caregivers, only 'time for self' and 'finances' differed significantly between the groups. A need for more time away from the patient

is a major QoL concern for highly burdened caregivers, and a perceived lack of adequate informal support and/or financial constraints are contributory factors.[13]

In our cross-sectional study, caregiver SEIQoL scores are related to various caregiver burden measures (Zarit Burden Interview - ZBI, Self-perceived pressure from informal care scale - EDIZ, and Self-Rated Burden scale - SRB), and cognition of the patients (Mini-Mental State Examination - MMSE). SEIQoL scores will also be compared to scores of healthy elderly and AD patients, which we measured in an earlier study. Knowledge about these relationships is necessary to be able to measure impact of interventions on caregiver QoL and burden and in understanding the value of caregivers' QoL and the best way to select starting points for the initiation of psychosocial interventions in dementia care practice.

Research questions we sought to answer are as follows: 1. What are the most prominent domains determining QoL in caregivers of patients with mild to moderate AD. 2. Are there any differences in QoL between the caregivers of AD patients, the patients themselves, and healthy non-caregiving elderly? 3. How are the different measures of caregiver burden related to the caregiver SEIQoL? 4. Does patient cognitive status affect caregiver QoL? The research questions did not involve other patient related factors than cognition, thus behavior and functional status of the patients were not included in the outcome measures.

Methods

Participants and design

Spouses of patients who received the diagnosis of mild to moderately severe AD after investigations at the outpatient memory clinic of the Slingeland Hospital between 1999 and 2006 participated in the study. Patients were diagnosed with probable AD according to the DSM-IV and NINCDS-ADRDA criteria. The degree of severity of dementia according to the Clinical Dementia Rating (CDR; 0-3) scale was 1-2.[14-16] Subsequently, 112 spouses completed measures of QoL and burden. Cognitive function of the patients was assessed with the MMSE (0-30). Subjects were excluded from further analysis if their internal validity score of the SEIQoL was below 0.7, and if the SEIQoL ratings explained less than 70% of the total variance in QoL (see below). Participants gave informed consent and the Internal Review Board of the Slingeland Hospital approved this research.

Assessment of quality of life

Participants were interviewed with the SEIQoL in a standardized semi-structured format by the same interviewer (C.S-D). The first step in the SEIQoL is cue elicitation. The respondent is asked to name five areas of life (cues) most important to his/her overall QoL ('What are the five most important areas of your life at present?'). Responses can be classified into one of the generally agreed QoL domains: Cognitive, Affective, Social, Physical, Ecological and Religious (CASPER model; http://www.brunswik.org). The respondent may be prompted by the researcher if fewer than 5 cues have been named.[8] The second step is determining current level for each cue ('How would you rate yourself on each of these areas at the moment, on a scale from the worst possible to the best possible?') by drawing a bar for each cue (written in the appropriate space under a rectangle). Along the left hand side of the rectangle there is a scale ranging from 'worst possible' (0) on the bottom to 'best possible' (100) on the top.[8] Step 3 is the relative weighting or importance of each cue to the overall QoL. In order to quantify the relative importance of each cue, respondents are asked to estimate the QoL they would expect to be enjoyed by 30 hypothetical individuals ('cases'). Each case profile is based on the cues chosen by the respondent and random, computer generated, values of these. A total of 30 cases is necessary to reliably quantify the 5 cues, 20 of these being unique profiles and 10 of these being randomly interspersed repeat profiles, which are needed to allow the estimation of internal reliability. The cue weights are extracted by multiple regression analysis.[17] Next, the SEIQoL Index score (0-100) is calculated by multiplying the five cue levels by the matching cue weights and summing up the products. SEIQoL scores of the respondents in the present study were compared to the results of two historical reference groups, AD patients and healthy elderly, assessed in an earlier study.[11;18]

Assessment of caregiver burden in a subgroup of the participants

Three caregiver burden scales were applied: EDIZ (self-perceived pressure from informal care, developed in Dutch; 0-9),[19] Zarit Burden Interview scale for burden of caregivers, short version (ZBI; 0-48), both having higher scores for higher burden,[20] and SRB (Self-Rated Burden scale) for rating of subjective feeling of burden on a visual analogue scale (VAS; range 0-100; 0 for lowest, 100 for highest burden). The stress measured by EDIZ refers to the demands the spouse perceives with respect to the personal interests, the psychological and psychosocial complaints, and to the stressors in the caregiving situation. ZBI assesses the feelings of burden of caregivers in caring for the person with dementia. ZBI identifies three dimensions of burden: effect on the social and personal life of caregivers, psychological burden and feelings of guilt.

Statistical analysis

The SEIQoL Policy PC package estimates the internal validity (R^2) which indicates the amount of variance in the overall QoL judgment policy (i.e. variance in length of the bars) explained by the five cues. R^2 values of 0.70. or higher, which demonstrate

the construct validity of Judgment Analysis in this context, are considered accepta-ble.[21] Intra-subject reliability is expressed as the correlation coefficient (Pearson r), which had to be 0.7 or more in each caregiver to be eligible for this study. Charac-teristics of caregivers who were included and who had to be excluded were compa-red using ANOVA. SEIQoL scores of the caregivers were compared with historical reference groups using a Cochrane review meta-analytical program (ReviewMana-ger), considering that these are respondents from a different study. We performed multiple regression analysis to assess which factors best predict SEIQoL scores.

Results

All AD patients lived at home with their spouse as the principal informal caregi-ver and received no or limited professional care. The patients had a mean age of 73.5 years, standard deviation (SD) 7.2 years, and their mean MMSE score was 20.3 (SD: 4.2). The characteristics of the caregivers and results of QoL assessment are presented in Table 1. Of 112 spouses fulfilling the inclusion criteria, 15 (13%) were unable to nominate the five necessary cues and were excluded. Of the remai-ning 97 participants, 87 (90%) completed the SEIQoL reliably, with a mean R^2 score of 0.82 and a mean Pearson r score of 0.85. Ten subjects had R^2 and/or Pearson r scores <0.70, they were excluded from further analysis because of unreliable judgment. The excluded subjects were significantly older and predominantly fema-le. The mean SEIQoL score for the 87 spouses was 68.6 (SD: 14.8). Female caregivers had slightly but nonsignificantly higher scores (M=70.6, SD=13.3, N=41) than male caregivers (M=66.8, SD=16.0, N=46), with F(1.85)=1.45, MSe=217.6, and p=.23.

The elicited cues are summarized in Table 2. Condition of partner and Marriage, both being aspects of Relation (CASPER domains: Social and Affective) were most frequently nominated as the most important domains of QoL. The next important determinant was Family (CASPER domain: Social). In the subgroup of female care-givers most important determinants were Family and Condition of partner, while in the subgroup of male caregivers Condition of partner and Marriage were most important. Differences between female and male caregivers are slight. The cue heights and weights of the first elicited cues are presented in Table 3.

The SEIQoL scores of the caregivers in the present study were compared with his-torical reference groups. In our previous studies, mean SEIQoL score for patients with mild AD was 79.9 (SD=14.8; N=12; mean age 71.3, SD=3.9 years; mean MMSE score 22, SD=3.9) while for the healthy elderly population it was 76.3 (SD=11.0; N=32; mean age 77.3, SD=5.5 years).[11;18] SEIQoL scores of spouses in the present study were significantly lower than either the scores of AD patients (Z=2.42, p<.05), or the scores of healthy elderly (Z=2.59 , p<.05).

Burden analyses were performed in a subgroup of N=46 participants for which reliable caregiver burden measures were collected. The results are presented in Table 4. Mean scores were: SEIQoL M=69.2 (SD=15.2); ZBI M=12.9 (SD=6.3); EDIZ M=4.7 (SD=2.3) and SRB M=45.6 (SD=25.0). Mean patient MMSE for this subgroup was 19.5 (SD=4.8). Caregiver gender differences were not significant. However, females scored higher on all dependant variables including the spousal MMSE. Overall, correlation between patients' MMSE and caregivers' SEIQoL was positive and significant (r=.287, N=46, p<.05). At the same time correlation between ZBI and caregiver SEIQoL was negative and significant (r=-243, N=45, p=.05). Correlations of the other two burden measures (EDIZ, SRB) with SEIQoL were not significant. Re-gression analysis, using Enter method, showed that MMSE showed a strong trend towards being a significant predictor of SEIQoL (Beta=.29, t=1.99 p=.05) from the first simple model, in which the other burden variables were excluded, to the most complex multivariate model, in which it was entered together with ZBI, EDIZ and SRB scores (Table 5).

Discussion

The aims of the study were to investigate which domains determine QoL in spousal caregivers of AD patients, and to explore differences in SEIQoL between caregi-vers, AD patients and healthy non-caregiving elderly. In a subgroup of caregivers caregiver QoL was also related to different measures of caregiver burden, and pa-tient cognitive status.

The domains Condition of patient and Marriage were the most prominent determi-nants for QoL in this study. Some differences between female and male caregivers were observed with respect to the primacy of the nominated cues. These slight gender differences deserve attention in future research. They may be important in deciding on the most suitable interventions for caregivers. The reported qua-litative findings are only partly in line with other SEIQoL studies and literature in patients with physical problems and healthy elderly. Here domains Family, Health, Social contacts, Hobbies, Psychological well-being, Leisure activities and Living environment were most frequently nominated.[18;22-26] Apparently, in case of demen-tia other domains of QoL are important for the spouse. These differences deserve attention in future studies.

In the present study SEIQoL scores of spouses of AD patients were significantly lower compared to historical controls of either patients with mild AD, or healthy elderly. This suggests a negative impact of caregiving in dementia. One of the ex-planations may be our finding that cognition of the patient is a significant predictor of QoL of the spousal caregiver. We are inclined to interpret the data quite straight

forward in that the quality of life of caregivers is indeed lower than quality of life of patients and healthy elderly, because of their heavy burden.

Two other possible explanations for the higher QoL in patients are response shift and anosognosia. Response shift (RS) is the psychological change in perception of QoL following a change in health status. RS is the result of changes in internal standards of measurement, recalibration of the measurement scale, changes in values or prioritization of domains within a construct, or changes in the definition or conceptualization of that construct.[27] One of the causes of RS is adaptation to illness.[28] It has been clearly evidenced that longitudinal measurements in dementia patients do not result in significant changes in QoL over time, while cognition deteriorates.[29] This make RS in dementia patients highly likely.[30] Besides RS, unawareness of deficits (anosognosia, lack of insight) may also play a role. Anosognosia has been frequently reported in later stages of dementia,[31] and may be associated with disruption of frontal-subcortical circuits. Unawareness may be one of the causes for discrepancies between reports from patients and caregivers.[32] However, the fact remains that QoL of caregivers is lower than that of healthy elderly, who were even older. This still underlines the burden of caregiving.

Caregiver gender differences regarding QoL, burden and spousal cognitive status were not significant. However, females scored higher on all variables, including the spousal MMSE. Speculatively, these higher scores could imply that, despite higher caregiver burden compared to male caregivers, females experience higher levels of QoL which may be due to a less severe dementia of the patient. However, further research is needed in order to reliably explore this possibility. Overall, the relationship between patient cognition and caregiver SEIQoL was positive and significant, while the relationship between caregiver burden on ZBI and SEIQoL was negative and significant, as can be expected. The three measures of burden did correlate significantly with each other.

Next to our study, two other studies have attempted to relate QoL and burden of caregivers of dementia patients. Serrano-Aguilar et al. related health-related QoL (European Quality of Life -5D; EQ-5D) and burden (ZBI) of 237 informal caregivers of AD patients. Variables having negative correlation with QoL were burden, time committed to care, and age.[33] Coen et al. divided caregivers of dementia patients into low- and high-burden groups. In the high-burden group caregiver QoL was lower and the patients displayed more neuropsychiatric symptoms.[13] Thus, in addition to cognitive impairment, the presence of neuropsychiatric symptoms may represent such a high burden that it may significantly affect caregiver QoL.[34] These authors found a negative correlation between only one burden measure (ZBI) and caregiver QoL (EQ-5D and IQoL respectively).[13;33] Others measured ZBI versus no

formal QoL measure.[35-37] Riedijk et al. studied the general QoL measure SF-36 and two burden measures: Burden due to Neuropsychiatric Disturbance of the Patient and VAS Burden, and also found no differences.[38] In sum, it is unlikely that the absence of a relationship is due to invalidity of the burden measures we applied.

There are several limitations to this study that need to be recognized. An important limitation concerns the study design, a cross-sectional analysis in a convenience sample. However, the participants are representative of the population of caregivers of AD patients referred to a multidisciplinary memory clinic. 21% of the participants had to be excluded because the SEIQoL results were unreliable by conventional criteria. Application of the short, more simple, version of the instrument using direct weighting (DW) may result in less exclusion of respondents.[39] Burden was only assessed in a subgroup, but without selection bias. We choose not to apply SEIQoL in assessing QoL of AD patients cared for by the caregivers because on average, their cognitive decline does not allow for reliable usage of the long form of SEIQoL instrument.[10] A final limitation might be that we only related caregiver status to patient's cognitive and not to behavioral or functional status.

In conclusion, in addition to the Condition of the partner, Marriage, and Family were seen as domains strongly affecting QoL, with slight differences between male and female caregivers. Caring for persons with dementia is a challenge in many respects. Possibly, negative effects of the partner condition can be compensated by well functioning family ties and adaptations in marital relationship.

Evidence of the impact of dementia caregiving on caregiver QoL warrants that new intervention programs (including drug trials) are evaluated for their impact on caregiver QoL and burden. Because most interventions have domain-specific outcomes, clinicians must tailor interventions according to the specific needs of the individual caregivers and address the domains they find most important. Our results further underline the importance of implementing health services already known to improve QoL of the principal caregiver, like occupational therapy or other forms of providing assistance to caregivers.[40;41]

References

1. Schölzel-Dorenbos CJM, van der Steen MJ, Engels LK, Olde Rikkert MG. Assessment of quality of life as outcome in dementia and MCI intervention trials: a systematic review. Alzheimer Dis Assoc Disord 2007;21:172-8.

2. Sörensen S, Duberstein P, Gill D et al. Dementia care: mental health effects, intervention strategies, and clinical implications. Lancet Neurol 2006;5:961-73.

3. Freyne A, Kidd N, Coen R et al. Burden in carers of dementia patients: higher levels in carers of younger sufferers. Int J Geriatr Psychiatry 1999;14:784-8.

4. Walker MD, Salek SS, Bayer AJ. A review of quality of life in Alzheimer's disease. Part 1: Issues in assessing disease impact. Pharmacoeconomics 1998;14:499-530.

5. Logsdon RG, Gibbons LE, McCurry SM et al. Assessing quality of life in older adults with cognitive impairment. Psychosom Med 2002;64:510-9.

6. Schölzel-Dorenbos CJM, Ettema TP, Bos J et al. Evaluating the outcome of interventions on quality of life in dementia: selection of the appropriate scale. Int J Geriatr Psychiatry 2006;22:511-9.

7. Thomas P, Lalloue F, Preux PM et al. Dementia patients caregivers quality of life: the PIXEL study. Int J Geriatr Psychiatry 2006;21:50-6.

8. McGee HM, O'Boyle CA, Hickey A et al. Assessing the quality of life of the individual: the SEIQoL with a healthy and a gastroenterology unit population. Psychol Med 1991;21:749-59.

9. Joyce CR, Hickey A, McGee HM et al. A theory-based method for the evaluation of individual quality of life: the SEIQoL. Qual Life Res 2003;12:275-80.

10. Coen RF, O'Mahony D, O'Boyle CA et al. Measuring the quality of life of dementia patients using the Schedule for the Evaluation of Individual Quality of Life. Irish J Psychology 1993;14:154-63.

11. Schölzel-Dorenbos CJM. Measurement of quality of life in patients with dementia of Alzheimer type and their caregivers: Schedule for the Evaluation of Individual Quality of Life (SEIQoL). Tijdschr Gerontol Geriatr 2000;31:23-6.

12. Coen RF, O'Boyle CA, Coakley D et al. Dementia carer education and patient behaviour disturbance. Int J Geriatr Psychiatry 1999;14:302-6.

13. Coen RF, O'Boyle CA, Coakley D et al. Individual quality of life factors distinguishing low-burden and high-burden caregivers of dementia patients. Dement Geriatr Cogn Disord 2002;13:164-70.

14. American Psychiatric Association. DSM-IV-TR. Diagnostic and Statistical Manual of Mental disorders, Fourth edition, Text Revision. Ed. 2000.

15. McKhann G, Drachman D, Folstein M et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984;34:939-44.

16. Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. Int Psychogeriatr 1997;S1:173-6.

17. Policy PC Judgment Analysis Software. Reference Manual., Third edition Ed. Executive Decision Services, Inc. Albany, New York, 1986.

18. Schölzel-Dorenbos CJM, Jellesma-Eggenkamp MJH. Een meetmethode voor individuele kwaliteit van leven bij Nederlandse ouderen. Ned Tijdschr Psychol 2001;56:16-8.

19. Pot AM, van Dyck R, Deeg DJ. Perceived stress caused by informal caregiving. Construction of a scale. Tijdschr Gerontol Geriatr 1995;26:214-9.

20. Bedard M, Molloy DW, Squire L et al. The Zarit Burden Interview: a new short version and screening version. Gerontologist 2001;41:652-7.

21. Joyce CRB, O'Boyle CA, McGee H. Individual Quality of Life. Approaches to Conceptualisation and Assessment. Amsterdam: Harwood academic publishers, 1999.

22. LeVasseur SA, Green S, Talman P. The SEIQoL-DW is a valid method for measuring individual quality of life in stroke survivors attending a secondary prevention clinic. Qual Life Res 2005;14:779-88.

23. Lhussier M, Watson B, Reed J et al. The SEIQoL and functional status: how do they relate? Scand J Caring Sci 2005;19:403-9.

24. Puts MT, Shekary N, Widdershoven G et al. What does quality of life mean to older frail and non-frail community-dwelling adults in the Netherlands? Qual Life Res 2007;16:263-77.

25. Smith HJ, Taylor R, Mitchell A. A comparison of four quality of life instruments in cardiac patients: SF-36, QLI, QLMI, and SEIQoL. Heart 2000;84:390-4.

26. Westerman M, Hak T, The AM et al. Problems eliciting cues in SEIQoL-DW: quality of life areas in small-cell lung cancer patients. Qual Life Res 2006;15:441-9.

27. Oort FJ. Using structural equation modeling to detect response shifts and true change. Qual Life Res 2005;14:587-98.

28. Schwartz CE, Andresen EM, Nosek MA et al. Response shift theory: important implications for measuring quality of life in people with disability. Arch Phys Med Rehabil 2007;88:529-36.

29. Selwood A, Thorgrimsen L, Orrell M. Quality of life in dementia--a one-year follow-up study. Int J Geriatr Psychiatry 2005;20:232-7.

30. Missotten P, Ylieff M, Di Notte D et al. Quality of life in dementia: a 2-year follow-up study. Int J Geriatr Psychiatry 2007;22:1201-7.

31. Snow AL, Norris MP, Doody R et al. Dementia Deficits Scale. Rating self-awareness of deficits. Alzheimer Dis Assoc Disord 2004;18:22-31.

32. Antoine C, Antoine P, Guermonprez P et al. Awareness of deficits and anosognosia in Alzheimer's disease. Encephale 2004;30:570-7.

33. Serrano-Aguilar PG, Lopez-Bastida J, Yanes-Lopez V. Impact on health-related quality of life and perceived burden of informal caregivers of individuals with Alzheimer's disease. Neuroepidemiology 2006;27:136-42.

34. Livingston G, Johnston K, Katona C et al. Systematic review of psychological approaches to the management of neuropsychiatric symptoms of dementia. Am J Psychiatry 2005;162:1996-2021.

35. Belle SH, Burgio L, Burns R et al. Enhancing the quality of life of dementia care-givers from different ethnic or racial groups: a randomized, controlled trial. Ann Intern Med 2006;145:727-38.

36. Davis JD, Tremont G. Impact of frontal systems behavioral functioning in dementia on caregiver burden. J Neuropsychiatry Clin Neurosci 2007;19:43-9.

37. Papastavrou E, Kalokerinou A, Papacostas SS et al. Caring for a relative with dementia: family caregiver burden. J Adv Nurs 2007;58:446-57.

38. Riedijk SR, De Vugt ME, Duivenvoorden HJ et al. Caregiver burden, health-related quality of life and coping in dementia caregivers: a comparison of fron-totemporal dementia and Alzheimer's disease. Dement Geriatr Cogn Disord 2006;22:405-12.

39. Hickey AM, Bury G, O'Boyle CA et al. A new short form individual quality of life measure (SEIQoL-DW): application in a cohort of individuals with HIV/AIDS. BMJ 1996;313:29-33.

40. Graff MJ, Vernooij-Dassen MJ, Thijssen M et al. Community based occupa-tional therapy for patients with dementia and their care givers: randomised controlled trial. BMJ 2006;333:1196-1202.

41. Kurz X, Scuvee-Moreau J, Vernooij-Dassen M et al. Cognitive impairment, dementia and quality of life in patients and caregivers. Acta Neurol Belg 2003;103:24-34.

Table 1. Results of SEIQoL* measurement in spouses of Alzheimer patients

	Valid SEIQoL scores	Invalid SEIQoL scores[†]
Number of spouses	87	10
Mean age (years)[‡]	72.2 ± 7.3	76.1 ± 4.9
Male vs. female[‡]	53% vs. 47%	10% vs. 90%
Mean SEIQoL Index score	68.6 ± 14.8	63.4 ± 16.4
R^2	0.82 ± 0.07	0.59 ± 0.08
Pearson r	0.85 ± 0.07	0.52 ± 0.17

*Schedule for the Evaluation of Individual Quality of Life (0: very low-100: perfect QoL).
[†]Scores were invalid for R^2 and/or Pearson r<0.70.[21] [‡]p<0.005

Table 2. Frequency (%) of SEIQoL domains for female and male caregivers of 87 AD patients

Domain	Female (N=41)					Male (N=46)				
	Cue 1	Cue 2	Cue 3	Cue 4	Cue 5	Cue 1	Cue 2	Cue 3	Cue 4	Cue 5
Condition of partner	24.4%	22.0%	7.3%	4.9%	4.9%	37.0%	6.5%	6.5%		4.3%
Marriage	14.6%	17.1%	7.3%		2.4%	37.0%	4.3%	6.5%	6.5%	2.2%
Family	31.7%	14.6%	7.3%	14.6%	4.9%	8.7%	19.6%	10.9%	10.9%	4.3%
Relatives	2.4%	4.9%	7.3%	22.0%	12.2%	15.2%	2.2%	8.7%	10.9%	15.2%
Health	12.2%	17.1%	22.0%	24.4%	2.4%	15.2%	32.6%	17.4%	8.7%	2.2%
Social life/relations	2.4%	7.3%	19.5%	24.4%	7.3%		2.2%	8.7%	23.9%	15.2%
Financial situation	2.4%	2.4%	7.3%	7.3%	14.6%		13.0%	4.3%	4.3%	6.5%
Hobbies	2.4%	2.4%	2.4%	9.8%	7.3%			10.9%	4.3%	15.2%
(Voluntary) work	2.4%		2.4%	2.4%	4.9%		2.2%	4.3%		6.5%
Spirituality/ religion	7.3%		4.9%	2.4%	4.9%		2.2%	6.5%	6.5%	8.7%
Car driving					2.4%	2.2%				
Holiday		4.9%			4.9%				10.9%	6.5%
Leisure activities		2.4%	9.8%	4.9%	14.6%		10.9%	4.3%	13.0%	4.3%
Sports		2.4%	2.4%							
Nature				2.4%					2.2%	
Sexuality									2.2%	
Attitude to life		2.4%								
Living environment		2.4%			9.8%		4.3%	10.9%		6.5%
Pets				2.4%						
Housekeeping					2.4%					
Self-determination			2.4%	2.4%					2.2%	4.3%
Total	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

Note: Cue 1 is the domain elected as most important by a spouse. Cue 2 was the second most important domain, etc.

