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Could the choice of patient versus proxy ratings for assessing quality of life in dementia affect resource allocation in health care?

ORIGINAL RESEARCH

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ABSTRACT

OBJECTIVE: The aim of this paper is to demonstrate how the choice of patient versus proxy ratings of patient health-related quality of life (HRQoL) in dementia, for use in cost-effectiveness analyses (CEAs), could potentially affect resource allocation in health care.

METHODS:A model of Alzheimer's disease (AD) based on cognitive ability was used to assess the consequences of using HRQoL ratings from either patients themselves or proxies if a new treatment was to be introduced. The model was based on previously published data on costs related to AD stages as well as HRQoL ratings from AD patients and from their caregivers as proxy raters.

RESULTS:The results show that there can be large differences in the results of the CEAs depending on whether the ratings of patients' HRQoL were made by the patients themselves or by the proxy. When patient self-ratings of HRQoL were used, the cost/quality-adjusted life year (QALY) gained was much higher as compared to the scenario when proxy ratings were used for the same analysis.

CONCLUSIONS: The choice of patient self-ratings compared to proxy ratings of patients' HRQoL can have a substantial effect on the results of CEAs. These differences in results may have an important impact on decision making and, ultimately, on resource allocation. In order to critically appraise the results of CEA studies in dementia we advise that both patient and proxy ratings are used in the CEA. To decide on methodology it is of great importance that focus is directed towards determining the most valid way to measure HRQoL in AD.

Keywords

Patient ratings; Proxy ratings; Dementia; Quality of Life; Resource allocation

INTRODUCTION

Decisions on resource allocation and priority setting are a reality in the health care sector. Decision makers need to battle the gap between available resources and the increasing demand for health care. In this context, health economic analyses studying costs and effects of technologies are important in enabling informed decisions about resource allocation. Several agencies, including the National Institute for Health and Clinical Excellence (NICE) in England and Wales, require economic evidence to be presented in the form of cost-effectiveness analyses (CEAs) [1]. In these analyses, the difference in cost between two or more treatment alternatives is weighted against the difference in effects in order to calculate the results expressed as a ratio: the incremental cost-effectiveness ratio (ICER). The recommended effect measure used by agencies such as the NICE when performing a CEA is quality-adjusted life years (QALYs) [1]. The QALY combines life years with the health state utility, often expressed in terms of health-related quality of life (HRQoL).

Health state utility (or HRQoL) for QALY calculations can be obtained in different ways. Health economics is often associated with the theories of welfare economics. Within the field of welfare economics, it is

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assumed that the judge of a person's utility should always be the affected individual. Summarizing the tenet of "Individual sovereignty" within the framework of welfare economics, Hurley (2000, p. 60) [2] writes: «Individual sovereignty asserts that individuals are the best judges of their own welfare; that any assessment of individual welfare should be based on a person's own judgment. It rejects paternalism, the notion that a third party may know better than the individuals themselves what is best for them».

Whose preferences for valuing HRQoL (HRQoL will be the term used hereafter in the present study) should be used is, however, a much debated subject. Many argue that the preferences of the public should be used rather than those of the individual, and one argument for this is that when a societal perspective (i.e., the argument that all relevant costs and effects that arise within society should be included) is advocated for the health economic analyses, then the preferences for different health states should be gathered from the general public [3]. Dolan (1999) argues that the issue boils down to whether or not the fact that persons in poor health states may adapt to, or cope with, their situation, and consequently not assign the health state the "true" value, should be taken into account [4].

Another dimension related to the issue of whose preferences to use arises when a person, due to, e.g., young age (small children) or cognitive impairment/dementia, has difficulties stating their own preferences or rating their own health state. In these situations, **proxy raters** are often used as a representative of the patient. A proxy is a person who is close to, and has knowledge about, the patient.

