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ADDRESSING THE BIAS PROBLEM IN THE ASSESSMENT OF THE QUALITY OF LIFE OF PATIENTS WITH DEMENTIA: DETERMINANTS OF THE ACCURACY AND PRECISION OF THE PROXY RATINGS

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Abstract: *Objectives:* We aimed to examine the discrepancy between patients and caregivers' ratings of quality of life in terms of accuracy and precision, and identify factors associated with it, in order to facilitate the use of this scale as dementia progresses. *Design:* Cross-sectional analytic study. *Setting:* Day care centres. *Participants:* Community-living patients with Alzheimer's disease in early or moderate stage and their principal caregivers. *Measurements:* Participants rated patients' quality of life using DEMQOL. The discrepancy was assessed using the individual difference score and the residuals for each domain of DEMQOL. The scores on Mini-Mental State Examination, Geriatric Depression Scale, Neuropsychiatric Inventory, Clinical Insight Rating Scale, Cumulative Illness Rating Scale, Health Utilities Index Mark 3 and Zarit Burden Interview were considered as possible predictors of the discrepancy. *Results:* A total of 276 subjects participated in the study (138 patients with Alzheimer's disease and their caregivers). Discrepancy measured by individual difference score was lower than that measured by the residuals. Burden and mood-related symptoms explained the positive differences and residuals, while pain, self-perceived depression and cognition determined the negative ones. *Conclusions:* Differences exist between patients and caregivers' perceptions about subjective states. The evaluations of each informant seem to be influenced by their own emotional state and the inner experience of the effects of the disease. Caregivers' ratings on DEMQOL could be useful to monitor the efficacy of any treatment whenever burden is low and patients have no great physical or emotional suffering.

Key words: Quality of life, discrepancy, Alzheimer's disease, DEMQOL.

Introduction

Alzheimer's disease (AD) is increasingly prevalent in aging societies (1). Therefore, there is increasing interest in developing cost-effective strategies to improve the health-related quality of life (HRQoL) of these patients (2). Althought HRQOL definitions vary widely, there is general agreement that it implies a subjective perception of the impact of health status on physical, psychological, and social functioning. In cognitively impaired patients, HRQoL has been assessed using self-reports, caregiver-reports and observational measures. There is general agreement that subjective evaluation should rely, as far as possible, on the patients' perspective, especially in early stages of AD (3). Several studies have reported notable differences between patients and caregivers' perceptions of HRQoL. Caregivers' ratings are, on average, lower than patients' ratings, and the agreement between observers is moderate at best (3-4). This discrepancy has been associated to characteristics of the patients such as lack of insight, severity of cognitive impairment or behavioral disorders (5), but also to caregivers-related factors such as depression, health or burden (6). These data suggest that proxy's report, though necessary in advanced stages, may not be a good substitute for the patient's report. Determining the factors that contribute to the discrepancy could help assess HRQoL more reliably. Little research has been conducted on this topic using DEMQOL scale (7-8). This study aimed to measure the discrepancy between patients and caregivers DEMQOL ratings and identify the factors potentially contributing to it. We used two methodological approaches to assess the discrepancy, and established comparisons between them. The results could be of practical importance, since we have considered a wide set of clinical variables as predictors and separately analyzed the discrepancy in different domains of HRQoL.

Methods

Participants

Patients were recruited from day centres in the area of Murcia, Spain. They were required to meet criteria for possible or probable AD (9), have a score of 4 or 5 in the Global Deterioration Scale score (10) and be residing with a caregiver in a community dwelling. Caregivers were selected from people who provide daily care to the patients and supervise them at home. They were non-professional caregivers.

