# Health Related Quality of Life in Caregivers and Family Members: A Systematic Review

Todd Gammie[1], Harpreet Singh[2], James Harris[2], Scott Metcalfe[2], Zaheer Ud-Din Babar[3]

1. University of Auckland, Auckland, New Zealand

2. Pharmaceutical Management Agency (PHARMAC), Wellington, New Zealand

3. University of Huddersfield

# Abstract:

## Objective

To systematically review the current literature which utilises health related quality of life instruments that investigate the health related quality of life effect associated with being an informal, unpaid caregiver or close family member to a primary patient.

## Methods

A systematic review of the literature (1998-2016) identified relevant, peer-reviewed articles. Narrative Synthesis was used to identify different approaches to quantifying the impact of caregiving upon the health related quality of life, and analysis of the burden of care for informal caregivers by type of disease. Inclusion criteria included the use of a preference-based measure to assess HRQOL, with studies reporting HRQOL differences between informal caregivers and/or family members and, preferably, a designated control population.

## Results

One hundred and one articles covering ten health conditions met the inclusion criteria. The health-related quality of life of informal caregivers and family members was assessed in some studies by general surveys, and in others by multi-attribute utility instruments that enable results to be mapped to preference-based quality of life weights. The literature review indicates that caregivers experience mild to moderate reductions in health related quality of life compared to the general population. Mental health and social functioning HR-QOL domains were the most commonly affected. This review discovered the use of several instruments used to determine the extent of carer burden. Several studies reported that a direct relationship between patient health related quality of life (or utility) and carer health related quality of life were poorly specified and had low explanatory power. Analysis of studies recognised that the HRQOL of the patient and the HRQOL of the caregiver may not be directly related and affect one another through a proxy measure; carer burden which is positively related to the severity of the primary patient’s health state.

## Conclusion

Primary informal caregivers and family members of individuals suffering from many health conditions experience lower health-related quality of life as compared to the general population. The extent to which an individual’s health state leads to quantifiable health-related quality of life loss in caregivers and family members appears to be determined by disease type, severity of disease and the burden of care experienced by the caregiver. Health-related quality of life in caregivers and family members is most affected in the domains of mental health and social functioning.

# 1 Introduction

Health Related Quality of Life (HRQOL) is widely used to quantify the health status of individuals. This is also often used in economic evaluations and other methodologies of health care evaluation (1, 2). The World Health Organisation defines quality of life (QOL) as an 'individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns' (1). While no consensus exists around a definition for HRQOL, definitions of and related to the concept tend to focus on an individual's multi-dimensional well-being, current health situation and expectations (1). HRQOL most often assesses the effect of physical and mental disorders and disability on the patient's general wellbeing (2).

Informal caregivers provide a range of services to assist those with disease in coping with the effects of their disease on their daily life. These services most often include personal care, housework, mobility assistance (3). The relationship between an individual's health state and its effect upon the HRQOL of primary informal caregivers and family members who may or may not be caregivers has been recognized in several reviews (4-6). These can include effects upon caregiver well-being, relationship stability and employment status (4, 7). For instance, a recent systematic review found that caring for an ill or disabled family member imposes a 'well documented' burden upon the caregiver, both in terms of health effects and quality of life (4). Another review (8), found a deterioration in HRQOL in primary informal caregivers of stroke survivors compared to the general population, particularly in mental health domains such as anxiety and depression.

Burden of care continues to emerge as a concept in the literature on informal caregiving and its relationship with individual patient health state and HRQOL. Evidence indicates that the act of informal caregiving can involve considerable time contributions for caregivers depending on the condition and functional status of the individual receiving care (9). Thus, caregivers can often find their caregiving tasks considerably demanding, feel lacking in time to themselves, or feel aspects of social isolation (9). As a result, informal caregivers can often experience feelings of strain, develop health problems such as anxiety and depression and thus can experience reductions in overall HRQOL (9). Increasingly, models and indexes quantifying the burden of caregiving have been developed and utilised. Several examples include the Zarit Burden Interview (ZBI), a 25 item self-rated scale for measuring caregiver perceived burden, caregiver reaction assessment (CRA) and the caregiver burden scale (CBS) (9-11).

The assessment of HRQOL in informal providers of care and family members is increasingly a major challenge for the economic evaluation of health interventions (2). Disease specific HRQOL instruments include questionnaires such as the Qol-AD for dementia, caregiver quality of life index- Cancer (CQOLC) for cancer and CAREQOL-MS for multiple sclerosis (2, 12, 13). Generic HRQOL instruments include questionnaires such as the SF-36 or multi-attribute utility instruments such as the EQ-5D, SF-6D or 15-D. Generic instruments allow a comparison of health outcomes across different conditions, different groups of patients, the general population and increasingly, informal caregiver groups and family members (2, 14, 15). Often communicated utilising quality-adjusted life years (QALYs), multi-attribute HRQOL utility instruments provide a common outcome measure in the economic evaluation of healthcare interventions (2). Most often, statistical analyses are conducted with the use of questionnaire only based models to determine a HRQOL effect or are 'mapped' to a multi-attribute utility model, such as from SF-36 to the SF-6D to facilitate health technology assessment (HTA) and further economic evaluations (2, 14).

It is becoming increasingly important for academics, policy-makers and governmental agencies to understand the effect an individual patient's health state may have upon the health of individuals other than that of the primary patient, including informal caregivers and family members. However literature is scant on this issue. Hence the articles in this review predominately summarised the effect of an individual disease upon caregivers and family members HRQOL, or only included a narrow scoping of HRQOL instruments utilised to measure HRQOL effects in informal caregivers and family members. The aim of this study was to review, as thoroughly and systematically as possible, the current literature on health related quality of life effects of caregivers and family members, when related to the primary patient's health state and measured by a multi-attribute HRQOL instrument. The review also sought to investigate other possible covariates affecting the link between the patient's condition and the caregiver's health related quality of life.

# 2 Methods

## 2.1 Search Strategy

The PRISMA guidelines for conducting systematic reviews were utilised (16). A search of the literature was conducted between December 10, 2015 and December 5 2016 to identify peer reviewed articles in English. The databases searched (by TG) included: Medline (1998- 2016), Pubmed (1998- 2016), Google Scholar (1998- 2016), Springer Links (1998- 2016), Scopus (1998- 2016) and the Cochrane Library (1998- 2016). The following journals were searched for relevant articles: Health policy (1998-2016), Health and Quality of Life Outcomes (1998- 2016), International Journal of Wellbeing (1998-2016), Pharmacoeconomics (1998- 2016), PLoS One (1998- 2016), PLoS Medicine (1998- 2016) and Quality of Life Research (1998-2016).

The search strategy of the paper was developed by TG, with input from HS and JH. Keywords included: (“Health” or “Health related”) and (“Quality of life” or “Burden of disease” or “utility” or “well-being” or “economic analysis”) and (“Measurement” or “Instruments”) and (“Loss” or “Benefit”) and (“Caregiver” or “Parent” or “Family member” or “Children” or “Partner” or “Spouse”). The keywords were connected and incorporated in database and journal searching. Search results (‘hits’) by database and journal are detailed in Appendix 2. In the search process, “Boolean Operator” rules were utilised. The search terms were combined using ‘AND’ and search duplication was removed utilising ‘OR’ where possible. MESH search terms were used where appropriate. The references of any retrieved articles were also searched for further relevant articles that the search may have neglected.

## 2.2 Article Selection and Data Collection

Thirty seven thousand three hundred and twenty three titles/abstracts were retrieved from the database and journal searching. The title and abstract of all retrieved articles were reviewed by the lead author (TG) for relevance with subsections of research results checked by a second author (HS or JH). If there was any ambiguity with regard to the paper, the full text (article) was retrieved and read in full. After removal of irrelevant articles and adjusting for duplication in the search process 185 peer-reviewed articles in English were retrieved. We included articles if they described or utilised instruments to quantify health related quality of life loss and the burden of care in caregivers and family members. We also measured quality of life differences between non-caregivers and caregivers or differences by disease type. In total 185 articles were relevant to quantifiable health related quality of life loss or burden of disease in caregivers and/or family members and so were read in full by TG. Twenty two more articles were obtained from the references lists of retrieved articles; thus 207 articles were considered against study inclusion/exclusion criteria with discussion of bias, if relevant. Based upon study exclusion and inclusion criteria 106 articles were excluded and 101 articles were included in the final analysis.

## 2.3 Analysis

We reviewed the literature in a systematic manner in accordance with the PRISMA guidelines for systematic reviews and meta-analyses (16). This was to ensure a comprehensive collection of relevant literature. Narrative synthesis of the literature was conducted, which generated the following categories regarding; instruments utilised to quantify HR-QOL loss in caregivers and family members, differences in the quality of life between caregiver groups and between caregivers and non-caregivers, factors which lower or exacerbate the burden of disease for caregivers and family members, all by type of patient condition. Additional categories were examined until no more categories could be generated and saturation was deemed to be reached. Using the categories generated by this analysis, we described the quantifiable health related quality of life loss or benefit in caregivers and family members of patients with variable health states. We defined caregivers as an informal caregiver or family member or other person who aids in, and supervises the daily care of an individual suffering from disease or illness. These individuals need not live in the same household, but are not paid formally to care for these individuals (3, 9).

**Fig 1. Study Selection Flow Diagram (PRISMA)**

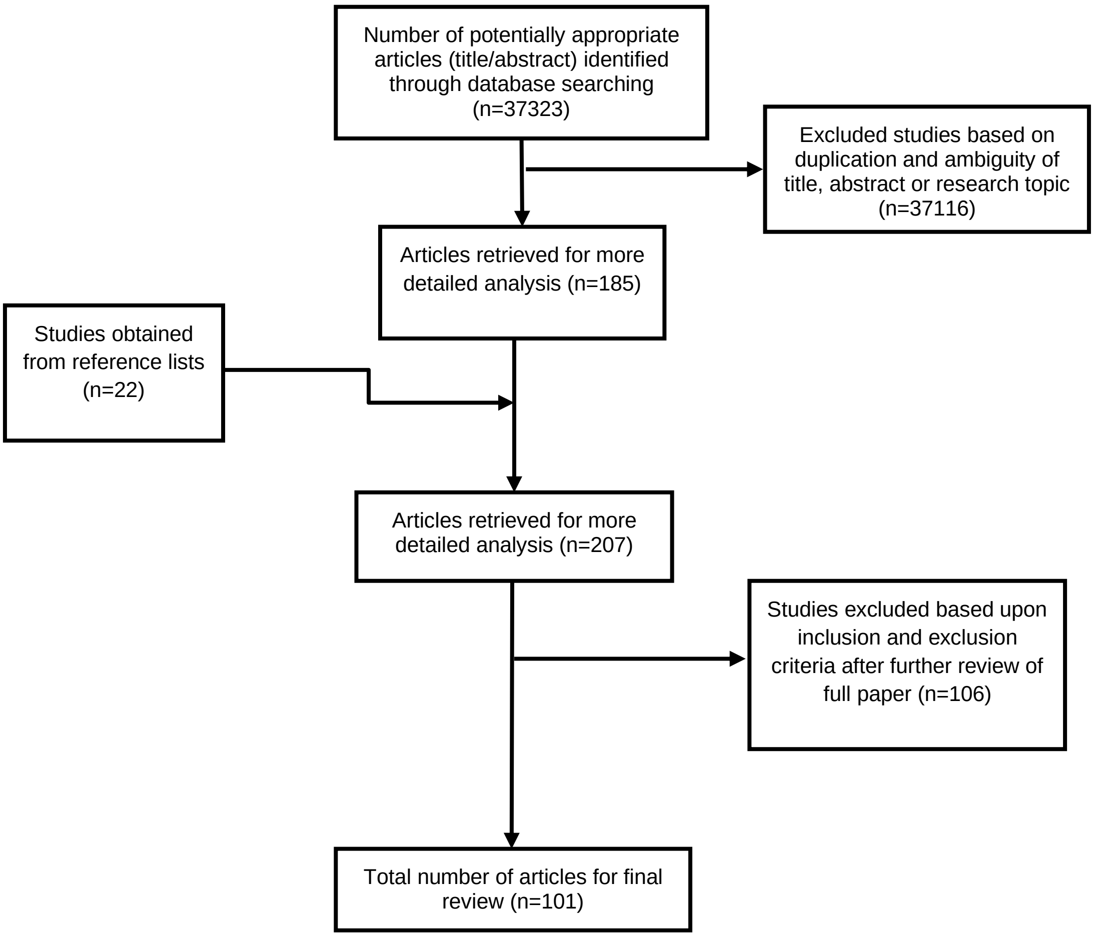


**Table 1.** Study inclusion & exclusion criteria

| *No.* | *Category* | *Inclusion Criteria* |
|---|---|---|
| 1 | Year of release | 1998-2016 |
| 2 | Publication Type | Full text articles in peer-reviewed scientific journals and in English. |

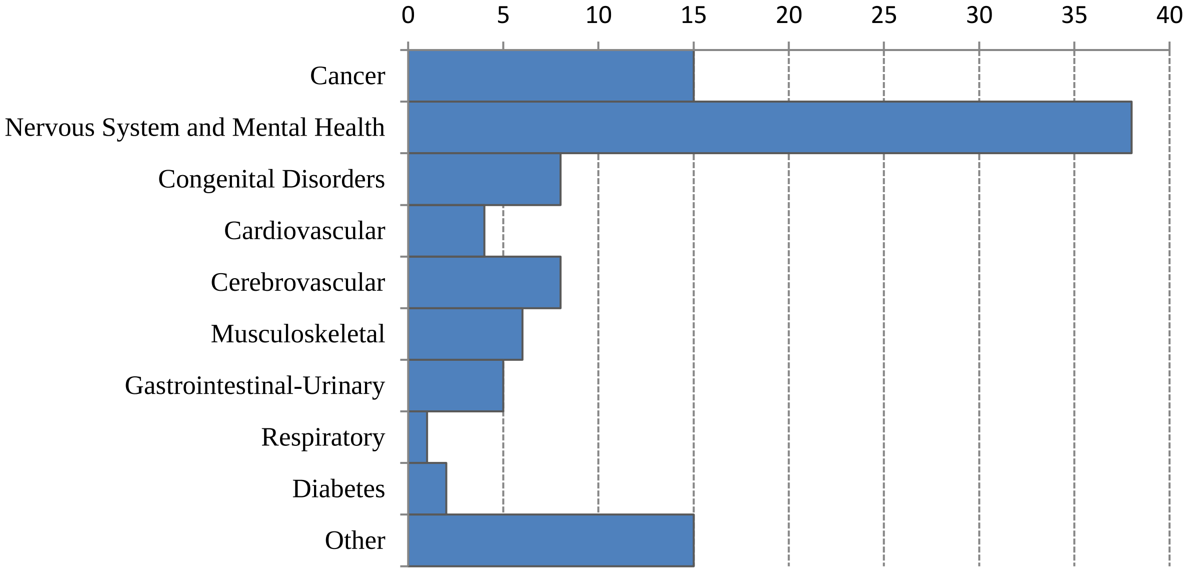
| ***No.*** | ***Category*** | ***Inclusion Criteria*** |
|---|---|---|
| 3 | Definition and issues to include | Quality of life, health related quality of life (HR-QOL), health state, informal caregivers, burden of disease, quality of life instruments.<br>Definitions of; health-related quality of life, caregivers, non-caregivers, family members, standard quality of life instruments, multi-attribute utility scales, burden of disease, health benefits<br>Quality of life; Health related quality of life, quality of life loss, quality of life benefits, wellbeing, utility<br>Quality of Life Instruments including but not limited to; EQ5D, SF6D, ADRQL, QWB-SA, HUI, AQOL, 15D<br>Burden of disease, Quality adjusted life years, Disease adjusted life years, economic analysis, burden of care, burden of care instruments i.e ZBI |
| 4 | Methodology and topic of research | Review of peer reviewed journal articles investigating health related quality of life benefits (loss) to caregivers and family members as a result of a (primary) patient's health state, with emphasis on finding studies that measure HR-QOL effects using standard instruments. Investigating:<br>Health related quality of life loss in informal caregivers: mechanisms and key aspects of HRQOL loss (and benefit) that exhibit in informal caregivers of primary patients as well as differences in QOL between (informal) caregiver groups and between (informal) caregivers and non-caregivers<br>Standard HRQOL Instruments: Common and key instruments such as multi-attribute utility scales, used worldwide for measuring HRQOL changes in informal caregivers and individuals other than the primary patient as a result of the health state of the primary patient<br>Burden of disease: Common and critical factors which lower or exacerbate the burden of disease for (informal) caregivers and family members, burden of care instruments |
| 5 | Outcomes | Mechanisms and factors which lead to quantifiable health related QOL loss and impacts upon burden of disease for (informal) caregivers and family members, with preference for studies which compared to other caregiver groups or non-caregiver groups where standard HRQOL measurement instruments have been utilised. |
| 6 | Bias | No presence of issues in study design, methods, data collection, analysis or any other factor of the study or article that could lead to bias of the individual study. |
| No. | | *Exclusion Criteria* |
| 1 | | Articles that are not published in English |
| 2 | | News Reports |

# 3 Results

## 3.1 Primary Patient conditions, Populations of Caregivers, and Family Members studied

One hundred and one articles described the health related quality of life of family members or caregivers with studies organised by the primary patient's condition according to 10 disease groups. Patient conditions included; cancers (n=15) (14, 17-30), nervous system and mental health illnesses such as, but not limited to, dementias, autism spectrum disorders (ASD) and multiple sclerosis (MS) (n=38) (3, 10, 13, 31-65) , congenital disorders (n=8) (15, 66-72) , cardiovascular conditions (n=4) (73-76), cerebrovascular conditions (n=8) (77-84) , musculoskeletal (n=6) (9, 85-89), gastrointestinal-urinary diseases (n=5) (90-94) , respiratory illnesses (n=1) (95), diabetes (n=2) (84, 96) and others (HRQOL effects on caregivers for diseases and/or treatments which did not fit into (only) one of the previous disease groups i.e bereavement effects or investigation of multiple conditions) (n=15) (11, 97-110). Figure 2 provides a summary of these findings.

**Fig 2.** Number of included studies by primary patient's disease type



The majority of included studies assessed the HRQOL of each patient's condition on informal caregivers (n=99) rather than on non-caregiving family members (n=2) (64, 78). Many studies found that mothers were the primary, informal caregivers of children (15, 31, 32, 66, 100). Two studies reported that 89.5% and 84% of the primary informal caregivers for children in the study were mothers respectively (31, 66). For adults, spouses or partners and the patient's children were most commonly the primary informal caregiver (13, 41, 49, 77).

## 3.2 Instruments used to measure Health-Related Quality of Life effects in Family Members and Caregivers

Health related quality of life effects assessed in caregivers and family members were measured with two main types of HRQOL instrument; questionnaires and multi attribute utility instruments. HRQOL questionnaires assess HRQOL generally by summing scores for a number of domains and are conducted by two main study designs. The first method involved distribution of questionnaires to caregivers/family members with these HRQOL scores often compared to established population norms. The second method was to compare HRQOL questionnaire results in primary caregivers with healthy control age-paired caregivers within the study itself. HRQOL questionnaires used included the; Short Form Health Survey 8, 12 and 36, Quality of life enjoyment and satisfaction questionnaire, caregiver quality of life index (cancer and multiple sclerosis), WHOQOL-BREF, KDQOL-SF, General Health Questionnaire 12 (GHQ-12), SWED-QUAL, SEIQOL-DW, Peds QL Family Impact Module and FACT-B. Health related quality of life questionnaires focus upon the experiences and perception of participants health-related quality of life over a previous time period and consist of closed-ended structured questions and calculate a summary scale score of which respondents are graded for their HRQOL.