Within the field of dementia, where the issue of patient self-ratings versus proxy ratings is a well-acknowledged methodological challenge, research has shown that there are differences between self-ratings of the persons with dementia and proxy ratings. Proxy ratings of the patients' HRQoL in dementia are lower than the patients' own ratings of their HRQoL [5-9]. Sands et al. (2004) [5] set out to explain the differences in subjective quality of life (QoL) ratings between patients with mild to moderate dementia and their caregiver proxies, and conclude that the difference could be related to factors such as level of caregiver burden, with a higher burden level meaning lower rating of the patients' QoL as compared to the patients' own rating. As there may be issues of bias concerning caregiver proxy ratings [5] and questions concerning patients' own ratings due to cognitive limitations and poor patient insight in dementia [7], both the proxy ratings and the patients' own ratings have been questioned regarding validity. It has been argued that since it is not established who is the most appropriate rater in dementia – the patient or the proxy – data should be gathered from both [10].

Depending on who the rater of a patient's HRQoL is, the patient or a proxy, the result of the CEA, i.e., the ICER, is likely to differ. The discrepancies between patient and proxy ratings in dementia are well known, but to what extent this has an impact on the results of CEAs has, to our knowledge, not been previously studied. This information is, however, of great importance when it comes to deciding on method and critically appraising results of CEA studies. If the differences are sufficiently large, the choice of rater could ultimately lead to different decisions concerning resource allocation in health care.

AIM

The aim of this paper is to demonstrate how the choice of rater, patient self-rater or caregiver proxy rater of the patient's HRQoL in dementia, for use in CEAs, could potentially affect resource allocation within health care.

METHODS

Using a health economic model, we investigated the impact of different raters (patient and proxy) of patient HRQoL on the ICER. The model simulates the natural history of Alzheimer's disease (AD) and calculates the cost-effectiveness of a new hypothetical treatment slowing the progression of AD.

THE HEALTH ECONOMIC MODEL

A Markov model was constructed to model the progression of AD in four health states, from the onset of cognitive impairment to severe cognitive impairment (Figure 1). 10,000 individuals enter the model in the onset of cognitive impairment health state and can thereafter progress to a more severe cognitive health state with a monthly probability (monthly cycle length). Onset of cognitive impairment, progression, and health states were modeled based on Mini-Mental State Examination (MMSE) scores. The MMSE [11] is a common instrument for measuring cognitive ability in dementia. It includes questions on orientation, registration, attention and calculation, memory, language, spatial ability, and ability to follow instructions. The score ranges from 0 to 30, where 30 represents high cognitive ability. In the model, onset of cognitive impairment was defined as a

MMSE score of ≤ 24 [12]. The progression in the model was based on a study by Mendiondo et al. [13]. In this study, Mendiondo et al. presented mean MMSE change per year for different MMSE values. These progression rates were incorporated in the model to model the MMSE progression, and thus transitions between the health states in the model. In each cycle, all individuals are at risk of death through all cause mortality [14]. The starting age of the patients in the model was 75. The simulations were run until all patients had moved through the model, from stage 1 to death.

Based on this model of the natural progression of AD, we created a strategy whereby a hypothetical treatment of AD was introduced. In the base case scenario, the treatment would decrease the monthly deterioration of MMSE by 10%, but add an additional cost of € 100 per month. In addition, we ran the model for scenarios of treatment effects of 5%, 6%, 7%, 8%, and 9% in order to illustrate how the result would differ depending on choice of rater and also depending on different treatment effects.

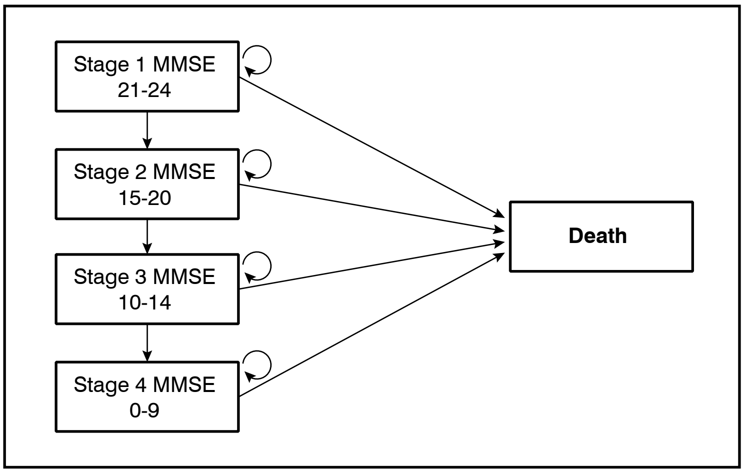

Figure 1. *Markov model describing the four different stages of dementia*
MMSE = Mini-Mental State Examination

