

Validation of the Care-Related Quality of Life Instrument in different study settings: findings from The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS)

J. E. Lutomski · N. J. A. van Exel · G. I. J. M. Kempen · E. P. Moll van Charante ·
W. P. J. den Elzen · A. P. D. Jansen · P. F. M. Krabbe · B. Steunenbergh ·
E. W. Steyerberg · M. G. M. Olde Rikkert · R. J. F. Melis

Accepted: 24 October 2014
© Springer International Publishing Switzerland 2014

Abstract

Purpose Validity is a contextual aspect of a scale which may differ across sample populations and study protocols. The objective of our study was to validate the Care-Related Quality of Life Instrument (CarerQol) across two different study design features, sampling framework (general population vs. different care settings) and survey mode (interview vs. written questionnaire).

Methods Data were extracted from The Older Persons and Informal Caregivers Minimum DataSet (TOPICS-MDS, www.topics-mds.eu), a pooled public-access data set

with information on >3,000 informal caregivers throughout the Netherlands. Meta-correlations and linear mixed models between the CarerQol's seven dimensions (CarerQol-7D) and caregiver's level of happiness (CarerQol-VAS) and self-rated burden (SRB) were performed.

Results The CarerQol-7D dimensions were correlated to the CarerQol-VAS and SRB in the pooled data set and the subgroups. The strength of correlations between CarerQol-7D dimensions and SRB was weaker among caregivers who were interviewed versus those who completed a written questionnaire. The directionality of associations between the CarerQol-VAS, SRB and the CarerQol-7D dimensions in the multivariate model supported the construct validity of the CarerQol in the pooled population. Significant interaction terms were observed in several dimensions of the CarerQol-7D across sampling frame and

On behalf of TOPICS-MDS Consortium.

Electronic supplementary material The online version of this article (doi:10.1007/s11136-014-0841-2) contains supplementary material, which is available to authorized users.

J. E. Lutomski (✉) · M. G. M. Olde Rikkert · R. J. F. Melis
Department of Geriatric Medicine, Radboud University Medical Center, Postbus 9101, 6500 HB Nijmegen, The Netherlands
e-mail: jennifer.lutomski@radboudumc.nl

J. E. Lutomski
Anu Research Centre, University College Cork, Cork, Ireland

N. J. A. van Exel
Institute of Health Policy and Management, Erasmus University, Rotterdam, Netherlands

G. I. J. M. Kempen
Department of Health Services Research, CAPHRI School for Public Health and Primary Care, Maastricht University, Maastricht, Netherlands

E. P. Moll van Charante
Department of Internal Medicine and Geriatrics, Academic Medical Center, Amsterdam, Netherlands

W. P. J. den Elzen
Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, Netherlands

A. P. D. Jansen
Department of General Practice and Elderly Care Medicine/EMGO + Institute for Health and Care Research, VU University Medical Center, Amsterdam, Netherlands

P. F. M. Krabbe
Department of Epidemiology, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands

B. Steunenbergh
Julius Center for Health Sciences and Primary Care, UMC Utrecht, Utrecht, Netherlands

E. W. Steyerberg
Department of Public Health, Erasmus MC University Medical Center, Rotterdam, Netherlands

survey mode, suggesting meaningful differences in reporting levels.

Conclusions Although good scientific practice emphasises the importance of re-evaluating instrument properties in individual research studies, our findings support the validity and applicability of the CarerQol instrument in a variety of settings. Due to minor differential reporting, pooling CarerQol data collected using mixed administration modes should be interpreted with caution; for TOPICS-MDS, meta-analytic techniques may be warranted.

Keywords CarerQol-7D · Caregivers · Quality of life · Geriatric health services · Visual analogue scale

Purpose

Informal care for older persons has long served as an integral part of the healthcare system. However, increased longevity coupled with decreased fertility has widened the ratio between very old persons requiring care and middle-aged persons who have historically provided informal care [1]. These demographic trends are further compounded by wider geographical dispersion of family members [2], the increasing number of women joining the labour market [2] and the increasing prevalence of minor functional impairment and chronic (co-) morbidity among older persons [3–5]. The combination of these population dynamics leads to fewer persons available to provide support for older persons with more complex care needs as well as increased physical and mental stress on caregivers [6–9]. As government policies shift towards informal care to offset increasing healthcare costs, understanding care-related burden has become increasingly important in public health and health policy arenas [10].

With this backdrop, the Dutch National Care for the Elderly Programme funded the development and implementation of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS; www.topics-mds.eu) to guide future policy decision making and health interventions for older persons and informal caregivers in the Netherlands [11]. TOPICS-MDS is a large, public access, pooled data set with information from various research projects across the country. Yet, challenges in the analysis of TOPICS-MDS remain. Although the same set of core questions were answered by all caregivers, heterogeneity between study protocols may result in differential measurement error which becomes obscured in the pooled data set. For instance, TOPICS-MDS contains mixed-mode data, i.e. caregivers responded to the same core questions either in a face-to-face interview or in a written questionnaire. Measurement error may vary across these two survey modes due to differences in auditory versus visual

processing or a preference to provide socially desirable answers when interviewed [12]. Such phenomena are well documented in other research settings [13]. Furthermore, variation in sampling frames (e.g. sampled from the general population vs. primary centres) may elicit different response patterns [14]. Projecting the directionality and degree of measurement error induced by different study designs is difficult and may not be uniform across all variables [12, 15].

In light of these issues, the objective of our study was to validate the Care-Related Quality of Life Instrument (CarerQol) across two different study design features available in TOPICS-MDS, sampling framework (general population vs. different care settings) and survey mode (interview vs. written questionnaire). Notably, the CarerQol was the primary instrument used in TOPICS-MDS to measure care-related quality of life. Although it has been validated in earlier research [16, 17], these findings were based on small (<250 participants), specialised settings using a written questionnaire. Since construct validity is contextual [15], further validation work has been recommended [17].

Methods

Data source

Data were derived from TOPICS-MDS (www.topics-mds.eu), which is a public access data repository designed to capture essential information on the physical and mental well-being of older persons and informal caregivers in the Netherlands. A detailed description of TOPICS-MDS has been presented elsewhere [11]. Briefly, the Dutch National Care for the Elderly Programme (<http://www.nationaalprogrammaouderenzorg.nl>) was established in 2008 to promote proactive, integrated health care for older persons with complex care needs. As part of this national agenda, TOPICS-MDS was developed to collect uniform information from all research projects funded under the Programme. Thus, TOPICS-MDS consists of pooled data from various research projects which differ across study design, sampling framework and inclusion criteria. All data were cleaned locally using a standardised protocol. Anonymised individual-level data were then submitted to a central institution (Radboud University Medical Center, Nijmegen, Netherlands) for further validation checks and creation of the pooled data set. Since various research projects submit information to TOPICS-MDS, the database is dynamic in nature and thus regularly updated with new observations. Our present analysis uses the first version of the data set available as of January 2013 and is based on 17 research projects with data available on 3,269 informal caregivers.