Measures

Dementia specific HRQoL measure

DEMQOL (4). The DEMQOL system consists of two interviewer-administered instruments (DEMQOL and DEMQOL proxy) that measure the HRQoL of dementia

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patients. DEMQOL is reported by patients and DEMQOL proxy is completed by caregivers, both have proved to have good psychometric properties in mild to moderate dementia patients (4). DEMQOL consists of 28 items answered on a 4-point Likert scale (a lot/quite a bit/a little/not at all). Total score ranges from 28 to 112, with higher scores indicative of better HRQoL. DEMQOL proxy has 31 items, some of which are different from DEMQOL items. Since we intend to measure the patient-caregiver agreement and to predict patients' ratings, we administered DEMQOL to both patients and caregivers and studied its psychometric properties. Studies about the factorial structure of DEMQOL have proposed solutions with three, four and five factors (4, 11). We choose the solution proposed by Lucas et al. (11) because this study was conducted with the Spanish version of the scale. This version has three factors: feelings, everyday life and memory. The "feelings" factor includes items 1 to 13 and item 27; "everyday life" includes items 20 to 26 and 28 and "memory" items 14 to 19.

Clinical measures of the participants

MINI-MENTAL STATE EXAMINATION (MMSE) (12). MMSE is a 30-point instrument widely used as a rough measure of cognitive severity. We used the score of a short version of MMSE (SMMSE) built from six memory items of MMSE, which has proved to be useful in screening dementia (13).

GERIATRIC DEPRESSION SCALE SHORT FORM (SGDS) (14). SGDS is a 15-item self-report questionnaire that has been validated to assess depression in both cognitively intact and demented elderly (15).

NEUROPSYCHIATRIC INVENTORY (NPI) (16). NPI is an interview-based tool designed for comprehensive evaluation of behavioral disturbances in patients with dementia. The 12-item version evaluates the frequency and severity of delusions, hallucinations, agitation, depression, anxiety, euphoria, apathy, nighttime behaviour disturbances, appetite disorders, disinhibition, irritability and aberrant motor behaviour. The score for each item is obtained by multiplying frequency (1-4) by severity (1-3). The total NPI score is the sum of the individual item scores. Recently, a study using confirmatory factor analysis has proposed a three-factor model for the 12-item NPI: mood (depression, apathy, eating disturbances, nighttime behaviour disturbances and anxiety), psychosis (delusions, hallucinations) and behavioral disturbances (anxiety, agitation, disinhibition, irritability, aberrant motor behaviour) and the item euphoria (17).

CLINICAL INSIGHT RATING SCALE (CIR) (18). CIR is a 4–item instrument that measures four components of insight: the awareness of the situation, cognitive deficits, functional disability, and progression of the disease. Each item is rated from 0 (totally unaware) to 2 (totally aware).

ZARIT BURDEN INTERVIEW (ZBI) (19). ZBI is an instrument for measuring caregivers' perceived burden of providing family care. It has 22 items and is self-administered. ZBI scores range from 0 (no burden) to 88 (highest burden).

HEALTH UTILITIES INDEX MARK 3 (HUI 3) (20). HUI 3 is a generic multi-attribute preference-based measure of health status and HRQoL widely used as an outcome measure in clinical and economic studies. HUI 3 includes 8 attributes of health status: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain with 5 or 6 levels per attribute, varying from highly impaired to normal. HUI 3 is scored using single- and multi-attribute utility as described by Ruiz et al. (21). In this study, we used the score of the pain attribute.

CUMULATIVE ILLNESS RATING SCALE (CIRS) (22). The modified Cumulative Illness Rating Scale was used to measure the total burden of medical illness. The questionnaire consists of 14 domains related to different body systems. Scoring on the different domains is weighted by the severity of the comorbid condition. Severity scores range from 0 (none) to 5 (extremely severe). The illness severity index is the average score of all the items, excluding the domain "psychiatric or behavioral disturbances". CIRS has proved to be valid and reliable in the geriatric population (23).

Procedures

Written informed consent was obtained from both patients and caregivers. Patients and caregivers were administered the tests separately to avoid the possibility of influence. Patients were interviewed about their quality of life (DEMQOL) and depressive state (SGDS). The severity of the dementia was assessed by using the MMSE and the GDS. A physician quantified medical comorbidity using the Cumulative Illness Rating Scale. Caregivers completed HUI 3, NPI and ZBI and were asked to rate the patients' HRQoL (DEMQOL) as a substituted judgment. Researchers completed CIR based on their judgments of patients' insight after the interviews with the patient and the relative.