AD stages	MMSE score	Mean annual cost/patient (€)*
Stage 1	21-25	8,699
Stage 2	15-20	17,044
Stage 3	10-14	21,007
Stage 4	0-9	34,718

Table I. *Model data – Mini-Mental State Examination (MMSE) scores and costs. Data retrieved from Jönsson et al [15]*
* Values for 2003
AD = Alzheimer's disease

COSTS

Costs associated with the different stages of AD were retrieved from a study by Jönsson et al. [15] that included 272 patients and their caregivers. In that article, the authors had calculated mean annual costs for each of the MMSE stages [15] (Table I). The mean costs included costs for medical care (pharmaceuticals), in- and outpatient care, community care (special housing, home help, day center visits, etc.), and informal care performed by family caregivers [15]. The costs were discounted using a 3% rate.

HEALTH-RELATED QUALITY OF LIFE

Data on HRQoL for the analysis were retrieved from a study by Jönsson et al. [7] which measured patient and proxy HRQoL weights for the different stages of dementia (Table II). The total population in the Jönsson et al. [7] study was 272 patients and their caregivers (proxies) who were mostly spouses or children. The proxies were asked to rate how they judged the patients' HRQoL [16]. The patients were diagnosed with possible or probable AD and the mean age was 75.9 years [7]. The ratings retrieved from the Jönsson et al. study [7] used in the present article are the ones where both patient and caregiver ratings were available. The HRQoL in the article [7] was collected using the EQ-5D instrument [17]. The EQ-5D instrument includes five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, and has three response options that correspond to: "no problems", "moderate problems", and "severe problems". The EQ-5D has a possible score ranging from -0.594 to 1, where 1 represents full health [18]. The patients in the Jönsson et al. [7] study answered the EQ-5D themselves or with help from an interviewer. The HRQoL values were discounted using a 3% rate.

RESULTS

The health economic model in the present study was used to illustrate the result of a

AD stages	MMSE score	EQ-5D HRQoL	
		Patient ratings	Proxy ratings
Stage 1	21-25	0.85	0.65
Stage 2	15-20	0.83	0.52
Stage 3	10-14	0.73	0.51
Stage 4	0-9	0.78	0.40

Table II. *Model data – Mini-Mental State Examination (MMSE) scores and health-related quality of life (HRQoL) scores. Data retrieved from Jönsson et al [7]*
AD = Alzheimer's disease

	Patient self-rated HRQoL	**Proxy-rated HRQoL**
Cost, untreated (€)	210,003	210,003
Cost, treated (€)	211,211	211,211
Incremental cost (€) (Cost, untreated – Cost, treated)	1,208	1,208
QALYs, untreated	7.087	4.360
QALYs, treated	7.109	4.439
Incremental QALYs (QALYs, untreated – QALYs, treated)	0.023	0.079
ICER	**€ 53,619**	**€ 15,213**

Table III. *Mean differences per patient in the results between patient-rated health-related quality of life (HRQoL) and proxy-rated HRQoL*
ICER = incremental cost-effectiveness ratio; QALYs = quality-adjusted life years

CEA when both patient and proxy ratings of the patient's HRQoL are used for the same analysis. The results show that there may be large differences in the results of a CEA, depending on whether patient-rated or proxy-rated HRQoL is used (Table III). When patient self-rated HRQoL was used for the analysis in the present study, the cost per QALY gained (the ICER) was approximately € 53,600. When proxy-rated patient HRQoL was used for the same analysis, the cost per QALY gained was considerably lower, approximately € 15,200 (Table III).