TOPICS-MDS is a fully anonymised data set available for public access, and therefore this analysis was exempt from ethical review (Radboud University Medical Centre Ethical Committee review reference number: CMO: 2012/120).

Informal caregivers

Informal caregivers were defined as individuals who provided long-term, unpaid care for another individual in their family, household or social network who has physical, mental or cognitive limitations. Sociodemographic information available on informal caregivers included sex, age, socio-economic status [11], the caregiver's relationship with the care recipient, whether the caregiver resided with the care recipient, self-reported health and objective and subjective care-related burden.

Objective care-related burden refers to indicators which independently measure the size of the care task, such as the frequency of care provision. In TOPICS-MDS, the average number of hours a caregiver assisted the care recipient with household tasks, personal care or practical support (such as transport or financial/administrative duties) was recorded for the previous week.

Subjective care-related burden refers to personal perceptions of care burden. Given that internalisation of burden may vary between caregivers, caregivers in similar situations may report varying levels of burden, which in turn influences care-related quality of life. The CarerQol instrument was used to measure subjective care-related quality of life (Fig. 1; original Dutch version available at www.topics-mds.eu). This instrument is comprised of two parts, the Carer-QoL-7D and the CarerQol-visual analogue scale (CarerQol-VAS). Modelled after the EuroQol-5D, the CarerQol-7D was developed to measure seven dimensions of care-related burden which can then be used to derive a care-related quality of life summary score. These dimensions include care-related fulfilment, relational problems with the care recipient, mental health problems, physical health problems, problems completing daily activities, financial security and social support. Caregivers can describe their personal situation by responding whether they have “no”, “some” and “a lot” of problems for each attribute [16–18]. To generate a single summary score for the CarerQol-7D, the two positive items (care-related fulfilment and social support) are reverse scored and a set of weights (also referred to as a “tariff”) are applied to each level of the seven dimensions. These weights were based on preferences derived from the Dutch general population [19]. The CarerQol-7D summary score represents a utility score for the care situation that ranges between zero (worst informal care situation) and 100 (best informal care situation).

The CarerQol-VAS represents an additional valuation component which asks caregivers to rate their general level

of happiness using the statement “Please indicate how happy you are currently feeling”. Responses are recorded on a horizontal scale ranging from “0” (completely unhappy) to “10” (completely happy). For the purposes of this analysis, scores were subsequently converted to a scale ranging from 0 to 100.

Two additional VAS were also assessed [20]: (1) self-rated care burden (SRB) and (2) transfer of care (Transfer). SRB is an independent measure of subjective care burden that provides an overall assessment of the negative and positive aspects of caregiving [21]. SRB was assessed using the following statement, “Draw an ‘X’ on the scale to indicate how hard you are finding it to care for the care recipient”. Transfer describes a hypothetical situation in which care tasks are taken over by a person selected by the carer and the care recipient without changing the living situation of the care recipient and free of charge [22]. Given this scenario, caregivers were asked to “Draw an ‘X’ on the scale to indicate how happy you would feel if this person would take over the care responsibilities from you”. Unlike SRB, Transfer was not developed as a stand-alone measure but rather with the CarerQol-VAS to measure the concept of process utility (PU, described below). Both scales ranged from “0” to “10”, and similarly to the CarerQol-VAS, were converted to scores ranging from 0 (not difficult at all, completely unhappy with transferring caregiving tasks) to 100 (far too difficult, completely happy with transferring caregiving tasks).

PU is a derived measure representing the value a carer attaches to the process of informal caregiving and is calculated by taking the difference in happiness between two situations: the current situation (measured by CarerQol-VAS) and a hypothetical situation in which care tasks are transferred (measured by Transfer) [22]. A positive PU score indicates that the carer would be unhappy transferring care tasks, thus attaching a positive value to caregiving, whereas a negative PU score indicates the opposite. A PU score of zero indicates that the carer is neutral towards caregiving.

Care recipient

Informal caregiver data were linked with data on the care recipient. To examine the relationship between caregiver quality of life and the severity of the care recipient's vulnerability, we constructed a 45-item frailty index [23] validated for use in TOPICS-MDS [24]. A frailty index is calculated by reviewing ≥ 30 health problems affecting different physiological systems; the total number of problems observed in an individual is then divided by the total number of problems reviewed to calculate a proportion. Frailty index scores ≥ 0.20 indicate a likely frail state [23].

CarerQol-7D

The following questions are about your situation as a caregiver. Place an “X” next to the word that best describes your care situation.

- a. I gain...
☐ no
☐ some
☐ a lot
 ...(of) fulfilment with carrying out my care tasks.
- b. I have...
☐ no
☐ some
☐ a lot
 ...(of) relational problems with the care receiver (for example, he/she is very demanding, he/she behaves differently, we have communication problems).
- c. I have...
☐ no
☐ some
☐ a lot
 ...(of) problems with my own mental health (for example, stress, fear, gloominess, depression, concern about the future).
- d. I have...
☐ no
☐ some
☐ a lot
 ...(of) problems with my own physical health (for example, being sick more often, tiredness, physical stress).
- e. I have...
☐ no
☐ some
☐ a lot
 ...(of) problems combining my daily activities (for example, household activities, work, study, family activities and free time) with my care tasks.
- f. I have...
☐ no
☐ some
☐ a lot
 ...(of) financial problems because of my care tasks.
- g. I have...
☐ no
☐ some
☐ a lot
 ...(of) support with carrying out my care tasks when I need it (for example, from family, friends, neighbors, acquaintances).

CarerQol-VAS

Please draw an “X” on the scale below to indicate how happy you are feeling right now.

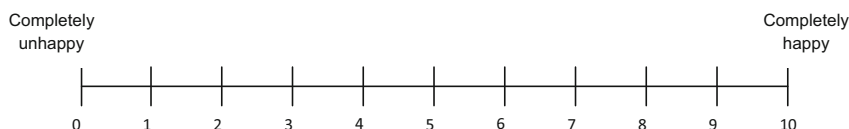


Fig. 1 CarerQol instrument

Statistical analysis

TOPICS-MDS is a pooled data set of individual-level information; subsequent analyses were performed using a one-step individual patient data meta-analysis. This type of

analysis, also referred to as a “mega-analysis”, allows the simultaneous analysis of data while accounting for the clustering effects. Since TOPICS-MDS is comprised of study projects with different sampling frameworks and implementation procedures, we decided a priori to perform

analyses in the pooled data set as well as across two subgroups: sampling framework (i.e. recruitment from the general population vs. hospital vs. primary care centres) and survey mode (i.e. caregivers who completed face-to-face interviews vs. written questionnaires). Notably, individual study protocols dictated survey mode.

We first described the characteristics of the study sample. We then assessed the distributional properties of the CarerQol-VAS, SRB and Transfer by examining mean scores, spread in variation (standard deviation), and the extent of floor or ceiling effects. Since there is no universally accepted threshold for identifying floor and ceiling effects, we considered these effects present if 15 % of caregivers reported either the lowest or highest scores [25]. We further examined the mean (standard deviation), range and floor and ceiling effects for PU and CarerQol-7D summary scores. Mean differences for the three VAS scores, PU and the CarerQol-7D summary score across subgroups were assessed using ANOVA.