The second type of instrument used to assess HRQOL effects were multi-attribute utility instruments which allow a comparison of health outcomes across different conditions, different groups of patients, the general population and increasingly, informal caregiver groups and family members (2, 14, 15). Communicated as quality adjusted life years (QALY's), most often calculated from instrument index values based upon individual or community preferences for a variety of different health states, multi-attribute HR-QoL utility instruments provide a common outcome measure in the economic evaluation of healthcare interventions (2). These measures calculate a common utility score and often compare caregiver's scores to a comparison population (i.e non-caregivers scores or caregivers of other conditions). Multi-attribute utility instruments utilised included the EQ-5D, SF-6D, HUI-2 and 15-D. Figure 3 summarises the use of these instruments below.

**Fig 3.** Bar Graph depicting the number of times each HRQOL instrument was used by included studies N.B. Some studies used more than one instrument in HRQOL analysis

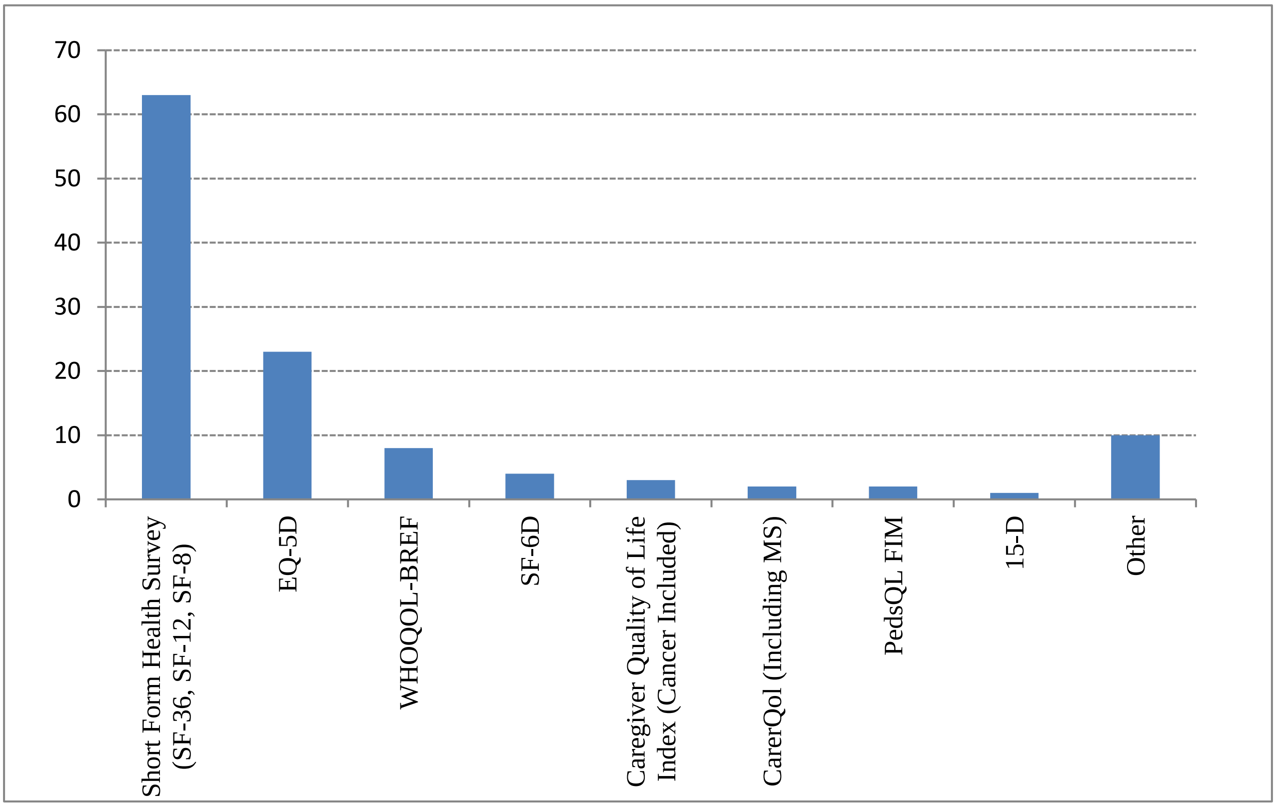


**Table 2.** Descriptive summary of the 9 major generic instruments used to measure caregiver and family member HRQOL in included studies

| Instrument | Domains covered | Description of Instrument |
|---|---|---|
| **SF-36** | • Physical Function<br>• Role-physical function<br>• Bodily pain<br>• General health<br>• Vitality<br>• Social function<br>• Role-emotional function<br>• Mental health | The Medical Outcomes Study 36-Item Short Form or SF-36 is a generic health related quality of life questionnaire consisting of 36 questions summarised into eight scales assessing its included domains grouped into a physical health component summary (PCS) and a mental health component summary (MCS). The SF-36 delivers a final summary scale score to determine HRQOL. A score of 0 corresponds to the worst overall health state and 100 to the best, general health state (45). |
| **SF-12** | • Physical Function<br>• Role-physical function<br>• Bodily pain<br>• General health<br>• Vitality<br>• Social function<br>• Role-emotional function<br>• Mental health | The Medical Outcomes Study 12-Item Short Form or SF-12 is a generic health related quality of life questionnaire containing 12 items from the SF-36 in its 8 domains grouped into a PCS and a MCS. The SF-12, much like the SF-36 delivers a final summary scale score to determine HRQOL. A score of 0 corresponds to the worst overall health state and 100 to the best, general health state (49). |
| **SF-8** | • Physical Function<br>• Role-physical function<br>• Bodily pain<br>• General health<br>• Vitality<br>• Social function<br>• Role-emotional function<br>• Mental Health | The Medical Outcomes Study 8-Item Short Form or SF-8 is a generic health related quality of life questionnaire containing 8 items from the SF-36 in its 8 domains grouped into a PCS and a MCS. The SF-8, much like the SF-36 delivers a final summary score to determine HRQOL. A score of 0 corresponds to the worst overall health state and 100 to the best, general health state (3). |
| **EQ-5D** | • Mobility<br>• Self-Care<br>• Usual Activities<br>• Pain/Discomfort<br>• Anxiety/Depression | The EQ-5D is a standardised, preference based utility measured generic instrument used to measure HRQOL. The EQ-5D is comprised of two components. The first is a self-classifier component and consists of the five aforementioned domains or dimensions of health. Participants are required to score on a 3 point scale generally, however some versions of the EQ-5D utilise a five point scale. For the three point scale; level 1 indicates no problems, level 2 indicates some/moderate problems and level 3 indicates extreme problems. The second part consists of the EQ-VAS which is a visual analogue scale ranging from 0 to 100. A value of 0 indicates the worst imaginable health state and 100 indicates the best imaginable health state. EQ-5D health states (generally 243 in total) may be converted into a single preference based index value (where 0.0 is death and 1.0 is the best possible health state) which are often presented in country specific value sets and are multiplied by the time in that state to calculate quality adjusted life years or QALYS (55). |
| **SF-6D** | • Physical Functioning<br>• Role Limitations<br>• Social Functioning<br>• Pain<br>• Mental Health<br>• Vitality | The SF-6D is a standardised, preference based utility measured generic instrument used to measure HRQOL. The SF-6D is a single index measure of health derived from the SF-36 and consists of the aforementioned six multi-level dimensions of health. The SF-6D defines 18,000 health states and utilises regression models to estimate a single index score (where 0.0 is death and 1.0 is the best possible health state) for all health states calculated by the SF-6D. These index values are often used to facilitate the calculation of quality adjusted life years or QALY's in economic evaluations of health-care (111). |
| **15-D** | • Mobility<br>• Vision<br>• Hearing<br>• Breathing<br>• Sleeping<br>• Eating<br>• Speech<br>• Excretion | The 15D is a standardised, preference based utility measured generic instrument used to measure HRQOL. The 15-D consists of the 15 aforementioned domains and combines a profile and preference based single index measure. A set of utility weights is used to generate the 15-D score on a 0-1 scale where 0 represents death and 1 represents perfect HRQOL. 15-D index values can be used to facilitate the calculation of quality adjusted life years or QALY's in economic evaluations of health-care (41). |

| Instrument | Domains covered | Description of Instrument |
|---|---|---|
| | Usual Activities<br>Mental Function<br>Discomfort and Symptoms<br>Depression<br>Distress<br>Vitality<br>Sexual Activity | |
| **WHOQOL-BREF** | Physical<br>Psychological<br>Social<br>Environmental | The WHOQOL-BREF is a generic health related quality of life questionnaire containing 26 questions corresponding to the four aforementioned domains. These domains are used to assess physical capacity, psychological wellbeing, social relationships and the environment where the individual exists. The answers for each domain are summed to scores ranging from 4 to 20, where higher scores indicate better HRQOL (72). |
| **Caregiver Quality of Life Index** | Physical<br>Emotional<br>Family<br>Social Functioning | The Caregiver Quality of Life Index is a standardised health related quality of life questionnaire aimed at measuring caregiver HRQOL in cancer research. The instrument consists of 35 items/questions and measures on a five point likert scale (0 to 4) measuring the four aforementioned domains. The total score for caregiver HRQOL is calculated by summing the score for all 35 items which are equally weighted (112). |
| **CarerQol** | Fulfilment<br>Relational Dimension<br>Mental Health Dimension<br>Social Dimension<br>Financial Dimension<br>Perceived support<br>Physical Dimension | The CarerQoL instrument is a preference based, standardised instrument utilised to measure caregiver HRQOL. The instrument consists of two parts, a questionnaire providing a description on seven burden dimensions and a valuation component in terms of general quality of life using a visual analogue scale (VAS). The instrument utilises utility tariffs to calculate a weighted sum score (index score) in order facilitate cost-utility analyses of interventions aimed at informal caregivers (113). |

## 3.3 Primary Patient Health State, Caregiver and Family Member Health Related Quality of Life and Differences between Caregiver Groups

Many studies found that the role of caregiving was associated with decreases in HRQOL compared to non-caregiver norms reflecting increased levels of stress, poor physical and mental health including depression and anxiety (14, 63, 82, 106, 107, 109, 110). We categorised studies into 10 primary patient conditions and/or treatment including; cancers, nervous system and mental health, congenital disorders, cardiovascular type, cerebrovascular, musculoskeletal, Gastrointestinal-urinary, Respiratory, Diabetes and Other.. The relationship between primary patient health state and the effect of caregiving for these patients on caregiver HRQOL is discussed below.

### 3.3.1 Cancers

15 studies involved informal caregivers and family members of patients with cancer including gynaecological, ovarian, lung, breast, brain, blood and unspecified cancer type. The primary patient's health state and the effect of caregiving for these patients had detrimental effects upon caregiver HRQOL in all cancer studies, ranging from mild to moderate effects (14, 17-30) . Lee et al (19) compared the HRQOL between cancer and non-cancer families and found that cancer families had slightly lower EQ-5D scores than non-cancer families with the average EQ-5D VAS score of non-cancer families at 94.11 and cancer families at 92.25. Butow et al (18) investigated caregiver HRQOL for women with ovarian cancer and found that primary informal caregivers had significantly lower mental and physical HRQOL than population norms. Additionally, the ability of the caregiver to

function normally i.e lead as normal life as possible, rather than the level of patient quality of life, predicted caregiver health related quality of life. In a study examining family caregiver HRQOL for advanced cancer patients in Sweden, compared with norm-based values of the SF-36, family members had considerably poorer mental HRQOL (mental component scores (MCS)) SF-36 scores of 39+/-2.2 at 3 months of study progression and 41 +/- 2.4 at 15 months for family members compared to the norm based MCS value of 51.1 +/- 0.97. These family members also scored worse on the EQ-5D VAS to a degree of statistical significance in all five time period assessments compared to norm based values (21). Goren and colleagues (14) reported that cancer caregivers reported significant impairment compared to a sample of non-caregivers, with a SF-12 MCS of 43.23 compared to 46.95 and significantly lower SF-6D health utilities of 0.681 compared to 0.732, 1.46 times as much work impairment and 1.97 times the odds of anxiety. All other cancer studies included in the review reported similar findings of minor to moderate HRQOL effects.

### 3.3.2 Nervous system and mental health

Thirty eight studies investigated HRQOL upon family members and informal caregivers caring for patients with nervous system conditions or mental health related disorders. These conditions were; multiple sclerosis (n=9), amyotrophic lateral sclerosis (n=1), epilepsy (n=1), brain injury (acquired or traumatic) (n=3), paraplegia (n=1), dementias (including Alzheimer's and Parkinson's disease) (n=14), autism spectrum disorders (ASDs) (n=4), schizophrenia (n=3), eating disorders (n=1) and general mental illness (n=1).

#### *Multiple Sclerosis*

In the studies that examined effects of caregiving on caregiver health related quality of life for multiple sclerosis patients, the adverse impact of caregiving upon family member and caregiver HRQOL was apparent. Acaster et al (51) found that caregivers reported considerably lower HRQOL compared to matched, non-caregiver controls were measured by the SF-36 and EQ-5D. Caregivers scored approximately 55 for the physical component summary score while non-caregivers scored approximately 58. For the MCS, caregivers scored approximately 40 and non-caregivers scored 48. EQ-5D utility values also differed between caregivers and non-caregivers, with a mean EQ-5D utility score of 0.82 for non-caregiver controls and 0.74 for caregivers. Additionally, a lower level of functioning in patients with MS had a surprisingly inverse relationship with caregiver HRQOL (51). Gupta and colleagues (52) reported that MS caregivers had greater activity impairment, poorer mental and physical health status, lower health utility scores and more hospitalizations than non-caregiver controls. In particular, the SF-6D health utility score was 0.70 for MS caregivers and 0.74 for non-caregiver controls and the difference was statistically significant. Argyriou et al (55) investigated the perceived emotional burden and HRQOL in a sample of Greek primary informal caregivers of MS patients. They found that in their comparison of EQ-5D-3L scores between caregivers and non-caregiver controls there was a statistically significant difference in scores in three of the five EQ-5D domains (Usual activities, Pain/discomfort and anxiety and depression) as well as the EQ-5D VAS scores. (55). Other MS studies included in this review showed similar findings with informal caregivers of MS patients reporting minor to moderately negative effects upon their HRQOL as a result of caregiving (3, 13, 49-55).

#### *Dementias*

Fourteen studies examined the HRQOL effects on informal caregivers and family members of patients with dementia including Alzheimer's disease (AD) (n=5), Parkinson's disease (PD) (n=3) and general or unspecified Dementias (n=6). Of the 5 Alzheimer's studies, one study found that caregivers had significantly lower HRQOL than age and gender standardised controls. The study utilised the 15-D and found that the mean index 15-D utility score for caregivers was statistically significant and different from that of non-caregivers with a mean difference in the utility index score of -0.018. Family caregivers also had significantly lower HRQOL in seven of the 15-D domains; vision, breathing, usual activities, depression, distress, vitality and sexual activity. In addition, severity of Alzheimer's disease was associated significantly (statistically) with the mobility and depression dimensions of caregiver HRQOL of the 15-D (41). Serrano et al (10) discovered that caregivers had a greater rate of problems compared to the general population for every EQ-5D dimension.. The study also found that the mean EQ-5D VAS score for caregivers of AD patients was 61.4 while the general population had a mean value of 65.9. Caregiver HRQOL was also associated inversely with the patients dependency level, i.e the more dependent a patient, the worse the caregiver HRQOL (10). Of the 3 Parkinson's studies, no studies specifically investigated differences in caregiver HRQOL and that of controls of the general population.

Carod-Artal and colleagues (47) investigated the main determinants of burden and HRQOL in caregivers of patients with Parkinson's disease and noted that the EQ-5D index mean utility scores were 0.7 and their VAS mean scores were 76.3. Of the general dementia studies, these studies all reported mild to moderate effects upon HRQOL. One such study, conducted by Takahashi et al (38) found that informal caregivers had the lowest quality of life out of the three studied groups in the study; informal caregivers, professional caregivers and controls. HRQOL was evaluated using the WHO-QOL 26. Informal caregivers compared to controls scored lower on every domain; physical, psychological, social, environment and QOL impression and results were statistically significant. The average QOL score for informal caregivers was 2.9+/-0.5 while controls scored 3.5+/-0.5 (38). Another study found that informal caregivers for patients with dementia scored worse on every SF-36 domain compared to healthy controls. All results were of statistical significance ($p<0.05$) (40).

### *Autism Spectrum Disorders*

Four studies investigated predictors of HRQOL among informal caregivers of children with Autism Spectrum Disorders (ASDs). Kuhlthau and colleagues (31) found that HRQOL scores in parents were slightly worse than the general population and that, in scores related to anxiety and depression, moderate effects upon HRQOL were seen. Kuhlthau et al found that the 45% of parents in the study reported moderate or severe issues with pain/discomfort and 51.1% had issues related to anxiety/depression. However the average EQ-5D score was similar to the general (US) population with 0.85 for caregiver parents and 0.89 for the general population. Analysis in the same study utilising the SF-6D experienced similar results, with 46.3% of caregiver parents experiencing moderate to severe problems with mental health and 65.3% reporting problems in the vitality domain on the SF-6D. However, only 20.9% reported moderate to severe problems with pain. Unlike the EQ-5D-3L, the SF-6D results indicated a clinically significant difference in HRQOL between caregiver parents and the general population (0.74 vs 0.80) (31). Other studies found similar results, with caregivers of children with ASD experiencing lower HRQOL scores than the general population (33, 34).

### *Other Nervous System and Mental Health Studies*

Other nervous system and mental health studies (n=11) were also investigated and included: amyotrophic lateral sclerosis, epilepsy, brain injury (acquired or traumatic), paraplegia, schizophrenia, eating disorders and general mental illness. For the studies investigating amyotrophic lateral sclerosis (ALS) and epilepsy, HRQOL was rated low by caregivers of ALS (overall QOL on the WHO-BREF of 3/5 and psychological status of 4/5 where higher scores indicate worse HRQOL). These scores were not evaluated with respect to a control population (56, 57). Caregivers of epilepsy rated their HRQOL comparable to the general (Dutch) population with both caregivers and the general population values reporting an EQ-5D utility score of 0.88. (56, 57). For informal caregivers of patients with paraplegia, caregivers rated low on the SF-36 domains of vitality (65.58) and bodily pain (65.02) (48). In informal caregivers of brain injury patients HRQOL was somewhat lower than normative scores of population based controls with mean EQ-5D VAS scores for caregivers of survivors of acquired brain injury of 70.4 compared to 73.0; and SF-36 scores of 45.40 in caregivers compared to 54.99 in controls for patients with traumatic brain injury (58, 59). For studies investigating schizophrenia, Gupta et al (63) found that informal caregivers of individuals with schizophrenia reported mildly worse HRQOL than non-caregiver controls (lower mental component summary of 40.3 compared to 42.7 and SF-6D health utility of 0.64 vs 0.67). Other schizophrenia studies investigated the relationship between HRQOL and burden of care. For eating disorder individuals, informal caregivers experienced worse HRQOL than in a normal reference sample. Specifically, mental health, vitality and emotional role functioning were the most impaired (64).