Table 3. Scores for absolute (level) and relative (weight) importance of most important quality of life domain (cue 1) of spouses (N=87)

Domain	N	Mean cue level (0-100)	Mean cue weight (0-1.00)
Condition of partner	27	51 ± 19	0.41 ± 0.08
Marriage	23	78 ± 19	0.38 ± 0.07
Family	17	83 ± 17	0.37 ± 0.05
Health	12	64 ± 20	0.34 ± 0.08
Spirituality/religion	3	79 ± 14	0.29 ± 0.04
Financial situation	1	77	0.42
Relatives	1	88	0.37
Social life/relations	1	75	0,30
Car driving	1	81	0.29
Work	1	77	0.27

Note: the SEIQoL Index score (0-100) is calculated by multiplying the cue levels by the matching cue weights of all 5 cues and summing up the products

Table 4. Mean scores and SD for caregiver quality of life (SEIQoL), Burden (SRB, EDIZ and ZBI), and patient cognition (MMSE) for the 46 respondents in the final set, split by gender

	Sex	Mean	Std. Deviation	N
SEIQoL	Female	71.6	14.5	24
	Male	66.5	15.8	22
	Total	69.2	15.2	46
SRB	Female	46.5	26.8	24
	Male	44.6	23.5	22
	Total	45.6	25.0	46
EDIZ	Female	4.8	2.6	24
	Male	4.6	2.1	22
	Total	4.7	2.3	46
ZBI	Female	13.8	6.7	24
	Male	11.9	6.0	22
	Total	12.8	6.3	46
MMSE	Female	20.5	4.9	24
	Male	18.5	4.7	22
	Total	19.5	4.8	46

Table 5. Regression coefficients obtained using enter method with SEIQoL as dependent variable and MMSE, ZBI, EDIZ and SRB scores as predictors in four progressively more complex models

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1*	(Constant)	51.539	9.124		5.649	.000	33.151	69.927
	MMSE	.901	.453	.287	1.987	.053	-.013	1.815
	ZBI							
	EDIZ							
	SRB							
2†	(Constant)	59.341	10.218		5.807	.000	38.734	79.947
	MMSE	.859	.447	.273	1.923	.061	-.042	1.759
	ZBI	-.543	.341	-.227	-1.593	.118	-1.230	.144
	EDIZ							
	SRB							
3‡	(Constant)	56.442	10.984		5.139	.000	34.276	78.608
	MMSE	.922	.457	.294	2.019	.050	.000	1.844
	ZBI	-.761	.450	-.317	-1.689	.099	-1.669	.148
	EDIZ	.944	1.267	.142	.745	.460	-1.613	3.501
	SRB							
4§	(Constant)	56.803	11.502		4.939	.000	33.575	80.031
	MMSE	.914	.467	.291	1.956	.057	-.030	1.858
	ZBI	-.750	.463	-.313	-1.619	.113	-1.686	.186
	EDIZ	1.000	1.363	.151	.734	.467	-1.752	3.752
	SRB	-.013	.107	-.022	-.122	.904	-.230	.203

* Predictors: (constant), MMSE; † Predictors: (constant), MMSE, ZBI; ‡ Predictors: (constant), MMSE, ZBI, EDIZ;
§ Predictors: (constant), MMSE, ZBI, EDIZ, SRB

CHAPTER 8

ASSESSMENT OF QUALITY OF LIFE AS OUTCOME IN DEMENTIA AND MCI INTERVENTION TRIALS A SYSTEMATIC REVIEW

C.J.M. Schölzel-Dorenbos
M.J.M.M. van der Steen
L.K. Engel
M.G.M. Olde Rikkert

ABSTRACT

Objectives: To provide a systematic review of the use of quality of life (QoL) measures as outcome in pharmacological and non-pharmacological intervention trials in patients with Mild Cognitive Impairment (MCI) or dementia, and their proxies. To record the responsiveness of the applied QoL measures, to detect minimal important differences.

Design and methods: Randomized controlled trials (RCTs) were identified from a search of the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group in April 2006. This register contains records from major healthcare databases like CENTRAL, MEDLINE, EMBASE, CINAHL and PsycINFO. We also checked references and systematic reviews, covering the period until September 2006. Primary and secondary endpoints were screened for QoL scales and it was registered whether information on responsiveness was provided.

Settings: Community-dwelling and institutionalized patients with MCI/dementia, and their proxies.

Results: We found 117 pharmacological and 108 non-pharmacological RCTs. One of the pharmacological and four of the non-pharmacological studies used QoL as primary outcome, and two and three as secondary endpoint, respectively. Altogether QoL was assessed in only 4,4% of the RCTs; two RCTs reported on responsiveness of QoL.

Conclusions: This review provides evidence that QoL instruments are seldom used as outcome measures in RCTs in dementia and MCI and that information on responsiveness is scarce. QoL measures should be applied more often in clinical trials as currently no disease modifying drugs are available, while there are valid and reliable QoL measures for dementia that reflect the aims of palliative care and provide transparent information about patient's and caregiver's treatment benefits.

Introduction

As Alzheimer's disease (AD), the most common cause of dementia, is one of the principal causes of disability and decreased quality of life (QoL) among older adults, there is a strong need for effective and efficient interventions, with meaningful outcomes on individual and societal levels.[1] While cognition has been previously viewed as the best outcome measure of efficacy in clinical trials in dementia and Mild Cognitive Impairment (MCI), at present a substantial number of researchers agree that measuring QoL is just as important as measuring cognition, disease severity, symptom response, behavioral disturbance, functional abilities, caregiver burden and resource utilization.[2;3] Rockwood et al. raised the question whether a treatment effect on cognition is really clinically important.[4] Less extremely, many authors stated that cognitive symptom response no longer suffices in anti-dementia trials.[3] However, patients, proxies, clinicians, investigators and drug companies all have different interests, resulting in different definitions of a positive response to treatments. Furthermore, small changes on responsive psychometric cognitive tests, even if statistically significant by including large numbers of patients, may not be clinically relevant. Registration authorities already require that response criteria are defined unambiguously in registered trial designs, which requires to define the changes in the outcome variables considered to be clinically relevant.[5-8] Interpreting health-related QoL outcomes from clinical trials can be difficult. The minimal important difference (MID) represents the smallest change that patients or proxies perceive as an advantage, or that could lead patient or clinician to consider a change in treatment. The responsiveness of outcome measures for these MIDs defines the sample size needed for trials to detect such a difference.

Research efforts are expanding towards novel types of interventions and towards pre- and early symptomatic phases, e.g. MCI, to be able to intervene as early as possible. Current regularly available treatment focuses on early start of cholinesterase inhibitors, N-methyl-D-aspartate receptor-targeted therapy, treatment of co-morbidities and neuropsychiatric symptoms and psychosocial interventions. The final goal of these interventions is to improve QoL of patients and proxies, as cure is still out of range.[9] Rating of QoL in dementia-trials first requires critical reflection on the available scales.[10] In general, three methods are used: self-rating (patient-reported outcomes; PROs), proxy-rating, and proxy observation scales. Persons with MCI and mild-moderately severe dementia can be considered good informants of their own subjective states. So at these stages PROs should be judged as the gold standard. At more severe stages proxy measures or direct observation may be preferred. The disadvantage of proxy-ratings is that they filter a subjective measure through the opinion of another person, with his or her own expectations, mood, burden of care, and a specific prior relationship with the person being rated.[11-13] Often it is not fully clear whether a proxy rates QoL of the patient as if he or she were the patient, or by taking into account what they know about the value system of the patient. Direct observation in more severe dementia may be subject to similar reporting biases. Acknowledging the problem of potential bias of proxy-reports, PRO is preferable and much effort should be put into acquiring this. In case PRO is impossible, observational evaluation by an uninvolved professional caregiver may be the best alternative.[11] Thus, using state of the art methods problematic issues can be sufficiently solved to use QoL measures in randomized controlled trials (RCTs). It is unknown how often these methods are elected as primary or secondary

outcomes at a stage where there is no formal obligation of registration authorities to do so. The aim of the present study is to systematically review how often QoL measures are used as endpoints in MCI and dementia intervention trials, in patients as well as proxies, and to report on their responsiveness. Furthermore the selected scales will be placed in the context of the currently available QoL measures.

Methods

Search strategy

The trials were identified in April 2006 using the search strategy of the Dementia and Cognitive Improvement Group of the Cochrane Review Groups (http://www.mrw.interscience.wiley.com/cochrane/clabout/articles/DEMENTIA/frame.html). This register contains records from major health care databases like CENTRAL, MEDLINE, EMBASE, CINAHL and PsycINFO, as well as many ongoing trial databases and is updated regularly. Additionally reference lists of the intervention studies and reviews selected were checked for studies until October 2006.

Inclusion and exclusion criteria

Patients were required to suffer from dementia or MCI. Papers focussing on proxies/informal caregivers could also be included. Patients were community-dwelling or institutionalized. All types of interventions, both drug and non-drug therapy, could be included if the trial design was a randomized controlled trial (RCT). Papers in non-English language were excluded.

Data extraction strategy

Results of the searches were entered into a standard case record form. Two researchers (L.E. and M.v.d.S.) independently screened the titles and abstracts and selected articles for inclusion in the study. In case of disagreement between the two researchers, the two other authors were involved and papers were finally included if based on consensus. Data extraction was more detailed for those articles, in which a QoL measure was one of the endpoints. Details extracted in these studies included a description of the type of study, intervention, other primary and secondary outcome measures, the type of QoL measure, outcome on QoL and data quantifying responsiveness.

Quality of life

QoL measures cover a range of domains: physical status, functional ability including role functioning, social and community interactions, economic status, psychological status, well-being, somatic sensation and life satisfaction.[14;15] Basically, QoL

is recognized as a concept representing individual responses to the physical, mental and social effects of illness on daily living, which influence the extent to which personal satisfaction with life circumstances can be achieved. It is an abstract and broad concept encompassing physical well-being, perceptions of well-being, satisfaction and sense of self-worth. Slightly more promising definitions are possibly: the ability of patients to manage their lives as they evaluate it. Or: the degree of need satisfaction within the physical, psychological, social, activity, material and structural area.[16;17] In this review an instrument was judged to be a QoL instrument if it was a published measure validated for measuring QoL as defined in one of the abovementioned definitions.

Responsiveness

Responsiveness/sensitivity to change is the ability of an instrument to detect small but important clinical changes.[18] One of the problems is to account for the score variability (often improvement) occurring in stable subjects. Demonstrating responsiveness is necessary to determine the MID, which can be calculated using anchor-based or distribution-based methods. Anchor-based methods assess which changes on the scale correspond with another, external criterion (anchor). This defines the clinical relevance. Distribution-based methods quantify and take into account the variability in a stable population, using effect size, standardized response mean and standard error of measurement.[8;19] Anchor-based approaches do not take measurement precision into account, while distribution-based methods do not provide a good indication of the importance of the observed change.[20] To judge whether a QoL measure is responsive it should be compared with changes in other endpoints within the same study. Therefore, we also registered effect sizes (and responsiveness measures) of the other outcome measures. We aimed to register all possible responsiveness measures on QoL measures or calculate effect sizes, if possible.

Results

The results are summarized in Table 1. We identified 225 RCTs that satisfied the inclusion criteria, 10 (4,4%) used QoL as outcome measure. For pharmacological studies a total of 117 papers satisfied the inclusion criteria. In 114 studies (97%) QoL was not an outcome variable. One drug study used QoL as a primary and two as a secondary outcome. Two QoL measures were applied, one dementia-specific: Quality of Life-Alzheimer Disease Scale (QOL-AD; 2 studies) and one non-dementia specific: Patient-rated scale according to Blau (PRB).

Pharmacological interventions

One RCT evaluated the effects of testosterone (75 mg applied daily to the skin) on cognition, neuropsychiatric symptoms, global functioning and QOL-AD as primary outcome in 16 male patients with mild AD and 22 healthy elderly men. Testosterone-treated AD patients had significantly greater improvements in caregiver-rated QOL-AD scores. In the control group, a nonsignificant trend toward greater improvement in self-rated QOL-AD score was observed in the testosterone-treated group compared with placebo. No significant difference between the groups was detected in the other outcome measures. The authors state that the results should be considered preliminary, a major limitation is the small sample size and the fact that QoL in AD was reported by proxies.[21] In the second trial mild-to-moderate AD patients received the nonsteroidal anti-inflammatory drugs (NSAIDs) rofecoxib and naproxen or placebo. NSAIDs had no significant effect on QOL-AD, cognition, Clinical Dementia Rating scale or neuropsychiatric symptoms.[22] The third study applied the PRB, evaluating patients' perceptions of their well-being.[23] The instrument is not validated in dementia. Donepezil treated patients with mild to moderate AD, produced statistically significant improvements in cognition and global functioning. The Intention-to-Treat (ITT) sample receiving placebo or 5 mg donepezil showed statistically significant improvement on the PRB. However, patients receiving 10 mg donepezil demonstrated worsening. The fully evaluable population showed no significant differences in PRB scores. Clinically meaningful improvements were reported for cognition, no such information was provided for QoL.[24] Information on responsiveness of the QoL measures was not provided in these three studies, and could not be calculated because of lack of clear effect on QoL.

Two other relevant drug studies are worth mentioning. The first study, not included because of lack of control group, reported on responsiveness of the QoL in Late Stage Dementia scale (QUALID) in a double-blind RCT of two antipsychotics (olanzapine and risperidone) for treatment of dementia-related behavioral symptoms in 31 patients. QUALID scores had a significant positive relationship with improvement in behavioral symptoms, and a negative association with adverse medication effects.[25] The second study (included in the 'pharmacological RCTs without QoL as outcome' group) measured the extent to which individualized goals of treatment was met, by means of Goal Attainment Scaling (GAS). 128 AD patients were treated with galantamine or placebo. As primary efficacy parameter treatment goals set before treatment were scored and evaluated every 2 months. The clinician-rated GAS scores showed a significantly greater improvement among patients in the galantamine group than in the controls. The patient-caregiver-rated GAS scores showed a similar improvement in the galantamine group. However, because of the improvement also seen in the placebo group, differences between groups were not statistically significant.[26]

Non-pharmacological interventions

For non-pharmacological studies a total of 108 studies was identified, 101 (94%) studies had no QoL related outcome measures. Four studies used QoL as a primary and three as a secondary outcome. Six types of QoL measures were applied, four dementia-specific: Dementia Care Mapping (DCM; 2 studies), QOL-AD (2 studies), Alzheimer Disease Related QoL scale (ADRQL) and Dementia Quality of Life scale (DQoL). Two scales were non-dementia specific: psychosocial domain of the Functional Limitation Profile (FLP) and Euro Quality of Life (Euro-QoL).

In the first study 72 patients with severe dementia received aromatherapy with Melissa essential oil or placebo. Changes in clinically significant agitation and QoL-indices (% of time spent socially withdrawn and % of time engaged in constructive activities, measured with DCM) were compared. QoL-indices improved significantly more in active treatment. 35% of patients receiving Melissa and 11% treated with placebo experienced a significant reduction in agitation.[27]

The second study used a single-blind, parallel-groups design, in 101 nursing home residents with severe dementia. This RCT investigated whether a reminiscence program would lead to higher levels of psychosocial well-being. Primary outcome measures were cognition, functional performance, Social Engagement Scale (SES) and Well-being/Ill-being Scale (WIB), which is one of the three measures in the DCM. Outcomes were examined at baseline (T0), immediately (T1), and after six weeks (T2). No significant differences were found for cognition and functional performance. The intervention produced a significant effect size of 0.374 for the SES score at T0 and T2 (with only 60% power), and of 0.476 for the WIB score at T0 and T1. The power of this test reached 80%. However, no significant changes were observed in the per protocol sample. In view of the narrow spread of the scores, the changes in the scores may be interpreted as having some clinical significance.[28]

In the third study a significant improvement was found in psychosocial health-related QoL in carers of 50 community-dwelling dementia patients after attending a memory clinic, as measured by the psychosocial domain of the FLP at 6 months (p<0.05), including improvement in the subgroups of alertness behavior (p<0.05) and social interaction (p<0.01). The improvement in social interaction was maintained at 12 months (p<0.05). There was no significant difference in carer psychological morbidity, burden or knowledge of dementia.[29]

The last study investigated whether community-based consultants (STAR-caregivers) could be trained by consultants (master's-level healthcare professionals) to

teach family-caregivers a systematic behavioral approach for reducing mood and behavioral problems in 95 AD patients. The family-caregivers were assigned to trained STAR-caregivers or usual care control groups. Community-based consultants successfully implemented a behavioral intervention with the family-caregivers. Caregivers receiving STAR-C training showed significant improvements in depression, burden, and reactivity to behavioral problems. The frequency and severity of behavioral problems reduced significantly, and QoL in patients and proxies, assessed with the QOL-AD patient and proxy version, improved.[30] No information on responsiveness or effect size was presented or could be calculated.

Three studies had QoL as secondary outcome. The first partially masked RCT evaluated the efficacy of a reminiscence-based intervention in 37 dementia patients, in reducing apathy and improving QoL, assessed with the ADRQL. Despite a substantial improvement in apathy-scores, there was no clear advantage to the reminiscence-based intervention on QoL.[31] In the second study participants were randomized to receive Cognitive Stimulation Therapy (CST) or treatment as usual. 201 people with dementia living in residential homes or attending day centres were assessed using the QOL-AD (self-report version) and measures of cognition, dementia level, mood, dependency and communication, at baseline and eight weeks later. The intervention had a significant positive effect on total QOL-AD score: mean difference pre and post intervention 1,3 for the experimental and –0,8 for the control group (F=6,87, p<0,01). CST also produced statistically significant improvement in cognition.[32] At baseline, higher QoL was significantly correlated with lower levels of dependency and depression, but not with cognitive function or dementia severity. Improvement in QoL was associated with being female, low QoL at baseline, reduced depression and increased cognitive function. Mediation analysis demonstrated that CST is related to change in both QoL and Mini-Mental State Examination (MMSE) and change in MMSE is significantly related tot change in QoL (correlation for total group 0,25, p<0,01). Changes in cognitive function mediated the effects of treatment in improving QoL. These results suggest that whilst QoL in dementia appears to be independent of level of cognitive function, interventions aimed at improving cognitive function can, nonetheless, have a direct effect on QoL.[33] The last study, FACT, is a two-by-two factorial RCT, examining the effect of a walking program aimed at improving cardiovascular endurance, and vitamin supplementation with B6, folic acid and B12, on the rate of cognitive decline of independently living elderly with MCI. Only the study design is available yet. Primary endpoints are measures of cognitive function. Secondary outcomes include two QoL measures: DQoL and Euro-QoL.[34]

Discussion

QoL is mentioned as one of the primary outcomes of interest in dementia drug trials in a recent Cochrane update on cholinesterase inhibitors for AD.[35] However, our review shows that QoL measures are used in only 4,4% of all dementia/MCI related RCTs as outcome measure. Where QoL measures were included, most papers included not enough details to quantify responsiveness or clinical relevance. In non-pharmacological RCTs QoL was measured few times more, and resulted in positive outcome more often than in pharmacological intervention studies (5 out of 7 vs 0 out of 3, respectively).

The responsiveness of outcome measures in dementia trials still lacks a firm empirical base, but is crucial for the interpretation of effectiveness of treatments.[4] From the included sample of RCTs we cannot draw valid conclusions on responsiveness, but some data are available from other naturalistic or validation studies. The QUALID seems to be sensitive to both treatment and adverse effects of medication.[25] Also, data were reported on the responsiveness of GAS. In 15 people the mean gain in GAS-scores was compared to changes in cognition, global functioning and clinical impression. GAS had the largest relative efficiency and the largest effect size.[4;36] GAS can be considered as a method to assess aspects of clinical meaningfulness and could be an interesting instrument for dementia research, that encompasses QoL aspects.[37] In a cross-sectional study comprising 101 people with dementia and their 99 family caregivers, QoL (measured by the DEMQOL-Proxy), cognition, functional impairment, behavioral and psychological symptoms in dementia (Neuropsychiatric Inventory; NPI), and carer mental health were assessed. In a multivariate model, decreased QoL was statistically significantly correlated with higher (worse) NPI scores and younger age of the patient.[7] Furthermore, three longitudinal studies of QoL change in dementia are published.[10;38;39] In the first study QoL was assessed in 47 dementia patients with the ADRQL and reassessed two years later. The ADRQL turned out to be a sensitive measure of change in QoL and seems appropriate as endpoint in intervention studies.[10] In the second study longitudinal change in QoL in 60 dementia patients was assessed with QOL-AD, DQoL and EuroQoL-5 Dimensions, at baseline and one-year later. There was no mean change in QoL. However, around half of the people had increases or decreases in their QoL. The only significant predictor of QoL at follow-up was initial QoL. The main finding of this study was that people with dementia did not perceive that their QoL declined over a period of one year.[38] Patterson et al. evaluated QoL of subjects with MCI around the time of conversion to AD using the QOL-AD. Converters did not differ at baseline with respect to self-rated or informant-rated QoL. After 1 and 2 years informant-rated QoL was significant lower for converters. There was no difference

for self-rated QoL, although converters felt more depressed than non-converters.[39] Lastly DCM is a valid tool for the longitudinal evaluation of QoL in care settings and some abbreviation of the method may facilitate its use more widely.[40]

Our study is the first systematic review of the use of QoL as endpoint in MCI and dementia trials, an increasingly important research area. To our knowledge all presently published RCTs were included. The major limitation is that many studies do not provide clear information on effect sizes, responsiveness and most important: MID. Nevertheless reliable QoL scales are available. In a previous study we found no QoL instrument that was valid for the entire course of dementia.[41] Four instruments represented domains of QoL important to patients and domains professional caregivers focus on, best. Two were self-rating instruments: SEIQoL,[42-44] applicable in mild to moderate dementia patients as well as proxies, and QOL-AD, remaining applicable during disease progression.[45] The CQOL-AD version assesses QoL of the proxy. If self-report is not possible the observational instruments Qualidem, for mild to severe dementia,[46] and DSDAT (Discomfort scale-Dementia of Alzheimer Type) for severe dementia can be applied.[47]

In this systematic review we showed that QoL instruments are seldom used as effectiveness endpoints in MCI and dementia trials, and that information on responsiveness is scarce. QoL measures should be applied more often in clinical trials as currently no disease modifying drugs are available, while there are valid and reliable QoL measures for dementia that reflect the aims of palliative care and provide important information about patient's and caregiver's perspective of treatment benefit. QoL assessment is the only format for patients, caregivers and professionals to express whether an intervention really caused a relevant difference to the patient's life.[38] Therefore, QoL should increasingly be seen as an important outcome in dementia research. We recommend further efforts and research aimed at determination of the MID of existing QoL measures and at including QoL assessment in both patients and their proxies as effectiveness endpoints in all intervention trials.