The results of the scenarios using different treatment effects are shown in Figure 2, together with different levels of willingness to pay (WTP) for 1 QALY gained, of € 20,000, € 30,000, and € 50,000, respectively. The results show that at lower treatment effects (5-7%), the ICERs based on both patient and proxy HRQoL ratings are above the WTP level of € 50,000. At higher treatment effects, the ICERs based on proxy ratings are under the WTP levels of € 50,000, around € 30,000 at a treatment effect of 9% and also under € 20,000 at the highest treatment effect used in the present study, of 10%. The ICERs from the analyses based on patient self-ratings are, however, never below the WTP level of € 50,000.

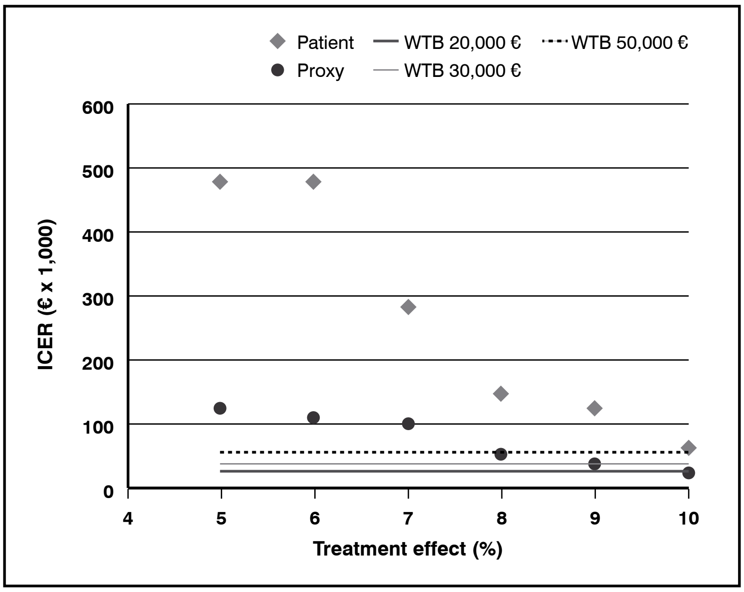

Figure 2. *Incremental cost-effectiveness ratios (ICERs) for different levels of treatment effect, based on patient self-ratings and proxy ratings of patient health-related quality of life (HRQoL). Three different levels of willingness to pay (WTP) for 1 quality-adjusted life year (QALY) gained are shown*

The National Institute for Health and Clinical Excellence (NICE) has defined a value range of £ 20,000-30,000 (approximately € 22,100-33,200) for cost per QALY gained to illustrate whether a technology is considered an effective use of resources [1]. Based on this value range, the choice of rater, patient or proxy, may have an important impact on resource allocation.

DISCUSSION

In the present paper, we have illustrated that the choice of rater of a patient's HRQoL in dementia has an important impact on the results of the CEA, and may also have an effect on decision making. Depending on the choice of rater, the value of the ICER will change dramatically. As shown in our analysis, the ICER would differ between € 53,600 for the new, hypothetical, treatment if patient ratings were used and € 15,200 if proxy ratings were used. Applying the value range of £ 20,000-30,000 (approximately € 22,100-33,200) for cost per QALY gained, set by the NICE [1], it is clear that the choice of rater could have a substantial impact on the decision on whether or not to fund the new treatment. For a technology with an ICER > € 33,200 per QALY gained, strong arguments concerning, e.g., considerable benefits not captured by the QALY are needed in order for the technology to be included in public funding [1]. From the example in the present study, this would mean that if proxy ratings were used for the analysis, the treatment under investigation would be considered cost-effective; by contrast, if the HRQoL ratings of the patients themselves were used, generating a substantially higher cost/QALY gained, the treatment would not be regarded as cost-effective.