### 3.3.3 Congenital Disorders

Eight Studies (15, 66-72) investigated patients suffering from congenital disorders, their informal caregivers and HRQOL effects in;down's syndrome, Rett Syndrome, Fragile X Syndrome, Cystic Fibrosis, Developmental Delays, Prune Belly Syndrome, Major Congenital anomalies and Osteogenesis imperfecta. For Down's syndrome, psychosocial variables rather than socio-demographics or child functioning were the best predictors of parent HRQOL (66). Sarajlija et al (15) investigated factors influencing HRQOL in mothers of Rett Syndrome children. The lowest scoring SF-36 domains of the mothers were mental health, vitality and role functioning emotional but none of these domains differed significantly compared to the general Serbian population. Mean EQ-5D-5L utility scores for caregivers for children with fragile X syndrome vs population norms were 0.75 +/- 0.24 for caregivers compared to the population norm of 0.83. In addition, utility scores were much lower for carers for patients with lower levels of functioning (67). One study investigated HRQOL for carers of patients with cystic fibrosis. The study found that the HRQOL of carers was 0.742 as assessed by the EQ-5D. This was stated to be lower than general population reference values in France of 0.83 for the French speaking adult general population (68). Hsieh et al (69) investigated the quality of life of caregivers of children with developmental delays in Taiwan. The study found no significant differences in the quality of life of carers for children with developmental delays. The remaining studies also found varying results. One study investigating parents caring for children with major congenital anomalies found significant HRQOL differences between parents caregiving for these children and the general population. Specifically, mothers of children with congenital anorectal malformations (ARM) between 25 and 34 years old had a statistically significant difference with the general population; EQ-5D utility values of 0.83 vs. 0.93 (71). HRQOL was discovered to be reduced in caregivers of OI. Statistically significant differences in mean scores in WHO-BREF domains were seen between caregivers and the general population in the physical psychological and environmental domains with caregivers scoring lower on all domains (72). All studies investigating congenital disorders thus reported generally mild to moderate effects upon informal caregivers or family member health related quality of life (15, 66-72).

### 3.3.4 Cardiovascular conditions

Studies investigating the heath related quality of life of informal caregivers of patients with cardiovascular conditions included studies on; heart failure, cardiac surgery and cardiothoracic transplant patients (73-76). One study, conducted by Pressler and colleagues (73) found in caregivers of patients with heart failure that caregivers of patient's with more severe symptoms had poorer physical health related quality of life and more time spent on caregiving tasks. A study investigating carers for cardiothoracic transplant patients found that caregiver HRQOL was generally high, but that with greater caregiver burden predicted worse HRQOL in carers (76). In parents of children suffering from heart disease and their HRQOL, the parents scored poorer than controls in every domain of the SF-36 besides bodily pain indicating lower HRQOL. The largest differences were for General Health, Vitality and role limitation physical. The factors having significant impacts upon HRQOL of parents were severity of illness, type of heart disease in addition to age of child, having multiple children, financial situation and presence of comorbid conditions. All results were statistically significant except for bodily pain (74).

### 3.3.5 Cerebrovascular Conditions

Eight studies examined the health related quality of life of carers and patients suffering from cerebrovascular conditions/stroke. The effect upon health related quality of life of carers caring for these patients was generally mild to moderate (77-84). One such study, investigating health related quality of life in carers of patients with stroke found that, compared to a 'normative sample', caregiver HRQOL was moderately lower for all SF-36 domains (77). Yu et al (78) found that higher education levels, planning and 'active coping' were associated positively with caregiver HRQOL while the number of chronic conditions, hours of care per day and 'functional dependence' of the survivor were associated negatively with HRQOL. Roth et al (82) who found that caregivers reported more quality of life problems than non-caregivers. However, these effects tended to be dependent upon the perceived level of caregiver burden or strain. Caregivers who reported no or less burden or strain experienced better HRQOL than those who experienced higher burden.

### 3.3.6 Musculoskeletal Conditions

Six studies investigated musculoskeletal conditions in: spinal cord injury, rheumatoid arthritis and juvenile idiopathic arthritis (9, 85-89). For the studies investigating spinal cord injury (SCI), studies by Ebrahimzadeh et al (86) and Middleton and colleagues (87) both found that the SF-36 scores of caregivers were lower than the scores of the general population. Moreover, Middleton and colleagues found that the mental component summary score (MCS) for informal caregivers of individuals with SCI was significantly lower than Australian national norms (87). One study investigated rheumatoid arthritis and established that informal caregivers of rheumatoid arthritis (RA) tend to be healthy, however the more severe the patients symptoms the worse the HRQOL of the caregivers. However, the study did not find significant differences in terms of health losses as a result of caregiving burden (9). One study investigated Juvenile idiopathic arthritis. The study discovered that the pain and mental health domains of the SF-36 were the most affected in caregivers but did not compare this to a comparator group (89).

### 3.3.7 Gastrointestinal-Urinary Conditions

Gastrointestinal-Urinary (GI-U) conditions and caregiver HRQOL were investigated in chronic renal failure and lower urinary tract dysfunction (90-94). Health related quality of life of carers for patients with chronic renal failure were studied in 4 articles. Shimoyama et al (91) evaluated caregiver HRQOL using the KDQOL-SF and the SF-36. It revealed that compared to national norms, caregivers scored lower in general health (61.5 vs 77.5), vitality (61.0 vs 76.5) and mental health (68.7 vs 81.6) on the SF-36. Another study found similar results, with the physical component summary and mental component summary of the SF-36 worse for family caregivers of patients with chronic renal failure needing dialysis than for the general population (92). One study looked at lower urinary tract dysfunction and found that health related quality of life was worse in caregivers in the pain and physical limitations components of the SF-36 when compared to non-caregiver controls (94).

### 3.3.8 Respiratory Conditions, Diabetes and 'Other Conditions'

One study investigated the HRQOL of caregivers and primary patients experiencing respiratory illnesses, 2 studies investigated diabetes and 15 studies investigated conditions or treatments that did not fall into the 7 other disease type categories and are discussed in the next section. Cedano and colleagues (95) investigated patients experiencing chronic obstructive pulmonary disease (COPD) and found diminished scores on the SF-36 for vitality and mental health. In addition, the greatest bearer of burden for caregivers of COPD was the environment. The environment referred to problems in: access to medical services, transport, medicines and the unsuitability of the domestic environment for the purpose of caregiving. Of the two diabetes studies, Li et al (84) found that, adjusting for age and gender, the mental component summary of the SF-36 was significantly lower when compared to the general population (45.80 +/-11.58 vs 50.5 +/-7.8).

#### *Other Conditions or Treatments*

The 15 studies investigated conditions and/or treatments that did not fall into the other 7 categories. These included neovascular age related macular degeneration, palliative care, children with disabilities, functional constipation, functional impairment, general chronic illness, studies investigating multiple diseases (many) and a study based investigating the effect upon HRQOL of caregivers due to bereavement (11, 97-110). Ho et al (110) investigated the impact upon HRQOL of primary informal caregivers of the elderly and noted that primary informal caregivers had 'significantly increased risks' for poorer health, greater health service utilisation, anxiety and depression. In addition, these caregivers reported worse scores for every domain of the SF-36 when compared to non-caregivers. Higher burden was also associated with poorer HRQOL in caregivers (110). Studies which investigated the effect of caregiving upon caregiver HRQOL in general or over multiple disease found similar mild to moderate effects upon HRQOL.  In particular, Wittenberg and colleagues (104) found evidence that lower EQ-5D health utility (HRQOL) scores were associated with family members in proximity to, or caring for, family members with chronic illness. Other studies reported similar findings for all diseases, including Rebollo et al (105) who investigated the health related quality of life of the main informal caregiver after the primary patient had died. The study found that caregivers SF-36 scores were lower than expected for the general population, particularly in the mental health, role-emotional and social functioning domains.

**Table 3.** Summary of lowest and highest health related quality of life losses between caregivers/family members of the primary patient and non-caregivers/population controls

| **Disease Group (Reference)** | **Specific Disease Indication (If relevant)** | **HRQOL Loss between Informal Caregivers/Family Members and Non Caregivers Lowest/Highest** | **Assessment Method(s)** |
|---|---|---|---|
| *Cancers* (19, 21) | Cancer/Advanced Cancer | 0.0186/ 0.051/ 0.107 | EQ-VAS/SF-6D/EQ-VAS |

| **Disease Group (Reference)** | **Specific Disease Indication (If relevant)** | **HRQOL Loss between Informal Caregivers/Family Members and Non Caregivers Lowest/Highest** | **Assessment Method(s)** |
|---|---|---|---|
| *Nervous System and Mental Health* (52, 55) | Multiple Sclerosis | 0.04/0.08/ 0.296 (0.28) | SF-6D/EQ-5D-3L/EQ-5D-3L (EQ-VAS) |
| (10, 41) | Alzheimer's Disease | 0.018/ 0.05 | 15-D/EQ-5D -VAS |
| | Parkinson's Disease | - | - |
| (38, 40) | General Dementias | 0.03 / 0.2078 | WHO-QOL 26 / SF-36 (General Health) |
| (31) | Autism Spectrum Disorders | 0.04 / 0.06 | EQ-5D-3L / SF-6D |
| | Amyotropic Lateral Sclerosis | - | - |
| (57) | Epilepsy | 0 | EQ-5D-3L |
| (58) | Acquired Brain Injury | 0.026 | EQ-5D |
| (59) | Traumatic Brain Injury | 0.1 | SF-36 |
| | Paraplegia | - | - |
| (63) | Schizophrenia | 0.03 | SF-6D |
| | Eating Disorders | - | - |
| | General Mental Illness | - | - |
| *Congenital Disorders* | Down's Syndrome | - | - |
| (15) | Rett Syndrome | 0 | SF-36 |
| (67) | Fragile X Syndrome | 0.08 | EQ-5D-5L |
| (68) | Cystic Fibrosis | 0.088 | EQ-5D-5L |
| (69) | Developmental Delays | 0 | WHOQOL-BREF |
| (71) | Major Congenital Anomalies (congenital anorectal malformations) (children) | 0.1 | EQ-5D |
| | Osteogenesis Imperfecta | - | - |
| *Cardiovascular Conditions* | Heart Failure | - | - |
| | Cardiothoracic Transplant | - | - |
| (74) | Heart Disease (Children) | 0.269 | SF-36 (General Health) |
| *Cerebrovascular Conditions* (77) | Stroke | 0.0731 | SF-36 (General Health) |
| *Musculoskeletal Conditions* | Spinal Cord Injury | - | - |
| | Rheumatoid Arthritis | - | - |
| | Juvenile Idiopathic Arthritis | - | - |
| *Gastrointestinal-Urinary* (91) | Chronic Renal Failure | 0.16 | SF-36 (General Health) |

| Disease Group (Reference) | Specific Disease Indication (If relevant) | HRQOL Loss between Informal Caregivers/Family Members and Non Caregivers Lowest/Highest | Assessment Method(s) |
|---|---|---|---|
| | Urinary Tract Dysfunction | - | - |
| *Respiratory Conditions* | Chronic Obstructive Pulmonary Disorder | - | - |
| *Diabetes (84)* | Diabetes Mellitus | 0.0838 | SF-36 (General Health) |
| *Other Conditions* | | - | - |

*Values in this table measure differences in health related quality of life between informal caregivers and family members of disease affected individuals and non-caregivers/ controls. These values reflect the *loss* or difference between the two groups in reported HRQOL as reported by different instruments (MAU Instruments and/or HRQOL (survey) instruments)

** A - is used to reflect situations where values were not given for general health or utilities (i.e SF-36 mental component scores or physical components scores were only given). For more detailed analysis see individual results sections.

## 3.4 The Burden of Care(giving) and Caregiver Health Related Quality of Life

An emerging theme among studies included in this review was the relationship between the burden of caregiving and its relationship with the health related quality of life of informal caregivers and family members. Many studies investigated the burden of care, either directly utilising ‘standard’ burden of care(giving) instruments or study specific measures and its relationship to caregiver HRQOL. These studies continued to demonstrate a relationship, whereby the greater the burden of care, the worse the caregiver health related quality of life (9, 36, 47, 53, 88, 108). In this review, we recorded the use of a number of burden of care(giving) instruments and the relationship between burden of care and caregiver health related quality of life.

### 3.4.1 Instruments used to measure Burden of Care(giving) in Family Members and Informal Caregivers

Increasingly, instruments to measure the burden of caregiving are being developed. These instruments were most often constructed as interviews or surveys where higher scores represent higher caregiver burden. Burden of care instruments utilised by the various studies in this review included: the Zarit Burden Interview (ZBI), Caregiver Burden Scale (CBS), Caregiver Strain Index (CSI), Caregiver Reaction Assessment (CRA), Caregiver Burden Index (CBI), Oberst Caregiving Burden Scale, Burden Scale for Family Caregivers (BSFC), Carer Burden Domain, Caregiver Strain Questionnaire, Feelings about Caregiving Scale and the Montgomery Caregiver Burden Scale. Figure 4 counts the use of these instruments in the included studies.

**Fig 4.** Bar Graph depicting the number of included studies using each Burden of Care(giving) instrument.

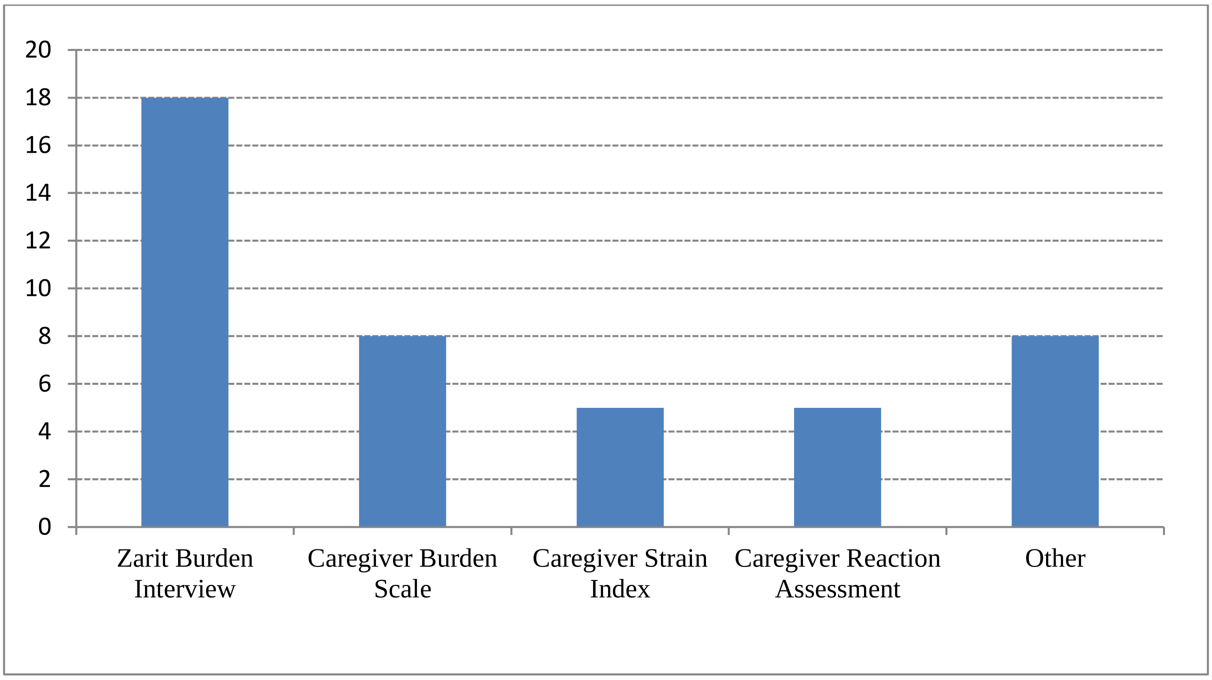


**Table 4.** Descriptive summary of the 4 major generic instruments used to measure caregiver and family member Burden of Care(giving) in included studies

| Instrument | Domains covered | Description of Instrument |
|---|---|---|
| **Zarit Burden Interview** | - Physical Health<br>- Emotional Health<br>- Social Impact<br>- Financial Impact | The Zarit Caregiver Burden Interview (ZBI) is used to ascertain the distress or burden experienced by informal caregivers. The ZBI includes 22 items regarding the impact of the primary patient's disabilities/illness on caregiver's physical and emotional health as well as social and financial impact. In each item, respondents (caregivers) indicate how often they have felt a suggested sentiment or opinion. The ZBI is scored on a scale of 0-88, with higher score indicative of higher caregiver burden (67). |
| **Caregiver Burden Scale** | - General Strain<br>- Isolation<br>- Disappointment<br>- Emotional Involvement<br>- Environment | The Caregiver Burden Scale (CBS) is divided into five domains and is a 22 item scale instrument. The CBS scores all items on a scale of 1 to 4, where 1 corresponds to 'not at all' and 4 to 'often'. The total burden index consists of the sum of all 22 items with higher scores indicating higher burden. Total scores range from 22 to 88 (88). |
| **Caregiver Strain Index** | - Health Impact<br>- Financial Impact<br>- Social Impact<br>- Time Impact<br>- Employment Impact | The Caregiver Strain Index (CSI) is a self-rated burden scale for assessing subjective (caregiver) burden. The CSI contains 13 statements to which the caregiver responds with a binary yes/no response. Total scores on the CSI range from 0 to 13 where the higher the score, the higher the (perceived) burden of informal caregiving (79). |
| **Caregiver Reaction Assessment** | - Disrupted Schedule<br>- Financial Problems<br>- (Lack of) Family Support<br>- Health Problems<br>- Self Esteem (Emotional) | The Caregiver Reaction Assessment (CRA) measures five dimensions and consists of 24 items. Within each domain, a score of 1 indicates no burden and 5 indicates high burden. This is the case for every domain except self-esteem, where a higher score indicates higher esteem and thus a lower burden. The CRA does not contain a total score combining all domains so is often used alongside a visual analogue scale assessing burden from 0 (lowest burden) to 100 (highest burden) (114). |

### 3.4.2 Health Related Quality of Life and Burden of Care in Informal Caregivers and Family Members

Burden of Caregiving and its relationship with caregiving health related quality of life was a key theme illustrated in this review. Many studies indicated an association between increased caregiver burden and decreasing caregiver health related quality of life (23, 38, 43, 80, 81, 103). This was particularly the case in the mental health domain whereby caregiver burden was an important predictive element of anxiety and depression in informal caregivers (23, 38, 43, 80, 81, 103). Moreover, caregiver burden was associated with increasing patient disability (symptom severity), anxiety and depression (81).

Song and colleagues (28) investigated the health related quality of life and burden of informal caregivers of terminal cancer patients. The study utilised the EQ-5D and caregiver reaction assessment (CRA) for caregiver HRQOL and burden. Within the CRA, the health problems or 'health impact' domain was (statistically) significantly and was negatively related to caregiver health related quality of life. In addition, the 'impact on health' domain of the CRA had a positive relationship with the level of perceived stress of the caregiver (Odds ratio = 3.21, 95% CI =1.53 – 6.74) (28). Another study, investigating the HRQOL and perceived burden of informal caregivers for Alzheimer's patients reported that caregiver HRQOL was significantly and negatively associated with higher feelings of caregiver burden and more time committed to care (10). The Zarit Burden Interview (ZBI) and the EQ-5D were used to assess burden and HRQOL independently. 83.3% of caregivers had a high level of burden (ZBI score of greater than 60) and this burden was negatively correlated with caregiver HRQOL to a degree of statistical significance ($p < 0.001$) (10).

Kelly et al (46) found no statistically significant relationships between caregiver HRQOL and caregiver strain (burden) in an examination of the relationship between HRQOL of patients with Parkinson's disease, their caregivers and caregiver strain. However, a relationship was suggested between poorer HRQOL in patients with Parkinson's disease and higher levels of caregiver strain or burden (Spearman rho for; EQ-5D VAS = -0.16 , EQ-5D TTO = -0.18) which were both statistically significant (46). These findings suggest that poorer (self-rated) HRQOL in patients with Parkinson's was related to increased caregiver burden/strain. Takahashi and colleagues (38) examined the factors associated with HRQOL of caregivers of patients with Dementia. Informal caregivers had the highest ZBI scores and lowest health related quality of life among the three studied groups (informal caregivers, professional caregivers and controls). Informal caregivers had an average ZBI index score of 45.1 +/-16.1, professional caregivers; 19.2 +/-7.2 and controls 0.00. Average HRQOL scores measured by the WHO-QOL-26 for each group were; 2.9+/-0.5, 3.1+/-0.4 and 3.5+/-0.5 (38). Institutionalisation of these patients may have resulted in lower burden for these informal caregivers, whereby the ZBI scores were moderate and not indicative of high burden (38). A study by Bleijlevens et al (36) investigated this scenario. The study looked to examine the differences in caregiver burden and HRQOL of informal caregivers of Dementia patients. Lower health related quality of life and higher levels of burden as assessed by the ZBI and EQ-5D respectively, were found in informal caregivers of Dementia patients living at home as compared to (informal) caregivers of recently institutionalised Dementia patients. More specifically, the mean ZBI scores of informal, home carers were 32.4 (Standard deviation (SD) = 15.8) as compared to informal caregivers of institutionalised patients at 24.9 (SD = 15.2). The mean EQ-5D-3L scores of home carers and informal caregivers of institutionalised patients were 0.76 and 0.78 respectively (36).