References

1. De Korte J, Mombers FM, Sprangers MA et al. The suitability of quality-of-life questionnaires for psoriasis research: a systematic literature review. Arch Dermatol 2002;138:1221-7.
2. Trial Designs and Outcomes in Dementia Therapeutic Research. London and New York: Taylor & Francis Group, 2006.
3. Winblad B, Brodaty H, Gauthier S et al. Pharmacotherapy of Alzheimer's disease: is there a need to redefine treatment success? Int J Geriatr Psychiatry 2001; 16:653-666.
4. Rockwood K, Stolee P. Responsiveness of outcome measures used in an anti-dementia drug trial. Alzheimer Dis Assoc Disord 2000;14:182-5.
5. Leber P. Observations and suggestions on antidementia drug development. Alzheimer Dis Assoc Disord 1996;S1:31-5.
6. Banerjee S, Smith SC, Lamping DL et al. Quality of life in dementia: more than just cognition. An analysis of associations with quality of life in dementia. J Neurol Neurosurg Psychiatry 2006;77:146-8.
7. Crosby RD, Kolotkin RL, Williams GR. Defining clinically meaningful change in health-related quality of life. J Clin Epidemiol 2003;56:395-407.
8. Walker MD, Salek SS, Bayer AJ. A review of quality of life in Alzheimer's disease. Part 1: Issues in assessing disease impact. Pharmacoeconomics 1998;14:499-530.
9. Desai AK, Grossberg GT. Diagnosis and treatment of Alzheimer's disease. Neurology 2005;64:S34-9.
10. Lyketsos CG, Gonzales-Salvador T, Chin JJ et al. A follow-up study of change in quality of life among persons with dementia residing in a long-term care facility. Int J Geriatr Psychiatry 2003;18:275-81.
11. Brod M, Stewart AL, Sands L et al. Conceptualization and measurement of quality of life in dementia: the dementia quality of life instrument (DQoL). Gerontologist 1999;39:25-35.
12. Logsdon RG, Gibbons LE, McCurry SM et al. Assessing quality of life in older adults with cognitive impairment. Psychosom Med 2002;64:510-9.
13. Scocco P, Fantoni G, Caon F. Role of depressive and cognitive status in self-reported evaluation of quality of life in older people: comparing proxy and physician perspectives. Age Ageing 2006;35:166-71.
14. Bowling A. Measuring health: a review of quality of life measurement scales. Open University Press. Milton Keynes. Philadelphia, 1993.
15. Spilker B. Quality of life assessment in clinical trials. New York: Raven Press, 1990.
16. De Haes JC, van Knippenberg FC. The quality of life of cancer patients: a review of the literature. Soc Sci Med 1985;20:809-17.
17. Joyce CRB, O'Boyle CA, McGee H. Individual Quality of Life. Approaches to Conceptualisation and Assessment. Harwood Academic publishers, 1999.
18. Deyo RA, Diehr P, Patrick DL. Reproducibility and responsiveness of health status measures. Statistics and strategies for evaluation. Control Clin Trials 1991;12:142-58.
19. Beaton DE, Bombardier C, Katz JN et al. A taxonomy for responsiveness. J Clin Epidemiol 2001;54:1204-17.

20. De Vet HC, Terwee CB, Ostelo RW et al. Minimal changes in health status questionnaires: distinction between minimally detectable change and minimally important change. Health Qual Life Outcomes 2006;4:54-9.

21. Lu PH, Masterman DA, Mulnard R et al. Effects of testosterone on cognition and mood in male patients with mild Alzheimer disease and healthy elderly men. Arch Neurol 2006;63:177-85.

22. Aisen PS, Schafer KA, Grundman M et al. Effects of rofecoxib or naproxen vs placebo on Alzheimer disease progression: a randomized controlled trial. JAMA 2003;289:2819-26.

23. Blau TH. Quality of life, social indicators and criteria of change. Prof Psychol 1977;8:464-73.

24. Rogers SL, Doody RS, Mohs RC et al. Donepezil improves cognition and global function in Alzheimer disease: a 15-week, double-blind, placebo-controlled study. Donepezil Study Group. Arch Intern Med 1998;158:1021-31.

25. Martin-Cook K, Hynan LS, Rice-Koch K et al. Responsiveness of the quality of life in late-stage dementia scale to psychotropic drug treatment in late-stage dementia. Dement Geriatr Cogn Disord 2005;19:82-5.

26. Rockwood K, Fay S, Song X et al. Attainment of treatment goals by people with Alzheimer's disease receiving galantamine: a randomized controlled trial. CMAJ 2006;174:1099-1105.

27. Ballard CG, O'Brien JT, Reichelt K et al. Aromatherapy as a safe and effective treatment for the management of agitation in severe dementia: the results of a double-blind, placebo-controlled trial with Melissa. J Clin Psychiatry 2002;63:553-8.

28. Lai CK, Chi I, Kayser-Jones J. A randomized controlled trial of a specific reminiscence approach to promote the well-being of nursing home residents with dementia. Int Psychogeriatr 2004;16:33-49.

29. Logiudice D, Waltrowicz W, Brown K et al. Do memory clinics improve the quality of life of carers? A randomized pilot trial. Int J Geriatr Psychiatry 1999;14:626-32.

30. Teri L, McCurry SM, Logsdon R et al. Training community consultants to help family members improve dementia care: a randomized controlled trial. Gerontologist 2005;45:802-11.

31. Politis AM, Vozzella S, Mayer LS et al. A randomized, controlled, clinical trial of activity therapy for apathy in patients with dementia residing in long-term care. Int J Geriatr Psychiatry 2004;19:1087-94.

32. Spector A, Thorgrimsen L, Woods B et al. Efficacy of an evidence-based cognitive stimulation therapy programme for people with dementia: randomised controlled trial. Br J Psychiatry 2003;183:248-54.

33. Woods B, Thorgrimsen L, Spector A et al. Improved quality of life and cognitive stimulation therapy in dementia. Aging Ment Health 2006;10:219-26.

34. Van Uffelen JG, Hopman-Rock M, Chin APM et al. Protocol for Project FACT: a randomised controlled trial on the effect of a walking program and vitamin B supplementation on the rate of cognitive decline and psychosocial wellbeing in older adults with mild cognitive impairment. BMC Geriatr 2005;5:18.

35. Birks J. Cholinesterase inhibitors for Alzheimer's disease. Cochrane Database Syst Rev 2006;CD005593.

36. Rockwood K, Stolee P, Howard K et al. Use of Goal Attainment Scaling to measure treatment effects in an anti-dementia drug trial. Neuroepidemiology 1996; 15:330-338.

37. Kaduszkiewicz H. An innovative approach to involve patients in measuring treatment effects in drug trials. CMAJ 2006;174:1117-8.

38. Selwood A, Thorgrimsen L, Orrell M. Quality of life in dementia-a one-year follow-up study. Int J Geriatr Psychiatry 2005;20:232-7.

39. Patterson M, Whitehouse P Barber M et al. Psychological assessment of QOL in drug trials. International Psychogeriatrics 2005;17,31-2.

40. Fossey J, Lee L, Ballard C. Dementia Care Mapping as a research tool for measuring quality of life in care settings: psychometric properties. Int J Geriatr Psychiatry 2002;17:1064-70.

41. Schölzel-Dorenbos CJM, Ettema TP Bos J et al. Evaluating the outcome of interventions on quality of life in dementia: Selection of the appropriate scale. Int J Ger Psychiatr 2007;22:511-9.

42. Coen R, O'Mahony D, O'Boyle C et al. Measuring the quality of life of dementia patients using the Schedule for the Evaluation of Individual Quality of Life. Irish J Psychology 1993;14:154-63.

43. McGee HM, O'Boyle CA, Hickey A et al. Assessing the quality of life of the individual: the SEIQoL with a healthy and a gastroenterology unit population. Psychol Med 1991;21:749-59.

44. Schölzel-Dorenbos CJM. Measurement of quality of life in patients with dementia of Alzheimer type and their caregivers: Schedule for the Evaluation of Individual Quality of Life (SEIQoL). Tijdschr Gerontol Geriatr 2000;31:23-6.

45. Hoe J, Katona C, Roch B et al. Use of the QOL-AD for measuring quality of life in people with severe dementia--the LASER-AD study. Age Ageing 2005;34:130-5.

46. Ettema T, Droës R-M, de Lange J et al. QUALIDEM: development and evaluation of a dementia specific quality of life instrument-validation. Int J Geriatr Psychiatry 2007;22:424-30.

47. Hoogendoorn LI, Kamp S, Mahomed CA et al. The role of observer for the reliability of Dutch version of the Discomfort Scale-Dementia of Alzheimer Type (DSDAT). Tijdschr Gerontol Geriatr 2001;32:117-21.

48. Aisen PS, Schafer KA, Grundman M et al. Effects of rofecoxib or naproxen vs placebo on Alzheimer disease progression: a randomized controlled trial. JAMA 2003;289:2819-26.

49. Logiudice D, Waltrowicz W, Brown K et al. Do memory clinics improve the quality of life of carers? A randomized pilot trial. Int J Geriatr Psychiatry 1999;14:626-32.

50. Politis AM, Vozzella S, Mayer LS et al. A randomized, controlled, clinical trial of activity therapy for apathy in patients with dementia residing in long-term care. Int J Geriatr Psychiatry 2004;19:1087-94.

Table 1. Quality of life (QoL) measures applied in patients and caregivers in randomized pharmacological and non-pharmacological trials in dementia or mild cognitive impairment

	Intervention	Subject	QoL I outcome Measure	QoL II outcome Measure	Effect on QoL; ES*
	Pharmacological	*Patient/proxy*	*Measure*	*Measure*	*Measure*
Lu[21]	Testosterone	Patient	QOL-AD	-	Inconclusive; NI
Rogers[24]	Donepezil	Patient	-	Scale Blau	No difference; NI
Aisen[48]	NSAID	Patient	-	QOL-AD	No difference; NI
	Non-pharmacological	*Patient/proxy*	*Measure*	*Measure*	*Measure*
Ballard[27]	Melissa essential oil	Patient	DCM	-	Improvement; NI
Lai[28]	Reminiscence program	Patient	WIB (DCM)	-	Improvement**
Logiudice[49]	Attendance memory clinic	Proxy	FLP	-	Improvement; NI
Teri[30]	Behavioral approach	Patient/proxy	QOL-AD	-	Improvement; NI
Politis[50]	Reminiscence-based activity	Patient	-	ADRQL	No difference; NI
Spector[32]	Cognitive stimulation therapy	Patient	-	QOL-AD	Improvement; NI
Van Uffelen[34]	Walking program; vit. B	Patient	-	DQoL, EQ-5D	In progress

*Effect size; **ES: 0.48; QOL-AD: Quality of Life-Alzheimer Disease Scale; NI: no information present; NSAIDs: nonsteroidal anti-inflammatory drugs; DCM: Dementia Care Mapping; WIB: Well-being/Ill-being Scale; FLP: Functional Limitation Profile; ADRQL: Alzheimer Disease Related Quality of Life scale; DQoL: Dementia Quality of Life
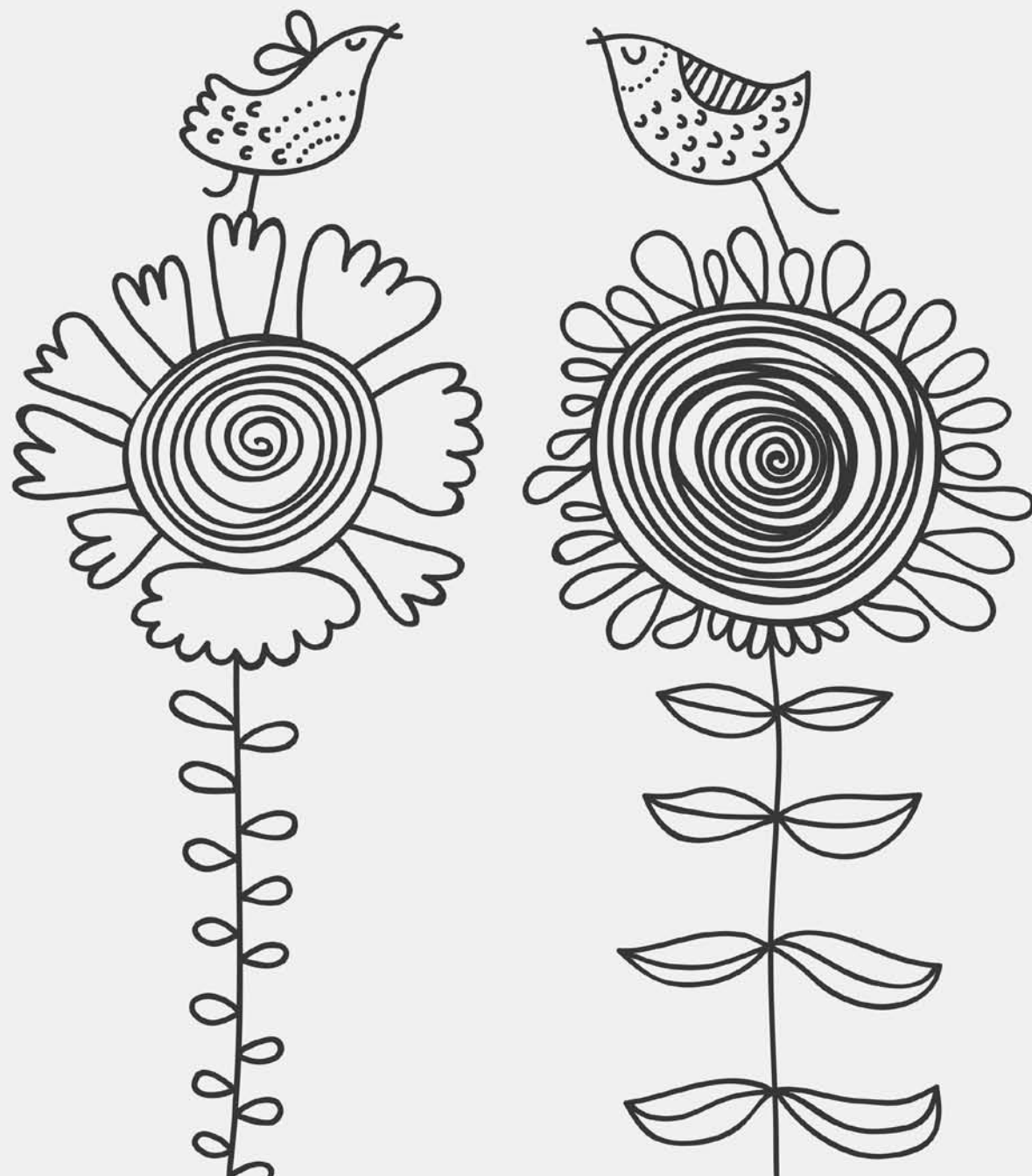
CHAPTER 9

QUALITY OF LIFE OF DEMENTIA PATIENTS AND INFORMAL CAREGIVERS BOTH DEPENDENT ON THEIR OWN DETERMINANTS IN A CROSS-SECTIONAL STUDY

C.J.M. Schölzel-Dorenbos
E.J. Meeuwsen
E.M.M. Adang
P.F.M. Krabbe
M.J. Vernooij-Dassen
F.R.J. Verhey
P. Scheltens
M.G.M. Olde Rikkert
R.J.F. Melis

ABSTRACT

Context: Dementia is still incurable and this makes health-related quality of life (HR-QoL) an important palliative outcome. Better understanding of key determinants of patients' and informal caregivers' QoL can help to improve dementia care.

Objectives: To assess if and how QoL of patients and caregivers are associated. To identify determinants of their individual QoL.

Design, setting and participants: Cross-sectional analysis (baseline data) of the AD-Euro study, a multicentre randomized controlled trial comparing (cost-)effectiveness of treatment and care-coordination of mild-moderate dementia patients and caregivers by memory clinics vs. general practitioners. Dutch community-living dyads were recruited from January 2008 through June 2009. Relationship between patient and caregiver QoL was evaluated using multivariable logistic regression.

Main outcome measures: Health-related (EuroQol-5D-VAS) and dementia-related QoL (QOL-AD). Baseline characteristics, general and dementia-related determinants.

Results: There was a modest but significant correlation between patient and caregiver HRQoL (univariable r=.17; p=.027), but not between their dementia-related QoL (univariable r=.07; p=.353). In the univariable linear regression analysis only patient factors determined patient HRQoL, while caregiver HRQoL was determined by both patient en caregiver factors. The bivariable model indicated that associations between HRQoL were decreased by patient factors but augmented by caregiver factors. In the multivariable regression model with patient HRQoL as dependent variable, the patient's own factors comorbidity (β=-.547; p=.035) and mood (β=-2.593; p=.000) remained significant, but caregiver factors lost significance. When caregiver HRQoL was the dependent variable, only caregiver's mastery (β=-.529; p=.030) and mood (β=-. 382; p=.009) remained significant, whereas patient factors lost significance.

Conclusions: There was only a modest association between HRQoL of patients and caregivers. HRQoL of each depended particularly on their own personal characteristics. Our main message is that HRQoL in dementia care may be best served if one specifically addresses the individual determinants of health status of patients as well as informal caregivers.

Trial Registration clinicaltrials.gov Identifier: NCT00554047

Introduction

As long as a cure for dementia is lacking, relief of symptoms and improvement of well-being of people suffering from dementia remain the most important therapeutic targets. This justifies a palliative policy. According to the definition of the World Health Organisation (WHO), improving the quality of life of patients and their families are specifically part of palliative care. Dementia is a devastating disease with adverse effects on health and quality of life of dementia patients as well as their informal caregivers.[1] Dementia patients and their informal caregivers are closely connected. This makes it desirable to investigate the relationship between the quality of life for both groups.

Quality of life of dementia patients is influenced by the severity and nature of the disease itself.[2-4] Additionally, the presence of dementia-related complications, co-morbidity, and limitations in daily life performance may play an important role. Mood disturbances,[5;6] neuropsychiatric symptoms,[2;6;7] and functional limitations all potentially reduce quality of life, but their impact has not been quantified.[2;4;5;8]

Many informal caregivers lack proper dementia care training as well as professional information and support for care-giving tasks. However, providing care has been proven to be an important risk factor for the physical, emotional, social and financial well-being of informal caregivers.

For example, it has recently been shown that stress in dementia caregivers leads to a chronic low-grade hypercoagulable state that increases cardiovascular disease risk.[9] Neuropsychiatric symptoms of patients,[10;11] burden and hours of informal care,[10;12] self-esteem and perceived social support also are important for the caregivers' quality of life.[10;13] Moreover, to ensure long term informal care, it is crucial to invest in improving quality of life of informal caregivers as an important precondition for care provision, because most people with dementia are living in the community.

Given the importance of maintaining quality of life in dementia patients and caregivers and the reciprocal relationship between patients and caregivers, it is remarkable that only three studies simultaneously examined the determinants of quality of life of patients and informal caregivers.[11;14;15] They suggested a positive relationship between the quality of life of the pair members. However, the studies were small and had methodological drawbacks. In the first study the caregivers rated both their own quality of life and the quality of life of the care recipients.[11] In the last study the factors underlying the quality of life relationship were not explored.[15] The fact that empirical information on quality of life in dementia is scarce can be partly explained by the difficulty to reliably measure quality of life. Empirical research is hindered by a lack of unequivocally defined dimensions and determinants of the concept.

Dementia patients often require formal and informal care. Including care for the (quality of life of the) informal caregivers is needed for successful care provision and dementia management. Therefore, factors affecting the associations between quality of life of dementia patients and their informal caregivers should be iden-

tified. The aim of our study was to: 1) Explore the relationship between quality of life of dementia patients and their caregivers, and: 2) Compare the strength of this relationship with how strongly the disease related determinants of patients and caregivers influenced the quality of life of both parties.

Methods

Study Design

The AD-Euro study is a multicentre randomized controlled trial that aimed to compare (cost-) effectiveness of post-diagnosis treatment and care-coordination of dementia patient-caregiver pairs by multidisciplinary memory clinics versus general practitioners. Details of the study design have been published elsewhere.[16] In this study, a cross-sectional analysis of baseline quality of life data and their potential determinants was performed.

Participants

175 Pairs of community-dwelling persons with dementia and their informal caregivers were enrolled in the study and have been included in the analysis. We included consecutive patients with a new dementia diagnosis fulfilling DSM-IV-TR criteria with a Clinical Dementia Rating (CDR) scale score 0.5-2.[17;18] Patients were excluded if data collection was impossible, in case of those with a short life expectancy, those awaiting nursing home admission, or patients who had a definite indication for specific memory clinic follow-up (e.g. rare dementia diagnosis), and therefore could not be randomized.

Measurements

Quality of life

The primary outcome of the study was quality of life. We investigated quality of life with two instruments. First with the European Quality of life-5 Dimensions Visual Analogue Scale (EQ-5D-VAS) for general health-related quality of life (HR-QoL),[19] and second with the Quality of Life-Alzheimer's Disease scale (QOL-AD) for dementia-related quality of life.[20] The EQ-5D is a generic tool for assessing the current health state. The instrument consists of two parts: self-administered health index, and VAS. The health index represents the perspective of the general population (utility aspect of the EQ-5D), while the EQ-5D VAS shows the perspective of individual subjects. The EQ-5D-VAS was therefore preferred as the outcome measure. The VAS assigns a global value to current health state on a 100-point scale, with 100 representing the 'best imaginable health state' and 0 representing the 'worst imaginable health state'. The QOL-AD is a dementia-specific 13-item

measure with scores ranging from 13 (poor) to 52 (excellent). We used the patient self report version (PQOL-AD) for patients. Caregivers reported on their own quality of life with the caregiver version of the QOL-AD that can be used in clinically nondemented samples.[21]

Figure 1 provides an overview of theoretical relationships between quality of life and determinants of quality of life of dementia patients and informal caregivers. The model proposed that quality of life of a member of the pair, be it patient or caregiver, is directly dependent on his or her own set of determinants. In addition, there may be a direct link between the determinants of the two members of the patient-caregiver pair and between the quality of life of the patient and the caregiver.