Rating HRQoL when diagnosed with dementia is linked to a number of challenges, such as lack of insight [6] and difficulties in comprehending the questions, due to cognitive impairment. The validity and reliability of patient self-ratings in dementia has been questioned [6,19]. Patients with AD, regardless of stage of the disease, rate their HRQoL as relatively high [7]. For example, the lowest ratings from the persons with AD used in the present model, data from Jönsson et al. [7], were from patients at AD stage 3, with a EQ-5D HRQoL weight of 0.73, while the highest were from AD patients at stage 1, with a HRQoL rating of 0.85 (shown in Table II). This could be compared to EQ-5D ratings from the Swedish general population, which on average are 0.79 in the age group 70-79 years [20]. Departing from the example in the present study, the use of self-ratings of the patients would mean that the treatment would not be considered cost-effective. Because of the difficulties of self-ratings in AD due to the nature of the disease, it can be argued that using patient self-ratings, with its potential consequences for resource allocation, would not be ethically just.

Proxy ratings of the patient's HRQoL are often used as an alternative to patient self-ratings when the patient is suffering from cognitive impairment (see e.g. [19]). Proxy ratings of patient HRQoL in AD using the EQ-5D have been shown to strongly relate to cognitive functioning [7]. Proxy ratings are, however, not without challenges. There is a low level of agreement between proxy ratings and patient self-ratings, and factors related to the proxy (level of caregiver burden), and not necessarily to the patient, have been shown to influence proxy ratings [5]. It could be argued that using the ratings of a proxy would be unethical as it is difficult to assess what the "real" HRQoL of the patient is. The validity of self-ratings of HRQoL by the patients themselves in the more severe stages of dementia is, however, probably considered as questionable due to the nature of the disease. But in milder stages of dementia, cognitive impairment may not be so prominent. Previous studies have recommended the use of patient self-ratings of subjective QoL in mild-moderate dementia [5]. Considering the discussion concerning whose preferences to use when it comes to the preferences of the individual or of the general public, Gold et al. (1996, p. 100) [3] write: «To inform public policy decisions, one would wish to have judgments that are informed, unbiased and competent. Problems emerge in meeting these measurement criteria simultaneously both for persons who are experiencing the health state and for those who are not».

The statement above is true also for the patient-proxy case. Patients may be regarded as not informed or competent at making self-ratings. Proxies, on the other hand, may not be seen as unbiased and consequently may not be competent at making ratings of patient HRQoL. This poses the problem of choosing whose ratings to use. It has further been debated who the most valid proxy is, as different proxies (family caregiver proxies or physician proxies) may yield different results when it comes to rating dementia patients' HRQoL [6]. Who the appropriate proxy rater is has yet to be established [6].

Due to the large differences in the ICERs, depending on whose ratings are used, a minimum requirement when performing a CEA in AD should therefore be to use ratings from both patients and proxies. As the scenarios with different treatment effect showed (see Figure 2), the choice of rater does not always affect the interpretation of the results of the CEA. This should therefore be displayed. Displaying the results of both patient and proxy ratings will make it possible to make comparisons and to critically appraise the results of the analysis. Including the ratings of both patients and proxies has been previously recommended when it comes to measuring QoL in dementia [10]. This methodological issue and these findings may also be found in other areas where proxy ratings are common and where there are differences between different raters.

METHODOLOGICAL CONSIDERATIONS

This article employs a modeling approach to illustrate the methodological question under investigation. The model used in the present article does not claim to reflect "medical actuality", but uses a fictitious scenario based on a hypothetical treatment. Several assumptions were made when designing the model, an important one being that AD stages are determined by cognitive ability (based on MMSE scores) only. Dementia is a complex disease including different symptoms, of which cognitive ability is one. To measure and model stages of AD based only on cognitive ability has its limitations [21] and has been criticized [22]. The progression of AD includes deterioration of cognitive and functional ability, behavioral aspects, and mood [22]. The aim of the present study was to examine differences between patient and proxy ratings of HRQoL and their potential consequences for decision making. The model only simulates deterioration of cognitive ability and consequences for decision making depending on rater. We suggest that further studies more comprehensively should reflect the complexity of dementia progression, also using longer term cost and utility data from clinical studies in the model in order to fully investigate these matters.

Health-related quality of life for CEAs aiming to calculate QALYs can be measured in different ways, either through so-called "direct" (e.g. Time-Trade-Off or Standard Gamble) or through "indirect" methods. In the present study, HRQoL weights based on the EQ-5D instrument (indirect method) were used for the model. These methods can also be discussed in relation to the theoretical framework of welfare economics; this will, however, not be explored further in the present study.