Statistical Analyses

The internal consistency of DEMQOL and its domains was calculated with Cronbach's alpha coefficient (24). The factor structure of the DEMQOL was examined by means of exploratory factor analysis using the using principal component analysis with varimax rotation.

The analysis of the discrepancies proceeded in several steps. First, we examined whether there were significant differences in both DEMQOL total and each domain scores between patients and caregivers using the ANOVA test. Where significant differences were found, we assessed the discrepancy by two statistical methods: individual difference score and regression residuals. Individual difference score was calculated by subtracting caregiver's rating score from the patient's rating score. Predictors were selected from the variables that correlate significantly with the difference score and with the scores of either patients or caregivers, as did Huang et al. (6). We used a Bonferroni adjustment to control for Type I Error.

The second method to assess the discrepancy is based on the

residuals of the regression equation of "patients' ratings" on "caregivers' ratings". We determined the predictors of positive and negative residuals. Positive residuals indicate that patients' scores are higher than predicted by caregivers' scores. Negative residuals indicate that patients gave lower scores than expected based on regression equation. Predictors were selected from among the variables significantly correlated with residuals and with the ratings of any of the observers.

Finally, we built multiple linear regression models separately to explain the individual difference score and the residuals using the default "enter" method.

To prevent collinearity between variables in the regression models, we used the score of the NPI factors instead of the NPI symptoms. Since euphoria was rare in our sample it was not considered as a predictor. Besides, we observed condition index, proportion of variance and variance inflation factor. Data were analyzed by the SPSS – version 17.

Results

Our sample consisted in 138 dyads patient-caregiver. Table 1 summarizes the demographic and clinical characteristics of the sample.

Psychometric properties and comparative analysis of patients and caregivers' ratings

The internal consistency of DEMQOL and its domains were high for patients and for caregivers, (alpha coefficient >0.70). In the exploratory factor analysis of patients' ratings, we found three factors, which explain 50.01% of the variance. The factors were similar to those reported by Lucas et al. (11), although some items (2, 4 and 20) cross-loaded on more than one factor. These factors were also found in the exploratory analysis of caregivers' ratings, explaining 57.87%. Only item 4 cross-loaded on factor feelings and factor memory. There were significant differences between patients and caregivers in the DEMQOL scores ($p = 0.025$) and in the domain "feelings" ($p = 0.001$). Because no differences in the mean scores were observed for the domains ADL and memory ($p = 0.617$ and 0.174, respectively), we did not analyze the discrepancy in these domains.

Discrepancy between patients and caregivers measured with the individual difference score.

The mean difference for the total DEMQOL scores was 4.45 ± 14.37 (range 26 - 43). In 49 dyads (35.5%) the difference score was positive while in 32 dyads (23.18%) the difference score was negative. Similarly, the mean difference for DEMQOL feelings was 3.74 ± 7.97 (range -11 - 27). In 62 dyads (44.92%) the difference score was positive and in 27 dyads (19.56%) the difference score was negative. Due to this heterogeneity, we separately examined the predictors of positive differences and negative differences. No differences between dyads with positive differences and negative differences in patients' gender ($F=2.933$; $p=0.058$) and age (Chi-square =0.260 $p=0.878$).

Table 1
Sample characteristics

	Mean	SD	Range
Patients characteristics			
Sex: female (%)	68.6		
GDS			
Age	72.09	6.39	60-85
Years of education	4.48	2.71	0-12
MMSE	18.51	4.29	14-27
SMMSE	0.67	0.98	0-3
SGDS	4.84	3.32	0-14
NPI	30.59	18.23	5-87
NPI-psychosis	2.63	3.53	0-12.94
NPI-mood	7.40	5.19	0-18.38
NPI-behavioural disorder	5.43	3.76	0-14.18
CIR	4.16	2.65	0-8
CIRS	11.24	4.71	2-23
HUI-3 pain	2.02	1.06	1-5
DEMQOL	84.31	12.62	53-106
DEMQOL-feelings	40.43	7.06	23-51
DEMQOL-ADL	23.80	4.86	16-32
DEMQOL-memory	17.52	4.75	6-24
Caregiver characteristics			
Sex: female (%)	70.6		
Caregiver type (%): spouse.			
child. no relative	41.2	50.9	7.8
Age	58.86	15.91	30-85
ZBI	31.05	14.08	7-69
DEMQOL	79.86	15.44	48-110
DEMQOL-feelings	36.68	8.04	21-50
DEMQOL-ADL	24.15	5.19	14-32
DEMQOL-memory	16.52	5.67	6-24