When testing the relationship between caregiver burden and caregiver HRQOL in another study of MS patients, utilising the ZBI and SF-36, SF-36 HRQOL domains, role-emotional functioning and vitality were significantly and negatively related with increasing burden (ZBI score) as was the disability status (disease severity) of the MS patient (53). The average ZBI score was 22.0 +/- 14.6 with 85.6% of caregivers reporting no burden (0-46), 4.3% reporting slight burden (47-55) and 1.4% reporting intense burden (56 to 88). 8.6% of respondents failed to complete the questionnaire (53).

One study investigated caregivers of patients with fragile X syndrome. The study utilised the EQ-5D for HRQOL and ZBI for caregiver burden. The study found no relationship between caregiver mean EQ-5D-5L utility score and ZCBI mean scores (r = -0.15, p=0.26). The study also recorded a mean Zarit Caregiver Burden Score of 39.9 which is most often interpreted as low burden (67). Pressler et al (73) explored health related quality of life and caregiver burden in caregivers of patients with heart failure using the SF-12 (HRQOL) and Oberst Caregiving Burden Scale (Caregiver burden). It was revealed that caregivers of patients with more severe symptoms reported higher burden (more time spent on tasks and more difficult tasks) and their health related quality of life was poorer (73). Cardiothoracic transplant patients and their caregivers HRQOL and care burden was assessed by Myaskovsky and colleagues (76). In the study, larger caregiver burden was associated with worse caregiver health related quality of life in several SF-36 domains. More explicitly, SF-36 scores in vitality and bodily pain were associated with higher ZBI burden scores (76).

The health related quality of life and burden of caregivers of stroke patients was evaluated by van Exel and colleagues (79). Both the level of objective and perceived burden were related negatively to caregiver HRQOL. The average perceived burden by caregivers was 4.3 as valued by the caregiver strain index. However, 30% of these caregivers indicated substantial burden and had a mean CSI score of 8.3/13 (79). Nogueira et al (88) analysed the impact and burden of care on the HRQOL of caregivers of individuals with spinal cord injury. An association between care burden and HRQOL was identified with increased carer burden predicting lower caregiver HRQOL. Analysis of the relationship between care burden (assessed by the caregiver burden scale) and HRQOL assessed by the SF-36 found that all correlations between the two in all CBS and SF-36 domains were negative and statistically significant (88).

Multiple other studies, investigating the relationship between caregiver health related quality of life and burden existed in this review, including studies for caregivers of chronic renal failure patients, chronic obstructive pulmonary disorder, neovascular age related macular degeneration, general palliative care and studies investigating multiple diseases recorded a relationship between HRQOL and carer burden. For example, Ho et al (110) investigated the impact of caregiving and noted that high caregiver burden was associated with both poorer physical and psychological health related quality of life. The relationship between caregiver HRQOL and burden was also studied by Dixon and colleagues (107). Interestingly, they reported that the relationship between carer utility (or health related quality of life) and patient utility was poorly specified and had low explanatory power. However, the relationship between carer utility and burden was statistically significant when socio-demographic covariates were introduced. It would therefore appear that the HRQOL of the patient and the HRQOL of the caregiver are not directly related and affect one another through a proxy measure; care burden or the burden of caregiving.

# 4. Discussion

This article reports a systematic and comprehensive review of the current literature on health related quality of life effects, measured by a standardised HRQOL instrument, to caregivers and family members as a result of a primary patient's health state. Existing reviews predominately summarised the effect of an individual disease upon caregivers and family members HRQOL, or only included a narrow scoping of HRQOL instruments utilised to measure HRQOL effects in informal caregivers and family members. The breadth and depth of our review, its individual consideration of different diseases and consideration of the impact of caregiver burden provides important understanding and appraisal of the topic. We summarized the effects of caregiving on caregiver health related quality of life and the relevant instruments utilised by studies to assess this relationship. We also discussed a key relationship increasingly emergent in the literature, the quantitative relationship between increasing carer burden and deceases in informal caregiver health related quality of life and investigated key instruments utilised to measure carer burden. We identified 10 different disease type categories including; cancers, nervous system and mental health, congenital disorders, cardiovascular type, cerebrovascular, musculoskeletal, gastrointestinal-urinary, respiratory, diabetes and other diseases and/or treatments.

We noted that the primary informal caregivers of children were most often parents, primarily mothers while the informal carers of adults and older people tended to be the individuals spouse or children (13, 15, 31, 32, 41, 66, 100). Health related quality of life in informal caregivers and family members of the primary patient was assessed by two different types of instruments, surveys and multi-attribute preference based utility instruments. Of the instruments, the most utilised survey measure was the SF-36 and its derivatives (SF-12 and SF-8) and the EQ-5D was the most utilised preference based utility instrument. The relationship between the primary patient's health state and caregiver HRQOL was considered by the 101 studies included in this review. Of the studies that investigated cancers, mild to moderate effects on caregiver HRQOL were experienced as compared to the general population. These effects were experienced in many domains in the aforementioned studies, but particularly in regard to caregiver mental health and social functioning (14, 17-30). Nervous system and Mental Health studies constituted the largest proportion of all studies with 38 studies in this disease group total. Similar to cancer studies, nervous system and mental health studies reported many statistically significant differences between caregiver health-related quality of life and the health related quality of life of non-carers to a mild and moderate effect. These differences were predominately experienced in caregiver HRQOL domains pertaining to mental health (anxiety or depression) and social functioning/ability to undertake usual activities (3, 10, 13, 31-65). Interestingly, a higher level of disease severity and symptoms were associated with lower caregiver and family member HRQOL in several studies including studies related to multiple sclerosis and dementia (10, 41, 51). Mild to moderate effects on caregiver health related quality of life as compared to non-caregivers were observed for family members and caregivers of individuals with congenital disorders, however, significant effects were seen for cancers of children with multiple congenital anomalies (15, 66-72). In particular, the HRQOL of informal caregivers of children with major congenital anomalies, cystic fibrosis, fragile X syndrome and OI were most affected. Several studies reported HRQOL differences between carers and the general population, with domains related to general health, vitality and role limitations the most severely affected in caregivers (73-76). The relationship between greater disease severity and lower family member and caregiver quality of life was also noted in regard to caregiving for individuals with cardiovascular conditions (73). Mild to moderate differences in the HRQOL of caregivers and family members of individuals with cerebrovascular conditions were experienced. More specifically, limitations in physical and emotional role were noted by caregivers and family members of these patients (77). Disease severity and its relationship with caregiver HRQOL, in particular, the functional dependence of the diseased individual was predominant in this relationship (78). Studies investigating musculoskeletal, gastrointestinal, respiratory and diabetes related conditions all reported similar findings, with informal caregiver and family member health related quality of life most often lower than the general population. These studies also reported the largest reductions were in the mental health and vitality quality of life domains of these individuals (9, 84-96). Studies investigating individuals with 'other' diseases and the HRQOL of their caregivers reported similar findings, with particular reductions in the mental health (anxiety and depression), role-emotional and social functioning domains (11, 97-110).

An inverse relationship between caregiver burden and health related quality of life of informal caregivers was revealed in this review. Many studies indicated varying strengths of a relationship between caregiver burden and caregiver health related quality of life where higher caregiver burden was associated with lower caregiver health related quality of life (23, 38, 43, 80, 81, 103). We noted four major instruments used to assess caregiver burden; the Zarit Burden Interview, Caregiver Burden Scale, Caregiver Strain Index and Caregiver Reaction assessment of which the ZBI was utilised by a large majority. Carer burden was associated with disease severity in several studies, which then exhibited an inverse association with caregiver health related quality of life. This would seem to suggest that with increasing severity of the primary patient's health state, the burden of care and thus the health related quality of life of the caregiver is more negatively affected (46, 53, 81). It was noted by the analysis of one study that the HRQOL of the patient and the HRQOL of the caregiver are not directly related and affect one another through a proxy measure; care burden or the burden of caregiving due to the lack of a direct relationship between patient and carer utility (107).

Differences in the experience and health related quality of life of caregivers and family members between countries while outside the scope of this review, was discussed by several papers. We noted that differences in the HRQOL of caregivers may be affected by additional factors such as access to and availability of health and economic resources for caregiving and cultural factors among others (62, 109). Differences in the distributions of the demographic characteristics of caregivers were also pervasive in the studies included in this review. Most often, women were the primary informal caregiver (15, 31, 32, 66, 100).

Our study has some limitations. Firstly, outcome reporting and publication bias may have led to the publication or non-publication of articles contingent on the particular findings of the article. Within the review, we only included English language publications and articles produced in other languages only, were not included. With consideration of additional research need, interestingly, no studies considering the health related quality of life of caregivers of patients with infectious disease or asthma related illness were picked up by our searches. Further research may provide useful information on the experiences of caregivers caring for individuals suffering from these diseases. Furthermore, we noted the existence of preference and utility based measures for health related quality of life of caregivers, however, no such measures were present to measure caregiver burden in a similar manner. Studies that provide suitable modelling would be of benefit in economic evaluations by policy makers and academics quantifying the effect of these diseases upon the burden of care experienced. These measures may be of particular benefit where no relationship between carer and patient utility can be established.

# 5. Conclusion

Overall, primary informal caregivers and family members of individuals suffering from disease appear to experience inferior health related quality of life as compared to the general population. The extent to which an individual's health state leads to quantifiable health related quality of life loss in caregivers and family members appears to be determined by disease type, and is also affected by  the severity of disease and the burden of care that caring for the primary patient imposes upon the caregiver. Health related quality of life in caregivers and family members is most affected in the domains of mental health, particularly anxiety, depression or emotional role functioning, the ability to conduct usual day to day activities and measures of vitality i.e the energy to function. Importantly, a relationship between the burden of caregiving and the health related quality experienced by informal caregivers indicates consideration should be given to how this can be included more formally in economic evaluations.

# Supporting Information

### S1 Appendix. PRISMA Checklist

### S2 Appendix. Search Results

### S3 Appendix. General Characteristics of Included Studies

# Author Contributions

Conceived the study: HS/JH. Performed the experiments. TG. Analysed the data: TG HS JH. Contributed reagents/materials/analysis tools: TG HS JH. Wrote the paper: TG HS JH

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| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 3,4 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 4 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 4 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 4-7 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 4-7 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 4-7 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 4-7 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 4-7 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 4-7 |

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| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 4-7 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 4-7 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 4-7 |

Number of Search Results (‘Hits’) by Database or Journal

| **DATABASES** | (“Health” or “Health related”) AND (“Quality of life”) AND (“Instruments” or “Measurement”) AND (“Caregivers” or “Family members”) | (“Health related”) AND (“Quality of life”) AND (“Caregivers” or “Family members”) | (“Health” or “Health related”) AND (“Quality of life” or “Burden of disease”) AND (“Measurement” or “Instruments”) AND (“Loss” or “Benefit”) AND (“Caregiver” or “Parent” or “Family member” or “Children” or “Partner” or “Spouse”) | (“Burden of disease”) AND (“Caregivers” or “Family members”) | (“Health” or “Health related”) and (“Quality of life” or “utility” or “wellbeing” or “Burden of disease” or “economic analysis”) and (“Measurement” or “Instruments”) and (“Loss” or “Benefit”) and (“Caregiver” or “Family member”) |
|---|---|---|---|---|---|
| Medline | 1 | 614 | 37 | 35 | 10 |
| Google Scholar | 18,400 | 17,500 | 14,800 | 23,000 | 15,600 |
| Pubmed | 433 | 932 | 86 | 63 | 22 |
| Scopus | 1249 | 2669 | 542 | 1281 | 201 |
| Cochrane Library | 1277 | 1560 | 1505 | 281 | - |
| Springer Links | 525 | 1967 | 179 | 5601 | 126 |

**JOURNALS**

| | | | | | |
|---|---|---|---|---|---|
| Health Policy | 17 | 39 | 1233 | 40 | - |
| Health and Quality of Life Outcomes | 341 | 392 | 327 | 186 | 202 |
| International Journal of Wellbeing | 14 | 22 | 5 | 1 | - |
| Pharmacoeconomics | 140 | 239 | 177 | 147 | 128 |
| PLoS One | 356 | 69 | - | 28 | - |
| PLoS Medicine | - | 5 | - | 11 | - |
| Quality of Life Research | 639 | 705 | 589 | 319 | 368 |

# Appendix 3: General Characteristics of Included Studies

| Study (First author's name) | Disease(s) covered (Of Primary Patient), Caregiver Type, Year of Publication | Caregiver HR-QOL Survey/ Instrument Used | Instrument for Measurement of Caregiver Burden (If any) | Objective (Aim) of Article | Research Methods, Collected data | Key Findings/Comments |
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| Acaster (51) | Multiple Sclerosis, Family Caregivers, 2013 | EQ-5D/EQ-VAS, SF-36 | - | To explore the overall HRQL of caregivers of people with Multiple Sclerosis compared to matched controls, and more specifically explore the impact of different levels of functioning in people with MS on caregivers' HRQL scores | A cross-sectional observational study of 200 caregivers of people with MS and 200 matched controls completed the EQ-5D, SF-36, HADS and a sociodemographic questionnaire. Caregivers also completed the Patient Determined Disease Steps questionnaire as a measure of MS severity. Differences in HRQOL between caregivers and controls were assessed using t-tests and chi square analyses as appropriate. Ordinary Least Squares regression was also used to evaluate the disutility of being a caregiver compared to controls stratified by MS severity | Caregivers reported significantly lower HRQOL compared to matched controls. A lower level of functioning in people with MS was mirrored by lower levels of caregivers' HRQOL. At the point at which mobility problems required wheelchair use caregivers reported better HRQOL. |
| Alshubaili (50) | Multiple Sclerosis, Family Caregiver, 2008 | WHOQOL-BREF | - | To compare the subjective QOL of family caregivers of persons with relapsing remitting and progressive MS, with those of a matched general population sample and caregivers of diabetes and psychiatric patients and to assess the relationship of QOL with caregiver attitudes to MS and patient's variables. | Consecutive MS clinic attendees were assessed with the 26 – item WHOQOL Instrument, and for depression and disability. Similarly, caregivers independently rated their own QOL as well as their impression of patients' QOL and attitudes to patients' illness | Caregivers had significantly lower QOL than the general population control group for five out of six domains and the general facet ($P < 0.01$), but higher QOL than the patients. The significant predictor of caregivers' overall QOL was their impression of patients' QOL. |
| Alvarez-Ude (92) | Chronic Renal Failure (Dialysis), Family Caregivers, 2004 | SF-36 | Zarit Burden Interview (ZBI) | To evaluate the health-related quality of life (HRQOL) and burden on family caregivers of chronic dialysis patients and to analyze which factors were associated with it | A cross-sectional multicentric study was carried out with 221 patient/caregiver pairs. SF-36 norms were used to estimate gender and age standardized physical component summary (PCS) and mental component summary (MCS) scores. The Duke-UNC Functional Social Support Questionnaire (FSS), the ZBI, and sociodemographic and clinical data were also collected | The PCS and MCS of caregivers were slightly worse than that of the Spanish population. Lower PCS was associated with younger age and higher ZBI. Lower MCS was associated with higher ZBI, lower FSS and lower MCS in the patient. Higher ZBI was associated with lower FSS, PCS and MCS of the caregiver. |
| Andren (37) | Dementia, Family Caregivers, 2007 | EQ-5D/EQ-VAS | Caregiver burden scale (CBS) | The aim of this study is to examine associations between caregiver burden, perceived health and sense of coherence in family caregivers to persons with dementia living at home. | Older persons, 2238 subjects, with any form of social services, were invited to an assessment of cognitive capacity. Those who had cognitive decline (255) were invited for a medical examination and 130 persons were diagnosed as having dementia. The family caregivers to persons with | The family caregivers experienced moderate burden, and strong associations were noted between burden, especially isolation, disappointment and emotional involvement with perceived health and sense of coherence, adjusted for age and relationship. Caregivers with lower burden reported significantly better perceived health and higher mean score of sense of coherence than caregivers with |

| Study (First author's name) | Disease(s) covered (Of Primary Patient), Caregiver Type, Year of Publication | Caregiver HR-QOL Survey/ Instrument Used | Instrument for Measurement of Caregiver Burden (If any) | Objective (Aim) of Article | Research Methods, Collected data | Key Findings/Comments |
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| | | | | | dementia answered a questionnaire including a caregiver burden scale, the Nottingham health profile scale, sense of coherence scale and the Euroqol (EQ-5D) instrument | higher burden. |
| Arafa (74) | Heart Disease, Parents, 2008 | SF-36 | - | To describe the Health related quality of life (HRQOL) of parents whose children are suffering from heart diseases and to identify the most important factors that could affect it | A cross sectional study was conducted in Alexandria, Egypt in the two main hospitals that treat children with heart diseases. 400 parents of children with heart diseases were recruited and a comparison group (400) of parents of children with minor illnesses were included from both hospitals. Socioeconomic and disease related data were collected, SF36 was used to collect data regarding the QOL. MANOVA was used to compare the SF-36 scores between groups and to explore the impact of different variables | In all SF-36 subscales, parents of children with heart diseases reported significantly poorer HRQOL, except for pain subscale. The largest differences were for General Health, Vitality and role limitation physical. Factors that had a significant impact on HRQOL were severity of illness, type of heart disease in addition to age of child, having multiple children, financial situation and presence of comorbid condition. The scores for each domain for parents vs controls were; 46.25 vs. 73.15 for general health, 75.76 vs 79.84 for physical functioning, 39.53 vs 61.81 for role limitations due to physical health problems, 38.25 vs 58.75 for role limitation due to emotional problems, 39.66 vs 75.81 for vitality, 72.90 vs 82.67 for emotional well-being, 93.63 vs 99.88 for social functioning and 82.60 vs 81.80 for bodily pain |
| Arango-Lasprilla (40) | Dementia, Family Caregivers, 2010 | SF-36 | - | To examine the HRQoL of a group of Colombian caregivers of individuals with dementia | The SF-36 measure of HRQOL was used with 99 caregivers of individuals with Dementia and 95 healthy individuals/controls. | Caregivers of individuals with dementia scored significantly lower on all of the SF-36 subscales than the healthy controls The adjusted mean for caregivers compared to healthy controls was: physical function 67.38 and 81.92, role-physical, 56.81 and 84.79, role emotional, 66.18 and 85.40, vitality, 61.96 and 73.96, mental health, 62.68 and 76.00, social function, 73.06 and 87.18, bodily pain, 70.55 and 79.33 and General Health with 55.06 and 75.84. |
| Arango-Lasprilla (59) | Traumatic Brain Injury (TBI), Family Caregivers, 2011 | SF-36 | - | To assess the health-related quality of life of a group of family caregivers of individuals with traumatic brain injury from Guadalajara, Mexico | 90 family caregivers of individuals with traumatic brain injury and 83 healthy controls completed the SF-36 for HRQOL. | Results showed significantly lower scores for traumatic brain injury caregivers compared with healthy controls on 6 Short-Form 36 subscales: role-emotional, vitality, mental health, social functioning, bodily pain, and general health |
| Argimon (39) | Dementia, Family Caregivers, 2004 | SF-36 | - | To assess the health-related quality of life of carers of patients with dementia compared with an age- and gender-matched sample from the general population | A cross-sectional study in 37 primary health care centres in Catalonia, Spain. Carers (*n* = 181; 78% females, mean age 63 years) of patients with dementia together with a random sample of 543 individuals from the general population, matched for age and gender, were assessed with the SF-36 questionnaire | With the exception of physical function category, seven of the scales showed lower scores for females in the carer group. The most important differences were observed in the emotional role, mental health and bodily pain categories. In contrast, male carers had higher scores in the physical function category, and no differences were observed on the other scales. |
| Argyriou (55) | Multiple Sclerosis, Family Caregivers, 2011 | EQ-5D/EQ-VAS | - | To assess the perceived emotional burden and quality of life (QOL) in a sample of Greek | Twenty-two male and 13 female primary caregivers, and an equal number of patients with MS, | Caregivers experienced higher degree of anxiety than depression. Twenty-two caregivers were diagnosed with manifesting anxiety, whereas 12 |