Determinants of patients

Determinants of patients that we investigated were: age, sex, marital status, material well-being, relationship with caregiver, living situation and household composition. The relevant dementia-related determinants were: cognition, mood, stage of illness, behavioral disturbances, physical health, co-morbidity and functional performance. Cognitive function was measured with the Mini-Mental State Examination (MMSE).[16] Mood of patients was assessed with the Geriatric Depression Scale-15 (GDS), a depression screening instrument.[22] Severity of dementia was assessed with the Clinical Dementia Rating scale (CDR).[18] Neuropsychiatric symptoms were assessed with the Neuropsychiatric Inventory Questionnaire (NPI-Q).[23] The Cumulative Illness Rating Scale-Geriatrics (CIRS-G) was used to quantify chronic medical illness burden. CIRS-G provides a review of medical problems by 14 organ systems, with common problems of elderly with emphasis on morbidity, yielding a cumulative score.[24] Functional performance has been measured with the Interview on Daily living activities in Dementia Diagnosis (IDDD) that assesses both the patients' initiative (IDDD-initiative) to perform daily activities and the amount of help actually needed (IDDD-help).[25]

Determinants of caregivers

With the caregivers we investigated the determinants: age, gender, marital status, material well-being, relationship with patient and living arrangements. Socio-economic state was assessed with the ISEI-92, based on Standard Occupational Classification (SOC).[26] Caregivers' depression was evaluated with the Center for Epidemiologic Studies Depression Scale (Ces-D).[27] Caregivers' distress associated with neuropsychiatric symptoms of patients was rated on a 0-5-point distress scale of the NPI-Q.[23] Pearlin Mastery Scale (PMS) was applied to measure capacity and

structure of coping.[16] Environmental determinants for caregivers were: caregiver time, resource utilization, socio-economic state, social support and social network. The Inventory for Measuring Social Involvement (ISB) was used to measure social support.[16]

Statistical analysis
Descriptive statistics were used to summarize sample characteristics. Pearson correlations between patients' and caregivers' HRQoL (EQ-5D-VAS) and patients' and caregivers' dementia-related quality of life (QOL-AD) were calculated. Univariable linear regression analysis was used to compare the associations between the significantly correlated quality of life measures in the first analysis with the effects of other possible determinants of patients' and caregivers' quality of life. Bivariable linear regression analyses with one outcome variable (quality of life measure of patient and caregiver, separately) and one independent variable (the individual determinants of patients and caregivers) were used to identify the factors possibly explaining the relationship between the quality of life measures of patients and caregivers.

Finally, multivariable linear regression was used to build models with the potential predictive and explaining factors that were identified in the univariable and bivariable analyses. Both caregivers' and patients' quality of life measures were modeled as dependent variable. The significant variables in the univariable model that remained significant in multivariable analyses, as well as all variables found to explain the relationship between patient and caregiver quality of life in the bivariable analyses, were kept in the final multivariable model.

Ethical Aspects
The study was approved by the Medical Ethics Committee of Radboud University Nijmegen Medical Centre. Written consent of both all patients and caregivers was acquired before start of the study.

Results
Sample demographics and characteristics
Baseline characteristics of the 175 patient-caregiver pairs are presented in Table 1. 54% Of the caregivers were spouses, 41% were daughters or sons (-in-law) and 5% had another relationship with the patient. On average, caregivers provided 5.1 hours per week of (instrumental) activities of daily life support (range 0-35 hours). Most patients had Alzheimer's disease and a majority of patients had mild dementia. Almost three-quarters of caregivers were women. Scores for dementia-related

quality of life (QOL-AD) were similar for patients and caregivers, while scores for HRQoL (EQ-5D-VAS) were slightly better for caregivers.

Regression models for HRQoL
Patient and caregiver HRQoL assessed with EQ-5D-VAS were significantly correlated (Pearson r=0.17, p=.027; Table 2). However, no association was found between patient and caregiver dementia-related quality of life, assessed with QOL-AD (Pearson r=0.07, p=.353). Therefore, we only further investigated the relationship between patient and caregiver HRQoL.

Findings from univariable analyses
Univariable analysis revealed significant associations between patient HRQoL (patient EQ-5D-VAS as dependent variable; Table 3a) and four patient determinants: severity of dementia (CDR score, r=0.16, p=.037), co-morbidity (CIRS-G score, r=0.27, p=.000), mood (GDS score, r=0.44, p=.000) and function (IDDD-help score, r=0.17, p=.029). More severe stage of dementia and higher levels of patient co-morbidity (disease burden), depression, and dependency from help of others were associated with decreasing patient HRQoL. No significant univariable associations were found between patient HRQoL and caregiver determinants.

Univariable regression analysis with caregiver HRQoL (EQ-5D-VAS) as dependent variable (Table 3b) showed statistically significant associations with three patient determinants: behavioral symptoms (NPI-B-score, r=0.28, p=.000), mood (GDS-score, r=0.16, p=.035) and function (IDDD-initiative-score, r=0.17, p=.023), and four caregiver determinants: mood (CES-D-score, r=0.40, p=.000), feelings of mastery (PMS-score, r=0.38, p=.000), social involvement (ISB-score, r=0.31, p=.000) and distress (NPI-Q-D-score, r=0.33, p=.000). Lower levels of caregiver mood and mastery, higher levels of distress, and lower levels of mood and functioning of the patients they cared for were associated with decreasing caregiver HRQoL.

Findings from bivariable analyses
Results of bivariable analyses (see Table 4) entering separate patient variables into a model regressing patient HRQoL (dependent variable) on caregiver HRQoL (independent variable), showed that patients' co-morbidity (CIRS-G), IDDD-help, IDDD-initiative, and mood (GDS) decreased the association between patient and caregiver HRQoL (CIRS-G: β=0.17; IDDD-initiative: β=0.17, IDDD-help: β=0.17 and GDS: β=0.10 for the estimate of the effect of caregiver HRQoL on patient HRQoL). Entering caregiver variables into the model augmented the association between patient and caregiver HRQoL. The relevant caregiver determinants were mood

(CES-D-score: β=0.267), feelings of mastery (PMS-score: β=0.245) and social involvement (ISB-score: β=0.220).

Results of bivariable analyses entering determinants into a model regressing caregiver HRQoL (dependent variable) on patient HRQoL (independent variable), showed that these either augmented or diminished the relationship between caregiver and patient HRQoL for the same seven determinants (CIRS-G, IDDD-help, IDDD-initiative, GDS, CES-D, PMS, and ISB).

Findings from multiple regression analyses
In the multivariable model (Table 3a) patient HRQoL was regressed on caregiver HRQoL and the determinants that were identified in the univariable and bivariable analyses. Patient comorbidity (CIRS-G-score, β=-0.547, p=.035) and mood (GDS-score, β=-2.593, p=.000) remained significant determinants in the multivariable analysis. Dementia severity (CDR) lost statistical significance and was therefore not included in the final model. The caregiver determinants mood (CES-D), mastery (PMS) and social involvement (ISB), as well as the patient determinants IDDD-help (despite losing statistical significance as a predictor) and IDDD-initiative, were kept in the final model on the basis of their effect in the bivariable analyses. Compared with their univariable relationship, the association between patient and caregiver HRQoL decreased from 0.19 to 0.17 and lost significance in the multivariable analyses.

In the multivariable model in Table 3b caregiver HRQoL was regressed on patient HRQoL and the determinants that were identified in the univariable and bivariable analyses. Only caregivers' mood (CES-D-score, β=-0. 382, p=.009) and mastery (PMS-score, β=-0.529, p=.030) were significant determinants in the multivariable analysis. The other univariable predictors of caregiver HRQoL (patient NPI-B, patient GDS, patient IDDD-initiative, caregiver ISB and caregiver NPI-Q-D) all lost statistical significance. Despite losing statistical significance as predictors, the patient determinants comorbidity (CIRS-G), function (IDDD-initiative) and mood (GDS), and the caregiver predictor ISB were kept in the final model on the basis of their effect in the bivariable analyses. Compared with their univariable relationship, the association between caregiver and patient HRQoL decreased from 0.15 to 0.12 and lost significance in the multivariable analyses.

Discussion
The purpose of this study was to investigate the relationship between quality of life of dementia patients and their caregivers and to identify the characteristics of patients and caregivers that affected their quality of life. We also compared the strength of the relationship of other patient and caregiver determinants which in-

fluenced the quality of life. We found a statistically significant but small association between HRQoL in this large sample of patient-caregiver pairs and no relationship between patient and caregiver dementia-related quality of life. Remarkably, the scores on the EQ-5D-VAS of the caregivers are rather high and thus good. This may be related to the relatively mild severity of the dementia which had, as of yet, little effect on quality of life of caregivers. We also saw that HRQoL was minimally determined by inter-individual, but mostly by intra-individual characteristics. Patient's HRQoL was mainly dependent on the patient's own determinants (i.e. disease severity, mood and co-morbidity), and not on caregiver determinants. Caregiver's own determinants (particularly mood and feelings of mastery) had a much stronger effect on their own HRQoL than patient determinants.

The results of our study (i.e. no association between dementia-related quality of life, only modest association between HRQoL) seemed to contradict the findings of three recently published studies.[11;14;15] Thomas et al. showed that dementia-related quality of life of caregivers was significantly related to patient's quality of life and vice versa.[11] However, patient dementia-related quality of life was rated by the caregivers, which may have introduced a correlation through information bias. Also, the study populations were not comparable with ours and some of the studies applied different quality of life measures for patients and caregivers than our study.

In the Inouye et al. study, which found a moderate association between patient and caregiver dementia-related quality of life,[15] the patients were already in treatment for over 3 years, while our patients were newly diagnosed. The patients in this study also had much lower lower quality of life scores than the patients in our study, while the scores of caregivers were comparable.[15] This difference may be explained by our finding that disease severity was a predictor of patients' and not caregivers' HRQoL. Finally, Gallrach et al. found that patient dementia-related quality of life was a predictor of caregiver quality of life and vice versa.[14]

The strengths of our study were the comprehensive approach in which we analyzed how a wide range of variables were related to the HRQoL of dementia patients and caregiver simultaneously, and the considerably larger and more homogeneous sample of patient-caregiver pairs than those of previous studies. In spite of these strengths, one limitation deserves comment. The study was cross-sectional, so direction of causation could not be ascertained.

We showed that in a large sample of dementia patient-caregiver pairs their HRQoL was only modestly interrelated. We demonstrated that patients as well as caregivers each have their own personal determinants of HRQoL. Further observational and intervention studies are needed to draw definite conclusions on the impact of these findings. Our study underscores the importance of ongoing medical manage-

ment in dementia to maintain the dementia patient's physical health and coexisting medical conditions that take into account the implications of their cognitive impairment.[28] Our study also lends support to the fact that explicit and separate attention should be paid to the caregivers. The results provide an empirical basis for dementia care that offers sufficient amount of time and attention to patients and caregivers separately. Success of most care plans, as well as continued living in the community of dementia patients, rests largely on informal caregivers. Our findings that HRQoL of both parties was predominantly dependent on their own personal determinants stress the need for dementia specialists and general practitioners to treat the dyad of the patient with dementia and his or her caregiver. The benefits of proper care and treatment for caregivers have already been shown, so the instruments are known and available.[29;30] The results of this study should encourage health care professionals to actually make efforts for the implementation of already existing knowledge and opportunities to improve dementia care.

References

1. Brodaty H, Donkin M. Family caregivers of people with dementia. Dialogues Clin Neurosci 2009;11:217-28.
2. Banerjee S, Smith SC, Lamping DL et al. Quality of life in dementia: more than just cognition. An analysis of associations with quality of life in dementia. J Neurol Neurosurg Psychiatry 2006;77:146-8.
3. De Vugt ME, Riedijk SR, Aalten P et al. Impact of behavioural problems on spousal caregivers: a comparison between Alzheimer's disease and fronto-temporal dementia. Dement Geriatr Cogn Disord 2006;22:35-41.
4. Ready RE, Ott BR. Quality of Life measures for dementia. Health Qual Life Outcomes 2003;1:11-20.
5. Byrne-Davis LM, Bennett PD, Wilcock GK. How are quality of life ratings made? Toward a model of quality of life in people with dementia. Qual Life Res 2006;15:855-65.
6. Samus QM, Rosenblatt A, Steele C et al. The association of neuropsychiatric symptoms and environment with quality of life in assisted living residents with dementia. Gerontologist 2005;45:19-26.
7. Samus QM, Rosenblatt A, Onyike C et al. Correlates of caregiver-rated quality of life in assisted living: the Maryland Assisted Living study. J Gerontol B Psychol Sci Soc Sci 2006;61:311-4.
8. Burgener S, Twigg P. Relationships among caregiver factors and quality of life in care recipients with irreversible dementia. Alzheimer Dis Assoc Disord 2002;16:88-102.
9. Von Känel R, Mausbach BT, Dimsdale JE et al. Problem Behavior of Dementia Patients Predicts Low-Grade Hypercoagulability in Spousal Caregivers. J Gerontol A Biol Sci Med Sci. 2010;10:1093-1101.
10. Belle SH, Burgio L, Burns R et al. Enhancing the quality of life of dementia caregivers from different ethnic or racial groups: a randomized, controlled trial. Ann Intern Med 2006;145:727-38.
11. Thomas P, Lalloue F, Preux PM et al. Dementia patients caregivers quality of life: the PIXEL study. Int J Geriatr Psychiatry 2006;21:50-6.
12. Vickrey BG, Hays RD, Maines ML et al. Development and preliminary evaluation of a quality of life measure targeted at dementia caregivers. Health Qual Life Outcomes 2009;7:56-68.
13. Chappell NL, Reid RC. Burden and well-being among caregivers: examining the distinction. Gerontologist 2002;42:772-80.
14. Gallrach F, Kirk R, Hornblow A et al. Quality of life in dementia: Clinical and economic findings from New Zealand. 2009;http://ir.canterbury.ac.nz/bitstream/10092/ 2646/1/ 12613469_Poster_Singapore_Finalx.pdf.
15. Inouye K, Pedrazzani ES, Pavarini SC et al. Perceived quality of life of elderly patients with dementia and family caregivers: evaluation and correlation. Rev Lat Am Enfermagem 2009;17:187-93.
16. Meeuwsen EJ, Melis RJ, Adang EM et al. Cost-effectiveness of post-diagnosis treatment in dementia coordinated by multidisciplinary memory clinics in comparison to treatment coordinated by general practitioners: an example of a pragmatic trial. J Nutr Health Aging 2009;13:242-8.
17. American Psychiatric Association. DSM-IV-TR. Diagnostic and Statistical Manual of Mental disorders, Fourth edition, Text Revision. Ed. 2000.
18. Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. Int Psychogeriatr 1997;9:173-6.
19. Brooks R. EuroQol: the current state of play. Health Policy 1996;37:53-72.
20. Logsdon RG, Gibbons LE, McCurry SM et al. Assessing quality of life in older adults with cognitive impairment. Psychosom Med 2002;64:510-9.
21. Revell AJ, Caskie GI, Willis SL et al. Factor structure and invariance of the Quality of Life in Alzheimer's Disease (QoL-AD) Scale. Exp Aging Res 2009;35:250-67.
22. Almeida OP, Almeida SA. Short versions of the geriatric depression scale: a study of their validity for the diagnosis of a major depressive episode according to ICD-10 and DSM-IV. Int J Geriatr Psychiatry 1999;14:858-65.
23. Kaufer DI, Cummings JL, Ketchel P et al. Validation of the NPI-Q, a brief clinical form of the Neuropsychiatric Inventory. J Neuropsychiatry Clin Neurosci 2000;12:233-9.

24. Miller MD, Paradis CF, Houck PR et al. Rating chronic medical illness burden in geropsychiatric practice and research: application of the Cumulative Illness Rating Scale. Psychiatry Res 1992;41:237-48.
25. Teunisse S, Derix MM. The interview for deterioration in daily living activities in dementia: agreement between primary and secondary caregivers. Int Psychogeriatr 1997;9:155-62.
26. Bakker B, Sieben I, Nieuwbeerta P et al. Scales for prestige, socio-economic status and social class for the Standard Occupational Classification 1992. Sociale Wetenschappen 1997;40:1-22.
27. Radloff LS. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. Applied Psychol Measurement 1997;1:385-401.
28. Attea P, Johns H. Confronting Alzheimer's Disease and Other Dementia. Editorial. J Am Geriatr Soc 2010;58:1587-90.
29. Graff MJ, Vernooij-Dassen MJ, Thijssen M et al. Community based occupational therapy for patients with dementia and their care givers: randomised controlled trial. BMJ 2006;333:1196-1202.
30. Lavretsky H, Siddarth P, Irwin MR. Improving depression and enhancing resilience in family dementia caregivers: a pilot randomized placebo-controlled trial of escitalopram. Am J Geriatr Psychiatry 2010;18:154-62.

Figure 1. Quality of Life and Determinants in Dementia

Table 1. Demographics and characteristics of dementia patient and caregiver dyads		
Characteristics	Patients (N=175)	Caregivers (N=175)
Age, mean (SD), years	78 (6)	64 (13)
Women, No. (%)	106 (61)	123 (70)
Living alone, No. (%)	61 (35)	
Alzheimer's disease, No. (%)	105 (60)	
Vascular dementia, No. (%)	15 (9)	
Mixed or other dementia, No. (%)	55 (31)	
Stage of dementia CDR 0,5, No. (%)	8 (5)	
Stage of dementia CDR 1, No. (%)	139 (79)	
Stage of dementia CDR 2, No. (%)	28 (16)	
MMSE, mean (SD)	22.7 (3.9)	
CIRS-G, mean (SD)	9 (4.5)[a]	
GDS-15, mean (SD)	2.6 (2.4)[b]	
NPI-Q-B, mean (SD)	7.4 (6.1)[c]	
IDDD-initiative, mean (SD)	12.8 (7.2)[d]	
IDDD-help, mean (SD)	18.5 (15.5)[d]	
NPI-Q-D, mean (SD)		9.7 (9.1)[d]
CES-D, mean (SD)		9.5 (7.6)[d]
PMS, mean (SD)		16.6 (4.4)[d]
ISB, mean (SD)		12.2 (3.1)[d]
PQOL-AD / CQOL-AD, mean (SD)	36.1 (4.3)	38 (4.2)[c]
EQ-5D-VAS, mean (SD)	72.4 (15.3)[d]	79.7 (13.5)

[a]N=168; [b]N=172; [c]N=174; [d]N=173. Abbreviations: SD, standard deviation; CDR, Clinical Dementia Rating scale (0-3); MMSE, Mini-Mental State Examination (0-30); CIRS-G, Cumulative Illness Rating Scale-Geriatrics (0-56); GDS-15, 15-item geriatric depression scale (0-15); NPI-Q-B, Neuropsychiatric Inventory Questionnaire, Behavior (12-36); IDDD, Interview on Daily living activities in Dementia Diagnosis: initiative (0-36), help (0-44); PQOL-AD, Patient version Quality of Life-Alzheimer's Disease scale (13-52); EQ-5D-VAS, European Quality of life-5 Dimensions Visual Analogue Scale (0-100); CES-D=Center for Epidemiologic Studies Depression scale (0-60); PMS=Pearlin Mastery Scale (7-35); ISB, Inventory for Measuring Social Involvement (4-16); NPI-Q-D, Neuropsychiatric Inventory Questionnaire, Distress (0-60); CQOL-AD, Caregiver version QOL-AD (13-52)
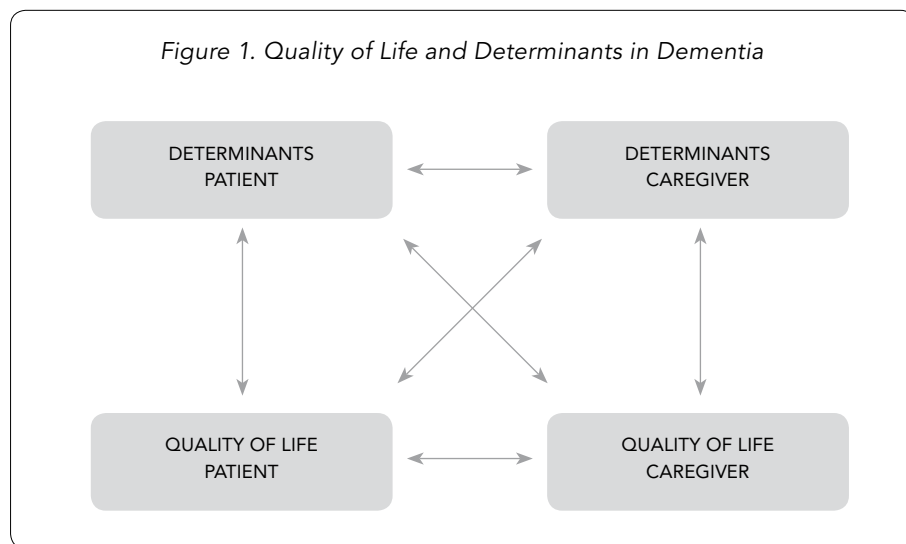
Table 2. Pearson correlations of patient and caregiver quality of life measures				
	PQOL-AD	P-EQ-5D-VAS	CQOL-AD	C-EQ-5D-VAS
PQOL-AD	1			
P-EQ-5D-VAS (N)	0.562[a] (173)			
p	<0.001	1		
CQOL-AD (N)	0.071 (174)	0.005 (172)		
p	0.35	0.95	1	
C-EQ-5D-VAS (N)	0.131 (175)	0.168[b] (173)	0.479[a] (174)	
p	0.08	0.03	<0.001	1

Abbreviations: P, patients; C, caregivers; QOL-AD, Quality of Life-Alzheimer's Disease scale; EQ-5D-VAS, European Quality of life-5 Dimensions Visual Analogue Scale. [a]Correlation is significant at the 0.01 level (2-tailed); [b]Correlation is significant at the 0.05 level (2-tailed)

Table 3a. Regression models with patient EQ-5D-VAS as dependent variable

Independent variable	Univariable model				Multivariable model			
	β[a]	p	R²	N	β	p	R²	N
C-EQ-5D-VAS	0.19	0.03	0.03	173	0.17	0.08	0.26	164
Patient variables								
CIRS-G	-0.91	<0.001	0.07	168	-0.55	0.04		
CDR	-6.67	0.034	0.03	173				
MMSE	0.09	0.78	<0.001	173				
GDS	-2.99	<0.001	0.20	171	-2.59	<0.001		
IDDD-initiative	-0.25	0.12	0.01	171	0.05	0.78		
IDDD-help	-0.17	0.03	0.03	171	-0.10	0.24		
NPI-Q-B	-0.13	0.51	0.003	172				
Age	-0.10	0.63	0.001	173				
Gender	-3.52	0.14	0.013	173				
Caregiver variables								
CES-D	0.12	0.44	0.003	171	0.12	0.51		
PMS	0.09	0.74	0.001	171	0.29	0.33		
ISB	-0.03	0.93	<0.001	171	-0.02	0.95		
Hours a week	-0.13	0.45	0.003	172				
NPI-Q-D	-0.02	0.88	<0.001	171				
Age	0.07	0.44	0.004	173				
Gender	-0.28	0.91	<0.001	173				
Education	0.66	0.53	0.002	172				