MMSE, Mini-mental State examination; SMMSE, Mini-mental State examination; GDS, Global Deterioration Scale; SGDS, Geriatric Depression Scale; NPI, Neuropsychiatric Inventory; CIR, Clinical Insight Rating Scale; HUI 3, Health Utilities Index; CIRS, Cumulative Illness Rating Scale; ZBI, Zarit Burden Interview.

Positive differences

The variables NPI Psychosis, NPI mood and ZBI were entered in the regression model as correlated with the differences and with caregivers' DEMQOL ratings (Table 2). The model explained 42.9% of the discrepancy. Since only NPI mood and ZBI retained significance, we estimated a model considering only these factors (Table 3). The explanatory power (Adjusted R2) was similar (41.1%). No collinearity was found between predictors (Tolerance > 0.99 VIF < 1.1; Condition index = 6.4).

The possible predictors of difference score for DEMQOL feelings were NPI psychosis and NPI mood (Table 2). Only NPI mood retained significance, explaining 30.8% of the total variance (Table 3).

Table 2
Correlations between positive and negative differences and clinical variables

	DEMQOL						DEMQOL feelings					
	Positive differences			Negative differences			Positive differences			Negative differences		
	P	C	Dif	P	C	Dif	P	C	Dif	P	C	Dif
CIRS	-0.253	-0.186	-0.030	-0.150	0.282	-0.627**	-0.361*	-0.451**	0.253	0.006	0.266	-0.536*
SMMSE	-0.198	0.044	-0.204	0.244	0.323	-0.123	-0.253	-0.159	0.017	0.325	0.502*	-0.350
MMSE	0.057	0.103	-0.051	0.039	0.151	-0.164	0.041	-0.058	0.083	0.126	0.405*	-0.570**
HUI 3 pain	0.048	0.021	0.020	-0.323*	0.080	-0.579**	-0.125	-0.143	0.074	-0.713**	-0.500*	-0.470*
GDS	-0.309*	-0.191	-0.071	-0.739**	-0.631**	-0.136	-0.261	0.079	-0.232	-0.868**	-0.765**	-0.251
CIR	0.036	0.111	-0.076	0.047	0.165	-0.175	-0.098	-0.171	0.119	0.133	0.092	0.090
ZBI	0.119	-0.378**	0.541**	-0.095	-0.093	-0.081	-0.052	-0.229	0.128	0.085	0.000	-0.203
NPI psychosis	-0.117	-0.467**	0.349*	0.146	0.165	-0.031	-0.070	-0.318*	0.285*	0.107	-0.030	0.286
NPI mood	-0.136	-0.558**	0.420**	-0.802**	-0.642**	-0.211	-0.151	-0.629**	0.556**	-0.583**	-0.639**	0.090
NPI behaviour	0.032	-0.236	0.251	-0.279	-0.347	0.108	-0.091	-0.197	0.149	-0.060	-0.209	0.304

MMSE, Mini-mental State examination; SMMSE, Mini-mental State examination; GDS, Geriatric Depression Scale; NPI, Neuropsychiatric Inventory; CIR, Clinical Insight Rating Scale; HUI 3, Health Utilities Index; CIRS, Cumulative Illness Rating Scale; ZBI, Zarit Burden Interview. P, patients' ratings; C, caregivers' ratings, Dif, difference. *0.01<p<0.05; **p<0.01; ***p<0.001.