| Study (First author's name) | Disease(s) covered (Of Primary Patient), Caregiver Type, Year of Publication | Caregiver HR-QOL Survey/ Instrument Used | Instrument for Measurement of Caregiver Burden (If any) | Objective (Aim) of Article | Research Methods, Collected data | Key Findings/Comments |
|---|---|---|---|---|---|---|
| | | | | primary caregivers of patients with multiple sclerosis (MS | completed the Greek validated version of the hospital anxiety and depression scale (HADS) and the Greek validated version of EuroQOL (EQ-5D). 35 age-, gender-, and education-matched healthy controls were used for comparison | of them also presented depression. Highly educated caregivers were more prone to manifest increased levels of anxiety and depression. In the EQ-5D: 27 reported a moderate level of anxiety/depression and three indicated an extreme degree. The caregivers reported a mean EQ-VAS value of 61.9 ± 13.8 (range 40–100), with 10 caregivers rating their health status a score of 50 or lower; the controls scored significantly higher (90.3 ± 7.1) The scores for caregivers and non-caregivers for each EQ-5D-3L domain were 1.2 +/- 0.4 and 1.0 +/- 0 for usual activities, 1.3 +/- 0.5 and 1.0 +/- 0 for pain/discomfort, 1.9 +/- 0.7 and 1.2 +/- 0.4 for anxiety and depression. The EQ-VAS scores were 61.9 +/- 13.8 for caregivers and 90.3 +/-7.1 for controls at a range of 0-100 |
| Arlen (70) | Prune Belly Syndrome, Family Caregivers, 2015 | Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q-SF) | - | To compare health-related quality of life (HRQoL) in children with prune-belly syndrome (PBS) and their caregivers to healthy controls. | Study participants completed the Pediatric Quality of Life Inventory Generic Core Scales (PedsQL) 4.0 generic core scales (children) or Quality of Life Enjoyment and Satisfaction Questionnaire Short Form (Q-LES-Q-SF) (caregivers) in an online, anonymous format. The PedsQL 4.0 is a 23-item, age-adjusted, validated questionnaire that assesses physical, emotional, social, and school functioning in pediatric patients. | Nineteen caregivers completed the Q-LES-Q-SF. Caregivers had a mean raw score of 54.8 ± 9.6, which was significantly lower (*P* = .02) than the comparative healthy adult cohort (59.8 ± 11.3). PBS profoundly impacts HRQoL in children, negatively affecting physical, emotional, social, and school functioning. Caregivers of PBS patients also report an overall lower quality of life than comparatively healthy, non-caregiver adults |
| Aymerich (54) | Multiple Sclerosis, Family Caregivers, 2009 | SF-12, GHQ-12 | - | To measure the health-related quality of life (HRQoL) of multiple sclerosis (MS) patients and their caregivers, and to assess which factors can best describe HRQoL | A cross-sectional multicenter study of nine hospitals enrolled MS patients and their caregivers who attended outpatient clinics consecutively. The instruments used were the SF-36 for patients and the SF-12 and GHQ-12 for caregivers. Classification and regression tree analysis was used to analyze the explanatory factors of HRQoL | Caregivers presented lower HRQoL than general population, especially in its mental domain. Moreover, according to GHQ-12, 27% of caregivers presented probable psychological distress |
| Barbosa (45) | Parkinson's disease, Family Caregivers, 2013 | SF-36 | - | To evaluate the general and oral health-related quality of life among caregivers of patients with Parkinson's disease. | A representative sample of caregivers from São José dos Campos, Brazil, answered Oral Health Impact Profile (OHIP-14) and Medical Outcomes Study 36-Item Short Form (SF-36) questionnaires, as well as another questionnaire regarding caregivers' characteristics and caring activities. | All domains of the SF-36 also showed negative correlations with OHIP-14 in the entire sample, but this correlation could not be observed among lower educated caregivers. There were significant differences between formal and informal caregivers for OHIP-14 and for the majority of SF-36 domains. Most caregivers were female, the mean scores for SF-36 and OHIP-14 were adequate, and formal caregivers had better results for the SF-36 and OHIP-14 when compared with informal caregivers. |

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|---|---|---|---|---|---|---|
| Belasco (90) | Chronic Renal Failure (Haemodialysis), Family Caregivers, 2002 | SF-36 | Caregiver Burden Scale (CBS) | To describe the characteristics of caregivers of chronic hemodialysis patients, assess their perceived burden and health-related quality of life, and investigate factors influencing this burden | 100 hemodialysis patients and their respective primary caregivers for more than 4 months, measuring quality of life by the SF-36. Subjective burden on caregivers was assessed by the Caregiver Burden scale. | Caregiver Mental Health and Vitality were the most affected emotional dimensions on the SF-36.<br>Mean score of total burden experienced was 2.07 +/- 0.05. Multiple regression analysis showed that independent and significant predictors of burden were Mental Health of the caregiver, Vitality of the patient, type of relationship of the caregiver, and Pain of the caregiver. |
| Belasco (93) | Chronic Renal Failure Hemodialysis/ Peritoneal Dialysis), Family Caregivers, 2006 | SF-36 | Caregiver burden scale (CBS) | To describe caregivers' characteristics and evaluate their burden and quality of life. | We studied caregivers of elderly patients (>65 years) on hemodialysis (HD) therapy (n _ 84), on peritoneal dialysis (PD) therapy (n _ 40), and a group of caregivers (n _ 77) of nonelderly HD patients. Their quality of life was evaluated by using the SF-36 questionnaire, Caregiver Burden scale, and Cognitive Index of Depression | The Mental Component Summary mean score, adjusted for patient race, educational level, primary diagnosis, hematocrit, comorbidities, and physical functional status, was worse for caregivers of PD than HD elderly patients. The most affected Caregiver Burden scale dimensions were General Strain and Environment. |
| Bell (44) | Alzheimer's disease, Family Caregivers, 2001 | HUI-2, SF-36 | - | To measure the mental health, caregiver burden, and amount of time spent on caregiving of those responsible for individuals with AD in different disease stages and care settings; to explore the relationship of caregiver HRQOL assessed with the Health Utilities Index Mark 2 (HUI2) to disease stage and setting; and determine whether increases in caregiving time and burden measures are associated with a decrease in HRQOL values as measured with the HUI2. | HUI2 was administered to a population of 679 caregivers to people with AD at 13 community and institutional sites in the United States. The study also administered the SF-36, a caregiver time questionnaire, and a caregiver burden instrument | The mean global HUI2 utility score for caregivers was 0.87 and varied little by the affected person's setting of care and AD stage. The caregiver burden scales all varied by the affected person's setting of care, and some also varied by disease severity. The mental health component summary score of the SF-36 for caregivers varied across both disease stage and setting. Caregiver time increased for caregivers of AD-affected persons with more severe cognitive impairment |
| Blanes (48) | Paraplegia, Family Caregivers, 2007 | SF-36 | Caregiver Burden Scale (CBS) | The assessment of the health-related quality of life (HRQoL) of primary caregivers of persons with paraplegia owing to traumatic SCI | The HRQoL was assessed by the Short Form-36 (SF-36) health survey questionnaire and caregiver burden was evaluated by the Caregiver Burden Scale (CBS) for 60 caregivers. | The subjects reported lower scores on bodily pain and vitality than the other dimensions of the SF-36. The mean global CBS score was 1.71 (SD¼0.50) and mean scores for each dimension ranged from 1.39 for emotional involvement to 2.44 for environment dimension |
| Bleijlevens (36) | Dementia, Family Caregivers, 2014 | EQ-5D/ EQ-VAS | Zarit Burden Interview (ZBI), Caregiver Reaction Assessment (CRA) | To describe differences in caregiver burden and health-related quality of life of informal caregivers of people with dementia in eight European countries and assess changes after transition from home to institutional long-term care | Data on burden and health-related quality of life were collected at baseline and follow-up (after 3 months) using face-to-face interviews. Two groups of informal caregivers included those: of people with dementia recently admitted to institutional long-term care facilities; | Lower HRQoL and higher levels of burden were expressed by informal caregivers of PwD living at home in comparison to the caregivers of recently institutionalised PwD in all participating European countries. Mild-to-moderate levels of burden were reported by informal caregivers in almost all countries. The perceived level of burden and HRQOL |

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| | | | | | and those of people with dementia receiving home care. | is lower in caregivers of people with Dementia who are residing in an institution. |
| Boyer (62) | Schizophrenia, Family Caregiver, 2012 | SF-36 | - | To assess QoL of the caregivers of individuals with schizophrenia in two countries characterized by different social, economic and cultural conditions, namely Chile and France | Data were collected from public mental health outpatient services in Arica (Chile), and in Marseille (France). QoL was measured with the short-form health survey scale - 36 items (SF36). QoL of 41 Chilean caregivers was firstly compared with 245 French caregivers. Univariate and multivariate analyses using linear regression were then performed to determine variables potentially related to QoL scores | The caregivers were primarily mothers in the two groups, but Chilean caregivers were younger, and lived more frequently with the individual with schizophrenia than French caregivers. The SF36 scores were globally low in the two groups, especially on the mental QoL scores. Chilean caregivers reported lower physical SF36 scores than French caregivers. In the multivariate analysis, being mother and Chilean caregivers were the most regular features associating to a lower QoL |
| Brouwer (9) | Rheumatoid Arthritis, Family Caregivers, 2004 | EQ-5D / EQ-VAS | Caregiver Reaction Assessment (CRA) | To improve understanding of the nature and magnitude of the burden of informal care and also to indicate important areas for improving the current ways in which informal care is investigated | Information on objective burden (such as care tasks performed and time investment), subjective burden (using the Caregiver Reaction Assessment instrument and a self-rated burden score), and quality of life (using the EuroQoL instrument) were collected in a postal questionnaire of 153 informal caregivers who provide care for rheumatoid arthritis (RA) patients | Caregivers had been caring for the RA patients on average for >11 years, reflecting the chronic nature of RA. They provide a substantial amount of care (27.4 hours per week) and are moderately strained (24.6 on the self-rated burden scale). Caregivers are relatively healthy on average but caregivers of more severe RA patients are relatively unhealthy, which may indicate health losses due to caregiving. |
| Bruns (89) | Juvenile Idiopathic Arthritis, Family Caregivers, 2007 | SF-36 | Caregiver Burden Scale (CBS) | To evaluate the quality of life and the disease burden on primary caregivers of patients with juvenile idiopathic arthritis (JIA) | 70 patients with JIA and their respective caregivers were enrolled in the study. Health, quality of life and psychological status were assessed by using the childhood health assessment questionnaire (CHAQ), the medical outcomes study 36-item short-form health survey (SF-36) and the psychiatric screening questionnaire (SRQ-20). Burden of disease on the caregivers was measured by the caregiver burden scale (CB Scale) | Pain and mental health were the items in the SF-36 questionnaire most affected in caregivers. The CB Scale was significantly correlated with the SRQ-20 (r= 0.6), number of limited joints (r = 0.3), number of visits (r = 0.2), family income (r = -0.3) and mental health (r = -0.6), emotional aspects (r = -0.4), social aspects (r = -0.4), vitality (r = -0.5) and general health state of the SF-36 (r = -0.4). |
| Buchanan (3) | Multiple Sclerosis, Family Caregivers, 2010 | SF-8 | - | To identify factors affecting the health-related quality of life (HRQOL) of informal caregivers assisting people with (multiple sclerosis) MS who have greater functional impairment | Data were collected in a national survey of 530 people who provided informal care to people with MS. Multiple linear regression models analysed these data | Poorer overall health for the person with MS, stronger agreement by caregivers that care giving was burdensome or emotionally draining, and the caregiver's need for mental health counselling in the past 12 months were associated with lower mental dimensions of HRQOL for the informal caregiver. Greater caregiver satisfaction with the access the person with MS had to MS-focused care was associated with higher mental dimensions of HRQOL among caregivers |

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| Buhse (49) | Multiple Sclerosis (Older People), Family Caregivers, 2015 | SF-12 | Zarit Burden Interview (ZBI) | To determine which factors (clinical and demographic) are associated with mental and physical health-related quality of life (HRQOL) for caregivers of older persons with multiple sclerosis (MS). | A cross-sectional descriptive design was used to examine the relationship between patient with MS and caregiver clinical and demographic factors with caregiver physical and mental HRQOL. Patients with MS aged 60 years or older and their caregivers were selected.<br>A caregiver survey was administered that collected demographic information and included validated questionnaires measuring HRQOL, caregiver burden, and caregiver perception of risk for neuropsychological impairment of patients with MS. Patient surveys collected demographic information and validated questionnaires measuring cognition, depression, and disability. | The caregivers in this study were older with existing comorbidities. Caregiver mental HRQOL was negatively associated with patient depression and positively associated with caregiver burden and caregiver comorbidity of heart disease. Caregiver physical HRQOL was negatively associated with caregiver comorbidities of arthritis and diabetes and lower household income. |
| Butow (18) | Ovarian Cancer, Family Caregivers, 2014 | SF-12 | - | To understand issues regarding Caregiver burden, quality of life (QOL) and unmet needs in caregivers of women with ovarian cancer at the end of life. | Ninety-nine caregivers of women participating in the Australian Ovarian Cancer Study (AOCS) QOL sub-study (88% response rate) rated their QOL (SF-12), psychological distress (HADS), optimism (LOT), social support (Duke) and unmet needs (SCNS-carers), and patients rated their QOL (FACT-O), every three months for two years. | Caregivers had significantly lower mental and physical QOL than population norms. Aspects of caregiver functioning, rather than patient quality of life, predict caregiver quality of life and distress. |
| Carod-Artal (47) | Parkinson's Disease, Family Caregivers, 2013 | EQ-5D/EQ-VAS | Zarit Burden Interview (ZBI) | To analyze the main determinants of burden and health-related quality-of-life (HRQoL) in caregivers of Brazilian Parkinson's disease (PD) patients. | Caregivers answered Hospital Anxiety and Depression Scale (HADS), Zarit caregiver burden interview (ZCBI) and EQ-5D, a generic measure of HRQoL. Patients were assessed with Hoehn and Yahr (H&Y) staging; Scales for Outcomes in Parkinson's disease (SCOPA) Motor, Cognition, Psychosocial and Sleep scales; Non-Motor Symptoms Scale; HADS; Clinical Impression of Severity Index; EQ-5D and Parkinson's Psychosis Rating Scale | ZCBI mean score was 20.2, and significantly worsened as severity of disease, based on H&Y, increased. Caregiver's EQ-5D Index and visual analog scale mean scores were 0.7 and 76.3 respectively. Weak to moderate association between EQ-5D Index and ZBCI mean scores was observed in caregivers. Patient outcomes (sleep disorders and behavioral-psychotic symptoms) and caregiver outcomes (mood, time of caregiving) were independent predictors of caregiver burden in the multivariate regression analysis. Caregiver's mood status was a significant determinant of caregiver's HRQoL, as measured by the EQ-5D Index. |
| Cedano (95) | Chronic Obstructive Pulmonary Disease (Receiving Oxygen | SF-36 | Caregiver Burden Scale (CBS) | To assess the quality of life and burden of caregivers to Chronic Obstructive Pulmonary Disease patients on Long-Term Oxygen Therapy and to investigate the factors influencing this burden. | An analytical, cross-sectional study of 80 persons with Chronic Obstructive Pulmonary Disease on Long-Term Oxygen Therapy who used the specialized outpatient center of the | The most compromised scores on the carers' quality of life questionnaire were for Vitality and Mental Health. On the Caregiver Burden Scale, the domain which created the greatest burden for carers was the Environment. With the exception of Emotional Involvement, all the domains of quality of life were |

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| | Therapy), Family Caregivers, 2013 | | | | Federal University of São Paulo, and their carers. | affected negatively by the domains of caregiver burden (increasing burden). |
| Chevreul (67) | Fragile X Syndrome, Family Caregivers, 2015 | EQ-5D/EQ-VAS, | Zarit Burden Interview (ZBI) | To provide data in order to increase awareness of the repercussions of FXS on patients and caregivers as well as on the health and social care systems in France. | Retrospective cross sectional study with 145 patients with Fragile X Syndrome and their caregivers. Data on their demographic characteristics and resource use were obtained from an online questionnaire, and costs were estimated by a bottom-up approach. HRQOL, caregiver burden and patient dependence were measured. | Mean EQ-5D utility scores were 0.49 for patients and 0.75 for caregivers. The mean burden for caregivers as measured by the Zarit Caregiver Burden Interview was 39.9. Compared with related diseases, it constitutes a particularly high burden for caregivers |
| Chevreul (68) | Cystic Fibrosis, Family Caregivers, 2015 | EQ-5D/ EQ-VAS | - | To provide data on the economic burden and health-related quality of life (HRQoL) associated with cystic fibrosis (CF) in France. | A retrospective cross-sectional study was carried out on adults and children with CF, who completed an anonymous questionnaire regarding their socio-demographic characteristics, healthcare consumption and presence of a carer. Costs were calculated with a bottom-up approach, and HRQoL was assessed using EQ-5D | The average utility was lower in adults (0.667 vs. 0.783 in children, p = 0.0015). The HRQoL of carers was also affected (0.742 and 0.765 for carers of adults and children with CF, respectively) being lower than that of the general population reference values. |
| Coco (56) | Amyotropic Lateral Sclerosis, Family Caregivers, 2005 | WHOQOL-BREF, SEIQoL-DW | - | To address the quality of life (QoL) and putative associated variables in amyotrophic lateral sclerosis (ALS) patients and their respective caregivers and to investigate concordance within patient–caregiver pairs for ratings of respective QoL | 37 patient– caregiver pairs were included in the study and their HRQOL was calculated using both HRQOL instruments. | QoL was rated low by both patients and caregivers, and there was no significant difference between them on scores of overall QoL No correlation could be found between QoL of both patients and caregivers and all the examined socio-demographic variables. Concordance between patients and respective caregivers was low for ratings of QoL, suggesting that their QoL is not necessarily interrelated, and that these couples do not actually represent a unique psychological entity. |
| Connell (98) | Palliative Care, Family Caregivers, 2013 | Caregiver Quality of Life Cancer Index (CQoLC) | - | This study aimed to investigate health-related quality of life of palliative care (PC) clients and their caregivers, at baseline and follow-up, following a referral to a community PC service. | Quality of life of clients and their caregivers was respectively measured using the McGill Quality of Life instrument (MQoL) and the Caregiver Quality of Life Cancer Index (CQoLC) instruments | Caregivers scored a total CQoLC of 63.9+ 21.4 and clients had a total QOL of 6.1+1.3. At follow up, matched data for 22 clients and 13 caregivers demonstrated no statistical differences in quality of life. |
| De La Rie (64) | Eating Disorders, Family Members, 2005 | SF-36 | - | To investigate the effect on QOL having a relative/ caring for a relative, may have on family members quality of life. | 40 caregivers of ED patients filled out a health-related quality of life questionnaire (SF-36) and a questionnaire on the impact of the ED on various areas of life domains, and on the relationship with the ED patient and the need for professional support. | Quality of life of caregivers was worse than in a normal reference group. Specifically, mental health, vitality and emotional role functioning were reported to be most impaired (SF-36 scores of 61.6 vs 76.8 for mental health, 56.2 vs 68.6 for vitality and 56.4 vs 82.3 for emotional role functioning). ED appeared to affect families' lives substantially. In response to the ED, caregivers felt anxious, powerless, sad, or desperate |