[a] β unstandardized coefficient. Regression analysis with EQ-5D-VAS scores of patients as dependent variables, by entering objective variables in the model analysis. Abbreviations: CDR, Clinical Dementia Rating scale; MMSE, Mini-Mental State Examination; CIRS-G, Cumulative Illness Rating Scale-Geriatrics; NPI-Q-B/D, Neuropsychiatric Inventory Questionnaire, Behavior/Distress; IDDD, Interview on Daily living activities in Dementia Diagnosis; EQ-5D-VAS, European Quality of life-5 Dimensions Visual Analogue Scale; CES-D, Center for Epidemiologic Studies Depression scale; PMS, Pearlin Mastery Scale; ISB; Inventory for Measuring Social Involvement

Table 3b. Regression models with caregiver EQ-5D-VAS as dependent variable

Independent variable	Univariable model				Multivariable model			
	β[a]	p	R²	N	β	p	R²	N
P-EQ-5D-VAS	0.15	0.03	0.03	173	0.12	0.08	0.22	164
Caregiver variables								
CES-D	-0.72	<0.001	0.16	173	-0. 38	0.009		
PMS	-1.18	<0.001	0.15	173	-0.53	0.03		
ISB	1.35	<0.001	0.10	173	0.37	0.26		
Hours a week	-0.27	0.07	0.02	174				
NPI-Q-D	-0.50	<0.001	0.11	173				
Age	-0.10	0.19	0.01	175				
Gender	-3.38	0.13	0.01	175				
Education	1.37	0.14	0.01	174				
Patient variables								
CIRS-G	-0.24	0.26	0.01	168	0.10	0.65		
CDR	-0.57	0.84	<0.001	175				
MMSE	-0.32	0.24	0.008	175				
GDS	-0.91	0.04	0.03	172	-0.45	0.31		
IDDD-initiative	-0.32	0.02	0.03	173	-0.22	0.17		
IDDD-help	-0.09	0.19	0.01	173	0.001	0.99		
NPI-Q-B	-0.63	<0.001	0.08	174				
Age	-0.14	0.43	0.004	175				
Gender	2.38	0.26	0.007	175				

[a] β unstandardized coefficient. Regression analysis with EQ-5D-VAS scores of caregivers as dependent variables, by entering objective variables in the model analysis. Abbreviations: CDR, Clinical Dementia Rating scale; MMSE, Mini-Mental State Examination; CIRS-G, Cumulative Illness Rating Scale-Geriatrics; NPI-Q-B/D, Neuropsychiatric Inventory Questionnaire, Behavior/Distress; IDDD, Interview on Daily living activities in Dementia Diagnosis; EQ-5D-VAS, European Quality of life-5 Dimensions Visual Analogue Scale; CES-D, Center for Epidemiologic Studies Depression scale; PMS, Pearlin Mastery Scale; ISB; Inventory for Measuring Social Involvement

Table 4. Bivariable regression model with patient and caregiver EQ-5D-VAS as dependent variable

Bivariable model; P-EQ-5D-VAS dependent variable						Bivariable model; C-EQ-5D-VAS dependent variable				
Independent variable	β	p	R^2	N		Independent variable	β	p	R^2	N
Patient variables						*Patient variables*				
C-EQ-5D-VAS CIRS-G	0.17 -0.87	0.06 0.001	0.09	168		P-EQ-5D-VAS CIRS-G	0.12 -0.13	0.06 0.56	0.03	168
C-EQ-5D-VAS CDR	0.19 -6.44	0.03 0.04	0.05	173		P-EQ-5D-VAS CDR	0.15 -0.26	0.03 0.93	0.03	173
C-EQ-5D-VAS MMSE	0.19 0.13	0.03 0.67	0.03	173		P-EQ-5D-VAS MMSE	0.15 -0.24	0.03 0.36	0.03	173
C-EQ-5D-VAS GDS	0.10 -2.87	0.22 <0.001	0.21	171		P-EQ-5D-VAS GDS	0.09 -0.90	0.22 0.07	0.05	171
C-EQ-5D-VAS IDDD-initiative	0.17 -0.19	0.05 0.23	0.04	171		P-EQ-5D-VAS IDDD-initiative	0.13 -0.29	0.05 0.04	0.05	171
C-EQ-5D-VAS IDDD-help	0.17 -0.15	0.05 0.05	0.05	171		P-EQ-5D-VAS IDDD-help	0.13 -0.07	0.05 0.32	0.03	171
C-EQ-5D-VAS NPI-Q-B	0.19 -0.01	0.04 0.968	0.03	172		P-EQ-5D-VAS NPI-Q-B	0.14 -0.60	0.04 <0.001	0.10	172
C-EQ-5D-VAS Age patient	0.19 -0.07	0.03 0.74	0.03	173		P-EQ-5D-VAS Age patient	0.15 -0.15	0.03 0.41	0.03	173
C-EQ-5D-VAS Gender patient	0.20 -3.93	0.02 0.10	0.04	173		P-EQ-5D-VAS Gender patient	0.16 2.61	0.02 0.21	0.04	173
Caregiver variables						*Caregiver variables*				
C-EQ-5D-VAS PMS	0.25 0.37	0.009 0.19	0.04	171		P-EQ-5D-VAS PMS	0.16 -1.17	0.009 <0.001	0.18	171
C-EQ-5D-VAS ISB	0.22 -0.32	0.02 0.42	0.03	171		P-EQ-5D-VAS ISB	0.16 1.29	0.02 <0.001	0.12	171
C-EQ-5D-VAS Hours a week	0.18 -0.08	0.04 0.66	0.03	172		P-EQ-5D-VAS Hours a week	0.14 -0.28	0.04 0.06	0.05	172
C-EQ-5D-VAS CES-D	0.27 0.31	0.005 0.07	0.05	171		P-EQ-5D-VAS CES-D	0.17 -0.72	0.005 <0.001	0.19	171
C-EQ-5D-VAS Education caregiver	0.19 0.41	0.03 0.70	0.03	172		P-EQ-5D-VAS Education caregiver	0.14 1.25	0.03 0.17	0.04	172
C-EQ-5D-VAS NPI-Q-D	0.21 0.08	0.02 0.54	0.03	171		P-EQ-5D-VAS NPI-Q-D	0.15 -0.49	0.02 <0.001	0.14	171
C-EQ-5D-VAS Age caregiver	0.20 0.09	0.02 0.34	0.03	173		P-EQ-5D-VAS Age caregiver	0.15 -0.09	0.02 0.26	0.04	173
C-EQ-5D-VAS Gender caregiver	0.19 0.43	0.03 0.87	0.03	173		P-EQ-5D-VAS Gender caregiver	0.15 -3.65	0.03 0.10	0.04	173

Abbreviations: CDR, Clinical Dementia Rating scale; MMSE, Mini-Mental State Examination; CIRS-G, Cumulative Illness Rating Scale-Geriatrics; NPI-Q-B/D, Neuropsychiatric Inventory Questionnaire, Behavior/Distress; IDDD, Interview on Daily living activities in Dementia Diagnosis; EQ-5D-VAS, European Quality of life-5 Dimensions Visual Analogue Scale; CES-D, Center for Epidemiologic Studies Depression scale; PMS, Pearlin Mastery Scale; ISB, Inventory for Measuring Social Involvement

CHAPTER 10

VALIDITY STUDY ON DEMENTIA
QUALITY OF LIFE INSTRUMENT (DQI)
IN PROFESSIONALS, DEMENTIA PATIENTS
AND CAREGIVERS

C.J.M. Schölzel-Dorenbos
A.M.M. Arons
J.J.G. Wammes
M.G.M. Olde Rikkert
P.F.M. Krabbe

ABSTRACT

Objectives: Disease-specific health-related quality of life (HRQoL) index measures are urgently needed to advance dementia research. Index measures quantify HRQoL into one single metric figure. A dementia-specific HRQoL index instrument was not available. We designed the Dementia Quality of life Instrument (DQI) and report on validity and feasibility.

Study design and setting: Expert Delphi procedure; survey under 241 dementia professionals; cross-sectional study in 145 mild-moderate dementia patient-caregiver dyads. Setting: outpatient clinics, nursing homes, patient residences. Measurements professionals: ranking/rating of five dementia-specific DQI domains: Memory, Orientation, Independence, Social Activities, Mood; simultaneously rating of nine DQI-derived health states on a visual analogue scale. Measurements patients-caregiver dyads: DQI feasibility and concurrent validity.

Results: All professionals judged the domains to be relevant. Differences in ranking/rating behavior were small. Mood was ranked/rated as most, Orientation as least important health domain. Concurrent validity was moderate. Completion rates for all domains were above 98% for patients and 100% for caregivers on patients.

Conclusions: Professionals judged all domains as relevant. Subgroup differences can be explained by their different working backgrounds. The DQI proved valid and feasible for patients and caregivers. Introducing the DQI Index will advance dementia-related HRQoL measurement, by overcoming the shortcomings of generic and non-index instruments.

Introduction

Dementia is a major public health concern due to its increasing incidence. It is a devastating condition for patients and caregivers. Assessing meaningful treatment benefits is complex. Many researchers state that cognitive response no longer suffices in anti-dementia trials.[1] There is emerging consensus that adding patient-reported outcomes such as health-related quality of life (HRQoL) is warranted.[2] There are two fundamentally different approaches to HRQoL measurement. The first is the standard 'questionnaire' approach, using descriptive or profile instruments.[3] The second is the 'index' approach, using preference-based instruments.[4,5]

Descriptive instruments summarize multiple dimensions of health status and are based on classical test theory.[6] A small set of related items covers the content of various health domains and a score for each dimension is generated. One such frequently used descriptive instrument is the SF-36.[7]

Index measures quantify multiple health domains into one single metric figure. In the case of HRQoL, index measures quantify the desirability of a certain health state.[8] The generated values, variously called utilities, (strength of) preferences, or weights, are often unambiguous; e.g., a value of 1.0 stands for 'perfect health', 0.0 for 'death'. HRQoL values with metric characteristics are especially useful because they provide vital information for health outcome research and economic evaluations. The EuroQol-5 D (EQ-5D) is the most widely used HRQoL index instrument.[9,10] It includes the five dimensions Mobility, Self-care, Usual activities, Pain/Discomfort and Anxiety/Depression.

Based on the extent to which illnesses are covered, both types of HRQoL measures can be categorized into disease-/domain-specific or generic instruments. The first target individual diseases or specific health problems, while generic instruments are more universal and cover general health aspects.

Recently, Riepe et al. concluded that current HRQoL instruments, which have been useful in other contexts, are ill-suited and insufficiently validated to play a major role in dementia research, decision making and resource allocation.[11] They reported that six cost-effectiveness studies, using quality-adjusted life years (QALY) measurements, were unsatisfactory, and that large gaps existed between published measurements of HRQoL and the quality standards required by guidelines. Their conclusion was supported by the consensus statement of the International Psychogeriatric Association that generic HRQoL index measures, such as the EQ-5D, are not validated satisfactorily in dementia and that this called into question previous health economic analyses.[12] The solution seems to be a disease-specific HRQoL index instrument. Such instruments have been developed for various diseases but not for dementia.[13-17] We therefore designed a dementia-specific index instrument, the Dementia Quality of life Instrument (DQI).

The DQI is a classification system based on the conceptual framework of the EQ-5D. However, we substituted the generic EQ-5D domains by more dementia related domains that are better able to describe dementia status. This study presents content evidence to support the construct validity of the DQI by detailed description of the steps that were taken to ensure that the selected domains indeed represented the construct.[18] Additionally, we undertook a survey under dementia professionals on the contents of the instrument. Next, relations to other variables were examined in dementia patients and their informal caregivers by correlating DQI scores with scores from two well-validated quality of life instruments, one generic and one dementia-specific. Finally, we report on the feasibility of the DQI in dementia patients and caregivers.

Methods

Development of the DQI

The following specific features and global constraints were formulated beforehand. 1. Classification of the dementia health states should be based on a limited set of key domains to prevent cognitive overload. 2. Each separate domain should consist of a limited number of levels to facilitate rating. 3. All items should be unequivocally understandable. 4. Consistency throughout domains and levels is mandatory. 5. Responses should be uniform as much as possible. The EQ-5D, for which broadly acknowledged valuation procedures are available to elicit corresponding values, is widely used due to its ease in use: answers to only five questions result in a HRQoL value. The format of the EQ-5D meets the above described criteria and was used as a template.

The first step was to identify the construct and corresponding content. We searched the literature, databases, ProQolid (www.proqolid.com) and systematic reviews on qualifications of HRQoL in dementia, for previously published instruments, and on HRQoL domains considered important in dementia. We also used qualitative and quantitative information from our earlier HRQoL research in Dutch dementia patients and professionals.[19] This generated a pool of potential scale items. The next step was expert evaluation and reduction of items by initiating a Delphi procedure. The selected items were subjected to discussion and challenge within the AD-Euro study group to establish an operational consensus on valid items. The AD-Euro study is a multicentre randomized controlled trial (RCT) that aimed to compare (cost-)effectiveness of post-diagnosis treatment and care-coordination of dementia patients-caregiver pairs by memory clinics versus general practitioners.[20] The experts (N=6; two geriatricians, master of science in nursing, psychologist, psychometrician and epidemiologist),[20] examined the items and selected the best in several rounds. After each round, a summary from the previous round was provided and judged again. Finally, consensus was achieved in a group meeting resulting in a set of domains judged to fulfill content validity criteria.

Participants

Professionals were eligible for this validation study if they were working regularly with dementia patients in the field of diagnosis, care, treatment, coordination, and/or counseling. Professionals were divided in subgroups, namely clinical geriatricians (and residents), elderly-care physicians, nurses/nursing assistants and social workers/psychologists. Participants were recruited after a brief introduction during a national conference and by mail through the secretary of their professional associations.

Additionally, 145 pairs of community-dwelling persons with dementia and their informal caregivers of the AD-Euro RCT were included in the current study, by performing a cross-sectional analysis of data at T=6 months. Patients with a new dementia diagnosis fulfilling DSM-IV-TR criteria and a Clinical Dementia Rating (CDR; 0-3) scale scores 0.5-2 were included: 0.5 for questionable/very mild, 1 for mild, 2 for moderate and 3 for severe dementia.[21,22] Patients were excluded if data collection was impossible, in case of a short life expectancy or awaiting nursing home admission, and in case of a definite indication for specific memory clinic follow-up (e.g. rare dementia diagnosis).

Validation of DQI domains in professionals

The survey consisted of three tasks. The first two were ranking (Task 1) and rating (Task 2) of the domains of the DQI. For Task 1, we asked respondents to choose the order of importance of the domains for dementia patients, from 1 (most important) to 5 (least important domain). For Task 2, respondents rated the value of each separate domain. The assigned rating was between 1 and 10. A value of 1 meant that this domain is totally invaluable, 10 that it is very valuable for dementia patients. Summarized: ranking indicates the order of importance of the five domains. Rating appreciates the value of each domain in itself. Task 3 (valuation) consisted of rating nine dementia health-states, each consisting of the selected DQI domains combined with one out of the levels of severity of impairment per domain. These states were created in such a way that they largely covered the total spectrum of dementia severity. For Task 3 respondents scored the nine states on a visual analogue scale (VAS) with poles ranging from 0 (worst imaginable health) to 100 (best imaginable health).

Validation of DQI outcomes in patients and caregivers

Concurrent validity for the DQI was examined by comparing the scores of the DQI to scores of the generic EQ-5D+C,[23-25] and the dementia-specific Quality of Life-Alzheimer's Disease (QOL-AD) Scale.[26] The EQ-5D+C is an extended version of the EQ-5D with an additional cognitive dimension. The outcome measures were collected through personal interviews. If patients were able to complete the tasks by themselves, they were instructed to do so, if not, a research assistant supported with the completion. Caregivers were given instructions and performed the tasks independently.

Statistical analysis

For data analyses of the professionals, Kruskal-Wallis tests were performed to exa-

mine differences in ranking behaviors. Different rating behaviors for the separate health domains were assessed with one-way ANOVAs. The same analysis was used to explore possible differences in rating behaviors for the assessment of the constructed DQI health states. Additional Tukey post-hoc tests were performed to examine professional sub-group differences.

To examine the concurrent validity, Spearman rank correlations were calculated between DQI and EQ-5D+C,[24,25] and between DQI and QOL-AD.[26] It was hypothesized that the following DQI (higher score=worse HRQoL) versus EQ-5D+C (higher score=worse HRQoL) scores on similar domains would show positive (correlation coefficient >0.2) and significant (P<0.05) correlations: Memory/Cognition, Orientation/Cognition, Independence/Self-care, Independence/Usual activities, Independence/Cognition, Social activities/Usual activities, Mood/Pain-Discomfort, and Mood/Anxiety-Depression. Furthermore, it was hypothesized that the following DQI (higher score=worse HRQoL) versus QOL-AD (higher score=better HRQoL) correlations were negative correlations (>-0.2) and that they would be significant (P<0.05): Memory/Memory, Orientation/Memory, Independence/Physical health, Independence/Ability to do chores around the house, Social activities/Energy, Social activities/Ability to do things for fun, and Mood/Mood. Additionally, it was hypothesized that correlations on patient-data would be lower than caregiver-data, because of the cognitive effects of dementia.

Data were analyzed using SPSS (version 17; SPSS, Inc., Chicago, IL). Patient-caregiver inter-rater agreement was examined by quadratic-weighted Kappa coefficients. Feasibility of the DQI, EQ-5D+C and the QOL-AD were assesed by a missing values analysis. Descriptive statistics were used to examine baseline characteristics.

Results
Design of the DQI
The first step in the design of the DQI resulted in the prototype (Figure 1). By consensus five domains were selected, which were deemed to comply with the formulated constraints and criteria: Memory; Orientation (in time and/or place); Independence (in daily activities); (engagement in) Social activities; and Mood. The present status of the patient on these domains is formulated as a simple statement. The resulting descriptions are combined with one of three severity levels: level 1= no problems; level 2= some problems; level 3= extreme problems. Thus, 11111 represents the best health state, 33333 the worst. Theoretically, this set of five domains and three levels allows for 243 (3^5) different health state descriptions across dimensions relevant in dementia.[9] The second part of the DQI consists of a visual analogue scale (VAS). It is a vertical 200 mm 'thermometer', with 0 indicating the

worst imaginable health state and 100 indicating the best imaginable health state (Figure 2).

Baseline characteristics
The mean age of the 241 professionals varied between 37±8 years (clinical geriatricians) and 48±8 years (elderly-care physicians). Nurses were 42±2 years of age, nursing assistants 39±10, and social workers/psychologists had a mean age of 44±13 years. Almost two-thirds were nursing assistants (N=77) or nurses (N=70). Almost one-third of the participants were physicians: 21% clinical geriatricians and 11% elderly-care physicians. A smaller fraction consisted of social workers/psychologists (together 7% of total). All participants were working in general hospitals or nursing homes. The majority of professionals were female (88% of total, 77-96% of the various subgroups).

The mean age of the patients varied between 80±6 years, 58% was female. Alzheimer's disease was the most prevalent diagnosis (62%), followed by mixed dementia (28%), vascular dementia (6%) and other (4%). Average patient CDR-scores were 1.1 (SD 0.41). Patient-caregiver relationships were defined as partners (57%), children (37%) or other (6%). Caregivers were 66±13 years of age, 71% was female.

Validation of DQI domains in professionals
Task 1: Domain Ranking Task
Ranking of the domains showed for the total group that Mood was ranked as the most important health domain for dementia patients, followed by Independence. Social activities, Memory, and Orientation were judged as less important. However, absolute differences were rather small (Table 1). We found differences in ranking behavior between subgroups of professionals. The mean ranking values varied from 1.74 (more important) for Mood by nursing assistants to 4.31 (less important) for Memory by elderly-care physicians. Significant differences (P<0.05) were found for Memory, Independence, and Social activities. Elderly-care physicians ranked Memory as the least important domain while nurses ranked it as most important. Independence was ranked least important by nursing assistants.

Task 2: Domain Rating Task
The results of the domain rating task of the total group of professionals showed exactly the same ordering as found for the ranking task (Table 1). Scores were highest (most valuable) for Mood (8.5) and lowest for Orientation (7.0). Rating behaviors differed between subgroups for Memory, Orientation and Independence. For Memory and Orientation the differences could be attributed to nurses, who judged these health domains as more valuable. Differences for Independence were fully

caused by nursing assistants, who judged this domain as less valuable. Differences in rating behavior on the other domains were non-significant. Results of comparisons between subgroups on rating as the least or most valuable domain showed significant differences (P<.05) for Memory, Orientation and Independence.

Task 3: Health State Valuation Task

This task showed that DQI state 33333 was scored lowest with a value of 11.3 on the VAS (0-100) whereas DQI state 12211 was scored as the best state with a value of 88.4 (Figure 2). Significant differences in scores between the subgroups of professionals were observed for states 12211, 21122, 12132, 22222, and 11133 (all P<0.05). For all these hypothetical health states, nursing assistants, nurses, or both valued these dementia states as better compared to other subgroups of professionals.

Validation of DQI outcomes in patients and caregivers

The a priori hypothesized DQI versus EQ-5D+C correlations that were significant in both patients and caregivers were: Memory/Cognition, Orientation/Cognition, Independence/Self-care, Independence/Usual activities, Independence/Cognition and Mood/Depression-Anxiety. Patients had an average significant ρ of 0.28 while caregivers had an average significant ρ of 0.44. The difference between these average correlations was significant (P<0.01). Correlations that were hypothesized a priori but were not significant for patients were: Social activities/Usual activities and Mood/Pain-Discomfort. These correlations were significant for caregivers.

A priori hypothesized DQI versus QOL-AD correlations that were significant in both patients and caregivers were: Memory/Memory, Orientation/Memory, Independence/Physical health, Social activities/Energy and Mood/Mood. Patients had an average significant ρ of 0.33, while caregivers had an average significant ρ of 0.36. The difference between these average correlations was not significant (P>0.05). Correlations that were hypothesized a priori but not significant for patients were: Independence/Ability to do chores around the house and Social activities/Ability to do things for fun. These correlations were significant for caregivers. Patient/caregiver inter-rater agreement was slight (K<0.2) for Memory and Independence, fair (K 0.2-0.4) for Orientation and Mood, and moderate (K 0.4-0.6) for Social activities. Feasibility of the DQI was assessed by completion rates. All five domains had a completion rate of above 98.6% for patients, whereas for caregivers the completion rate was 100% in all domains. Patient completion rates for the EQ-5D+C were 97.9% for Self-Care and Cognition, 98.6% for Mobility and Daily Activities and 99.3% for Pain/Discomfort and Anxiety/Depression. Caregivers had a completion rate of 100% in all domains. Patient completion rates for the QOL-AD were 77.1% for Marriage (missing data was marked as 'not applicable'), 98.6% for Friends and Ability to

do chores around the house, 99.3% for Self as a whole and 100% for the remaining domains. Caregivers had a completion rate of 90.9% for Marriage (missing data marked as 'not applicable'), 99.3% for Mood and Ability to do things for fun and 100% for the remaining domains.