Negative differences

Only HUI-3 pain was considered as possible predictor of differences in DEMQOL because of its correlation with patients' ratings (Table 2). This factor explained 30.5% of the variance (Table 3). Regarding DEMQOL feelings difference score, both MMSE and HUI 3 pain score were considered as predictors. As Table 2 shows, MMSE correlates negatively with caregivers' ratings and HUI 3 pain correlates more negatively with patients' ratings than with caregivers' ratings. The model was significant and explained 72% of the variance (Table 3). HUI 3 pain explained 41.2 % and MMSE accounted for 28.8% of the variance. There was no collinearity (condition index = 9.72, tolerance > 0.92 and VIF < 1.1).

The results obtained by multiple linear regression for both positive and negative differences were confirmed using logistic regression analyses considering the difference between the two ratings as a binary variable (<10% vs ≥10% of total score).

Discrepancy between patients and caregivers measured with the residuals

Caregivers' total DEMQOL scores explained only 23.3% of patients' ratings. In 81 dyads (58.69%) the residuals from this regression were negative, and in 57 dyads (41.31%) were positive. As Table 4 shows, positive residuals were predicted only by ZBI (Adjusted R2=37.2%). To explain the negative residuals, SMMSE, HUI 3 pain, SGDS, and NPI mood were entered in the regression analysis. Only SGDS and HUI 3 pain retained significance, explained 51.2% of the variance (Table 4).

Patients' scores on DEMQOL feelings were explained in 32.5% by caregivers' scores. The residuals were positive in 79 cases (57.15 %) and negative in 59 cases (42.75%). There were differences between dyads with positive and negative residuals in patients' age (F=0.272; p=0.603) and gender (Chi-square=0.895 p=0.393). Possible predictors of the positive residuals were ZBI, NPI mood and NPI psychosis because of their negative correlations with caregivers' ratings (r=-0,309, 0,734 and -0.303, respectively). Only NPI mood retained significance in the final model (Adjusted R2 =13.8). Negative residuals were explained by up to 45.9% by SGDS (Table 4).

Regarding DEMQOL ADL, we found that 30.6% of patients' ratings was explained by caregivers' ratings. In 66 dyads (47.83%) the residuals were positive and in 72 dyads (52.17%) they were negative. There were no statistical differences between dyads with positive and negative residuals in patients' age (F=0.298; p=0.587) and gender (Chi-square=0.191; p=0.137). We did not find possible predictors for the negative residuals. Conversely, both ZBI and NPI psychosis correlated with caregivers' ratings (r=-0.557 and -0.267, respectively) and with the positive residuals (r = 0.333 and 0.471, respectively). Both factors explained 24.7% of the variance of the residuals (Table 4).

Only 8% of patients' scores on DEMQOL memory were explained by caregivers' ratings. The residuals were positive in 65 cases (47.11 %) and negative in 73 cases (52.89%). No differences were found between dyads with positive and negative residuals in patients' age (F=0.434; p=0.511) and gender (Chi-square=0.687; p=0.425). The variance of negative residuals was explained in 8% by MMSE. Possible predictors for positive residuals were ZBI, comorbidity and NPI mood. The final model explained 40.5% of the variance (Table 4).

Discussion

The agreement between observers can be estimated by different statistical methods. For continuous variables, the concordance correlation coefficient (25) seems to be more appropriate since it includes components of both

Table 3
Regression models to explain positive and negative differences

		Predictors	B	SE	β
Positive differences N=62	DEMQOL Dif				
	Model 1				
		Constant	-9.299	4.897	
		NPI mood	0.445	0.152	0.351***
		NPI psychosis	0.463	0.307	0.185
		ZBI	0.491	0.124	0.479***
	Model 2				
		Constant	-9.294	4.977	
		NPI mood	0.486	0.152	0.384**
		ZBI	0.527	0.123	0.514***
	DEMQOL feelings Dif				
	Model I				
		Constant	2.669	1.833	
		NPI mood	0.363	0.087	0.522***
		NPI psychosis	0.256	0.168	0.191
	Model 2				
		Constant	0.387	0.087	
		NPI mood	0.759	0.166	0.568***
Negative differences N=27	DEMQOL Dif				
		Constant	-0.880	3.080	
		HUI 3 pain	-4.976	1.494	-0.579**
	DEMQOL feelings Dif				
		Constant	9.463	2.045	
		MMSE	-0.355	0.059	-0.756***
		HUI 3 pain	-3.240	0.603	-0.677***