For comparative purposes [17], we evaluated each of the seven dimensions of CarerQol-7D separately. We first calculated the distribution of responses. To assess whether construct validity, i.e. the degree to which scores are consistent with hypotheses [26], of the CarerQol-7D was upheld in the pooled data set and predefined subgroups, we calculated random effects meta-correlations (Spearman's rho) between CarerQol-VAS, SRB and PU scores and the seven dimensions of the CarerQol-7D with the *meta*-package in R [27]. A random effects meta-correlation was performed to allow for heterogeneity between individual studies in the pooled data set. Correlation coefficients were classified as trivial (≤ 0.1), weak (0.1 to <0.3), moderate (0.3 to <0.5), strong (0.5 to <0.7) and very strong (≥ 0.7) [28]. In line with previous research [17], we posited several hypotheses reading the directionality and magnitude of these associations (Supplemental Table 1). We presumed that construct validity was upheld if the strength of association and directionality of correlations coincided with most (~ 75 %) of our hypotheses [25].

Caregiver happiness and self-perceived burden have been shown to be associated with the CarerQol-7D [17]. Thus, to further examine construct validity, we conducted linear mixed models between these measures while allowing for clustering effects between study projects. Given the observed correlation between CarerQol-VAS and SRB, we applied a multivariate repeated measures approach to simultaneously model both outcomes as a function of the seven dimensions of the CarerQol-7D [29]. In the adjusted models, consideration was also given to caregiver's sex, age, socio-economic status, self-reported health and the care recipient's sex, age and frailty status.

To demonstrate the potential impact on multivariate analysis, interaction terms were assessed to determine if associations differed significantly across sampling framework (general population vs. different care settings) and survey mode (interview vs. written questionnaire). Covariates of interest in these models only included the seven dimensions of the CarerQol-7D and their interaction terms between sampling framework or survey mode. All statistical analyses were carried out using SAS (Version 9.3; SAS Institute Inc., Cary, NC, USA) and R (2013: Vienna, Austria).

Results

Sample characteristics

Data were pooled from 17 different research projects resulting in a data set of 3,269 caregivers. The pooled data set comprised of two large projects (>500 caregivers recruited), nine mid-sized projects (100 to <500 caregivers recruited) and six small projects (<100 caregivers recruited); a more detailed description of individual studies is available at www.topics-mds.eu. The majority of caregivers were recruited from primary care centres (59.3 %; $n = 1,940$), followed by the general population (23.0 %; $n = 753$) and hospitals (17.6 %; $n = 576$). Information on survey mode was available for two-thirds of caregivers (61.7 %; $n = 2,195$). Among caregivers with data on survey mode, most (86.3 %; $n = 1,895$) completed a written questionnaire. The majority of caregivers completing a written questionnaire were recruited from a primary care centre (59.5 %; $n = 1,127$).

Several differences in caregiver and care recipient characteristics were observed across sampling frames and survey mode (Table 1). Relative to those sampled from the general population or primary care centres, caregivers sampled from hospitals were more likely to be the care recipient's spouse and consequently reside with the care recipient. Care recipients sampled from hospitals were less likely to be female and on average reported a lower frailty index score. Caregivers who were interviewed were more likely to be older, the care recipient's spouse and reside with the care recipient; their care recipients were more likely to have at least one ADL limitation and to report higher frailty index scores.

Visual analogue scales and summary scores

Mean (SD) scores for the CarerQol-VAS, SRB and Transfer were 70.1 (16.5), 43.0 (25.4) and 50.0 (26.2), respectively (Table 2). Based on a 15 % threshold, no disproportionate clustering of responses was observed at

Table 1 Characteristics of informal caregivers by sampling frame and survey mode, The Older Persons and Informal Caregivers Minimal Dataset, 2013

	Overall (<i>N</i> = 3,269)	Sampling frame			Survey mode		
		General population (<i>N</i> = 753)	Hospital (<i>N</i> = 576)	Primary care (<i>N</i> = 1,940)	Interview (<i>N</i> = 300)	Questionnaire (<i>N</i> = 1,895)	Not indicated (<i>N</i> = 1,074)
Caregiver characteristics							
Women	70.1	68.5	68.1	71.3	69.0	69.4	71.8
Age in years (mean, SD)	63 (12)	64 (12)	65 (12)	63 (13)	66 (12)	63 (12)	63 (12)
Relationship with care recipient							
<i>Spouse/life partner</i>	43.9	46.0	53.9	40.2	57.0	41.3	44.7
<i>Child</i>	46.0	43.2	38.5	49.2	36.0	47.0	47.0
<i>Other</i>	10.1	10.9	7.6	10.6	7.0	11.7	8.3
Residence with care recipient	46.0	43.9	54.4	44.3	60.1	44.5	44.6
Care h/week (median, IQR)	8 (16)	9 (17)	11 (18)	8 (16)	12 (25)	9 (16)	7 (13)
Socioeconomic status quartile							
<i>Low</i>	27.2	19.8	35.4	27.6	19.6	32.3	20.3
<i>Lower middle</i>	22.7	17.8	22.4	24.7	25.3	21.2	24.6
<i>Upper middle</i>	22.3	21.3	14.5	24.9	31.8	21.7	20.6
<i>High</i>	27.9	41.2	27.7	22.8	23.3	24.8	34.5
Self-reported health							
<i>Excellent/Very good</i>	24.2	25.1	25.8	23.4	24.0	24.0	24.7
<i>Good</i>	45.0	45.4	44.2	45.1	46.3	45.4	44.0
<i>Fair/poor</i>	30.8	29.5	30.0	31.5	29.7	30.6	31.4
Care recipient characteristics							
Women	61.4	61.6	55.4	63.1	52.3	63.6	60.2
Age in years (mean, SD)	80 (7)	80 (8)	78 (7)	80 (7)	80 (7)	80 (7)	80 (7)
Multimorbidity	85.1	81.3	77.9	87.8	91.3	86.9	80.8
≥1 ADL limitation	89.3	83.3	84.0	94.0	95.1	89.0	87.4
Frailty index score (mean, SD)	0.33 (0.14)	0.33 (0.16)	0.26 (0.14)	0.34 (0.13)	0.35 (0.14)	0.31 (0.13)	0.33 (0.16)

Percentages are shown unless otherwise stated. Socio-economic status was based on an index score derived from geospatial data on average income, employment type and educational level for the Dutch population. Multimorbidity was defined as the presence of >2 conditions based on a list of 17 morbidities. ADL limitations were identified using an extended version of the Katz Index of Independence Activities of Daily Living. The frailty index ranges from 0 to 1 with higher scores indicating higher levels of frailty

SD standard deviation, IQR interquartile range, ADL activities of daily living

the scale extremes to indicate floor or ceiling effects. However, for SRB, a notably higher proportion of caregivers sampled from hospitals reported no self-perceived burden (11.0 %) relative to those sampled from the general population (2.3 %) or primary care centres (3.3 %). None of the caregivers who were interviewed reported the highest possible score for Transfer, whereas 2.4 % of caregivers who completed a written questionnaire did.