Discussion

HRQoL index measures are not validated satisfactorily in dementia. Therefore, previous health economic analyses have been called into question.[11,12] To face the upcoming medical and health economic challenges of dementia, a dementia-specific index instrument seems necessary. This led us to design the DQI. The present study provides evidence for validity and feasibility of the DQI in dementia. Its development was based on a literature search, patient information, and a Delphi procedure among experts. The format was adapted from the widely used generic index instrument EQ-5D. A survey under dementia professionals showed that the selected DQI health domains were considered as relevant and important for HRQoL of dementia patients. Overall rating values were well in the upper range from 1 (not valuable) to 10 (very valuable). Mood was judged as most important and Orientation as least important domain. Small differences between professional subgroups could be explained by their different professional backgrounds, different types of professional contact, and stage of dementia that they face while working with their patients. In more advanced stages of dementia other needs, priorities and symptoms emerge.

Our concurrent validation study, in dementia patients and in caregivers on patients, showed that the DQI (a dementia-specific HRQoL index instrument) correlated moderately with the EQ-5D+C (a generic HRQoL index instrument) and the QOL-AD (a dementia-specific HRQoL instrument). Correlations were highest when the dimensions were (nearly) identical between the instruments. The differences in correlations imply that the DQI indeed provides other information than the EQ-5D. Caregiver correlations were higher than patient correlations. This can probably be attributed to the cognitive effects of dementia. Nevertheless, patient-caregiver inter-rater agreement was fair on average and the results are in line with other instruments used with dementia patients and caregivers.[27,28] The feasibility of the DQI was very high and comparable to that of the EQ-5D+C and the QOL-AD. Nearly all patients and all caregivers were able to complete the instrument. Therefore, we conclude that the DQI performs well for evaluating HRQoL in a mild to moderate dementia population.

To advance the DQI into a standardized two-step disease-specific index instrument for describing and valuing dementia-related HRQoL, our research will now
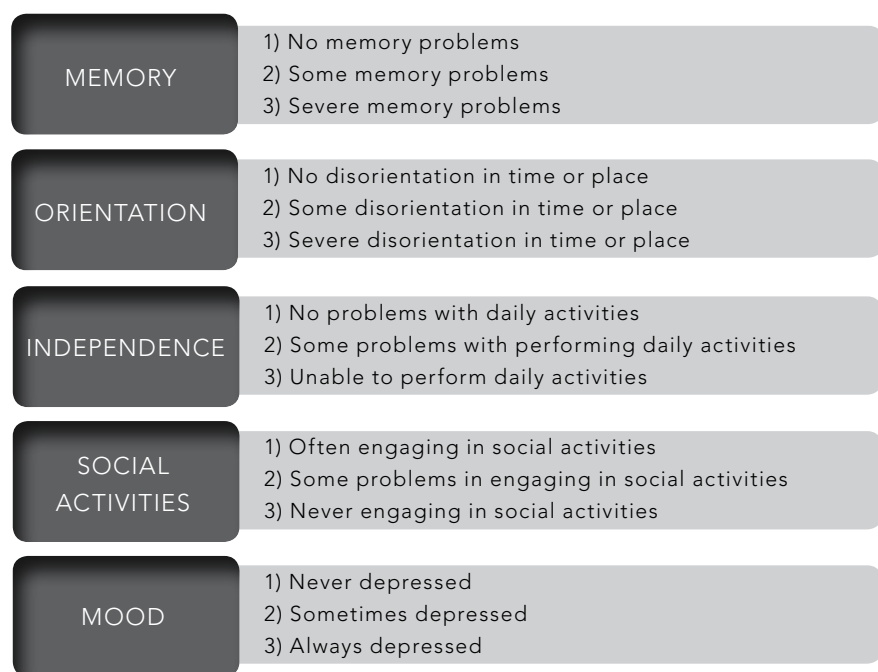
focus on generating values for each of the possible DQI states. These values will be generated in a large general population, with sufficient older persons, to derive an algorithm that converts the five separate DQI domain scores into one single DQI index score. This metric figure will enable unequivocal interpretation of subjective dementia HRQoL states. The DQI Index is the 'raison d'être' for the DQI. The EQ-5D does provide HRQoL values, but is too generic (lacks content validity) to acknowledge the specific problems of dementia. The QOL-AD is dementia-specific, but has been developed to produce a sum score for a set of separate domains. The DQI Index will advance HRQoL measurement in dementia by overcoming both these shortcomings, and therefore provide the field with an outcome measure of added value for evaluation research in dementia.

References

1. Trial designs and outcomes in dementia therapeutic research. London and New York: Taylor & Francis Group, 2006.
2. Banerjee S, Samsi K, Petrie CD et al. What do we know about quality of life in dementia? A review of the emerging evidence on the predictive and explanatory value of disease specific measures of health related quality of life in people with dementia. Int J Geriatr Psychiatry 2009;24:15-24.
3. Schölzel-Dorenbos CJM, Krabbe PFM, Olde Rikkert MGM. Quality of life in dementia patients and their proxies; a narrative review of the concept and measurement scales. In: Preedy VR, Watson RR, eds. Handbook of Disease Burdens and Quality of Life Measures. Heidelberg, Germany: Springer-Verlag 2010;3671-91.
4. Fanshel S, Bush JW. A Health-Status Index and its application to health-services outcomes. Operations Research 1970;18:1021-66.
5. Langenhoff BS, Krabbe PF, Wobbes T et al. Quality of life as an outcome measure in surgical oncology. Br J Surg 2001;88:643-52.
6. Streiner DL, Norman GR. Health measurement scales: a practical guide to their development and use. Oxford: Oxford University Press 2008.
7. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473-83.
8. Krabbe PF. Thurstone scaling as a measurement method to quantify subjective health outcomes. Med Care 2008;46:357-65.
9. Brooks R. EuroQol: the current state of play. Health Policy 1996;37:53-72.
10. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med 2001;33:337-43.
11. Riepe MW, Mittendorf T, Forstl H et al. Quality of life as an outcome in Alz-
heimer's disease and other dementias - obstacles and goals. BMC Neurology 2009;9:47-69.
12. Katona C, Livingston G, Cooper C et al. International Psychogeriatric Association consensus statement on defining and measuring treatment benefits in dementia. Int Psychogeriatr 2007;19:345-54.
13. Buxton MJ, Lacey LA, Feagan BG et al. Mapping from disease-specific measures to utility: an analysis of the relationships between the Inflammatory Bowel Disease Questionnaire and Crohn's Disease Activity Index in Crohn's disease and measures of utility. Value Health 2007;10:214-20.
14. Kirsch J, McGuire A. Establishing health state valuations for disease specific states: an example from heart disease. Health Econ 2000;9:149-58.
15. Lenert LA, Rupnow MF, Elnitsky C. Application of a disease-specific mapping function to estimate utility gains with effective treatment of schizophrenia. Health Qual Life Outcomes 2005;3:57-65.
16. Peacock S, Misajon R, Iezzi A et al. Vision and quality of life: development of methods for the VisQoL vision-related utility instrument. Ophthalmic Epidemiol 2008;15:218-23.
17. Wasserman J, Aday LA, Begley CE et al. Measuring health state preferences for hemophilia: development of a disease-specific utility instrument. Haemophilia 2005;11:49-57.
18. Cook DA, Beckman TJ. Current concepts in validity and reliability for psychometric instruments: theory and application. Am J Med 2006;119:166-75.
19. Schölzel-Dorenbos CJM, Ettema TP, Bos J et al. Evaluating the outcome of interventions on quality of life in dementia: selection of the appropriate scale. Int J Geriatr Psychiatry 2007;22:511-9.
20. Meeuwsen EJ, Melis RJ, Adang EM et al. Cost-effectiveness of post-diagnosis treatment in dementia coordinated by Multidisciplinary Memory Clinics in comparison to treatment coordinated by general practitioners: an example of a pragmatic trial. J Nutr Health Aging 2009;13:242-8.
21. American Psychiatric Association. DSM-IV-TR. Diagnostic and Statistical Manual of Mental disorders, Fourth edition, Text Revision, 2000.
22. Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. Int Psychogeriatr 1997;9:173-6.
23. Hoeymans N, van Lindert H, Westert GP. The health status of the Dutch population as assessed by the EQ-6D. Qual Life Res 2005;14:655-63.
24. Krabbe PF, Stouthard ME, Essink-Bot ML et al. The effect of adding a cognitive dimension to the EuroQol multiattribute health-status classification system. J Clin Epidemiol 1999;52:293-301.

25. Wolfs CA, Dirksen CD, Kessels A et al. Performance of the EQ-5D and the EQ-5D+C in elderly patients with cognitive impairments. Health Qual Life Outcomes 2007;5:33-43.
26. Logsdon RG, Gibbons LE, McCurry SM et al. Assessing quality of life in older adults with cognitive impairment. Psychosom Med 2002;64:510-9.
27. Coucill W, Bryan S, Bentham P et al. EQ-5D in patients with dementia: an investigation of inter-rater agreement. Med Care 2001;39:760-71.
28. Naglie G, Tomlinson G, Tansey C et al. Utility-based quality of life measures in Alzheimer's disease. Qual Life Res 2006;15:631-43.

Figure 1. DQI health states: combinations of 5 health domains and 3 levels of severity

MEMORY
1) No memory problems
2) Some memory problems
3) Severe memory problems

ORIENTATION
1) No disorientation in time or place
2) Some disorientation in time or place
3) Severe disorientation in time or place

INDEPENDENCE
1) No problems with daily activities
2) Some problems with performing daily activities
3) Unable to perform daily activities

SOCIAL ACTIVITIES
1) Often engaging in social activities
2) Some problems in engaging in social activities
3) Never engaging in social activities

MOOD
1) Never depressed
2) Sometimes depressed
3) Always depressed

For example, '12122' corresponds to the dementia health state:

No memory problems
Some disorientation in time or place
No problem wit daily activities
Some problems in engaging in social activities
Sometimes depressed

Figure 2. Valuation: scoring of 9 DQI health states on a visual analogue scale

Best imaginable health state

100
90 — 12211
80 — 21122
12132
70 — 22222
13311
60
50
11133 — 40 — 33232
30
32313 — 20
10 — 33333
0

Worst imaginable health state
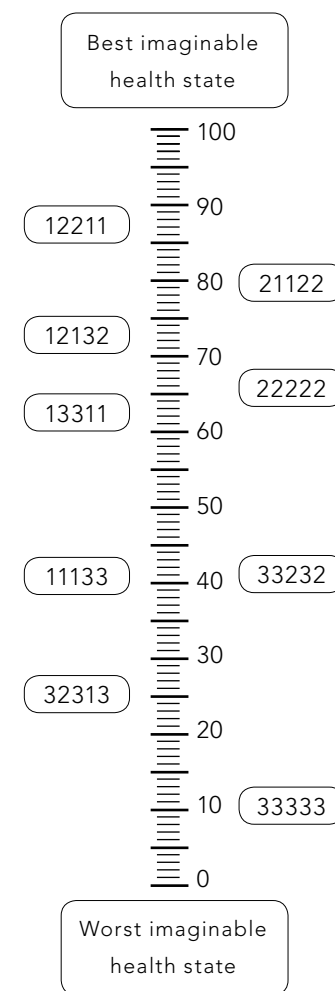
The health states are described by five dementia health domains each combined with one of three severity levels: level 1= no problems; level 2= some problems; level 3= extreme problems

Table 1. Results of ranking and rating of Dementia Quality of life Instrument (DQI) domains by professionals					
Ranking Values; Range: 1 (highest importance) to 5 (lowest importance)					
	Memory	Orientation	Independence	Social activities	Mood
Total group	3.45*	3.70	2.32	3.31	2.22
Nurses	3.23	3.61	2.14	3.34	2.69
Nursing assistants	3.34	3.61	2.86	3.46	1.74
Geriatricians and residents	3.48	4.00	1.98	3.12	2.39
Elderly-care physicians	4.31	3.81	2.04	2.96	1.89
SW[†] and psychologists	3.56	3.39	2.11	3.56	2.44
Rating Values; Range: 1 (not valuable) to 10 (very valuable)					
	Memory	Orientation	Independence	Social activities	Mood
Total group	7.2 (2.0)[‡]	7.0 (1.6)	8.2 (1.5)	7.7 (1.3)	8.5 (1.4)
Nurses	7.9 (1.5)	7.5 (1.4)	8.5 (1.4)	7.8 (1.3)	8.3 (1.4)
Nursing assistants	6.9 (2.3)	6.9 (1.5)	7.5 (1.5)	7.6 (1.4)	8.9 (1.1)
Geriatricians and residents	7.0 (1.9)	6.6 (1.8)	8.4 (1.4)	7.6 (1.1)	8.2 (1.4)
Elderly-care physicians	6.7 (1.8)	6.9 (1.4)	8.4 (1.6)	7.7 (1.5)	8.8 (1.0)
SW and psychologists	7.4 (1.7)	7.5 (1.5)	8.6 (1.6)	7.7 (1.0)	8.6 (1.2)

* Mean; † Social workers; ‡ Mean (Standard Deviation)

CHAPTER 11

SUMMARY OF RESULTS

DISCUSSION

SUMMARY

The aim of this thesis is to translate the theoretical overarching concept of quality of life into practical implications for dementia research and care planning. We recap previous and new knowledge and end with future plans and final remarks.

Quality of life in dementia. Theoretical part

Chapter 2 discusses definitions of quality of life and the methods of assessment. It explains the phenomenon of response shift, a term for the decrease in negative self-reports by dementia patients as the disease progresses. It shows that dementia caregiving affects quality of life of caregivers and recommends the use of quality of life as an endpoint in dementia intervention studies. Chapter 3 describes the results of a literature study on relevant domains of quality of life in different settings. Four instruments best represented domains important to patients, and domains pertinent to professional caregivers. Two are self-rating instruments: the Schedule for the Evaluation of Individual Quality of Life (SEIQoL), applicable in mild dementia, measuring individual quality of life of patient and informal caregiver, and the Quality of Life-Alzheimer's Disease Scale (QOL-AD), which can be applied up to moderately severe dementia. Both enable measurement of quality of life of patients as well as informal caregivers. For patients with advanced dementia receiving residential care, the observational instruments Qualidem and Discomfort scale-Dementia of Alzheimer Type (DSDAD) are recommended. Care-type, care-setting, severity of dementia, and the specific domains of an intervention determine which instrument is most appropriate in a specific situation. Chapter 4 presents available needs assessment instruments for dementia patients and caregivers, explores the interaction between unmet needs and quality of life, and relates these needs to individual goal setting instruments and Maslow's Hierarchy of needs model. Domains of unmet needs and quality of life overlap. Our Hierarchy Model of Needs in Dementia (HMND) offers a new theoretical framework to address the interplay between meeting of needs and improving of quality of life in dementia. By identifying unmet needs in dementia-research, and focusing on unmet needs in dementia-care, much can be done to improve quality of life. Chapter 5 addresses issues that threaten the accuracy of quality of life assessment. It describes factors that hamper measurement procedures in dementia and frail elderly patients. It illustrates reasons for differences between self-report and proxy-rating, such as the subjective nature of the concept, the own experience of living with dementia, and the effect of changing intellectual and other capacities. When interpreting quality of life outcomes in dementia, researchers must also take into account stage of disease, the disability paradox and response shifting. Altogether the relation between (severity of) dementia and HRQoL is neither simple nor direct. As patient-reported outcomes become more established, these measurement issues need to be addressed.

Quality of life in dementia. Empirical part

Chapter 6 reports the results of a pilot study of quality of life measurement of twelve patients with mild to moderate Alzheimer's disease (AD) and their caregivers with the Schedule for the Evaluation on the Individual Quality of Life (SEIQoL). The SEIQoL measures individualized quality of life by taking into account the relevant determinants for a particular individual. Persons rate five areas in life most important to their quality of life. A multiple regression analysis programme developed for the purpose then calculates the relative contributions of each area to the overall quality of life. Next the researchers computed the SEIQoL Index score, validity and reliability. One patient was unable to complete the interview. The remaining (8 women, 3 men, age 71.3 years) had a mean SEIQoL Index score (range 0-100) of 79.9, which is comparable to healthy Dutch elderly. The caregivers (10 spouses, 2 daughters; mean age 67.4 years) on the other hand had a lower SEIQoL Index score: 62.2. Validity and reliability were good for both groups. Thus, caregivers experienced a significantly (p<0.5) lower quality of life than either AD patients or healthy Dutch elderly. Chapter 7 presents the results of a cross-sectional study of a sample of 97 spousal caregivers of patients with mild to moderate AD. The SEIQoL assessed caregiver quality of life. The three caregiver burden scales that were used are: self-perceived pressure from informal care scale (EDIZ); Zarit Burden Interview scale for burden of caregivers (ZBI); and SRB (Self-Rated Burden scale) for rating of subjective feeling of burden on a visual analogue scale. The mean SEIQoL score of the spousal caregivers was 69±15. These scores were compared to historical control scores of healthy elderly (76±11) and AD patients (80±15) and were significantly (p<0.05) lower. The most important quality of life domains were condition of patient (31%) and marriage (26%). Spouses perceived moderate levels of burden according to their SRB, EDIZ and ZBI scores. The multiple regression analysis indicated factors that best predict quality of life. In this sample, patient cognition was a significant predictor of caregiver quality of life. Burden, measured with the ZBI, was significantly negatively correlated with caregiver quality of life.

It is not known how frequently quality of life is used as outcome measure at a stage where there is no formal obligation of registration authorities to do so. Chapter 8 systematically reviews how often quality of life measures are used as endpoints in pharmacological and non-pharmacological intervention randomized controlled

trials (RCTs) in MCI and dementia. In 117 pharmacological and 108 non-pharmacological RCTs quality of life was assessed in only 4.4% of the RCTs. We emphasize that quality of life measures should be applied more often in clinical trials because they reflect the aims of palliative care and provide transparent information about patient's and caregiver's treatment benefits. Chapter 9 presents the results of a cross-sectional study in 175 pairs of newly diagnosed mild-moderate stage dementia patients and their principal caregivers. Since disease-modifying therapies for dementia are still lacking, quality of life is an important palliative outcome. Better understanding of the key determinants of quality of life can help to improve dementia care. Associations between patient and caregiver quality of life were analyzed using linear regression analysis. There was a modest but significant correlation (univariable r=0.17, p=0.027) between health-related quality of life (HRQoL) assessed with the EQ-5D of patients and caregivers, but not between dementia-related quality of life assessed with the QOL-AD (univariable r=0.07, p=0.353). Especially the addition of patients' mood diminished the association between HRQoL of patients and caregivers. We also investigated which were the individual determinants for patients' and caregivers' HRQoL. Caregivers' mood, mastery, social involvement and distress (univariable r=0.40, 0.38, 0.31 and 0.33) were more important than patient determinants (univariable r=0.16 for mood and r=0.28 for behavioral symptoms) in explaining caregivers' quality of life. Patients' quality of life depended on their need for help from others, severity of dementia, mood and co-morbidity (univariable r=0.17, 0.16, 0.44 and 0.27), and not on caregiver determinants. In sum, quality of life of dementia patients and caregivers were only modestly associated. HRQoL of each depended particularly on their own personal characteristics. Our main message is that quality of life in dementia care may be best served if the individual determinants of health status of patients as well as informal caregivers are specifically addressed. Chapter 10 deals with the urgent need for a dementia-specific quality of life measure to advance the field of clinical research. The solution appears to be a dementia-specific index instrument to quantify quality of life into one single metric figure. This type of measure is not yet available. We therefore developed the Dementia Quality of life Instrument (DQI), which can be used in medical practice, research, and policy making. The DQI has a format analogous to the widely applied generic index instrument EQ-5D. We report on the design and construct validity of the prototype. The important aspects of quality of life were drafted on the basis of existing literature and on statements made by dementia patients, by caregivers and by health professionals in a variety of settings. The following five health domains are relevant for dementia: 'memory', 'orientation', 'independence', 'engagement in social activities' and 'mood'. The present status of the patient on these domains is formulated as a statement, with three levels of increasing severity. The resulting 243 (3^5) different states combine descriptions of each of five domains with one of three severity levels: 11111 represents best state, 33333 represents worst state. We carried out a cross-sectional study in dementia patient-caregiver pairs and a survey of dementia professionals. In the patients and caregivers sample feasibility and concurrent validity of the DQI were examined. The professionals ranked and rated the five dementia-specific DQI health domains, and simultaneously rated nine DQI-derived health states on one visual analogue scale. Completion rates for all five domains were above 95% for patients and 100% for caregivers. Concurrent validity was acceptable. Professionals judged the DQI domains to be relevant, and 'mood' as the most important one. Thus, the DQI proved feasible and valid.

Previous knowledge on the topic of this thesis

Most people regard dementia as a devastating end of life. Hugo Claus, a contemporary Flemish author, suffering from Alzheimer's disease, expressed this opinion in March of 2008. He deliberately chose to end his own life by euthanasia. Quality of dying has received much attention recently (www.eiu.com). Both quality of dying and quality of life are important for good palliative care. People with progressive chronic diseases often report a higher quality of life than expected, probably because of the way they adapt and cope. Nevertheless, dementia profoundly threatens the quality of life of patients as well as their family and caregivers. Persons with dementia mention happiness, sadness and loneliness as key areas for the quality of their life. Feeling attached, accepted and understood has a positive effect on quality of life, as well as the presence of a partner, social relationships and access to activities. Many patients report physical and mental health as essential factors.[39;40] Dementias are more complex than other chronic conditions such as hypertension and osteoarthritis. Dementias have multiple etiologies, especially when familial Alzheimer's disease is compared to non-familial, or early onset dementia to late onset dementia.[41-43] Given this complexity, there is emerging consensus that patient reported outcomes such as quality of life are warranted for comprehensive outcome measurement. Quality of life assessment demonstrates whether interventions are perceived as meaningful by patients and caregivers. However, the link between symptoms and quality of life is not clear, simple or predictable.

Many clinicians consider quality of life the most relevant global outcome measure as long as dementias cannot be cured. Nevertheless quality of life is rarely used as endpoint in research practice. In our research, as reported in this thesis, we notice the lack of definitions of quality of life, or its gold standard, and the challenges of its measurement. Furthermore, decreased self-reporting capabilities ge-

nerally make ratings more cumbersome. Measurement problems associated with anosognosia,[44;45] response shift,[30;46-48] and bias of proxy-rating have previously been proven.[23;36;38] Quality of life is regarded as a problematic outcome measure, especially by the regulatory authorities such as Food and Drug Administration (FDA) and European Medicines Agency (EMEA).