MMSE, Mini-Mental State Examination; NPI, Neuropsychiatric Inventory; HUI 3, Health Utilities Index; CIRS, ZBI, Zarit Burden Interview; Dif, difference score; B, unstandarized regression coefficient; SE, standard error of the regression coefficient. β, standardized regression coefficient. *0.01<p<0.05; **p<0.01; ***p<0.001.

accuracy and precision. Thus, the discrepancy, defined as the lack of agreement, should be measured in a double way: lack of precision and lack of accuracy. Most papers on the measurement of discrepancy between patients and caregivers have used the method of the difference score. However, this method has some limitations. The difference score is an unreliable variable when the correlation between the measures is high, the reliability of any of the measures is moderate and their variances are similar (26). Such situation did not occur in this study. The residual standardized scores have the advantage of not being correlated with the initial scores, although are still plagued with low reliability (27). Briefly, we used both methods as complementary ways of estimating discrepancy. We have considered the mean difference as a measure of lack of accuracy and the residuals as a measure of lack of precision.

We found a modest discrepancy, in terms of mean difference, between raters in DEMQOL scores. In fact, there is no difference in both DEMQOL total and domain "feelings" scores in 41% and 35% of the dyads, respectively. Moreover, there is no significant difference between means in the domains "ADL" and "memory". This may be because the agreement is higher for observable aspects of life (28). Another possible explanation is the existence of two groups of patient-caregiver dyads, as also reported Buckley et al. (29). One group, the most numerous, includes dyads in which patients score higher than caregivers; the other comprises those dyads in which patients' scores are lower than caregivers' scores. In the first group, we observed that burden is the main determinant of the discrepancy because of the negative influence on caregivers' ratings. These findings are consistent with previous research (7, 30-32). In line with this, we found that NPI "mood" score predicted discrepancy in the domain "feelings" because it influences only caregivers' ratings. This factor measures the behavioral manifestations of depression and, like other NPI symptoms, is related to caregivers' burden (31-33). Several studies have noted that NPI symptoms are associated with poor agreement between patients and caregivers ratings of HRQoL (5-6, 32). This could be due to the influence of NPI symptoms

Table 4
Regression models explaining the positive and the negative residuals

		Predictors	B	SE	β
Positive residuals N=57		Constant	2.140	1.930	
		ZBI	0.300	0.060	0.623***
Negative residuals N=81	Model 1	Constant	0.608	1.261	
		SMMSE	0.241	0.537	0.047
		HUI 3 pain	-1.937	0.633	-0.361**
		GDS	-0.764	0.161	-0.514***
		NPI mood	0.007	0.062	0.012
	Model 2	Constante	0.572	1.199	
		HUI 3 pain	-1.835	0.553	-0.342**
		GDS	-0.745	0.153	-0.501***
DEMQOL feelings					
Positive residuals N=79					
	Model 1	Constant	0.397	1.699	
		ZBI	0.048	0.036	0.169
		NPI mood	0.092	0.042	0.289*
		NPI psychosis	0.103	0.094	0.142
	Model 2	Constant	2.600	0.754	
		NPI-mood	0.119	0.040	0.371**
Negative residuals N=59	Model 1	Constant	-2.533	1.306	
		NPI behaviour	0.100	0.059	0.199
		GDS	-0.601	0.126	-0.620***
		HUI 3 pain	-0.266	0.533	-0.064
	Model 2	Constant	-1.710	0.805	
		GDS	-0.665	0.109	-0.686***
DEMQOL Memory					
Positive residuals N=65					
		Constant	4.026	0.881	
		ZBI	0.053	0.020	0.321*
		CIRS	-0.300	0.066	-0.567***
		NPI mood	0.089	0.030	0.385**
Negative residuals N=73		Constant	-5.164	0.994	
		MMSE	0.113	0.054	0.281*
DEMQOL ADL					
Positive residuals N=66		Constant	1.227	.862	
		ZBI	0.047	0.027	0.225*
		NPI psychosis	0.331	0.102	0.424**

MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Scale; NPI, Neuropsychiatric Inventory; CIR, Clinical Insight Rating Scale; HUI 3, Health Utilities Index; CIRS, Cumulative Illness Rating Scale; ZBI, Zarit Burden Interview; B, unstandarized regression coefficient; SE, standard error of the regression coefficient. β, standardized regression coefficient. *0.01<p<0.05; **p<0.01; ***p<0.001.

on caregivers' burden and depression. Additionally, in the case of NPI mood, we should consider that this reflects caregivers' perception of patients' depression (34-35). We cannot exclude the presence of rater bias.