The distributional properties of PU and CarerQol-7D summary scores were broadly similar across sampling frame and survey mode (Table 2). The mean (SD) PU score was 20.0 (31.3), indicating that on average caregivers attached a positive value to providing care. None of the caregivers scored the lowest or the highest possible scores for the CarerQol-7D (i.e. 0, 100, respectively). When examining lower and upper thresholds (i.e. summary scores

≤5 or ≥95), overall, no caregivers scored ≤5, whereas 6.9 % scored ≥95.

Dimensions of the CarerQol

The vast majority of caregivers reported fulfilment in care giving and few reported financial difficulties due to their care-giving responsibilities (Fig. 2). Reporting levels across the individual dimensions of the CarerQol-7D varied minimally by sampling frame and survey mode (Supplemental Figures 1 and 2); yet, there were several key differences. Caregivers sampled from primary care centres were less likely to report “no” relational issues compared to caregivers sampled from the general population or hospitals (50.2, 63.7, 64.9 %, respectively) and more likely to report “some” relational issues (40.1, 28.6, 27.9 %,

Table 2 Distribution of visual analogue scales, process utility and CarerQoL-7D summary scores by sampling frame and survey mode

	Overall (<i>N</i> = 3,269)	Sampling frame		Survey mode					
		General population (<i>N</i> = 753)	Hospital (<i>N</i> = 576)	Primary care (<i>N</i> = 1,940)	<i>p</i> value	Interview (<i>N</i> = 300)	Questionnaire (<i>N</i> = 1,895)	Not indicated (<i>N</i> = 1,074)	<i>p</i> value
CarerQoL-VAS									
<i>Mean (SD)</i>	70.1 (16.5)	71.3 (17.4)	68.0 (19.2)	70.3 (14.7)	0.07	68.7 (13.5)	69.7 (16.7)	72.3 (17.0)	0.11
<i>Floor (%)</i>	0.3	0	0.8	0.2		0	0.4	0	
<i>Ceiling (%)</i>	3.6	6.0	3.4	2.5		1.3	3.2	6.6	
SRB									
<i>Mean (SD)</i>	43.0 (25.4)	39.4 (24.5)	37.4 (26.2)	46.0 (25.1)	0.58	57.2 (25.7)	39.5 (24.9)	45.1 (24.5)	0.34
<i>Floor (%)</i>	4.3	2.3	11.0	3.3		4.0	6.5	0.7	
<i>Ceiling (%)</i>	0.6	1.0	0.4	0.5		0.3	0.4	1.0	
Transfer									
<i>Mean (SD)</i>	50.0 (26.2)	49.4 (25.8)	49.7 (27.5)	50.5 (26.0)	0.83	48.7 (26.5)	50.4 (26.2)	49.6 (26.1)	0.30
<i>Floor (%)</i>	3.3	1.8	5.9	3.2		4.4	4.1	0	
<i>Ceiling (%)</i>	2.3	2.6	2.4	2.0		0	2.4	3.1	
Process utility									
<i>Mean (SD)</i>	20.0 (31.3)	22.0 (30.6)	17.9 (33.1)	19.6 (30.9)	0.57	20.1 (31.1)	19.2 (31.5)	22.7 (30.5)	0.07
<i>Range</i>	−90 to 100	−90 to 100	−80 to 100	−90 to 100		−50 to 100	−90 to 100	−90 to 90	
<i>Score <0</i>	20.9	18.2	23.7	21.3		22.2	21.8	17.2	
<i>Score = 0</i>	17.5	16.4	18.8	17.5		15.4	18.0	16.8	
<i>Score >0</i>	61.6	65.3	57.5	61.2		62.5	60.2	66.0	
CarerQoL-7D									
<i>Mean (SD)</i>	79.2 (14.7)	81.0 (13.5)	79.3 (14.9)	78.5 (15.1)	0.98	78.1 (15.5)	80.5 (14.0)	77.3 (15.4)	0.95
<i>Range</i>	14 to 98	19 to 98	21 to 98	14 to 98		21 to 98	19 to 98	13 to 98	
<i>Summary score ≤ 5 (%)</i>	0	0	0	0		0	0	0	
<i>Summary score ≥ 95 (%)</i>	6.9	6.8	6.9	6.9		9.2	7.6	5.0	

CarerQoL-VAS refers to the statement, “Please indicate how happy you are currently feeling”. SRB refers to the statement, “Please indicate how burdensome you feeling care for loved one is at the moment”. Transfer refers to the statement, “Please indicate how happy you would feel if your caregiver responsibilities were taken over by someone else”. CarerQoL-VAS, SRB and Transfer are visual analogue scales ranging from 0 to 100. Process utility is a derived measure representing the value a carer attaches to the process of informal caregiving. Statistical significance between sampling frame and survey mode subgroups were tested using ANOVA

SD standard deviation

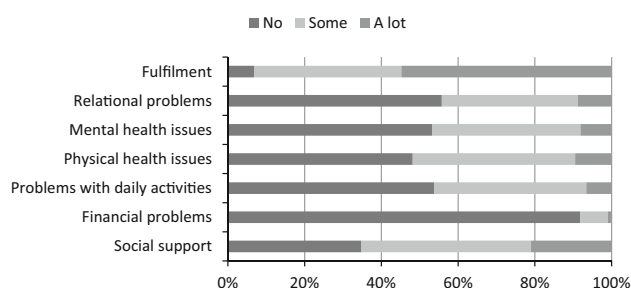


Fig. 2 Distribution of CarerQol-7D dimension ($N = 3,269$)

respectively). Compared to those who completed a written questionnaire, caregivers who were interviewed reported higher levels of social support and relational problems though lower levels of fulfilment in caregiving.

Random effects meta-correlation

In the pooled data set, a weaker negative correlation was observed between the CarerQol-VAS and SRB, whereas a stronger positive correlation was observed between the CarerQol-VAS and PU (Table 3). There was a weak to moderate negative correlation between the CarerQol-VAS and five of the CarerQol-7D dimensions (relational problems, mental health issues, physical health issues, problems with daily activities and financial problems). SRB was negatively correlated with PU and fulfilment and positively correlated with the remaining CarerQol-7D dimensions. Similar patterns were observed for PU though in contrasting directionality. Observed correlations in the pooled data set generally coincided with hypothesized magnitude and directionality (Table 3, Supplemental Table 1). The magnitudes of observed correlations differed modestly by

sampling frame and survey mode. Specifically, correlations between SRB and the CarerQol-7D dimensions were weaker among caregivers who were sampled from primary care centres and who were interviewed (Supplemental Tables 2 and 3).