| Study (First author's name) | Disease(s) covered (Of Primary Patient), Caregiver Type, Year of Publication | Caregiver HR-QOL Survey/ Instrument Used | Instrument for Measurement of Caregiver Burden (If any) | Objective (Aim) of Article | Research Methods, Collected data | Key Findings/Comments |
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| Dixon (107) | Many, Family Caregivers, 2006 | EQ-5D/ EQ-VAS | CDQLP (Carer Burden Domain) | To examine whether patient QOL is associated with carer time and carer QOL | 40 312 cases from the Health Outcomes Data Repository (HODaR) were analysed to assess the relationship between patient utility, and the number of days care needed from friends and relatives. The stability of the relationship across patient subgroups was assessed by replicating the analysis in ten disease groups. 64 cases from a study of patients with Alzheimer's disease and their primary carer was also used. This was used to estimate the relationships between patient and carer utility. | Problems with self-care and usual activities have the greatest impact on carer time. For carer utility, the relationships between carer and patient utility have low explanatory power and are poorly specified. A clearer relationship is shown between carer burden and utility, such that when sociodemographic covariates are introduced, the relationship reaches conventional levels of statistical significance ($p < 0.05$). |
| Ebrahimzadeh (86) | Chronic Spinal Cord Injury, Spouses, 2013 | SF-36 | - | To evaluate the health related quality of life of spouses who act as primary caregivers of veterans with chronic spinal cord injuries in Iran | The study consisted of 72 wives of 72 veterans who were categorized as spinal cord injured patients based on the American Spinal Injury Association (ASIA) classification. Health related quality of life was assessed by the SF-36 Health Survey. Pearson's correlation was carried out to find any correlation between demographic variables with SF-36 dimensions. To find the effect of the factors like age, employment status, duration of care giving, education, presence or absence of knee osteoarthritis, and mechanical back pain on different domains of the SF-36 health survey, Multivariate analysis of variance (MANOVA) was used | All of the SF-36 scores of the spouses were significantly lower than the normal population. Pearson's correlation demonstrated a negative significant correlation between both age and duration of caring with the PF domain. The number of children had a negative correlation with RE and VT. The burden of caregiving can impact the QOL of caregivers and cause health problems. |
| Fleming (99) | Palliative Care, Family Caregivers, 2006 | SF-12 | Feelings about Caregiving Scale (FAC) | To explore the association between perceptions of health care quality and quality of life in patients with advanced metastatic cancer and their informal caregivers | 39 Patients' and caregivers' perceptions of health care quality, mental health, health-related quality of life, symptoms, and burden were measured. | Patients' mental health and depression scores correlated with those of caregivers, suggesting that the mental health of patients and their caregivers are associated; patients and caregivers shared similar perceptions regarding health care quality; the presence of depression in caregivers correlated with caregivers being less satisfied with the health care being given to their patients. |
| Godwin (83) | Stroke, Spouses, 2013 | SF-36 | Zarit Burden Interview (ZBI) | To measure HRQOL, and its related determinants, in long-term survivors of stroke (SS) and their spousal caregivers (CG) who were more than 2 years post stroke | Health related quality of life (HRQOL) and related outcomes were measured for SS and CG. Data from baseline to 12 months were used in conjunction with data from the present study. Linear mixed models were used to analyze the change in repeated | Increased number of illnesses and older age were associated with CG lower physical HRQOL score. Higher depression was associated with lower mental HRQOL score for both CG and SS |

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| | | | | | measures over time. Multiple linear regression was used to analyze the relationship of generic HRQOL to related psychosocial outcomes. | |
| Gohil (97) | Neovascular Age Related Macular Degeneration, Family Caregivers, 2015 | EQ-5D/EQ-VAS | Caregiver reaction assessment (CRA) | To assess the caregiver burden and factors determining the burden in patients receiving ranibizumab therapy for neovascular AMD (nAMD | A cross-sectional questionnaire survey of 250 matched patient caregiver dyads. The primary outcome was the subjective caregiver burden measured using caregiver reaction assessment scale (CRA). Objective caregiver burden was determined by the caregiver tasks and level of care provided. The factors that may predict the caregiver burden and the health status of the dyads were also collected and assessed in a hierarchical regression model | The mean CRA score was 3.2±0.5. Caregiver tasks including accompanying for hospital appointments for eye treatment and patient's visual acuity in the better eye were the biggest contributors to the caregiver burden hierarchical model explaining 18% and 11% of the variance respectively. Ranibizumab therapy for nAMD is associated with significant caregiver burden. Both disease impact and treatment frequency contributed to the overall burden. The carer's perception of patient's symptoms of nAMD and visual difficulties experienced by the patient also contributed to the carer's HRQOL. |
| Goren (14) | Cancer, Family Caregivers, 2014 | SF-12, SF-6D | - | To expand the understanding of cancer-related caregiving burden in Europe | Caregivers (n=1,713) for patients with cancer and non-caregivers (n=103,868) were identified through the 2010 and 2011 European Union National Health and Wellness Survey. Respondents completed measures of sociodemographics and health behaviours, health-related quality of life, work productivity and activity impairment, healthcare resource use (emergency room visits, hospitalizations, and traditional provider visits), and reported diagnosis of stress-related comorbidities (depression, anxiety, insomnia, headache, migraine, and gastrointestinal problems). Two sided tests of means or proportions compared caregivers against Non-caregivers. | Caregivers for patients with cancer vs. non-caregivers reported significant ($P<0.05$) impairment across all health outcomes, even after adjusting for several confounds (e.g., 3.26-point lower mental health status, 0.043-point lower health utilities, 1.46 times as much work impairment, and 1.97 times the odds of anxiety). |
| Grov (20) | Cancer (Palliative) Family Caregivers, 2005 | SF-36 | - | To examine anxiety, depression, and QOL in PCs of patients with cancer in the late palliative phase | The sample consisted of 49 PCs of women with breast cancer and 47 PCs of men with prostate cancer. QOL was rated with the Medical Outcome Study Short Form (SF-36), and mental health with the Hospital Anxiety and Depression Scale (HADS). The findings were compared with age-adjusted norm data (norm) | Physical QOL was significantly higher than norm in both genders, while mental QOL was significantly lower in male PCs. The level of anxiety was significantly higher than norm in both genders.<br>No significant difference for level of depression was found in either gender, while caseness of HADS-defined depression was significantly more prevalent in female PCs compared with norm |

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| Grov (22) | Cancer, Family Caregivers, 2012 | SF-36 | - | To compare caregivers of cancer patients during the curative and a palliative phases with respect to their mental health and health-related QOL | A descriptive, cross-sectional study combines data from two studies. The first group consists of caregivers of patients with cancer in the late palliative phase and the second group consists of caregivers of outpatients with cancer who suffer from pain and/or use analgesics. Data were collected by means of standardized measures and analysed with descriptive statistics | No significant differences in mental health and health related QOL were revealed for caregivers of cancer patients in the palliative and the curative phases, respectively. Neither education level in the caregivers, nor the patients' functional status influenced caregivers' mental health or QOL. Younger caregivers seem to have better physical QOL. |
| Grunfeld (24) | Cancer (Breast), Family Caregivers, 2004 | SF-36 | Zarit Burden Interview (ZBI) | To prospectively examine the psychosocial, occupational and economic impact of caring for a person with a terminal illness. | 89 caregivers of women with advanced breast cancer and their caregiver were followed until their death or study completion at 3 years. The Karnofsky Performance Status (KPS) index, the SF-36, the Hospital Anxiety and Depression Scale, the ZBI, FAMCARE and the Medical Outcomes Study Social Support Survey were administered during follow-up. Economic data were collected by means of a questionnaire | Significantly more caregivers than patients were anxious (35% v. 19%, $p = 0.009$). More caregivers were depressed (30% v. 9%, $p = 0.02$) and had a higher level of perceived burden (26.2 v. 19.4, $p = 0.02$) at the start of the terminal period than at the start of the palliative period. Burden was the most important predictor of both anxiety and depression. |
| Gulin (60) | Traumatic Brain Injury (TBI), Family Caregivers, 2014 | SF-36 | Zarit Burden Interview (ZBI) | To uncover the system of connections between Mexican TBI caregivers' HRQOL and their mental health | A cross-sectional survey was conducted at a public medical facility in Guadalajara, México. Ninety family caregivers of individuals with TBI completed measures of HRQOL, satisfaction with life, depression, and burden | The better the caregivers' HRQOL, the better their mental health was, with the effect reaching a large sized effect. Caregiver burden was significantly related to all HRQOL domains, with correlation coefficients ranging from -.26 (physical functioning) to -55 (vitality). |
| Gupta (52) | Multiple Sclerosis (MS), Family Caregivers, 2012 | SF-12, SF-6D | - | To examine the extent of multiple sclerosis (MS) caregiver burden compared with that of non-caregivers and Alzheimer's disease (AD) caregivers | Data was obtained from the 2009 National Health and Wellness Survey administered online to a US representative adult sample (N = 75,000). Respondents reported health status, quality of life, work productivity, health-care utilization, and caregiver status. Multivariable regressions, adjusting for key characteristics (eg, age, gender, marital status, depression), were conducted to explore differences between MS caregivers (n = 215) and non-caregivers (n = 69,224) and between MS caregivers and AD caregivers (n = 1341). | MS caregivers had significantly greater activity impairment, poorer mental and physical health status, lower health utility scores, and more traditional health-care provider visits, emergency room (ER) visits, and hospitalizations than non-caregivers, MS caregivers had greater activity impairment, more ER visits, and more hospitalizations than AD caregivers. MS caregivers had significantly more burden than non-caregivers, and for some measures, even AD caregivers |

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| Gupta (63) | Schizophrenia, Family Caregivers, 2015 | SF-12, SF-36, SF-6D | Caregiver reaction assessment (CRA) | To examine health-related quality of life (HRQoL) and comorbidities experienced by informal schizophrenia caregivers compared with non-caregivers and caregivers of adults with other conditions | Respondents provided information on HRQoL; SF-36v2: and SF-6D (health utility) scores), items from the Caregiver Reaction Assessment and comorbidities experienced in the past 12 months. Schizophrenia caregivers (n = 398) were matched to non-caregivers (n = 158,989) and caregivers of other conditions (n = 14,341) on baseline characteristics via propensity scores. Chi-square tests and ANOVAs were used to determine significant differences across groups | Schizophrenia caregivers reported worse HRQoL than non-caregivers and caregivers of other conditions. Schizophrenia caregivers were more likely to experience sleep difficulties, insomnia, pain, headaches, heartburn, anxiety, and depression than non-caregivers. Schizophrenia caregivers were more likely to experience sleep difficulties, insomnia, pain, and anxiety than other caregivers |
| Ho (110) | Many (Older People/ Elderly Care), Family Caregivers, 2009 | SF-36 | Zarit Burden Interview (ZBI) | To investigate the impact of caregiving on the health status and quality of life (QOL) of primary informal caregivers (PCGs) of elderly care recipients in Hong Kong | 246 PCGs and 492 matched non-caregiver (NCG) controls were identified in a population-based cross-sectional study through random telephone dialling. Their health status and QOL were assessed based on structured questionnaires and Short Form 36 (SF-36) Health Survey | Compared with NCGs, PCGs had significantly increased risks for reporting worse health, more doctor visits, anxiety and depression, and weight loss. Female PCGs were more likely to report chronic diseases, symptoms, and insomnia. PCGs, particularly women, had significantly lower scores in all eight domains of SF-36. High caregiver burden score was positively associated with adverse physical and psychological health and poorer QOL |
| Hsieh (69) | Developmental Delays (Children), Family Caregivers, 2009 | WHOQOL-BREF | - | To study the quality of life, health satisfaction and family impact on caregivers of children with developmental delays in Taiwan. | A Cross-Sectional Study of 48 male and 22 female children with developmental delays were recruited. WHOQOL-BREF for health-related quality of life (HRQOL), PedsQL-Health Satisfaction for health satisfaction, PedsQL-Family Impact Module and Impact on Family Scale for family impact were evaluated. The correlation of caregivers' HRQOL, health satisfaction and family impact were also studied | Caregivers in nuclear families had higher health satisfaction scores (78.2 for nuclear families vs. 66.9 for extended families, $P < 0.05$) when assessed by the PedQL-Health Satisfaction questionnaire. Children's age was negatively correlated with family impact, including parent ,family and total scores as assessed using the PedsQL-Family Impact Module. |
| Hughes (11) | Many (Veterans), Family Caregivers, 1999 | SF-36 | Montgomery Caregiver Burden Scale | To test the cross-sectional relationship between caregiver burden and health-related quality of life (HRQOL) among 1,594 caregivers of veterans identified to qualify for formal home care | 1594 caregivers of Veterans qualified for formal home care were assessed for HRQOL using the SF-36 and for caregiver burden using the Montgomery Caregiver Burden Scale. | Spousal relationship, low income, and burden were associated with poor HRQOL scores. Total variance explained in HRQOL ranged from 14% to 29%, with objective burden contributing more than subjective burden |
| Isa (100) | Children with disabilities, Parents, 2013 | PedsQL Family Impact Module | - | To determine the impact of having children with disabilities on parents' health-related quality of life (HRQOL), family | A total of 425 parents/caregivers of children with disabilities who were registered to community-based rehabilitation centers in 5 districts in Kelantan, Malaysia, participated in this | Mothers, non-Malays, and widowed parents/caregivers, parents/caregivers having male children with disabilities, and children with more complex disability had significantly lower parent HRQOL and family functioning. Both parents/caregivers' characteristics and children's |

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| | | | | functioning, and total family impact and to identify the associated factors | study. The Malay version of PedsQL Family Impact Module was used as research instrument. | characteristics contributed to family impact in local setting. Results of this study emphasize the importance of the whole family involvement as the focus of services and supports by health care providers. |
| Ji (32) | Autism Spectrum Disorder (ASD), Family Caregivers, 2014 | SF-36 | Caregiver Burden Index (CBI) | To identify the predictors of health-related quality of life (HRQOL) among caregivers of children with autism spectrum disorders (ASD) in China | Two hundred and seventy-three caregivers were surveyed using questionnaires on HRQOL, family functioning, coping style, social support, and caregiver burden. | Family functioning, coping style, social support, caregiver burden are predictors of HRQOL in caregivers of children with ASD, and these predictors correlated with each other |
| Kelly (46) | Parkinson's Disease, Family Caregivers, 2012 | EQ-5D/EQ-VAS | Caregiver Strain Index (CSI) | To examine the relationship between HRQOL in people with Parkinson's disease and their caregivers, as well as the effect of caregiver strain (burden). | Using the generic EuroQol and disease-specific Parkinson's Disease Questionnaire-39 Item (PDQ-39), HRQoL was evaluated in a sample of 97 people with PD and their caregivers. Caregiver strain was assessed using the Modified Caregiver Strain Index. Associations were evaluated between: caregiver and care-recipient HRQoL; caregiver HRQoL and caregiver strain, and; between caregiver strain and care-recipient HRQoL | No statistically significant relationships were found between caregiver and care-recipient HRQoL, or between caregiver HRQoL and caregiver strain. Although this Australian sample of caregivers experienced relatively good HRQoL and moderately low strain, a significant correlation was found between HRQoL of people with PD and caregiver strain (rho 0.43, p<.001). Poor HRQoL in people with PD is associated with higher strain in caregivers |
| Khanna (33) | Autism Spectrum Disorders (ASD), Family Caregivers, 2011 | SF-12 | Caregiver Strain Questionnaire (CGSQ) | To compare the HRQOL scores of caregivers of children with autism to those of the general US population and to identify the factors that influence HRQOL | A total of 304 usable survey responses were received after three mailings, yielding a usable response rate of 35%. Caregiver burden was assessed using the Caregiver Strain Questionnaire (CGSQ). HRQOL among caregivers of children with autism was assessed using the Medical Outcomes Study Short-Form Health Survey version 2 (SF-12v2) | Caregivers of children with autism had lower HRQOL scores than the general population. Care recipient level of functional impairment, social support, use of maladaptive coping, and burden influenced caregiver mental HRQOL. Care recipient extent of behavioural problems and social support influenced caregiver physical HRQOL. |
| Kuhlthau (31) | Autism Spectrum Disorder (ASD), Parents, 2014 | SF-6D, EQ-5D, CarerQOL | - | To understand quantitatively which aspects of HRQoL were most commonly reported by parents of children with an ASD, to determine qualitatively whether there were domains that were important but were not assessed in the quantitative evaluation, and to understand whether parents attributed aspects of their own HRQoL to their child's health condition. | A Mixed methods where parents of children with ASDs (N = 224) reported on their HRQoL, depression, and caregiving burden using quantitative tools. | Parents reported average HRQoL scores from SF-6D of 0.74, which was clinically significant lower than an average normative U.S. population. Families with three or more children with special health care needs (CSHCN) reported lower HRQL and higher caregiving burden than families with less CSHCN. |
| Labiano-Fontcuberta (13) | Multiple Sclerosis, Family Caregivers, 2014 | CAREQOL-MS | - | To examine the extent to which cognitive impairment in MS | A total of 63 MS patients, 63 caregivers and 59 matched controls were recruited. Patients and | Cognitive impairment in MS patients was significantly associated with worse caregiver HRQoL.. MS |

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| | | | | patients contributes to caregiver's HRQoL | controls underwent a neuropsychological assessment, including tests of working memory, speed of information processing, executive function, and verbal fluency. HRQoL of the caregivers was assessed by CAREQOL-MS | patient's caregivers HRQoL is significantly influenced by information processing speed impairment of MS patients. |
| Lee (19) | Cancer, Family Caregiver, 2015 | EQ-5D/EQ-VAS | - | To compared the health-related quality of life (HRQOL) between members of families of cancer patients (hereafter, cancer families) and members of cancer-free families (non-cancer families) | The data were from the Community Health Survey (2012). The study population included respondents at least 30 years of age. Data were adjusted for the following covariates: sex, age, education, marital status, household income, economic activity, household type, chronic disease, and perceived health status. Frequency analysis, analyses of variance, and multiple linear regression analysis were performed. | Cancer families had lower EQ-5D scores than non-cancer families. However, by subgroup, the scores had significant association between cancer and non-cancer families only for females and for those who worked |
| Lee (34) | Autism Spectrum Disorder (ASD), Parents, 2009 | SF-36 | - | To determine if parents of children with High Functioning Autism Spectrum Disorders (HFASDs) report lower health-related QOL as compared to parents of children without a disability and to identify the relationship among various demographic and psychosocial variables and health-related QOL | The physical and mental health-related quality of life (QOL) of 89 parents of children with high-functioning autism spectrum disorders (HFASDs) was compared to the health-related QOL of 46 parents of children without disabilities. Parents completed a packet of surveys measuring demographics, parenting stress, coping, resources, and QOL. | For parents of children with HFASDs, demographics and psychosocial variables accounted for a significant amount of variance for physical health-related QOL, with income, number of children, and stress being significant variables |
| Li (84) | Cerebrovascular disease/ diabetes mellitus (hospitalised/acute ), Family Caregivers, 2003 | SF-36 | - | To use the SF-36 to determine the extent to which HRQOL is decreased among primary caregivers of patients with cerebrovascular accident (CVA) or diabetes mellitus (DM) compared to normal Taiwanese population and to identify the determinants of this decrease. | Data from a cross-sectional survey of 187 primary caregivers who had responsibility for inpatients with a medically verified diagnosis of CVA or DM were compared to those of randomly selected residents. Data were collected by face-to-face interviews with trained interviewers | The age- and gender-adjusted mean differences of caregivers on primarily mental scales of SF-36 were significantly negative compared to general population, as much as a 3–12 points reduction on this 100-point scale. Effects of caregiving on the perceived social life of the caregiver and disability of inpatients in eating and getting in/out of bed were associated with the SF-36 Physical Component Scale (PCS) score while female gender, type of caregiver, care conflicts, degree of care demand of daily living, and effects of caregiving on perceived social life of caregivers were negatively associated with the SF-36 Mental Component Scale (MCS) score |
| Litzelman (106) | Many, Family Caregivers, 2015 | SF-12 | Caregiver Strain Index (CSI) | To determine if and to what extent caregiving characteristics were associated with caregiver strain and | Data were from the 2008–2010 Survey of the Health of Wisconsin, a representative sample of Wisconsin | More hours per week of care and greater duration of caregiving were associated with higher levels of strain. Greater caregiver strain was in turn associated with worse mental HRQoL. However, most caregiving |