In contrast, pain is the best predictor of discrepancy in the cases where patients score less than caregivers do. Pain is a prevalent symptom in dementia patients, which increases the risk of depression, and dependency in activities of daily living (34) and affects the self-perceived HRQoL (37). This symptom is often undetected and untreated in patients with cognitive impairment (38). The communications problems of patients make it difficult for caregivers to recognize this symptom (39).

In this study, patients' anosognosia was not found to be a significant predictor of patient-caregiver discrepancy. In fact, the effect of insight on both HRQoL ratings and patient-caregiver agreement seems to be small and be related with the level of cognitive impairment (8, 40-42). This could be due to the lack of reliability of the ratings of low-insight patients. However, we did not observe this situation. Overall, insight is a difficult ability to assess with the tools available due to its multidimensional character and the influence of contextual factors on its expression (43). More studies are necessary to establish the influence of patients' insight on their HRQoL and the ability to rate it.

The discrepancy, in terms of lack of precision, is higher than that measured by the mean difference. Caregivers

explained a low percent of patients' ratings in all the domains of DEMQOL. However, the sources of discrepancy are quite similar to those identified using the difference of means. Patients' ratings are underestimated by caregivers' ratings as burden increases. This was observed particularly for the domains ADL and memory. Conversely, patients with more pain and higher SGDS scores rated their HRQoL worse than expected. SGDS is a tool that measures self-perceived depression (14), a rather different construct from proxy perception of depression. The latter could be influenced by proxy personal beliefs, expectations or mood. Indeed, several studies show that SGDS is a good predictor of patients' ratings of HRQoL while proxy-rated depression predicts proxy's ratings (43-45). In line with this, we observed that, in the "feelings" domain, higher scores of proxy-rated depression (NPI mood) are associated with an underestimation by caregivers of patients' HRQoL. We also observed a relation between health and self-ratings of HRQoL. The more diseases patients have, the closer are their HRQoL ratings to their caregivers' ones. These results are consistent with previously reported data (29-30), providing support for convergent validity of patients' ratings. The reason that SGDS and comorbidity were not found as predictors of discrepancy using the mean difference score is methodological. The method of residuals allows us to identify factors that correlate similarly with both patients' and caregivers' ratings. However, when assessing the discrepancy with the method of difference mean, the effect of these factors is often unmasked.

Whether cognition has an impact on either HRQoL ratings or patient-caregiver agreement is still a controversial issue (5, 41). Some studies have suggested that agreement patient-caregiver decreases as cognition does (8, 30). In this study, cognitive function is important in the agreement only in the dyads where patients score less than caregivers. In domain feelings domain, the agreement is lower in less cognitively impaired patients because caregivers give higher scores. This could be because caregivers are influenced by their expectations of patients functioning when assessing patients' feelings. Surprisingly, patients' ratings about their memory abilities are lower as cognition decreases indicating convergent validity.

However, these results must be interpreted with caution. Since our sample includes only patients from day care centres, the data may not be generalizable to patients from other settings.

In conclusion, our data highlight the limitations of assessing HRQoL based on proxies' ratings. Caregivers do not seem to identify with accuracy patients' pain and emotional wellbeing. In addition, they are highly influenced by their burden when rating patients' HRQoL, even when they do from the patients' perspective. In these situations, caregivers' ratings are not adequate surrogates for patients' ones. Other sources of information about HRQoL should be used when patients suffer from pain and depression. This is especially important when using HRQoL as an outcome measurement of any therapy o care. Self-reports on DEMQOL are valid and reliable, even in moderate dementia and should be preferred.

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