Multivariate analysis

The directionality of associations in the multivariate model between the CarerQol-VAS, SRB and the seven CarerQol dimensions supported the construct validity of the CarerQol in the pooled population (Table 4). The positive dimensions of the CarerQol-7D (fulfilment, social support) were positively associated with the CarerQol-VAS, whereas the negative dimensions (relational problems, mental health issues, physical health issues, problems with daily activities and financial problems) were negatively associated with the CarerQol-VAS; contrasting associations were observed for SRB. Similar associations persisted in the adjusted model. Poor self-rated health and frailty of the care recipient were negatively associated with the CarerQol-VAS and positively associated with increased SRB, further supporting the validity of the measures.

In the last analysis, the CarerQol-VAS and SRB were modelled as a function of the seven dimensions of the CarerQol-7D and their interaction terms with sampling frame or survey mode; significant interaction terms were primarily observed for SRB (Tables 5, 6). The patterns of association between the positive and negative dimensions of the CarerQol-7D and the CarerQol-VAS and SRB were similar to the unadjusted model. However, the interaction terms did impact the strength of these associations. Relative to caregivers sampled from primary care centres, there

Table 3 Random effects meta-correlation coefficient (Spearman's rho)

	CarerQol-VAS (95 % CI)	SRB (95 % CI)	PU (95 % CI)
SRB	−0.25 (−0.40, −0.10)		
PU	0.52 (0.49, 0.54)	−0.35 (−0.44, −0.24)	
CarerQol domains			
Fulfilment	0.19 (0.15, 0.24)	−0.16 (−0.22, −0.09)	0.28 (0.22, 0.34)
Relational problems	−0.27 (−0.32, −0.22)	0.36 (0.27, 0.44)	−0.30 (−0.33, −0.27)
Mental health issues	−0.43 (−0.48, −0.38)	0.36 (0.26, 0.46)	−0.29 (−0.33, −0.25)
Physical health issues	−0.35 (−0.38, −0.31)	0.33 (0.21, 0.45)	−0.26 (−0.31, −0.21)
Problems with daily activities	−0.27 (−0.31, −0.24)	0.40 (0.27, 0.52)	−0.32 (−0.37, −0.28)
Financial problems	−0.17 (−0.21, −0.12)	0.15 (0.05, 0.24)	−0.14 (−0.18, −0.09)
Social support	0.09 (0.03, 0.14)	0.002 (−0.05, 0.05)	0.01 (−0.04, 0.06)

CarerQol-VAS refers to the statement, “Please indicate how happy you are currently feeling”. SRB refers to the statement, “Please indicate how burdensome you feeling care for loved one is at the moment”. PU, process utility, is a derived measure representing the value a carer attaches to the process of informal caregiving

95 % CI 95 % confidence interval

Table 4 Multivariable multivariate analysis of CarerQol-VAS and Self-Rated Burden (SRB)

	CarerQol-VAS				SRB			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	β	95 % CI	β	95 % CI	β	95 % CI	β	95 % CI
Intercept	88.41	83.90, 92.92	92.17	86.67, 97.66	-1.86	-7.48, 3.76	-4.48	-12.04, 3.08
Fulfilment	2.34	1.38, 3.31	2.27	1.24, 3.29	-2.03	-3.25, -0.80	-2.76	-4.23, -1.29
Relational problems	-2.81	-3.80, -1.82	-2.38	-3.45, -1.32	8.97	7.71, 10.22	7.73	6.20, 9.26
Mental health issues	-7.96	-9.02, -6.89	-7.41	-8.57, -6.24	5.67	4.32, 7.03	5.48	3.81, 7.15
Physical health issues	-3.53	-4.57, -2.50	-1.37	-2.66, -0.09	3.82	2.49, 5.14	2.97	1.13, 4.81
Problems with daily activities	-1.00	-2.08, 0.08	-1.47	-2.65, -0.29	11.04	9.68, 12.40	10.30	8.61, 12.00
Financial problems	-2.12	-3.93, -0.30	-1.00	-3.04, 1.04	2.15	-0.20, 4.49	2.49	-0.43, 5.42
Social support	0.58	-0.20, 1.36	0.19	-0.65, 1.03	0.89	-0.12, 1.90	0.25	-0.96, 1.46
Caregiver's sex (referent: female)			-1.07	-2.58, 0.44			-0.58	-2.74, 1.59
Caregiver's age			0.03	-0.03, 0.08			0.02	-0.06, 0.10
Socioeconomic status quartile								
Low			-0.41	-2.07, 1.24			1.23	-1.11, 3.57
Lower middle			0.01	-1.78, 1.79			-0.82	-3.35, 1.71
Upper middle			-1.48	-3.19, 0.24			-0.63	-3.07, 1.80
High			Reference				Reference	
Self-reported health								
Excellent/very good			Reference				Reference	
Good			-4.59	-6.14, -3.04			-1.58	-3.80, 0.65
Fair/poor			-6.89	-8.91, -4.87			-0.16	-3.07, 2.75
Care recipient's sex (reference: female)			-1.05	-2.49, 0.38			1.47	-0.59, 3.53
Care recipient's age			0.11	0.02, 0.20			0.02	-0.11, 0.15
Care recipient's frailty index score			-9.38	-13.98, -4.78			31.50	24.91, 38.09
Cluster effects								
Cluster variance (σ_u^2)		1.83		4.37		70.46		84.59
Error variance (σ_e^2)		201.41		186.73		381.24		368.34
Intraclass correlation coefficient (ρ)		0.009		0.02		0.16		0.19

CarerQol-VAS refers to the statement, "Please indicate how happy you are currently feeling". SRB refers to the statement, "Please indicate how burdensome you feeling care for loved one is at the moment". Unstandardised beta (β) estimates are presented. Models are adjusted for all variables listed on the table. The centred mean age was used in the multiple multivariate analysis

95 % CI 95 % confidence interval

was a weaker association between relational problems and SRB in caregivers sampled from hospitals; in contrast, the association between mental health issues and SRB was stronger (Table 5). Moreover, a stronger association between problems with daily activities and SRB was observed for caregivers sampled from the general population. A significant interaction between survey mode and physical health was observed for both the CarerQol-VAS and SRB, underscoring meaningful differences in the reporting of this item in an interview versus a written questionnaire (Table 6). Relative to caregivers who completed a written questionnaire, a weaker association was found between physical health issues and the CarerQol-VAS and SRB in caregivers who were interviewed. Similarly, the association between problems with daily activities and SRB was weaker.