What does this thesis add to existing knowledge?

This thesis provides an overview of current knowledge about methodological quality of life issues and about measurement problems in frail and demented elderly persons. It is important to include both generic and dementia-specific quality of life indicators, because factors outside the domain dementia are also very important for both people with dementia and their caregivers.

Quality of life is an important topic in geriatric medicine including dementia care. This is true in considering it an endpoint as well as a starting point of treatment, counseling, and selection and prioritization of interventions. Besides employing quality of life instruments to evaluate interventions, quality of life can also be used as a guide to the selection of the type of clinical intervention based on the preferences of the individual. Providing choices to patients has become a tenet of good quality clinical care.

Efficiency studies in macroeconomic research enable policymakers to obtain patient oriented relevant data for evidence based policy planning. The newly developed DQI has the potential to become a more accurate quality of life outcome measure for trials and economical decision making. The DQI can become the first dementia-specific HRQoL index measure allowing overall quantification of relevant health domains into one single figure.

Quality of life analysis, in clinical research, may contribute to better targeted dementia care for patients and caregivers. The concept of quality of life provides the opportunity for needs based and goal-oriented dementia care. Dementia is still an incurable disease. This justifies a palliative policy. According to the WHO definition improving quality of life of patients and informal caregivers, and addressing their needs, are a specific part of palliative care. We introduced a theoretical framework to address the interplay between meeting of needs and consequent improvement of quality of life in dementia: the Hierarchy Model of Needs in Dementia (HMND; see chapter 4). We encourage a goal-oriented treatment based on analysis of needs of patient and caregiver pairs. The method will be described in the section on future plans.

We showed that caregivers experienced a worse quality of life than healthy elderly and patients with mild to moderate Alzheimer's dementia (see chapter 7). Based on the principles of palliative care and the results described in this thesis, we advise clinicians that caregivers should be supported as well, to prevent caregiver burnout and unnecessary early institutionalization of dementia patients.

During the course of dementia a great deal of heterogeneity exists regarding the manifestation of, and the coping with, cognitive and non-cognitive symptoms, also dependent on type of caregiver and type of dementia. This means that dementia care should be individualized. Unfulfilled needs of patients as well as caregivers play an important role in decreasing quality of life. By identifying unmet needs in dementia research, and focusing on unmet needs in dementia care, much can be done to improve quality of life of both patients and caregivers. Preparation of patients and caregivers to participate with professionals in making the best possible treatment decisions, consistent with realistic goals of patients and caregivers, will enable optimal dementia care. In the future plans section of this thesis we introduce Dementia Personalized Care Planning (DPCP) as a practical tool.

Based on our data and the determinants of quality of life in patients and caregivers (chapter 9), an important focus for patient care is adequate treatment of co-morbidity and mood, whereas the main focus during caregivers' guidance is to strengthen their sense of mastery and to treat any caregiver depression. Longitudinal research is needed to confirm this. Based on this data the original conceptual model of quality of life (figure 2, page 23) was converted into a practical simplified model of health outcomes in dementia with only the relevant determinants (figure 3).

Figure 3. Empirical model of health outcomes in dementia

PATIENT

OBJECTIVE
Co-morbidity
Mood
Behavior
Functional performance

SUBJECTIVE
Quality of life
Health status

CAREGIVER

OBJECTIVE
Social involvement
Mood
Distress
Mastery

SUBJECTIVE
Quality of life
Health status
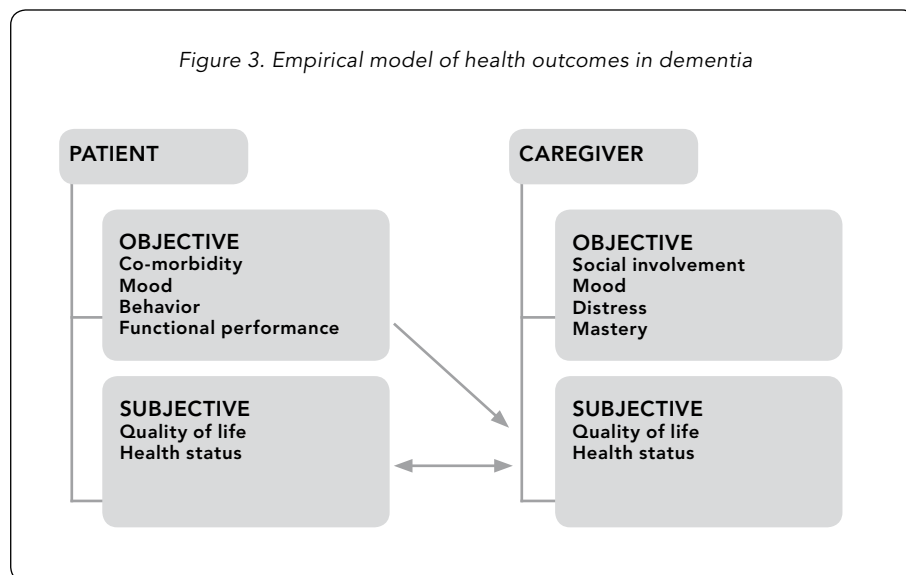
The explicit inclusion of quality of life of patients and caregivers into one single model is a new approach to quality of life understanding. In our cross-sectional analysis quality of life of patients and caregivers is only modestly associated and both are primarily dependent on their own personal determinants. The consequence is that caregivers should be considered and treated like the second patients. High quality clinical dementia care is combined care for patients and caregivers!

Recently a broad general intervention program by memory clinics showed no benefit in activities of daily living in patients with Alzheimer's disease and may, therefore, have little public health value.[49] Apart from the question whether this study targeted the appropriate outcome, results may likely also be explained by the fact that dementia is a complex and heterogeneous condition. Consequently, to have a beneficial effect on care management, interventions must target the specific and individual needs of patients, as well as caregivers. To advance the field of clinical dementia care we propose Dementia Personalized Care Planning (DPCP), as described in the future plans.

Future plans beyond this thesis

Involving quality of life in research and treatment of dementia is necessary to do justice to the increasing health, societal and economical problems associated with dementia. Quality of life evaluation plays a key role in delivering successful dementia care, and in assessing the efficacy and efficiency of disease-modifying interventions once they become available. Research in quality of life can employ quantitative and qualitative methods. Quantitative methods have value in facilitating reproducibility in clinical

research studies, but have a concomitant risk of losing the subtlety and distinctions experienced by patients living with health problems. Qualitative methods offer the opportunity for studying the lived experience of a disease and its treatment.[50] The conclusion of this thesis is that the role of quality of life measurement in research, decision making and resource allocation is still insufficient. Inclusion of quality of life, be it quantitative or qualitative, is necessary to meet the upcoming medical, social and economic challenges associated with increasing prevalence of this still incurable disease. Frequency and burden of informal care will increase with the rising number of dementia patients and declining availability of professional care. This adds to the necessity to involve quality of life of caregivers in successful clinical care of the dementia patient. A communication style in which healthcare professionals acknowledge the needs of both parties and address physical health problems and psycho-social issues of patients as well as caregivers will contribute to a higher satisfaction and better health outcomes.

How can we involve quality of life qualitatively and quantitatively in dementia care and research? At this time, benefits can be gained by explicitly including quality of life assessment and treatment in clinical care for dementia patients and caregivers. For the future we intend to further develop and introduce Dementia Personalized Care Planning (DPCP) to realize the qualitative improvement and the Dementia Quality of life Instrument (DQI) to achieve the quantitative improvement.

Our DPCP will be based on the choices and choosing (C-C) model of Gurland et al.[3;51;52] This model introduced a science base for understanding and guiding interventions that can assist people to achieve their quality of life goals. The C-C process is the personal management of accessing choices and choosing among them. This leads to rational and person-specific clinical interventions. People are then in a position to participate, with clinical help and guidance, in the relief of their distress.[53] The expected result is improved quality of life. DPCP is a pivotal procedure to guide treatment based on personal needs and goals of both patients and caregivers. DPCP will be based on a standard protocol according to the C-C model, supplemented with structured eliciting of realistic most urgent problems and needs that can be converted into corresponding concrete goals. These goals are used for care planning, treatment and evaluation during follow-up visits, to enhance the chance of successful combined care for patients and caregivers. In clinical practice the DPCP gives valuable information that can indicate areas in which patients and caregivers are most affected and help practitioners in making the best choices in patient care. DPCP has the potential to become a novel tool for post-diagnosis treatment by multidisciplinary memory clinics. Based on former research, the 19 most frequently occurring needs and quality of life domains in dementia were identified and translated into Dementia Need Cards. Dyads of dementia patients and caregivers will be offered 20 cards, including a 'wild card' to

nominate one personal need not provided by the predefined ones. The dyads subsequently select three need cards most relevant for their situation at this moment. The needs are converted into corresponding concrete goals, on which realistic milestones are set. These goals and milestones may be applied for care planning and treatment in the upcoming half year, and for evaluation during regulatory memory clinic visits. This approach enables individualized post-diagnosis dementia care, may enhance efficient use of scarce resources, promote quality of life of patients and caregivers, and add to prevention of caregiver burnout and unnecessary institutionalization.

And the next specific research step concerning the DQI is to conduct a large general population study to derive an algorithm that converts the five separate DQI domains scores into one overall metric health-related quality-of-life value, the DQI Index. This process is called valuation. A grant from the Netherlands Organization for Health Research and Development provides funds for the study which has recently started. The DQI Index will enable unequivocal interpretation of subjective dementia-related quality of life scores. The valuation system and DQI will together form the first dementia-specific health-related quality of life index instrument, applicable for evaluation of efficacy and efficiency of large-scale intervention studies in dementia.

Final remarks

Quality of life deserves a leading role in dementia treatment. The challenge lies in convincing professionals and decision-makers to recognize the integrated burden of the disease, including its interaction with co-morbidities and burden on caregivers. A paradigm shift in thinking about dementia is necessary: it is important to recognize quality of life as the start- and endpoint of the palliative treatment of this still incurable chronic disease.

This thesis is intended to contribute to the awareness for quality of life in all fields of dementia research and clinical practice. This will be beneficial for both patients and caregivers. Therefore, and from deep respect for the daily struggle of all dementia patients and their caregivers, this thesis is dedicated to all persons confronted with dementia.

NEDERLANDSE SAMENVATTING

Achtergrond

Steeds meer mensen worden oud. Sommige mensen lijden daaronder: oud worden wil iedereen, oud zijn wil niemand. Ouder worden kan gepaard gaan met achteruitgang van lichamelijke en/of geestelijke functies, met verlies van onafhankelijkheid, sociale contacten en rollen, gezondheid, geheugen, en de hierbij horende rouw. Veel mensen beschouwen dementie als een afschrikwekkend levenseinde en als bedreiging voor de kwaliteit van hun laatste levensfase. De schrijver Hugo Claus maakte dit in 2008 heel duidelijk door, na een persoonlijke afweging van zijn (verwachte) kwaliteit van leven, in het beginstadium van de ziekte van Alzheimer bewust voor euthanasie te kiezen. Kwaliteit van leven en kwaliteit van sterven liggen dicht bij elkaar. Beide zijn belangrijke onderdelen van de palliatieve zorg die hoort bij een nog steeds onbehandelbare ziekte als dementie. In dit proefschrift bespreken wij definitie, theorie en dagelijkse praktijk van kwaliteit van leven bij dementie. Wij stelden de volgende onderzoeksvragen: welke valkuilen en problemen zijn er bij het meten van kwaliteit van leven bij dementie? Wie moet de kwaliteit van leven van mensen met dementie beoordelen? Welke meetschalen kunnen het best worden gebruikt? Ook brengen we verslag uit over ons eigen onderzoek en mogelijke nieuwe ontwikkelingen.

Definitie en meten van kwaliteit van leven

Er bestaat geen overeenstemming over wat kwaliteit van leven precies is. Kwaliteit van leven is niet direct observeerbaar, maar uit zich in gedachten, gedrag en emoties. Ook het meten ervan is moeilijk. Bovendien wisselt kwaliteit van leven, zowel binnen één persoon als tussen mensen. De beste beoordelaar is de betrokkene zelf. Dementiegerelateerde kwaliteit van leven is het deel van kwaliteit van leven dat wordt bepaald door de dementie. Bij twijfel over het oordeelsvermogen van mensen met dementie kan men een ander vragen hun kwaliteit van leven te beoordelen. Buitenstaanders kunnen dit echter slechts indirect afleiden, bijvoorbeeld uit iemands gedrag. Onderzoek laat zien dat mantelzorgers de kwaliteit van leven van mensen met dementie slechter vinden dan de betrokkenen zelf (zie de alinea hieronder).

Het is belangrijk om onderscheid te maken tussen oorzaken van kwaliteit van leven en gevolgen van kwaliteit van leven. Somberheid kan bijvoorbeeld een gevolg zijn van een slechte kwaliteit van leven. Het verschil is niet altijd vast te stellen, maar is wel van belang. Oorzakelijke factoren kunnen namelijk soms worden beïnvloed of behandeld om de kwaliteit van leven te verbeteren.

Theorie

Mensen met dementie ervaren soms een betere kwaliteit van leven dan buiten-

staanders verwachten én dan zijzelf tevoren hadden (kunnen) voorzien. Dit staat bekend als de 'disability paradox': het verschijnsel dat mensen met een ernstige chronische ziekte hun kwaliteit van leven goed vinden, terwijl anderen dat leven onwenselijk achten. Het is een vorm van aanpassing en acceptatie die het onderwerp euthanasie bij dementie nog ingewikkelder maakt. Dit verschijnsel uit zich bij het meten van kwaliteit van leven als zogenaamde 'response shift'. Response shift is het veranderen van de eigen waardering van kwaliteit van leven door herijking en wijziging van prioriteiten of concepten.

Dit alles, en het feit dat dementie meerdere oorzaken kan hebben, maakt dementie een complexe ziekte. Dementie heeft nog meer dan andere ziekten invloed op allerlei facetten van het leven. De opvatting wint dan ook terrein dat juist bij een nog niet te genezen ziekte als dementie mensen zelf moeten bepalen wat het belangrijkste behandeldoel is. Kwaliteit van leven meting is een goede manier om aan te tonen of een behandeling betekenisvol is voor mensen met dementie en mantelzorgers. Het verband tussen ernst van ziekte en kwaliteit van leven is echter niet altijd duidelijk voorspelbaar. Bovendien wordt kwaliteit van leven ook bepaald door andere factoren die niets met de ziekte te maken hebben, zoals inkomen of woonomstandigheden.

Kwaliteit van leven is een belangrijke maar moeilijke uitkomstmaat. Het is een subjectief begrip, dat objectief moet worden gemeten. Bovendien bestaat er geen overeenstemming over wat kwaliteit van leven nu precies inhoudt. Kwaliteit van leven(meting) is complex. Daarom is een duidelijk theoretisch model nodig.

Meetpraktijk kwaliteit van leven

Dit proefschrift geeft een overzicht van meetinstrumenten en meetproblemen bij kwetsbare ouderen en dementie. Wij hebben eerst onderzocht welke gebieden belangrijk zijn voor mensen met dementie en of we die gebieden ook terugvinden in bestaande meetschalen. Vier instrumenten leken het meest geschikt. Dit waren twee zelfbeoordelingschalen: voor milde dementie de Schedule for the Evaluation of Individual Quality of Life (SEIQoL) en voor matig ernstige dementie de Quality of Life-Alzheimer's Disease Scale (QOL-AD). Beide kunnen kwaliteit van leven van zowel patiënten als mantelzorgers meten. Bij ernstige dementie zijn observatieschalen beter bruikbaar: de Qualidem of de Discomfort scale-Dementia of Alzheimer Type (DSDAT).

Dementie kan zelfbeoordeling moeilijker maken door afname van geheugen en oordeelsvermogen. Maar ook beoordeling door mantelzorgers is problematisch. Zij ervaren de dementie niet zelf, waardoor hun aanpassingsproces aan de ziekte anders verloopt. Informele mantelzorgers vinden de kwaliteit van leven van mensen met dementie slechter dan de betrokkenen zelf. Waarschijnlijk zijn mantelzorgers

door de zorgtaken zodanig (over)belast dat dit hun oordeel negatiever maakt. Maar ook beoordeling door professionele verzorgers heeft nadelen en wordt bijvoorbeeld beïnvloed door tevredenheid over het werk. Zelfbeoordeling van kwaliteit van leven bij dementie heeft dus de voorkeur. Bij longitudinaal onderzoek, waarbij men mensen meerdere jaren volgt en onderzoekt, is gelijktijdige beoordeling door patiënten zelf en hun mantelzorgers een optie. Hiermee wordt voorkomen dat er onvoldoende gegevens over het beloop zijn als de dementie erger wordt.

Onderzoek naar kwaliteit van leven bij dementie

De AD-Euro studie is een Nederlands onderzoek naar doelmatigheid van zorg en kwaliteit van leven bij mensen met milde tot matig ernstige dementie en hun mantelzorgers. De studie is uitgevoerd door Alzheimer Centra en geheugenpoliklinieken. De helft van de mensen werd na het stellen van de diagnose gedurende een jaar behandeld door de eigen huisarts en de andere helft door de geheugenpolikliniek. Uit de eerste analyse bleek dat er maar een beperkte relatie was tussen kwaliteit van leven van patiënten en mantelzorgers. Kwaliteit van leven van beiden werd ook voornamelijk bepaald door hun eigen kenmerken. Voor patiënten waren dit ziektelast en stemming, voor mantelzorgers stemming en het gevoel de situatie te beheersen. Op basis van deze resultaten pasten we het model voor kwaliteit van leven bij dementie aan (zie figuur 3, pagina 172).

Het geven van mantelzorg bij dementie leidt vaak tot slechtere gezondheid en welzijn. Er bestaat grote variatie in optreden van en omgaan met dementiesymptomen.[4] Dit hangt ook af van het type zorgverlener en het type dementie. We toonden in eerder onderzoek aan dat mantelzorgers hun kwaliteit van leven slechter vinden dan gezonde ouderen en mensen met dementie (hoofdstuk 7). Kwaliteit van leven van de mantelzorgers wordt dus evenzeer beïnvloed. Dit kan leiden tot mantelzorger burnout en onnodig snelle verpleeghuisopname. Aandacht voor kwaliteit van leven van mantelzorgers is daarom belangrijk! Ons onderzoek geeft aan op welke factoren speciaal gelet moet worden.

Bij het onderzoeken van kwaliteit van leven is het gebruiken van de juiste meetschaal erg belangrijk. Die meetschaal moet ook geschikt zijn voor het berekenen van de kosteneffectiviteit van een behandeling. Dit gebeurt met specifieke instrumenten die iemands gezondheidstoestand op bepaalde gebieden met enkele vragen in kaart brengen. Die gebieden zijn bijvoorbeeld gezichtsvermogen, mobiliteit, geheugen, emotie en pijn. Hieraan wordt vervolgens een waardering toegekend en dat is de utiliteit. Dit is meestal een getal tussen nul en één, waarbij nul staat voor dood en één voor perfect gezond.

De DQI (Dementia Quality of life Instrument) die in dit proefschrift wordt beschreven is een dementiespecifiek waarderingsinstrument. Het brengt de gezondheidstoestand dementie in kaart. Dit type meetinstrument bestond wel voor andere ziekten maar nog niet voor dementie. Het invullen van de DQI is niet moeilijk. We hebben de betrouwbaarheid ervan getest in de AD-Euro studie. Ook vroegen we dementieprofessionals naar hun oordeel over de inhoud. De resultaten hiervan zijn beschreven in hoofdstuk 10. De volgende stap is het uitdrukken van de Nederlandse waardering van de gezondheidstoestand dementie gemeten met de DQI. ZonMW heeft hiervoor een subsidie verstrekt. Binnenkort begint een onderzoek onder een deel van de Nederlandse bevolking. Daarna kan met moderne analysetechnieken een algoritme (computerrekenprogramma) worden geconstrueerd dat de individuele scores op de DQI omrekent naar de maatschappelijke waardering ervan. Met de combinatie van deze waardering en de tijdsduur van de betreffende gezondheidstoestand worden de zogenoemde 'kwaliteit-van-leven gecorrigeerde levensjaren' (QALYs) berekend. In de afgelopen jaren zijn QALYs voornamelijk uitgerekend met algemene meetschalen zoals de EQ-5D. In de toekomst kan de DQI hiervoor mogelijk worden gebruikt bij dementieonderzoek. Dit kan de maatschappelijke last van dementie in een getal uitdrukken. Het is dan ook mogelijk om de resultaten van verschillende behandelingen met elkaar te vergelijken.

Hoe nu verder?

Recent bleek uit een Frans onderzoek, de PLASA studie, dat het functioneren op het gebied van activiteiten van het dagelijks leven van mensen met de ziekte van Alzheimer niet verbeterde na behandeling door geheugenpoliklinieken.[49] Deze studie vergeleek twee vormen van begeleiding door geheugenpoliklinieken: zeer gestructureerd versus ongestructureerd. In de AD-Eurostudie vergelijken wij twee vormen van ongestructureerde gebruikelijke behandeling, namelijk die door geheugenpoliklinieken en huisartsen.

Dementie is een complexe en heterogene ziekte. Wij pleiten er dan ook voor dat de behandeling wordt afgestemd op de individuele behoeften van mensen met dementie en hun mantelzorgers. Het 'choice en choosing' (C-C) model geeft toegang tot mogelijke keuzen en het hieruit kunnen kiezen. Het kan mensen helpen bij het bereiken van hun kwaliteit van levendoelen.[3;51;52] Dit sluit aan bij ons theoretische model: het Hierarchy Model of Needs in Dementia (HMND; zie hoofdstuk 4). Door signaleren van onvervulde behoeften en proberen deze te verbeteren, kan veel worden gedaan voor de kwaliteit van leven van patiënten en mantelzorgers. Goede zorg (h)erkent de behoeften van beide partijen. Gepaste behandeling van patiënten en mantelzorgers draagt bij aan verbetering van kwaliteit van zorg en leven. Om dit in de praktijk te verwezenlijken kan Dementia Personalized Care Planning

(DPCP) worden gebruikt. Dit is een methode om de behandeling af te stemmen op persoonlijke behoeften en realistische doelen van patiënten en mantelzorgers. Wij willen DPCP in de praktijk gaan gebruiken. Op grond van eerder onderzoek zijn de 19 meest voorkomende behoeften en gebieden van kwaliteit van leven geïdentificeerd en omgezet in 'Dementia Need Cards'. Uit deze kaarten kiezen patiënten en mantelzorgers er samen drie die het belangrijkst zijn voor hun huidige situatie. Daarna worden concrete en haalbare doelen afgesproken. Die worden gebruikt voor de planning van zorg en behandeling in de komende periode. Deze aanpak vergroot de kans op inhoudelijke verbetering van de dementiezorg. Door gericht te proberen onvervulde behoeften te verminderen kan kwaliteit van leven worden verbeterd.