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| | | | | health-related quality of life (HRQoL), and whether caregiver strain mediated this association | adults aged 21–74 years. Participants completed questionnaires about their caregiving, sociodemographics, and HRQoL; 264 caregivers were identified. | characteristics were not directly associated with mental or physical HRQoL. |
| Lopes (94) | Lower Urinary Tract Dysfunction (Pediatrics), Family Caregivers, 2011 | SF-36 | - | To describe the QoL of children and adolescents with urological or neurourological conditions, managed with incontinent or continent urinary stomas, or by urethral clean intermittent catheterization (CIC), and their caregivers and compare them to a control group, | The study evaluated the QoL of 28 children and adolescents with urinary malformations and their caregivers using the Autoquestionnaire Qualité de Vie Enfant Imagé (AUQUEI) and Short-Form 36 (SF-36), respectively, and compared the results with 38 healthy control age-paired children/caregivers | A tendency for worse QoL scores in caregivers was detected in the SF-36 pain and physical limitation domains when compared to non-caregiver controls. |
| Lopez-Bastida (42) | Alzheimer's Disease, Family Caregivers, 2006 | EQ-5D/EQ-VAS | - | To examine the economic burden of Alzheimer's disease and to analyse the impact on HRQOL for patients with AD and caregivers in 2001 in the Canary Islands. | 237 patients were recruited. HRQOL was measured for patients and caregivers with the EQ-5D. | The HRQOL with the EQ-5D social tariff was 0.29 for patients and 0.67 for caregivers. The EQ-5D VAS score was 42 for patients and 62 for caregivers. The degree of severity of the patients with AD substantially influenced the quality of life of the patients but not that of caregivers. |
| Lucke (85) | Spinal Cord Injury (SCI), Family Caregivers (FC), 2004 | SF-36 | - | To describe and compare QOL in 10 adult SCI individuals and their family caregivers (FCs) during the initial 6 months following rehabilitation. | Participants completed the instruments and a face-to-face in-depth interview at 1-, 3-, and 6-months following inpatient rehabilitation | SCI individuals reported low physical function, role physical (RP), and role emotional (RE) scores on the SF-36, while reporting high general health (GH), mental health and social functioning on the SF-36. FCs reported lower RP, GH and vitality scores, while reporting higher physical functioning and RE scores. On the visual analog scales, persons with SCI reported lower QOL while FCs reported more pain at 3 and 6 months. |
| Marchal (66) | Down's Syndrome, Parents, 2013 | TNO-AZL Questionnaire for Adult's HRQOL | - | To explore which socio-demographics, child functioning and psychosocial variables were related to the HRQOL domains of cognitive functioning, social functioning, daily activities and vitality in parents of children with DS | Parents of 98 children with DS completed the TNO-AZL adult quality of life questionnaire (TAAQOL) and a questionnaire assessing socio-demographic, child functioning and psychosocial predictors. Using multiple linear regression analyses for each category of predictors, we selected relevant predictors for the final models | Cognitive functioning was best predicted by the sleep of the child and by the parent having given up a hobby, social functioning by the quality of the partner relation, daily activities by the parent having to care for an ill friend or family member, and vitality by the parent having enough personal time. Overall, psychosocial variables rather than socio-demographics or child functioning showed most consistent and powerful relations to the HRQoL domains of cognitive functioning, social functioning, daily activities and vitality. |
| Markowitz (43) | Alzheimer's Disease, Family Caregivers, 2003 | SF-12 | - | To investigate the relationship of caregivers' health related quality of life (HRQOL) to the burden of caring for patients with Alzheimer disease (AD) and resource utilization | Data were collected by a consumer-based survey of 2477 informal AD caregivers. Caregiver HRQOL was assessed using the SF-12 Mental and Physical Summary scores | Compared with a normative, age-adjusted sample, the 2477 caregivers had lower mental and physical scores (for the latter, only those <54 years of age). Increased caregiver mental functioning was associated with caregiver support and perceived quality of patient medical care, fewer hours of caregiving, and fewer patient behavioural symptoms. |

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| | | | | | | The burden of caregiving also had substantial effects on HRQOL |
| McCullagh (81) | Stroke, Family Caregivers, 2005 | EQ-5D/EQ-VAS | Caregiver Burden Scale (CBS) | To identify patient, caregiver, and support characteristics that influence caregiving burden, caregiver QOL, and institutionalization in the first year after stroke | Data on patient, caregiver, and health and social support characteristics were collected prospectively over 1 year in 232 stroke survivors in a randomized trial of caregiver training. The contribution of these variables to caregiver burden score (CBS) and quality of life (QOL) measures at 3 months and 1 year was analysed using regression models | CBS and QOL correlated with each other and with patient (age, dependency, and mood), caregiver (age, gender, mood, and training), and support (social services and family networks) variables. Of these, only patient and caregiver emotional status, caregiver age and gender, and participation in caregiver training were independent predictors of either outcome at 3 months. Caregiver QOL had a significant inverse relationship with caregiver burden and correlated with the same patient and caregiver variables as caregiver burden |
| McPherson (77) | Stroke, Partners, 2011 | SF-36 | - | To examine the relationships between caregiver quality of life (HRQOL), caregiver role, relationship satisfaction, balance and reciprocity in caregivers of partners who had experienced a stroke. | Fifty-six partner caregivers completed a postal survey that included measures of HRQL (SF-36), caregiver role (negative and positive aspects), relationship satisfaction, reciprocity and balance. Data were also collected on the care recipients' quality of life (Stroke Specific Quality of Life scale). | Compared to a normative sample, caregivers' HRQL was lower for all SF-36 domains. The differences between caregiver HRQOL and a normative sample for each of the SF-36 domains were: 70.52 vs 84.15 for limitations in physical functioning, 50.96 vs 80.96 for limitations in physical role, 71.24 vs 75.15 for bodily pain, 64.64 vs 71.95 for general health, 56.18 vs 60.86 for vitality, 77.50 vs 83.28 for limitations in social functioning, 62.65 vs 81.26 for limitations in emotional role and 70.55 vs 74.74 for mental health (77). Care recipient and caregiver age, care recipient quality of life and caregiver role (negative) significantly predicted physical component summary scores on the SF-36, while care recipient quality of life and caregiver role (negative) significantly correlated with mental component summary scores. Relationship satisfaction and intrinsic rewards of caregiving were found to be important predictors of positive aspects of the caregiver role. Caregivers who viewed their relationship as less balanced in terms of give and take had significantly greater caregiver burden than those who viewed their relationship as more equitable |
| Middleton (87) | Spinal Cord Injury, Family Caregivers, 2014 | SF-36 | Caregiver Strain Index (CSI) | To examine relations between psychological distress, health-related quality of life (HR-QOL), and burden among caregivers of people with traumatic spinal cord injury (SCI) over time, and to determine whether the data are more consistent with a wear and tear or adaptation trajectory. | Prospective longitudinal cohort study with measurements at 4 time points 6wk prior to discharge from subacute inpatient rehabilitation and 6wk, 1y, and 2y postdischarge to community. The study had 44 participants nominated as the primary caregiver for the individual with SCI. | At the pre-discharge time point, the caregivers'mental component summary score on the SF-36 was significantly lower than Australian national norms. The scores improved from pre-discharge to 6 weeks post-discharge. At all 3 postdischarge time points, the mental component summary scores were not significantly different to national norms. The trajectory of scores for psychological distress and HR-QOL was consistent with caregiver adaptation to the challenge of providing support to a person with SCI in the early postdischarge period. Caregiver burden did not display similar reductions but did not worsen over the study period |

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| Miura (103) | Functional Impairment (Older People), Family Caregivers, 2005 | SF-36 | Zarit Burden Interview (ZBI) | To examine the relationship between feelings of burden and health-related quality of life (HRQOL) among family caregivers looking after the impaired elderly residing in a community located in southern Japan | 85 pairs comprising elderly individuals requiring care and their respective family caregivers. Questionnaire items for the family caregivers related to demographic variables, caregivers' burden, HRQOL, use of public services, hours spent caregiving, duration of caregiving, and satisfaction with verbal communication with family. Questionnaire items for the elderly recipients of care concerned demographic variables, activities of daily living, and cognitive status | Caregivers' burden was significantly related to cognitive status, hours spent caregiving, and each HRQOL subscore except physical function. |
| Morimoto (80) | Stroke, Family Caregivers, 2003 | SF-12 | Zarit Burden Interview (ZBI) | To examine the relationship between caregiver burden and health-related quality of life in family caregivers of older stroke patients in Japan; and to examine which characteristics of the caregiving situation significantly relate to increased burden | 100 subjects were recruited from seven randomly selected neurological hospitals with out-patient rehabilitation clinics in western Japan and interviewed using the Zarit Burden Interview, the Modified Barthel Index, the Geriatric Depression Scale and the SF-12 for HRQOL. | Increased caregiver burden was significantly related to worsening health-related quality of life, particularly worsening mental health, even after controlling for caregiver age, sex, chronic illness, average caregiving hours/day, and functional dependence of the care-recipient. |
| Myaskovsky (76) | Cardiothoracic Transplant, Family Caregivers, 2012 | SF-36 | Zarit Burden Interview (ZBI) | To determine how the HRQOL of caregivers to cardiothoracic transplant recipients changes over the first year posttransplant; compare the trajectory of change in HRQOL in caregivers of lung versus heart transplant recipients; determine whether we can predict caregiver HRQOL at 1-year posttransplant with caregiver demographic and psychosocial factors assessed early after transplant; and determine whether caregiver HRQOL at 1-year posttransplant would predict subsequent cardiothoracic recipient survival. | Caregiver health-related quality of life was examined during the first year after their family member's transplant, its predictors and its relationship to subsequent patient survival. Adult (aged 18+) caregivers of 242 cardiothoracic transplant recipients (lung = 134; heart = 108) completed assessments of demographics, psychosocial characteristics and caregiver burden at 2 months posttransplant, and HRQOL at 2, 7 and 12 months posttransplant. Recipients' survival time was obtained from medical records | Caregiver HRQOL was generally high across the first-year posttransplant in emotional and social functioning; caregiver physical functioning significantly worsened. There were no differences by type of recipient transplant. Greater caregiver burden predicted poorer caregiver HRQOL in several physical domains at 12 months posttransplant. Transplant recipients whose caregivers had lower perceived general health at 12 months posttransplant showed poorer survival rates during the subsequent 7 years of follow up |
| Nabuurs-Franssen (96) | Diabetic Foot Ulcers, Family Caregivers, 2005 | SF-36 | - | To prospectively evaluate the effect of a foot ulcer on health-related quality of life (HRQoL) of patients with diabetes mellitus and their caregivers | HRQoL according to the SF-36 of 294 patients and 153 caregivers was analysed at baseline (time-point zero [T0]), once the ulcer was healed or after 20 weeks (time-point 1 [T1]), and 3 months later (time-point 2 [T2]). | The caregivers of patients with a persisting ulcer had more emotional difficulties at T2. HRQoL of the caregivers were correlated with the HRQoL of the patients |

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| Nogueira (88) | Spinal Cord Injury, Family Caregivers, 2012 | SF-36 | Caregiver Burden Scale (CBS) | To analyse the impact and burden of care on the Health-Related Quality of Life (HRQOL) of caregivers of individuals with a spinal cord injury (SCI). | A cross-sectional observational study carried out by reviewing medical records and applying questionnaires. The scale Short Form 36 (SF-36) was used to assess HRQOL and the Caregiver Burden Scale (CBScale) for care burden. Results were analysed quantitatively. | Tetraplegia and secondary complications stand out among the clinical characteristics that contributed to greater care burden and worse HRQOL. Association between care burden with HRQOL revealed that the greater the burden the worse the HRQOL. In particular, overall burden was correlated with; functional capacity (-0.28), physical aspects (-0.44), pain (-0.64), overall health condition (-0.30), vitality (-0.52), social aspects (-0.66), emotional aspects (-0.42) and mental health (-0.52) |
| Northouse (29) | Cancer (Breast), Family Caregivers, 2002 | FACT-B, SF-36 | - | To assess patients' and family members' quality of life within 1 month after recurrence, and effects of multiple factors on quality-of-life scores | Patient/family member dyads (N _ 189) participated in this study. A stress appraisal model guided selection of person factors, social/family factors, illness-related factors, appraisal factors, and quality of life, measured with psychometrically sound instruments. Quality of life was measured with both the SF-36 and cancer-specific Functional Assessment of Cancer Therapy scales. | Patients reported significant impairments in physical, functional, and emotional well-being. Family members reported significant impairments in their own emotional well-being. Structural equation modeling revealed that self-efficacy, social support, and family hardiness had positive effects on quality of life, whereas symptom distress, concerns, hopelessness, and negative appraisal of illness or caregiving had detrimental effects. |
| Perrin (35) | Dementia, Family Caregivers, 2014 | SF-36 | Zarit Burden Interview (ZBI) | To examine the association between health related quality of life and mental health in 90 Dementia caregivers. | A Researcher created questionnaires were used to gather demographic information. HRQOL was assessed using the SF-36 and caregiver burden by the Zarit Burden Interview. | Higher caregiver HRQOL was related to better mental health. Vitality, role limitations due to physical problems and pain were associated with caregiver burden. Caregivers with high vitality and low role limitations due to physical problems tended to have low depression and high life satisfaction. |
| Persson (25) | Cancer (Lung), Partners, 2008 | SWED-QUAL | - | To compare HRQOL in significant others of patients dying from lung cancer with that of a general population, in the beginning of the disease trajectory and after the patient's death | 140 Caregivers completed the SWED-QUAL questionnaire to study the course of HRQOL from the time of patient diagnosis (T1) to six months after patient death (T3). | Group comparisons at T1 showed that the significant others scored significantly lower on the scales in the mental domain compared with a general population sample. At T3, significant others also scored lower on most of the scales in the physical and social domains |
| Poley (71) | Major Congenital Anomalies, Parents, 2012 | EQ-5D/EQ-VAS | - | To find suitable methods to assess caregivers' HRQoL, using a population of parents of children with major congenital anomalies | 306 parents of children born with either congenital anorectal malformations (ARM) or congenital diaphragmatic hernia were surveyed. They rated their current HRQoL on the EQ-VAS. After that, they rated their HRQoL again on the assumption that someone would take over their caregiving activities completely and free of charge. The parents classified their HRQoL on the EQ-5D. The caregivers' scores on the EQ-VAS and the EQ-5Dwere compared | Significant HRQoL differences exist between parents caring for children with congenital anomalies and the general population. General HRQoL measures, as used in patients, may be able to detect HRQoL effects in caregivers |

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| | | | | | with scores elicited in the general population | |
| Pressler (73) | Heart Failure, Family Caregivers, 2013 | SF-12 | Oberst Caregiving Burden Scale | To evaluate changes in caregiver burden (perceived time spent and difficulty with caregiving tasks), perceived control, depressive symptoms, anxiety, perceived life changes, and physical and emotional health-related quality of life; to determine differences in perceptions between caregivers of patients with low HF symptoms and caregivers of patients with high HF symptoms; and to the estimate time spent performing caregiving task | Sixty-three HF patients and 63 family caregivers were enrolled; 53 caregivers completed the longitudinal study. Data were collected from medical records and interviews conducted by advanced practice nurses at baseline and 4 and 8 months later | Caregivers who completed the study had significant improvements in perceived time spent on and difficulty of caregiving tasks from baseline to 4 and 8 months, and depressive symptoms decreased from baseline to 8 months. Perceived life changes resulting from caregiving became more positive from baseline to 4 and 8 months. Perceived control, anxiety, and health-related quality of life did not change. Compared with caregivers of patients with low symptoms, caregivers of patients with high symptoms perceived that they spent more time on tasks and that tasks were more difficult, had higher anxiety, and had poorer physical health-related quality of life. |
| Rebollo (105) | Bereavement, Family Caregivers, 2005 | SF-36 | - | To evaluate the HRQL of the main caregiver after the death of a close elderly relative | General population SF-36 norms were used to calculate the gender and age standardised physical component summary (PCS) and mental component summary (MCS) scores. A MCS below 43 was used as an indicator of possible depression. Databases of several patient studies were additionally used to facilitate interpretation of results. 130 caregivers (91.5%) participated, the majority being women (80%), middle aged (56 years), and the spouse (22%) or son/daughter (56%) of the deceased person. | Caregivers' SF-36 scores were lower than expected for mental health, role emotional and social functioning |
| Reis (102) | Functional Impairment, Family Caregiver, 2013 | WHOQOL-BREF | - | To evaluate the QOL and associated factors for caregivers of functionally impaired elderly people | A cross-sectional study that analyzed data from a home-based care survey. The sample consisted of 40 caregivers of functionally impaired elderly people. The instrument consisted of demographic data, health status, the Perceived Family Support Inventory, the Social Support Satisfaction Scale, and the World Health Organization Quality of Life Assessment (WHOQOL-BREF). | In this study, the presence of sequelae showed statistically significant effects on both the physical and psychological domains of WHOQOL-BREF.<br>An association was found between the WHOQOL-BREF physical domain and the presence of sequelae, affective-cognitive inconsistency, and being the primary caregiver. |
| Ringdal (24) | Cancer, Family Caregivers, 2004 | SF-36 | - | To compare the health-related quality of life (HRQOL) of family members of patients who participated in a program of palliative care (intervention | A longitudinal study measuring HRQOL by the SF-36. | HRQOL of the family members deteriorated over time in the terminal phase and reached a low point a few months after the death of the patients, and thereafter gradually increased for all SF-36 scales other than |