Discussion

Our examination of the CarerQol instrument in different study settings demonstrates that construct validity was maintained. Although good scientific practice emphasises the importance of re-evaluating instrument properties in individual research studies [15], our findings lend support to the applicability of the CarerQol instrument in a variety of settings. Nonetheless, pooled analyses based on the full TOPICS-MDS may not be appropriate for all research questions due to minor differential reporting. Survey mode in particular seemed to modestly influence self-reported burden. Given the available data, we are unable to discern why such differences arose, and we cannot exclude that some findings may be due to statistical chance alone. Still, different survey administration modes have been shown to

Table 5 Interaction estimates for sampling frame in the multivariate analysis of CarerQol-VAS and self-rated Burden (SRB)

	CarerQol-VAS		SRB	
	β	95 % CI	β	95 % CI
Intercept	85.58	79.09, 92.07	6.39	−14.27, 0.51
Fulfilment	3.66	2.28, 5.06	−2.89	−4.51, −1.27
Relational problems	−2.49	−3.86, −1.12	9.21	7.61, 10.81
Mental health issues	−7.94	−9.41, −6.47	4.35	2.63, 6.07
Physical health issues	−2.90	−4.32, −1.48	3.93	2.25, 5.61
Problems with daily activities	−0.93	−2.43, 0.57	9.56	7.82, 11.31
Financial problems	−3.57	−6.22, −0.92	2.54	−0.61, 5.68
Social support	0.72	−0.38, 1.82	0.90	−0.42, 2.23
Sampling frame				
Primary care	Reference			
General	9.28	−0.38, 18.94	−15.93	−28.24, −3.62
Hospital	−0.22	−10.77, 10.32	−18.24	−32.06, 4.42
Fulfilment*				
General	−3.01	−5.25, −0.77	2.02	−0.92, 4.95
Hospital	−1.46	−3.99, 1.06	0.67	−2.71, 4.05
Relational problems*				
General	−1.35	−3.63, 0.94	0.56	−2.46, 3.58
Hospital	0.93	−1.78, 3.64	−3.81	−7.48, −0.15
Mental health issues*				
General	−0.38	−2.87, 2.11	2.54	−0.75, 5.83
Hospital	0.62	−2.25, 3.49	4.15	0.21, 8.09
Physical health issues*				
General	−1.33	−3.73, 1.08	−1.15	−4.34, 2.03
Hospital	−1.41	−4.25, 1.42	1.00	−2.86, 4.87
Problems with daily activities*				
General	−0.20	−2.70, 2.31	3.56	0.26, 6.89
Hospital	0.02	−2.86, 2.91	3.66	−0.23, 7.55
Financial problems*				
General	1.34	−3.09, 5.76	−0.96	−6.82, 4.90
Hospital	3.90	−0.48, 8.29	−0.01	−5.90, 5.87
Social support*				
General	0.72	−1.09, 2.54	−0.61	−3.02, 1.80
Hospital	−1.48	−3.52, 0.57	1.12	−1.65, 3.90
Cluster effects				
Cluster variance (σ_u^2)		1.70		75.72
Error variance (σ_e^2)		200.83		379.79
Intraclass correlation coefficient (ρ)		0.008		0.17

CarerQol-VAS refers to the statement, “Please indicate how happy you are currently feeling”. SRB refers to the statement, “Please indicate how burdensome you feeling care for loved one is at the moment”. Unstandardised beta (β) estimates are presented. Statistically significant interaction terms are indicated in bold. An asterisk (*) indicates an interaction term

influence response patterns [12, 13, 30], and caregivers may have underreported certain difficulties to frame their responses as more “socially desirable”. Importantly, these findings should encourage future users of the CarerQol-7D and TOPICS-MDS to be mindful that certain outcome measures, such as SRB, may be more heavily influenced by study design features than others.

In our present study, we expanded on previous research by validating the CarerQol among caregivers who were sampled from the general population, hospitals and

primary care centres. Reassuringly, observed associations between the CarerQol dimensions and outcomes of interest were similar [16, 17]. However, complementary research examining other care settings, such as retirement communities or nursing homes, would also be of benefit. Such settings are unique given the integration of informal and formal care. TOPICS-MDS did contain two studies sampled from nursing homes though these studies were excluded due to small numbers (100 observations in total).

Table 6 Interaction estimates for survey mode in the multivariate analysis of CarerQol-VAS and Self-Rated Burden (SRB)

	CarerQol-VAS		SRB	
	β	95 % CI	β	95 % CI
Intercept	87.09	81.77, 92.42	-6.88	-14.27, 0.51
Fulfilment	2.51	1.35, 3.66	-2.34	-3.99, -0.69
Relational problems	-1.86	-3.07, -0.66	8.83	7.11, 10.54
Mental health issues	-8.51	-9.76, -7.26	5.77	3.98, 7.57
Physical health issues	-4.13	-5.38, -2.89	5.60	3.83, 7.38
Problems with daily activities	-0.20	-1.47, 1.06	11.49	9.69, 13.30
Financial problems	-2.45	-4.50, -0.39	4.15	1.21, 7.10
Social support	0.79	-0.14, 1.71	-0.01	-1.32, 1.30
Survey mode (questionnaire = reference)	-8.78	-21.38, 3.82	55.97	38.17, 73.77
Fulfilment * mode	2.09	-0.99, 5.17	-1.81	-6.17, 2.54
Relational problems * mode	-2.13	-4.87, 0.61	-2.79	-6.69, 1.10
Mental health issues * mode	1.18	-2.03, 4.39	-3.07	-7.64, 1.49
Physical health issues * mode	4.82	1.80, 7.84	-9.35	-13.64, -5.07
Problems with daily activities * mode	-2.97	-6.23, 0.30	-7.62	-12.26, -2.98
Financial problems * mode	0.15	-5.76, 6.05	-7.89	-16.31, 0.53
Social support * mode	-0.30	-2.70, 2.11	3.34	-0.09, 6.76
Cluster effects				
Cluster variance (σ_u^2)		2.77		80.43
Error variance (σ_e^2)		190.85		372.33
Intraclass correlation coefficient (ρ)		0.01		0.18

CarerQol-VAS refers to the statement, "Please indicate how happy you are currently feeling". SRB refers to the statement, "Please indicate how burdensome you feeling care for loved one is at the moment". Statistically significant interaction terms are indicated in bold. Mode was defined as either interview or written questionnaire (reference group). An asterisk (*) indicates an interaction term

Although we reported the distributional properties of Transfer, it is important to emphasise that this VAS was developed in conjunction with the CarerQol-VAS with the intention of measuring PU. Transfer has not been independently validated for use in health services research, and thus should not be used as an individual marker of care-related burden. Nonetheless, we felt it was informative to present the distributional properties of Transfer since these measures directly influence the range of PU scores. If differential reporting was observed for one VAS and not the other, then the PU measurement may need to be re-evaluated. However, we found that neither VAS seemed to be disproportionately influenced by sampling frame or survey mode.

Our work is subject to several limitations. Firstly, the operationalisation of concepts may raise concerns, specifically how caregivers interpret the CarerQol-VAS (happiness) and SRB (burden). However, using a VAS to measure general happiness has been widely applied in psychological and economic research [31] as well as specifically in the context of informal care [32, 33]. Similarly, when compared with different burden scales, SRB produced a valid measure of burden [21]. Furthermore, the lack of a universally accepted operational definition for informal care may impede the applicability of findings. TOPICS-MDS applied a broad definition, defining informal care as long-term, voluntary and unpaid care for individuals with limitations impeding their ability to meet their daily needs.

This definition did not specify a time duration for "long-term" care, though recent guidelines developed in the Netherlands have defined "long-term" as care provision lasting at least 2 weeks [34].