Opdracht

De conclusie van dit proefschrift is dat kwaliteit van levenmeting nog niet zover is dat het een hoofdrol kan spelen bij onderzoek, behandeling en besluitvorming. Maar het betrekken van kwaliteit van leven bij onderzoek en behandeling van dementie is onvermijdelijk om de medische, sociale en economische uitdagingen van het toenemende aantal mensen met deze nog steeds ongeneeslijke ziekte het hoofd te bieden. Kwaliteit van leven, kwaliteit van zorg en kwaliteit van sterven staan dicht naast elkaar en er is een omslag in dementiezorg nodig. Zorg kan pas succesvol zijn als deze zich richt op het vervullen van individuele behoeften en op factoren waarvan door onderzoek is aangetoond dat ze belangrijk zijn voor kwaliteit van leven. Gemiddeld zijn bij de zorg voor één demente oudere bijna 4 mantelzorgers betrokken. De mantelzorglast wordt groter door het toenemende aantal mensen met dementie en de afnemende financiële middelen voor professionele zorg. Begeleiding en als het nodig is behandeling van mantelzorgers moet dus een nadrukkelijk onderdeel van dementiezorg worden.

Méér aandacht voor levenskwaliteit is belangrijk om op de juiste manier het hoofd te bieden aan de medische, sociale en economische uitdagingen van dementie. Bovendien moet begeleiding van mantelzorgers een routinematig en dus normaal vergoed onderdeel van dementiezorg worden. Dit zal bij afname van de beschikbare beroepsbevolking zeker een doelmatige investering blijken!

Hopelijk draagt dit proefschrift bij aan bevordering van aandacht voor kwaliteit van leven en zorg bij dementie. Zowel patiënten als mantelzorgers hebben hier recht op. Het proefschrift wordt dan ook opgedragen aan alle mensen die worden geconfronteerd met dementie.

APPENDICES

LIST OF REFERENCES

1. McKhann G, Drachman D, Folstein M et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984; 4:939-44.
2. Dubois B, Feldman HH, Jacova C et al. Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS-ADRDA criteria. Lancet Neurol 2007;6:734-46.
3. Gurland BJ, Gurland RV. The choices, choosing model of quality of life: description and rationale. Int J Geriatr Psychiatry 2009;24:90-5.
4. Streiner DL, Norman GR. Health measurement scales: a practical guide to their development and use. Oxford: Oxford University Press, 2008.
5. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473-83.
6. Krabbe PF. Thurstone scaling as a measurement method to quantify subjective health outcomes. Med Care 2008;46:357-65.
7. Brooks R. EuroQol: the current state of play. Health Policy 1996;37:53-72.
8. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med 2001;33:337-43.
9. Schölzel-Dorenbos CJM, Krabbe PFM, Olde Rikkert MGM. Quality of life in dementia patients and their proxies; a narrative review of the concept and measurement scales. In: Preedy VR, Watson RR, eds. Handbook of Disease Burdens and Quality of Life Measures. Heidelberg, Germany: Springer-Verlag, 2010,3671-91.
10. Fanshel S, Bush JW. A Health-Status Index and its application to health-services outcomes. Operations Research 1970;18:1021-66.
11. Langenhoff BS, Krabbe PF, Wobbes T et al. Quality of life as an outcome measure in surgical oncology. Br J Surg 2001;88:643-52.
12. Trial designs and outcomes in dementia therapeutic research. London and New York: Taylor & Francis Group, 2006.
13. Moniz-Cook E, Vernooij-Dassen M, Woods R et al. A European consensus on outcome measures for psychosocial intervention research in dementia care. Aging Ment Health 2008;12:14-29.
14. Banerjee S, Samsi K, Petrie CD et al. What do we know about quality of life in dementia? A review of the emerging evidence on the predictive and explanatory value of disease specific measures of health related quality of life in people with dementia. Int J Geriatr Psychiatry 2009;24:15-24.
15. Brown J, Bowling A, Flynn T. Models of Quality of Life: A Taxonomy, Overview and Systematic Review of the Literature. http://www ageingresearch group shef ac uk/pdf/qol_review_complete pdf 2004.
16. Flanagan JC. Measurement of quality of life: current state of the art. Arch Phys Med Rehabil 1982;63:56-9.
17. Alzheimer's Society. My name is not dementia; people with dementia discuss quality of life indicators. Report Alheimer's Society 2010;843:1-64.
18. Bowling A, Gabriel Z. An integrated model of quality of life in older age: results from the ESRC/MRC HSRC quality of life survey in Britain. Social Indicators Research 2004;69:1-36.
19. Patrick DL, Erickson P. Concepts of health-related quality of life. Health Status and Health Policy: Quality of Life in Health Care Evaluation and Resource Allocation. New York: Oxford University Press 1993.
20. Anderson RT, Aaronson NK, Bullinger M et al. A review of the progress towards developing health-related quality-of-life instruments for international clinical studies and outcomes research. Pharmacoeconomics 1996;10:336-55.
21. Carr AJ, Gibson B, Robinson PG. Measuring quality of life: Is quality of life determined by expectations or experience? BMJ 2001;322:1240-3.
22. Smith KW, Avis NE, Assmann SF. Distinguishing between quality of life and health status in quality of life research: a meta-analysis. Qual Life Res 1999;8:447-59.
23. Naglie G, Tomlinson G, Tansey C et al. Utility-based Quality of Life measures in Alzheimer's disease. Qual Life Res 2006;15:631-43.
24. Essink-Bot ML, de Haes JCJM. Kwaliteit van leven in medisch onderzoek. Een inleiding, ISBN 90-5356-206-0 Ed. Amsterdam: Amsterdam University Press 1996.
25. Hoe J, Hancock G, Livingston G et al. Changes in the quality of life of people with dementia living in care homes. Alzheimer Dis Assoc Disord 2009;23:285-90.
26. Albrecht GL, Devlieger PJ. The disability paradox: high quality of life against all odds. Soc Sci Med 1999;48:977-88.
27. Ubel PA, Loewenstein G, Schwarz N et al. Misimagining the unimaginable: the disability paradox and health care decision making. Health Psychol 2005;24:S57-62.
28. Paul C, Ayis S, Ebrahim S. Disability and psychosocial outcomes in old age. J Aging Health 2007;19:723-41.
29. Selwood A, Thorgrimsen L, Orrell M. Quality of life in dementia-a one-year follow-up study. Int J Geriatr Psychiatry 2005;20:232-7.
30. Missotten P, Ylieff M, Di Notte D et al. Quality of life in dementia: a 2-year follow-up study. Int J Geriatr Psychiatry 2007;22:1201-7.
31. Lyketsos CG, Gonzales-Salvador T, Chin JJ et al. A follow-up study of change in quality of life among persons with dementia residing in a long-term care facility. Int J Geriatr Psychiatry 2003;18:275-81.

32. Barclay-Goddard R, Epstein JD, Mayo NE. Response shift: a brief overview and proposed research priorities. Qual Life Res 2009;18:335-46.
33. Rabins PV, Black BS. Measuring quality of life in dementia: purposes, goals, challenges and progress. Int Psychogeriatr 2007;19:401-7.
34. Mack JL, Whitehouse PJ. Quality of Life in Dementia: state of the art--report of the International Working Group for Harmonization of Dementia Drug Guidelines and the Alzheimer's Society satellite meeting. Alzheimer Dis Assoc Disord 2001;15:69-71.
35. Alzheimer's Society. My name is not dementia. Literature review. Report Alheimer's Society 2010;842:1-64.
36. Boyer F, Novella JL, Morrone I et al. Agreement between dementia patient report and proxy reports using the Nottingham Health Profile. Int J Geriatr Psychiatry 2004;19:1026-34.
37. Logsdon RG, Gibbons LE, McCurry SM et al. Assessing quality of life in older adults with cognitive impairment. Psychosom Med 2002;64:510-9.
38. Sands LP, Ferreira P, Stewart AL et al. What explains differences between dementia patients' and their caregivers' ratings of patients' quality of life? Am J Geriatr Psychiatry 2004;12:272-80.
39. Dröes R-M, Boelens ECC, Bos J et al. Quality of life in dementia in perspective; an explorative study of variations in opinions among people with dementia and their professional caregivers, and in literature. Dementia: Int J Social Research and Practice 2006;5:533-58.
40. Schölzel-Dorenbos CJM. Measurement of quality of life in patients with dementia of Alzheimer type and their caregivers: Schedule for the Evaluation of Individual Quality of Life (SEIQoL). Tijdschr Gerontol Geriatr 2000;31:23-6.
41. Olde Rikkert MG, Teunisse JP, Vernooij-Dassen M. One hundred years of Alzheimer's disease and the neglected second lesson of Alois Alzheimer on multicausality in dementia. Am J Alzheimers Dis Other Demen 2005;20:269-72.
42. Olde Rikkert MG, van der Flier WM, de Leeuw FE et al. Multiple diagnostic tests are needed to assess multiple causes of dementia. Arch Neurol 2006;63:144-6.
43. Savva GM, Wharton SB, Ince PG et al. Age, neuropathology, and dementia. N Engl J Med 2009;360:2302-9.
44. Snow AL, Norris MP, Doody R et al. Dementia Deficits Scale. Rating self-awareness of deficits. Alzheimer Dis Assoc Disord 2004;18:22-31.
45. Antoine C, Antoine P, Guermonprez P et al. Awareness of deficits and anosognosia in Alzheimer's disease. Encephale 2004;30:570-7.
46. Sprangers MA, Schwartz CE. Do not throw out the baby with the bath water: build on current approaches to realize conceptual clarity. Response to Ubel, Peeters, and Smith. Qual Life Res 2010;19:477-9.
47. Norman G. Hi! How are you? Response shift, implicit theories and differing epistemologies. Qual Life Res 2003;12:239-49.
48. Visser MR, Oort FJ, Sprangers MA. Methods to detect response shift in quality of life data: a convergent validity study. Qual Life Res 2005;14:629-39.
49. Nourhashemi F, Andrieu S, Gillette-Guyonnet S et al. Effectiveness of a specific care plan in patients with Alzheimer's disease: cluster randomised trial (PLASA study). Brit Med J 2010;340:c2466.
50. Ring L, Gross CR, McColl E. Putting the text back into context: toward increased use of mixed methods for quality of life research. Qual Life Res 2010;19:613-5.
51. Gurland BJ, Gurland RV, Mitty E, Toner J. The choices, choosing model of quality of life: clinical evaluation and intervention. J Interprof Care 2009;23:110-20.
52. Gurland BJ, Gurland RV. The choices, choosing model of quality of life: linkages to a science base. Int J Geriatr Psychiatry 2009;24:84-9.
53. Gurland BJ, Cheng H, Maurer MS. Health-related restrictions of choices and choosing: implications for quality of life and clinical interventions. Patient Related Outcome Measures 2010;1:73-80.

LIST OF PUBLICATIONS

Journals

Schölzel-Dorenbos CJM. Meting van kwaliteit van leven bij patiënten met dementie van het Alzheimertype en hun verzorgers: Schedule for the Evaluation of Individual Quality of Life (SEIQoL). Tijdschr Gerontol Geriatr 2000;31:23-7. PMID: 10726294.

Schölzel-Dorenbos CJM. Parkinson: bij geriatrische patiënten soms een valkuil! Nederlands Tijdschrift voor Neurologie 2000;6:413-6.

Schölzel-Dorenbos CJM, Jellesma-Eggenkamp MJH. Een meetmethode voor individuele kwaliteit van leven bij Nederlandse ouderen. Nederlands Tijdschr voor de Psychologie 2001;56:16-8.

Rhebergen GA, Schölzel-Dorenbos CJM. Orthostatische en postprandiale hypotensie in de dagelijkse praktijk bij 70-plussers opgenomen op een interne afdeling. Tijdschr Gerontol Geriatr 2002;33:119-24. PMID 12122885.

Spronk GS, Schölzel-Dorenbos CJM, Jellesma-Eggenkamp MJH. Verwarde verhalen, soms iets anders dan verwardheid! Tijdschr Gerontol Geriatr 2003;34:222-7. PMID: 14694801.

Schölzel-Dorenbos CJM. Prioriteit voor dementie. Geheugenpolikliniek verbetert diagnostiek en behandeling. Medisch Contact 2003;43:1655-8.

Schölzel-Dorenbos CJM. Medicamenteuze behandeling van de ziekte van Alzheimer. De klinische praktijk in Nederland. Tijdschr Gerontol Geriatr 2005;36:122-6. PMID 16078659.

Schölzel-Dorenbos C, Lange J de. Kwaliteit van leven bij dementie: het perspectief van de patiënt. Denkbeeld 2005;17:6-9.

Schölzel-Dorenbos CJM. Mild Behavioral Impairment (MBI), a prodromal stage of frontotemporal dementia. J Am Ger Soc 2006;54:180-2. PMID 16420228.

Schölzel-Dorenbos C. Mild Behavioral Impairment (MBI), een mogelijk voorstadium van frontotemporale lobaire degeneratie. Tijdschr voor VerpleeghuisGeneesk 2006;31:128-32.

Dröes RM, Boelens-van der Knoop ECC, Bos J, Meihuizen L, Ettema TP, Gerritsen DL, Hoogeveen F, de Lange J, Schölzel-Dorenbos CJM. Quality of life in dementia in perspective; an explorative study of variations in opinions among people with dementia and their professional caregivers, and in literature. Dementia: Int J Social Research and Practice. 2006;5:533-58. DOI: 10.1177/1471301206069929.

Schölzel-Dorenbos CJM, Ettema TP, Bos J, Boelens-van der Knoop E, Gerritsen DL, Hoogeveen F, de Lange J, Meihuizen L, Dröes RM. Evaluating the outcome of interventions on quality of life in dementia: Selection of the appropriate scale. Int J Ger Psychiatr 2007;22:511-9. PMID 17133655.

Schölzel-Dorenbos CJM, van der Steen MJJM, Engels LK, Olde Rikkert MGM. Assessment of quality of life as outcome in dementia and MCI intervention trials; a systematic review. Alzh Dis Assoc Disord 2007;21:172-8. PMID 17545745.

Gerritsen DL, Ettema TP, Boelens E, Bos J, Hoogeveen F, de Lange J, Meihuizen L, Schölzel-Dorenbos CJM, Dröes RM. Quality of life in dementia: do professional caregivers focus on the significant domains? Am J Alzh Dis and Other Dementias 2007;22:176-83. PMID 17606526.

Vliek S, Melis RJF, Faes M, Golüke-Willemse GA, de Leest BJ, Meeuwsen EJ, van Raak FHJM, Schölzel-Dorenbos CJM, Olde Rikkert MGM. Single versus multicomponent intervention in frail elderly: simplicity or complexity as precondition for success? J Nutrition, Health & Aging 2008;12:319-23. PMID: 18443714.

Meeuwsen EJ, Melis RJF, Adang EM, Golüke-Willemse GA, Krabbe PF, de Leest BJ, van Raak FHJM, Schölzel-Dorenbos CJM, Visser MC, Wolfs CA, Vliek S, Olde Rikkert MGM. Cost-effectiveness of post-diagnosis treatment in dementia coordinated by multidisciplinary memory clinics in comparison to treatment coordinated by general practitioners: an example of a pragmatic trial. J Nutrition, Health & Aging 2009;13:242-9. PMID: 19262961.

Schölzel-Dorenbos CJM, Draskovic I, Vernooij-Dassen MJ, Olde Rikkert MGM. Quality of life and Burden of Spouses of Alzheimer's Disease Patients. Alzh Dis Assoc Disord 2009;23:171-7. PMID 19484919.

Schölzel-Dorenbos CJM, Olde Rikkert MGM, Adang EMM, Krabbe PFM. The challenges of accurate measurement of health-related quality of life in frail elderly and dementia. J Am Ger Soc 2009;57:2356-58. PMID: 20169632.

Schölzel-Dorenbos CJM, Meeuwsen EJ, Olde Rikkert MGM. Integrating unmet needs into dementia health-related quality of life research and care; Introduction of the Hierarchy Model of Needs in Dementia (HMND). Aging & Mental Health 2010;14:113-9. PMID 20155528.

Schölzel-Dorenbos CJM, Meeuwsen EJ, Adang EMM, Krabbe PFM, Vernooij-Dassen MJ, Verhey FRJ, Scheltens P, Olde Rikkert MGM, Melis RJF, on behalf of the AD-Euro study group. Quality of life of dementia patients and informal caregivers: both dependent on their own determinants in a cross-sectional study. Submitted for publication.

Schölzel-Dorenbos CJM, Arons AMM, Wammes JJG, Olde Rikkert MGM, Krabbe PFM. Validity study on Dementia Quality of life Instrument (DQI) in professionals, dementia patients and caregivers. Submitted for publication.

Gerritsen DL, Dröes RM, Ettema TP, Boelens E, Bos J, Meihuizen L, de Lange J, Schölzel-Dorenbos CJM, Hoogeveen F. Kwaliteit van leven bij dementie in perspectief: een oriënterende studie naar variaties in opvattingen onder mensen met dementie, hun zorgverleners en in de literatuur, en de weerslag daarvan op de dagelijkse praktijk. Tijdschr Gerontol Geriatr 2010, in press.

Letters
Schölzel-Dorenbos CJM. Disorders of concentration and memory in young adults and middle-aged persons. Ingezonden brief. Ned Tijdschr Geneesk 2005;149:1539. PMID 16033000.

Schölzel-Dorenbos CJM. Rivastigmine for Alzheimer disease; evaluation of preliminary results and of structured assessment of efficacy. Ingezonden brief. Ned Tijdschr Geneesk 2006;146:464. PMID 11913117.

Schölzel-Dorenbos CJM. Totaal atrioventriculair blok tijdens behandeling met galantamine. Ingezonden brief. Ned Tijdschr Geneesk 2006;150:989-91.

Book
Schölzel-Dorenbos CJM, Krabbe PFM, Olde Rikkert MGM. Quality of life in dementia patients and their proxies; a narrative review of the concept and measurement scales. In: Handbook of Disease Burdens and Quality of Life Measures. Springer-Verlag, Heidelberg, Germany. Victor R. Preedy, Ronald R. Watson (Eds.) Handbook of Disease Burdens and Quality of Life Measures 2010;3671-91. ISBN-13: 978-0-387-78664-3. Electronic publication 978-0-387-78665-0. Print and electronic bundle ISBN 978-0-387-78666-7 Library of Congress Control nr. 2009927296.

Posters and congress proceedings
Schölzel-Dorenbos CJM. Het effect van rivastigmine op het welzijn van Alzheimer-patiënten. In: Symposiumverslag 2000 Leo Cahn stichting: Het beoordelen van kwaliteit van leven bij demente ouderen. Redactie: Gerritsen DL, Steen van der JT, Jonker C. 2001;41-8.

Schölzel-Dorenbos CJM. Quality of life, mood and burden of partners of Alzheimerpatients. Age and Ageing. 2003;S1:29.

Schölzel-Dorenbos CJM, van Hees F, Krabbe P, Adang E, Olde Rikkert MGM. AD-Euro study: clinical and economic evaluation on how to organize post-diagnosis care for dementia patients and exploration of the relationship between patient and proxy HRQL measurement. International Psychoger 2007;S1:80.

Schölzel-Dorenbos CJM, Draskovic I, Vernooij-Dassen M, Olde Rikkert MGM. Quality of life and burden of spouses of Alzheimer's disease patients; individualized assessment with the Schedule for the Evaluation of Individual Quality of Life (SEIQoL). International Psychoger 2007;S1:339.

Schölzel-Dorenbos CJM, van der Steen M, Engels L, Olde Rikkert MGM. Assessment of quality of life (QoL) as outcome in dementia and MCI intervention trials; a systematic review. International Psychoger 2007;S1:254.

Schölzel-Dorenbos CJM, Krabbe P, Meeuwsen E, Adang E, Olde Rikkert MGM. An overview of quality of life measurement in dementia. International Psychogeriatric Association 2008 European Meeting, Dublin. 2008;41-42.

Schölzel-Dorenbos CJM, Meeuwsen EJ, Adang EMM, Krabbe PFM, Olde Rikkert MGM, Melis RJF. A cross-sectional study on how dementia patients' and their caregivers' quality of life are associated provides possibilities to improve dementia care. European Ger Med 2010;1:S10.

CURRICULUM VITAE

DANKWOORD

CURRICULUM VITAE

Carla Schölzel werd op 12 maart 1951 in Amsterdam geboren. Zij volgde het atheneum aan het Pius X college in Amsterdam en begon in 1969 met de studie geneeskunde aan de Universiteit van Amsterdam. In haar eerste studiejaar trouwde ze met Justien. In 1976 begon ze aan de specialisatie Inwendige Geneeskunde in het Zuiderziekenhuis in Rotterdam, met als opleider Prof. Dr. W.H. Birkenhäger. In 1982 volgde inschrijving in het specialistenregister Inwendige Geneeskunde. Van 1982-1984 deed ze wetenschappelijk onderzoek op de afdeling Hematologie van het Rotterdams Radiotherapeutisch Instituut in combinatie met klinisch werk op de afdeling Hematologie. Toen trok de volledige patiëntenzorg toch weer en werkte ze enkele jaren als internist in Leerdam. Na een kort intermezzo in het verpleeghuis begon ze in juli 1989 aan de specialisatie Klinische Geriatrie in het Rijnstate Ziekenhuis in Arnhem, met als opleider Dr. E. Bruijns. In februari 1994 volgde overschrijving naar het specialistenregister Klinische Geriatrie. Zij werkt sinds 1994 als klinisch geriater in het Slingeland Ziekenhuis in Doetinchem waar zij samen met anderen het Geriatrisch Onderzoek en Adviescentrum uitbouwde tot de huidige afdeling klinische geriatrie met geheugencentrum, valkliniek, dagkliniek, polikliniek en uitgebreide consultfunctie. Het aantal medewerker breidde zich in de loop van de jaren uit tot nu 5 klinisch geriaters, 2 psychologen, 2 psychodiagnostisch werkenden, 2 maatschappelijk werkers, 4 verpleegkundigen waaronder een verpleegkundig consulent en een verpleegkundig specialist, en de uitgebreide en gewaardeerde ondersteuning van doktersassistenten en secretaressen. Naast het klinisch werk was er (niet nodig, maar goed en leuk) gelegenheid om te promoveren, onder de stimulerende leiding van vooral Prof. Dr. Marcel Olde Rikkert (en veel incasseringsvermogen en steun van het geliefde en onmisbare thuisfront!). Tijdens de afronding van dit proefschrift begonnen (iets te vroeg) de nieuwe uitdagingen al weer, zoals het samen met Klaas Jansma en Pieter Wolswijk maken van een professionele film over 'Winst en het verlies van ouder worden', het met de afdeling pastoraal werk organiseren van een symposium over dit onderwerp in 2011 en vooral de start van het Zowel NWA: het 'Zorg voor ouderen en welzijn Netwerk West Achterhoek' (zie www.zowelnwa.nl). Kortom, geen gevaar voor het beroemde zwarte gat na deze dag!