CONCLUSIONS

In the present study, we have shown that the choice of rater – patient self-ratings versus proxy ratings – of patients' HRQoL in AD has an important effect on the results of the CEA. Following the present value ranges given by the NICE for what is considered cost-effective [1], these differences in results may have an important impact on decision making and, ultimately, on resource allocation. Based on these results we therefore advice that both patient and proxy ratings should be used in CEA's.

The best way to measure HRQoL in AD for CEAs has yet to be established. In order to critically appraise health economic assessments in AD and, further, to make informed decisions on resource allocation, the issues of measuring HRQoL in dementia should be given more attention in future research.

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PRIOR/DUPLICATE PUBLICATION

An earlier version of this manuscript has previously been published in a Ph.D. thesis by Jenny Alwin [23]. The manuscript has not been previously published in any scientific journal.

REFERENCES

1. National Institute for Health and Clinical Excellence, Guide to the methods of technology appraisal. London: NICE, 2008. http://www.nice.org.uk/niceMedia/pdf/TAP_Methods.pdf
2. Hurley J. An overview of the normative economics of the health care sector. In: Culyer AJ, Newhouse J (eds). Handbook of health economics. Amsterdam: Elsevier Science, 2000
3. Gold MR, Patrick DL, Torrance GW, et al. Indentifying and valuing outcomes. In: Gold M, Siegel JE, Russell LB, et al. (eds). Cost-effectiveness in health and medicine. Oxford University Press, 1996
4. Dolan P. Whose preferences count? *Med Decis Making* 1999; 19: 482-6
5. 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
6. 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
7. Jönsson 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
8. 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
9. Crespo M, Bernaldo de Quiros M, Gomez MM, et al. Quality of Life of Nursing Home Residents With Dementia: A Comparison of Perspectives of Residents, Family, and Staff. *Gerontologist* 2012; 52: 56-65
10. 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
11. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatric Res* 1975; 12(3): 189-98
12. Svensk förening för Kognitiva sjukdomar (SKF), Mini Mental Test/MMT, 2000 (test sheet, Swedish version. From: 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
13. Mendiondo MS, Ashford JW, Kryscio RJ, et al. Modelling mini mental state examination changes in Alzheimer's disease. *Stat Med* 2000; 19: 1607-16

14. Statistics Sweden. Life tables for 2006, divided into men and women. Available at: www.ssd.scb.se [latest accessed February 2012]
15. Jönsson L, Eriksdotter Jönhagen M, Kilander L, et al. Determinants of costs of care for patients with Alzheimer's disease. *Int J Geriatr Psychiatry* 2006; 21: 449-59
16. Jönsson L. Economic evaluation of treatments for Alzheimer's disease.Doctoral Thesis. Division of Geriatric Epidemiology, the Neurotec Department. Stockholm, Sweden: Karolinska Institutet, 2003
17. Brooks R. EuroQol: the current state of play. *Health Policy* 1996; 37: 53-72
18. Dolan P. Modeling valuations for EuroQol health states. *Med Care* 1997; 35: 1095-108
19. Busschbach JJ, Brouwer WB, van der Donk A, et al. An outline for a cost-effectiveness analysis of a drug for patients with Alzheimer's disease. *Pharmacoeconomics* 1998; 13: 21-34
20. Burström K, Johannesson M, Diderichsen F. Swedish population health-related quality of life results using the EQ-5D. *Qual Life Res* 2001; 10: 621-35
21. Jönsson L, Lindgren P, Wimo A, et al. Costs of mini mental state examination-related cognitive impairment. *Pharmacoeconomics* 1999; 16: 409-16
22. Green C. Modelling disease progression in Alzheimer's disease: a review of modelling methods used for cost-effectiveness analysis. *Pharmacoeconomics* 2007; 25: 735-50
23. Alwin J. Assessment of support interventions in dementia. Methodological and empirical studies. Department of Medical and Health Sciences. Linköping, Sweden: Linköping University, 2010