Secondly, due to extensive missingness in the survey mode, we were inhibited from stratifying our analysis by both sampling frame and survey mode. Since the majority of interviews were conducted on caregivers sampled from primary care centres, we were unable to ascertain the interaction between these two study design features. Further stratification may have exposed additional complexities in the data set. It is also important to note that survey mode was determined according to individual study protocols. The majority of included studies used written questionnaires, three were mixed mode and one was interview only. To reduce bias, data collection was performed using standardised forms, and we accounted for clustering effects within individual studies by performing linear mixed models.

Lastly, our current analysis revealed minor differential reporting by survey mode; we have not discussed treatment of differential reporting in TOPICS-MDS. Since the magnitude and directionality of bias may vary across individual survey items, quantifying the sole impact of a study design feature is challenging. We speculate that uniform solutions are unlikely given that differential reporting is dependent upon the outcomes and covariates of interest. We do, however, encourage future users of TOPICS-MDS to apply

meta-analytic techniques to examine heterogeneity and assess the feasibility of using pooled data [35]. Such techniques may include the a priori decision to perform subgroup or sensitivity analyses by survey mode [36]. Whereas random effects meta-analyses may be suitable for certain research questions, it is critical to emphasise that such analyses do not “fix” issues of heterogeneity [36].

In this regard, a major strength of our study was that we were able to perform an individual patient data meta-analysis using TOPICS-MDS, a standardised, pooled master database. There are numerous advantages of using individual patient data over aggregate data, such as the ability to include unpublished data (thus reducing publication bias) and the ability to perform standardised statistical analyses across studies [37]. As data sharing becomes increasingly encouraged in the scientific community [38], attempted retrieval of individual patient data should be encouraged in the protocol phase of a meta-analysis. Although individual patient data meta-analysis cannot circumvent all the challenges associated with pooled data [39, 40], it can enhance researchers’ understanding of the data and the effects of heterogeneity.

An additional strength is that we defined measurement properties (i.e. validity) in line with previous work published by CONSENSUS-based Standards for the selection of health Measurement INSTRUMENTS (COSMIN) Initiative [26]. Variation in terminology and definitions for measurement properties frequently occurs in scientific research. By adhering to recommended terms and definitions reached through international consensus, we aimed to create a greater transparency in our work.

In conclusion, our analysis supports the overall validity of the CarerQol instrument. This finding is not only relevant for individuals who wish to access TOPICS-MDS data, but also individuals who would like to apply the CarerQol instrument in future studies of care-related quality of life. Due to minor differential reporting, pooling mixed-mode CarerQol data should be interpreted with caution; for TOPICS-MDS, meta-analytic techniques may be warranted.

Acknowledgments The authors thank TOPICS-MDS Consortium members for their contribution to this research. The National Care for the Elderly Programme on behalf of the Organisation of Health Research and Development (ZonMw—The Netherlands). TOPICS-MDS Consortium: *Project Group* W.P.J. den Elzen (Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, Netherlands); A.P.D. Jansen (Department of General Practice and Elderly Care Medicine/EMGO + Institute for Health and Care Research, VU University Medical Center, Amsterdam, Netherlands); G.I.J.M. Kempen (CAPHRI School for Public Health and Primary Care, Department of Health Services Research, Maastricht University, Netherlands); P.F.M. Krabbe (Department of Epidemiology, University of Groningen, University Medical Center Groningen, Netherlands); R.J.F. Melis (Department of Geriatric Medicine, Radboud University Medical Center, Nijmegen, Netherlands); E.P. Moll

van Charante (Department of General Medicine, Academic Medical Center, Amsterdam, Netherlands); B. Steunenberg (Julius Center for Health Sciences and Primary Care, UMC Utrecht, Netherlands); E.W. Steyerberg (Department of Public Health, Erasmus MC University Medical Center, Rotterdam, Netherlands); *Steering Committee* E. Buskens (Department of Epidemiology, University of Groningen, University Medical Center, Groningen, Netherlands); J. Gussekloo (Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, Netherlands); H.E. van der Horst (Department of General Practice and Elderly Care Medicine, EMGO Institute for Health and Care Research, VU University Medical Centre Amsterdam, Netherlands); M.G.M. Olde-Rikkert, (Department of Geriatric Medicine, Radboud University Medical Center, Nijmegen, Netherlands); S.E.J.A. de Rooij (Department of Internal Medicine, Academic Medical Center, Amsterdam, Netherlands); J.M.G.A. Schols (Department of Family Medicine and Department of Health Services Research, CAPHRI School for Public Health and Primary Care, Maastricht University, Maastricht, Netherlands); M.J. Schuurmans (Department of Rehabilitation, Nursing Science and Sports, University Medical Center Utrecht, Netherlands); D. Smilde (Department of Research Policy, Erasmus MC University Medical Centre, Rotterdam, Netherlands); R.G.J. Westendorp (Leyden Academy on Vitality and Ageing, Leiden University Medical Center); *Working group* D. van den Brink, J.E. Lutonski, L. Qin (Department of Geriatric Medicine, Radboud University Medical Center, Nijmegen, Netherlands).

References

- Robine, J. M., Michel, J. P., & Herrmann, F. R. (2007). Who will care for the oldest people in our ageing society? *BMJ*, 334(7593), 570–571.
- Agree, E. M., & Glaser, K. (2009). Demography of informal caregiving. In P. Uhlenberg (Ed.), *International handbook of population aging* (pp. 647–668). Netherlands: Springer.
- Ward, B. W., & Schiller, J. S. (2013). Prevalence of multiple chronic conditions among US adults: Estimates from the National Health Interview Survey, 2010. *Preventing Chronic Disease*, 10, E65.
- Caughey, G. E., Vitry, A. I., Gilbert, A. L., & Roughead, E. E. (2008). Prevalence of comorbidity of chronic diseases in Australia. *BMC Public Health*, 8, 221.
- Uijen, A. A., & van de Lisdonk, E. H. (2008). Multimorbidity in primary care: Prevalence and trend over the last 20 years. *European Journal of General Practice*, 14(Suppl 1), 28–32.
- Bevans, M., & Sternberg, E. M. (2012). Caregiving burden, stress, and health effects among family caregivers of adult cancer patients. *JAMA*, 307(4), 398–403.
- Schulz, R., & Beach, S. R. (1999). Caregiving as a risk factor for mortality: The Caregiver Health Effects Study. *JAMA*, 282(23), 2215–2219.
- Joling, K. J., van Hout, H. P., Schellevis, F. G., van der Horst, H. E., Scheltens, P., Knol, D. L., et al. (2010). Incidence of depression and anxiety in the spouses of patients with dementia: A naturalistic cohort study of recorded morbidity with a 6-year follow-up. *The American Journal of Geriatric Psychiatry*, 18(2), 146–153.
- Bobinac, A., van Exel, N. J., Rutten, F. F., & Brouwer, W. B. (2011). Health effects in significant others: Separating family and care-giving effects. *Medical Decision Making*, 31(2), 292–298.
- Mestheneos, E., & Triantafyllou, J. (Eds.). (2005). *Supporting family carers of older people in Europe: The Pan-European background report. Empirical evidence, policy trends and future perspectives*. Hamburg: Lit Verlag.