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| | | | | family members) with those in conventional care (control family members). | | physical functioning, bodily pain and general health perception. |
| Rivera-Navarro (53) | Multiple Sclerosis, Family Caregivers, 2009 | SF-36 | Zarit Burden Interview (ZBI) | To describe the characteristics of a sample of caregivers of persons with MS, assess their perceived burden, health-related quality of life, and investigate factors influencing this burden | 278 caregivers of persons with MS, recruited from a Spanish cross-sectional survey, measuring health-related quality of life by the 36-Item Short-Form Health Survey (SF-36) and burden by the Zarit Caregiver Burden Interview. | Caregiver General Health, Mental Health, Bodily Pain, and Role-emotional Functioning were the most affected dimensions on the SF-36. Multiple regression analysis showed that independent and significant predictors of burden were Role-emotional Functioning and Vitality dimensions SF-36 scores of caregivers, and the Expanded Disability Status Scale scores. Emotional factors and the disability of the person with MS were major predictors of burden |
| Robinson (75) | Cardiac Surgery, Family Caregivers, 2012 | SF-36 | - | To assess the changes in Health-Related Quality of Life (HRQL) experienced by the carers of cardiac surgical patients who were discharged to home; and to gauge whether carers felt they needed an additional support group or network to be established | 96 primary carers of cardiac patients who had received elective surgery at one tertiary referral hospital were recruited. The majority were female spouses of patients who had undergone bypass and/or cardiac valve surgery. Participants completed a self-administered questionnaire that included the SF-36v2 quality of life health survey and asked about their need for support 6 weeks and 6 months following patient discharge | Carers reported a significant improvement in five out of eight HRQL dimensions (Physical functioning, Physical role, Vitality, Social functioning, Role-emotional) over the study period ($P < 0.05$). Those who completed the survey at 6 weeks but not 6 months reported higher scores across all dimensions. Carers' need for support need was higher at 6 weeks than 6 months |
| Roth (82) | Stroke, Family Caregivers, 2009 | SF-12 | - | To examine the quality of life correlates of family caregiving and caregiving strain in a large national epidemiological sample | Structured telephone interviews were conducted with 43,099 participants as part of the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study. Participants completed the SF-12 and brief measures of depressive symptoms, social contacts, and caregiving strain. | Caregivers reported more quality of life problems than non-caregivers, but these effects were largely dependent on the perceived level of caregiving strain. High strain caregivers reported more problems with emotional distress, worse physical functioning, and fewer social contacts than non-caregivers. Conversely, caregivers who reported no strain from caregiving reported better quality of life than non-caregivers |
| Sarajlija (15) | Rett Syndrome (RTT), Family Caregivers, 2013 | SF-36 | - | To investigate factors influencing health-related quality of life (HRQoL) and depression in mothers who care for children with Rett syndrome in Serbia | The cross-sectional study was conducted on 49 mothers giving care to females with RTT. Caregivers` HRQoL was assessed by using the SF-36 questionnaire. Clinical severity score (CSS) of RTT patients and Beck Depression Inventory II (BDI -II) scale were used to quantify RTT severity and mothers` depression, respectively. Statistical assessment included descriptive statistics, *t*- test, Pearson correlation coefficient and multiple logistic regression. | Lowest scoring domains of HRQoL in mothers giving care to RTT children were mental health, vitality and role functioning emotional. Multiple linear regression analysis revealed that severity of RTT patients` disability (CSS) and caregivers` age are factors with strongest influence to HRQoL and depression in care giving mothers |

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| Serrano-Aguilar (10) | Alzheimer's disease, Family Caregivers, 2006 | EQ-5D/EQ-VAS | Zarit Burden Interview (ZBI) | To assess the impact on health-related quality of life (HRQL) and the perceived burden of informal caregivers of individuals with Alzheimer's disease (AD) on the Canary Islands (Spain) | A multi-center, cross-sectional design, based on questionnaire responses of 237 informal caregivers of AD patients. Patients were classified according to the degree of severity utilizing the Clinical Dementia Rating Scale. Sociodemographic, HRQL (EQ-5D) and functional dependency data were gathered together with the degree of caregiver burden. | Caregivers had a higher frequency of problems than did the general population for every EQ-5D dimension. These rates were approximately: 30% of caregivers and 15% of the general population for mobility, 5-6% of caregivers and 2-3% of the general population for self-care, 40% of caregivers and 10% of the general population for usual activities, 65% of caregivers and 35% of the general population for pain/discomfort and 75% of caregivers and 20% of the general population for anxiety/depression. Caregivers' HRQL was inversely associated with the subject dependency level and caregiver age. HRQL was higher for more educated caregivers. Variables with a negative and/or significant effect on caregivers' HRQL were high feelings of burden, more committed time to care, and older age. The caregiver burden quantified by the Zarit scale showed 83.3% of caregivers with a high level of burden |
| Seven (17) | Gynaecological Cancer, Family Caregivers, 2014 | Caregiver Quality of Life Cancer Index (CQoLC) | - | To determine the factors influencing the general quality of life and the quality-of-life sub dimensions of family members caring for gynaecological cancer patients. | A descriptive study was conducted at a training and research hospital in Turkey. A total of 168 caregivers who were family members were included in the study sample. The data collection form and the Caregiver Quality of- Life Index Cancer Scale were used to collect data. The mean age of family caregivers was 42.6±12.30 and 81%were female. | The caregivers had the most problem with coping with the depressive symptoms and the nausea of the patient and with medication use for the patient. Information on care was requested by 35.7 %, whereas 70 % of this group felt they needed information on every subject regarding disease and its treatment. It is also found that although some factors did not influence the general quality of life of caregivers, they did have a negative effect on various areas such as burden, disruptiveness, positive adaptation, and financial concerns. |
| Shimoyama (91) | Chronic Renal Failure (Peritoneal Dialysis), Family Caregivers, 2002 | SF-36, KDQOL-SF | Zarit Burden Interview (ZBI) | To examine the relationship in Japan between peritoneal dialysis (PD) patients and caregivers with regard to health-related quality of life (HRQOL) and caregiver burden | 60 subjects,26 patients on continuous ambulatory peritoneal dialysis (CAPD), and 34 caregivers. The Kidney Disease Quality of Life Short Form (KDQOL-SF) and the SF-36 was used to measure HRQOL. The ZBI was used to measure caregiver burden. Data was also collected on each patient's duration of illness, treatment modality, age, sex, and medical history | Mean caregiver burden on the ZBI was 14.1, which is considerably lower than that reported among caregivers for patients with dementia or stroke. Caregivers and patients both rated their general health and vitality among the lowest of the eight dimensions on the KDQOL-SF. Compared to national normative data for their age group, caregivers scored substantially lower in general health, vitality, and mental health |
| Sjolander (21) | Cancer (advanced), Family Caregivers, 2012 | SF-36. EQ-5D/EQ-VAS | - | To investigate health-related quality of life (HRQOL) in family members of patients with advanced lung or gastrointestinal cancer 3 to 15 months after diagnosis | Data on mental and physical dimensions of HRQOL were collected from family members of these patients in this prospective quantitative study. Five assessments using the Short Form 36 Health Survey (SF-36) and EuroQol (EQ-5D) were conducted during a 1-year period starting 3 months after | No statistically significant changes in physical or mental HRQOL within the study group appeared over the 1-year follow-up. Compared with norm-based scores, family members had significantly poorer mental HRQOL scores throughout the year as measured by the SF-36. Family members also scored statistically significantly worse on the EQ-5D VAS in all five assessments compared to the norm-based score with family members scores of 73 +/- 3 |

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| | | | | | diagnosis. Thirty-six family members completed the study, i.e. participated in all five data collections. | at 3 month study progression and 69 +/- 3.3 at 15 months compared to 79.7 +/- 0.83 for the normal population. Findings showed that older family members and partners were at higher risk for decreased physical HRQOL throughout the 1-year period, and younger family members were at higher risk for poorer mental HRQOL. |
| Song (28) | Cancer (terminal), Family Caregivers, 2011 | EQ-5D/EQ-VAS | Caregiver Reaction Assessment (CRA) | To describe the QOL and mental health of family caregivers in Korea compared with those of the general population and investigated the associated factors. | The study surveyed the family caregivers of terminal cancer patients who received palliative care services in Korea. Control individuals were selected from participants in the first round of the fourth Korea National Health and Nutrition Examination Survey and were matched with family caregivers using the propensity score method to optimize our comparative analysis. | Health-related QOL was significantly lower in the caregiver group than in the controls. Caregivers experienced more frequent episodes of depression during the previous year than did controls. Caregiver burden, such as "impact on health," "financial problems," and "lack of family support" had a negative influence on the health-related QOL and mental health. However, "disrupted schedule" had a positive influence on the QOL and mental health. |
| Spencer (109) | Many (American Indians), Family Caregivers, 2013 | SF-12 | - | To examine the influence of caregiving on the health-related quality of life (HRQoL) of American Indians enrolled in the Education And Research Towards Health (EARTH) study | Participants were classified as caregivers if at least one adult relied on them for personal care or as non-caregivers (n = 3,736). Caregivers were further classified according to type; those caring for an adult with unspecified needs (CAU, n = 482) and those caring for an adult with mental or physical difficulties (CAD, n = 295). HRQoL was measured using the SF-12 | Across both regions, non-caregivers reported significantly better mental and physical health than CAD (caregiving for mental or physical difficulties), and the health of participants classified as CAU (caregiving for unspecified needs) did not differ from that of non-caregivers. The health of American Indian caregivers depends on the kind of care provided, |
| Takahashi (38) | Dementia, Family Caregivers/Professional Caregivers, 2005 | WHO-QOL 26 | Zarit Burden Interview (ZBI) | To examine the differences in depressive state and associated factors between informal and professional caregivers, | A cross-sectional study was carried out in 23 informal home-based caregivers of demented patients, 24 professional caregivers working in the dementia ward of a psychiatric hospital, and 31 controls. Measurements included severity of dementia and levels of caregivers depression, care burden and quality of life | Informal caregivers had the highest Beck Depression Inventory (BDI) score and ZBI and the lowest QOL among the three studied groups. The BDI and ZBI scores were significantly high when patients exhibited behavioural problems. Regarding informal caregivers, there was a strong positive correlation between BDI and ZBI scores. |
| Valimaki (41) | Alzheimer's Disease, Family Caregiver, 2015 | 15-D | - | To examine caregivers' health-related quality of life (HRQoL) and well-being during the first 3 years after their family member's Alzheimer's disease (AD) diagnosis and assessed the relationship between caregivers' HRQoL, | Longitudinal design (36 months) after AD diagnosis of 236 caregiver–patient dyads. Linear regression was used to assess age- and gender-adjusted association between repeated measurements of caregiver's HRQoL and the severity of AD. For comparison with general population, the National | Caregivers had significantly lower HRQoL than age- and gender-standardized counterparts. Severity of AD was significantly (p\0.05) associated with the mobility and depression dimensions of caregiver's HRQoL but not with the total HRQoL index score |

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| | | | | well-being, and the severity of AD. Further, to compare of caregivers' HRQoL to general population | Health 2011 Health Examination Survey data was utilized | |
| Van Andel (57) | Epilepsy, Family Caregivers, 2011 | EQ-5D/EQ-VAS, RAND-36 | - | To investigate HRQOL and coping style of both patients and caregivers and their interaction | Epilepsy patients attending the outpatient clinic of the University Medical Centre in Utrecht and their caregivers were sent EQ5D and RAND-36 questionnaires. The Utrecht Coping List was used to chart personal coping styles. HRQOL scores of patients and caregivers were compared to the general Dutch population. The association between patient and caregiver HRQOL scores was calculated.<br>A stepwise backward multivariate linear regression analysis was used to explain variances in caregiver HRQOL | Caregiver HRQOL scores were comparable to the general Dutch population. caregivers of epilepsy patients have normal HRQOL, but there are significant associations between patient and caregiver HRQOL scores. Passive coping style explained 50% of variation in HRQOL scores of caregivers. |
| Van Exel (79) | Stroke, Family Caregivers, 2005 | EQ-5D/EQ-VAS | Caregiver Strain Index (CSI) | To assess the objective and subjective burden of caregiving for stroke patients and to investigate which characteristics of the patient, the informal caregiver and the objective burden contribute most to subjective burden and to the condition of feeling substantially burdened. | A study of a sample of 151 stroke survivors and their primary informal caregivers. Data was collected through patient and caregiver interviews 6 months after stroke | Both the level of subjective burden and the condition of feeling substantially burdened were associated with both caregiver's and patient's health-related quality of life, patient's age, and the number of caregiving tasks performed |
| Vanz (72) | Osteogenesis Imperfecta, Family Caregivers, 2015 | WHOQOL-BREF | - | The aim of this study is to assess the quality of life (QoL) of caregivers of patients with OI | A cross-sectional study, a convenience sampling strategy was used to enrol adult caregivers of children and adolescents with OI who attended a referral center in southern Brazil. The WHOQOL-BREF instrument was used to assess QoL. | QoL appears to be impaired in caregivers of patients with OI. The caregivers of patients with OI had significant lower scores for the physical health, psychological, and environmental domains |
| Vogler (58) | Acquired Brain Injury (ABI), Family Caregivers, 2014 | EQ-5D/EQ-VAS | Caregiver Strain Index (CSI), Burden Scale for Family Caregivers (BSFC) | To assess long-term health-related quality-of-life (HRQoL) and potential predictors as well as burden in caregivers of patients with acquired brain injury. | Data of 104 caregivers and 30 patients were analysed. A multiple linear regression model was calculated to identify independent predictors for HRQoL in caregivers. Additionally, correlation analysis was conducted to evaluate associations between patient questionnaire results and caregiver HRQoL | HRQoL and perceived health status in caregivers remained below normative scores of age-matched controls. HRQoL in caregivers was predicted by well-being, caregiver strain, depressive symptoms and caregiver age. Furthermore, HRQoL of caregivers was correlated with depressive symptoms and happiness in patients |
| Wadhwa (27) | Cancer (advanced), Family Caregivers, 2013 | SF-36, CQOLC | - | To evaluate the quality of life (QOL) and mental health (MH) of caregivers of patients with advanced cancer who are | Patients with advanced gastrointestinal, genitourinary, breast, lung or gynaecologic cancer, and their caregivers, were recruited from 24 | Better caregiver QOL was associated with better caregiver MH and patient physical well-being and with not providing care for other dependents. Worse |

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| | | | | receiving ambulatory oncology care and associations with patient, caregiver and care-related characteristics | medical oncology clinics for a cluster randomized trial of early palliative care. Caregivers completed the Caregiver QOL—Cancer scale and the SF-36, and a questionnaire including care-related factors such as hours/day providing care and change in work situation. Patients completed a demographic questionnaire and measures of their QOL and symptom severity. Associations of these factors with caregiver QOL and MH were examined using linear regression analyses. | caregiver MH was associated with female caregiver sex, worse patient emotional well-being, more hours spent caregiving and change in the caregiver's work situation |
| Wang (101) | Functional Constipation (Preschool Children), Family Caregivers, 2013 | PedsQLTM 4.0 Family Impact Module (FIM) | PedsQLTM 4.0 Family Impact Module (FIM) | To investigate the health-related quality of life (HRQOL) in preschool children diagnosed with FC and the impact of the condition on affected families | In this cross-sectional, case-control study, 152 children aged 3-6 years with FC, 176 healthy children aged 3-6 years without FC, and their primary caregivers were selected. Chinese versions of the PedsQLTM 4.0 Generic Core Scale and the Family Impact Module (FIM) were used to assess childhood HRQOL and the impact of FC on family members, respectively. HRQOL scores were compared between children with FC and healthy children. | FC had a significant impact on HRQOL of affected children and their caregivers, as well as their family functions. Social characteristics of children and caregivers, duration and symptoms of FC and family economic status significantly affected HRQOL of children and caregivers, as well as family functions of children with FC. |
| Wittenberg (104) | Chronic Illness, Household Members, 2012 | EQ-5D/ EQ-VAS | - | To identify evidence of spillover of illness onto household members' health-related quality of life | Medical Expenditures Panel Survey (MEPS) data from 2000–2003 were analyzed to identify spillover of household members' chronic conditions onto individuals' health-related quality of life (N = 24,188). Spillover was assessed by disease category, timing of occurrence (pre-existing or new conditions), and age of the household member (adult or child). | Evidence from a US sample suggests that individuals who live with chronically ill household members have lower EQ-5D (HR-QOL) scores than those who live either alone or with healthy household members. |
| Wong (65) | Mental Illness, Family Caregivers, 2012 | WHOQOL-BREF | - | To explore the quality of life (QoL) of Chinese caregivers with mentally ill relatives. It also aimed to examine the differential roles of caregiving burdens, caregiver characteristics, and satisfaction with psychiatric services in caregivers' QoL | 276 caregivers with relatives attending community psychiatric facilities in Hong Kong were invited to fill out a questionnaire. One sample t-tests were conducted to compare the results of this study with that of other Chinese populations in Hong Kong, Taiwan, and mainland China. A hierarchical regression analysis was performed to examine the relative | Caregivers had significantly lower QoL scores than other Chinese populations. Results also suggest that Chinese caregivers who had chronic illness, younger in age, a lower education level, experienced more difficulties in handling negative symptoms, and were more dissatisfied with mental health services had poorer quality of life. Caregiver characteristics displayed a much stronger association with caregivers' QoL than did caregiving burdens and satisfaction with psychiatric services. |

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| | | | | | influence of different factors on caregivers' QoL. | |
| Yamazaki (26) | Cancer (Leukemia), Mothers, 2005 | SF-36 | - | To compare the health-related quality of life (HRQOL) of Japanese mothers of children with leukemia to that of mothers of children without leukemia. | The SF-36 was used to measure the HRQOL of 97 mothers of children with leukemia diagnosed between 1999 and 2000, and compared their scores to those of 240 mothers of children without leukemia matched to the children with leukemia | Of the eight unadjusted domain scores of the SF-36, five were significantly low among mothers of children with leukemia compared to mothers of children without leukemia: 'role-physical functioning' (RP), 'general health perception' (GH), 'vitality' (VT), 'social functioning' (SF) and 'mental health' (MH). |
| Yang (108) | Many (Older Adults)<br>Family Caregivers, 2012 | SF-36 | Zarit Burden Interview (ZBI) | To describe the health-related quality of life (HRQOL) among Chinese caregivers of the older adults living in the community and explore the predictors of caregivers' HRQOL | A cross-sectional study was conducted through convenience sampling. The study population was composed of 1,144 caregivers of older adults who suffered from one or more types of chronic diseases in 15 communities in 3 eastern cities of China. Family caregivers were interviewed face-to-face using the SF-36 and the ZBI scales. The Antonovsky's Sense of coherence (SOC) scale was also used to measure personal coping capability of the caregivers. Hierarchical multiple regression analysis (HMR) was performed to explore the predictors of caregivers' HRQOL | The majority of the caregivers were females (60.0%) or adult children (66.5%). Mental QOL was significantly lower than physical QOL. Hierarchical multiple regression analysis showed that Demographic Characteristics of Caregivers, Patients' Characteristics, and Subjective Caregiver Burden explained most of the total variance of all aspects of HRQOL. While, Objective Caregiving Tasks was only associated with physical QOL. Subjective Caregiver Burden was the strongest predictor of both physical and mental QOL. SOC was also a strong predictor of physical and mental QOL. |
| Yu (78) | Stroke, Family Members, 2013 | SF-36 | - | To examine the relationships of social support and coping strategies to health-related quality of life among primary caregivers of stroke survivors in China | A quasi-random, point of reference sample of 121 survivor–caregiver dyads was recruited from three community health centres and six health service stations in a city in central China. Data were collected in face-to-face interviews at participants' homes using structured questionnaires | Higher educational levels, planning and active coping were positively associated with health-related quality of life. The number of chronic conditions, hours of care per day and functional dependence of the survivor were negatively related to quality of life. |
| ZamZam (61) | Schizophrenia, Family Caregivers, 2011 | WHOQOL-BREF | - | To highlight the socio-demographic, clinical and psychosocial factors associated with the subjective Quality of Life (QOL) of Malaysian of primary family caregivers of subjects with schizophrenia attending an urban tertiary care outpatient clinic in Malaysia. | A cross-sectional study was performed to study patient, caregiver and illness factors associated with the QOL among 117 individuals involved with caregiving for schizophrenia patients. The study used WHOQOL-BREF to assess caregivers' QOL and Brief Psychiatric Rating Scale (BPRS) to assess the severity of patients' symptoms. Social Readjustment Rating Scale (SRRS) assessed the stress level due to life events. | Shorter duration and later onset of illness, not attending day care program, lower BPRS scores and higher education among patients were found to be significant predictors of higher scores in one or more QOL domains in caregivers. Secondly, caregivers with higher educational level, not having medical problems and facing less social readjustment to recent life events were predictive of higher QOL in one or more domains |