11. Lutonski, J. E., Baars, M. A., Schalk, B. W., Boter, H., Buurman, B. M., den Elzen, W. P., et al. (2013). The development of the older persons and informal caregivers survey minimum dataset (TOPICS-MDS): A large-scale data sharing initiative. *PLoS ONE*, 8(12), e81673.
12. Martin, P., & Lynn, P. (2011). *The effects of mixed mode survey designs on simple and complex analyses*. Centre for comparative social surveys working paper series: Paper no. 04: Centre for comparative social surveys, City University London.
13. Hood, K., Robling, M., Ingledew, D., Gillespie, D., Greene, G., Ivins, R., et al. (2012). Mode of data elicitation, acquisition and response to surveys: A systematic review. *Health Technology Assessment*, 16(27), 1–162.
14. Groves, R. M., & Peytcheva, E. (2008). The impact of nonresponse rates on nonresponse bias: A meta-analysis. *Public Opinion Quarterly*, 72(2), 167–189.
15. Streiner, D. L., & Norman, G. R. (2008). *Health measure scales: A practical guide to their development and use* (4th ed., pp. 167–210). Oxford University Press: New York.; 247–276.
16. Hoefman, R. J., van Exel, N. J., Foets, M., & Brouwer, W. B. (2011). Sustained informal care: The feasibility, construct validity and test-retest reliability of the CarerQol-instrument to measure the impact of informal care in long-term care. *Aging & Mental Health*, 15(8), 1018–1027.
17. Hoefman, R. J., van Exel, N. J., Looren de Jong, S., Redekop, W. K., & Brouwer, W. B. (2011). A new test of the construct validity of the CarerQol instrument: Measuring the impact of informal care giving. *Quality of Life Research*, 20(6), 875–887.
18. Brouwer, W. B., van Exel, N. J., van Gorp, B., & Redekop, W. K. (2006). The CarerQol instrument: A new instrument to measure care-related quality of life of informal caregivers for use in economic evaluations. *Quality of Life Research*, 15(6), 1005–1021.
19. Hoefman, R. J., van Exel, J., Rose, J. M., van de Wetering, E. J., & Brouwer, W. B. (2014). A discrete choice experiment to obtain a tariff for valuing informal care situations measured with the CarerQol instrument. *Medical Decision Making*, 34(1), 84–96.
20. Hoefman, R. J., van Exel, J., & Brouwer, W. (2013). How to include informal care in economic evaluations. *Pharmacoeconomics*, 31(12), 1105–1119.
21. van Exel, N. J., Scholte op Reimer, W. J., Brouwer, W. B., van den Berg, B., Koopmanschap, M. A., & van den Bos, G. A. (2004). Instruments for assessing the burden of informal caregiving for stroke patients in clinical practice: A comparison of CSI, CRA, SCQ and self-rated burden. *Clinical Rehabilitation*, 18(2), 203–214.
22. Brouwer, W. B., van Exel, N. J., van den Berg, B., van den Bos, G. A., & Koopmanschap, M. A. (2005). Process utility from providing informal care: The benefit of caring. *Health Policy*, 74(1), 85–99.
23. Searle, S. D., Mitnitski, A., Gahbauer, E. A., Gill, T. M., & Rockwood, K. (2008). A standard procedure for creating a frailty index. *BMC Geriatrics*, 8, 24.
24. Lutonski, J. E., Baars, M. A., van Kempen, J. A., Buurman, B. M., den Elzen, W. P., Jansen, A. P., et al. (2013). Validation of a frailty index from the older persons and informal caregivers survey minimum data set. *Journal of the American Geriatrics Society*, 61(9), 1625–1627.
25. Terwee, C. B., Bot, S. D., de Boer, M. R., van der Windt, D. A., Knol, D. L., Dekker, J., et al. (2007). Quality criteria were proposed for measurement properties of health status questionnaires. *Journal of Clinical Epidemiology*, 60(1), 34–42.
26. Mokkink, L. B., Terwee, C. B., Patrick, D. L., Alonso, J., Stratford, P. W., Knol, D. L., et al. (2010). The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *Journal of Clinical Epidemiology*, 63(7), 737–745.
27. Schwarzer, G. (2013). *meta: Meta-analysis with R*. <http://cran.r-project.org/web/packages/meta/meta.pdf>. Version = 3.1-2.
28. Hopkins, W. G. (2002). *A new view of statistics: Effect magnitudes*. Retrieved from <http://www.sportsci.org/resource/stats/effectmag.html> on 27 February 2014.
29. Singer, J. D. (1998). Using SAS PROC MIXED to fit multilevel models, hierarchical models, and individual growth models. *Journal of Educational and Behavioral Statistics*, 23(4), 323–355.
30. De Leeuw, E. D. (2005). To mix or not to mix data collection modes in surveys. *Journal of Official Statistics*, 21, 233–255.
31. van Praag, B. M. S., Frijters, P., & Ferrer-i-Carbonell, A. (2003). The anatomy of subjective well-being. *Journal of Economic Behavior & Organization*, 51, 29–49.
32. Bobinac, A., van Exel, N. J. A., Rutten, F. F. H., & Brouwer, W. B. F. (2010). Caring for and caring about: Disentangling the caregiver effect and the family effect. *Journal of Health Economics*, 29, 549–556.
33. van den Berg, B., & Ferrer-i-Carbonell, A. (2007). Monetary valuation of informal care: The well-being valuation method. *Health Economics*, 16, 1227–1244.
34. Hoefman, R. J., Van Exel, N. J. A., & Brouwer, W. B. F. (2011). *iMTA Valuation of Informal Care Questionnaire (iVICQ)*. Version 1.0 (December 2011). Rotterdam: iBMG/iMTA, 2011. Retrieved from www.bmg.eur.nl/english/imta/publications/manuals_questionnaires/ on 25 September 2013.
35. Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & Group, P. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *BMJ*, 339, b2535.
36. Higgins, J. P. T., & Green, S. (eds) (2009). *Cochrane handbook for systematic reviews of interventions version 5.0.2* [updated September 2009]. The Cochrane Collaboration, 2009. www.cochrane-handbook.org.
37. Riley, R. D., Lambert, P. C., & Abo-Zaid, G. (2010). Meta-analysis of individual participant data: Rationale, conduct, and reporting. *BMJ*, 340, c221.
38. Boulton, G., Rawlins, M., Vallance, P., & Walport, M. (2011). Science as a public enterprise: The case for open data. *Lancet*, 377(9778), 1633–1635.
39. Riley, R. D. (2010). Commentary: Like it and lump it? Meta-analysis using individual participant data. *International Journal of Epidemiology*, 39(5), 1359–1361.
40. Ahmed, I., Sutton, A. J., & Riley, R. D. (2012). Assessment of publication bias, selection bias, and unavailable data in meta-analyses using individual participant data: A database survey. *BMJ*, 344, d7762.