Factors related to the quality of life in family carers of people with dementia: a meta-analysis

Milena L Contreras (MSc) [1], Eneida Mioshi (PhD) [1] and Naoko Kishita (PhD) [1]

[1] School of Health Sciences, University of East Anglia, Norwich, UK

Funding

MC's PhD studentship is supported by the National Institute for Health Research (NIHR) Applied Health Research and CARE East of England (ARC EoE), Norfolk and Suffolk Primary and Community Care Research Office and Faculty of Medicine and Health Sciences, University of East Anglia. NK and research assistant's time is funded by the NIHR ARC EoE (Grant reference number: DEM-17). EM is also supported by the ARC EoE programme. The views expressed are those of the authors, and not necessarily those of the NIHR, NHS or Department of Health and Social Care.

This manuscript has not been published and is not under consideration for publication in any scientific journals. Some key findings were presented at the 29th Alzheimer Europe Conference (October 2019) as a poster presentation.

Abstract

Objectives: This meta-analysis aimed to 1) quantitatively synthesise evidence of factors related to the Quality of Life (QoL) of family carers of people with dementia (PwD); and 2) explore moderating factors that may influence the strength of the relationship between such potential predictive factors and carer QoL.

Methods: Studies that investigated correlations between patient/carer-factors and QoL in unpaid family carers of PwD and were published in English, Spanish, Portuguese or Japanese were included.

Results: Thirty-three studies were identified. The pooled correlations with carer QoL (effect size) were significantly large for depression (-0.58), significantly moderate for subjective burden (-0.47) and significantly small for PwD's neuropsychiatric symptoms (-0.24). These results indicated to be robust in the context of publication bias. The results of subgroup analyses demonstrated the social and economic development status of the country where study participants resided did not moderate these effects.

Conclusion: Carer depression, subjective burden and people with dementia's neuropsychiatric symptoms may play a critical role in maintaining QoL of family carers regardless of the social and economic circumstances.

Keywords

Dementia; Family Caregivers; Quality of life; QoL; Alzheimer's

Introduction

The number of people living with dementia worldwide is currently estimated at 35.6 million and this number is expected to double by 2030 and more than triple by 2050[1]. Dementia is one of the most expensive health conditions and the current annual worldwide cost of dementia is estimated to be US$ 818 billion[2]. As such, dementia is considered as one of the greatest health challenges we face today.

Dementia is a progressive condition and while some individuals maintain their independence for many years, many require progressively more support with daily activities, particularly in the later stage of the condition[3]. Family members are considered as a primary resource for this type of care in many countries. For example, in the UK, people affected by dementia and their relatives are currently shouldering two-thirds of all dementia care costs, saving the UK economy billions each year[4]. In Latin-American countries, such as Brazil, there are fewer healthcare services specialised in dementia, which reinforces the belief that families should be responsible for the person with dementia[5]. The lack of provision of dementia services within the public healthcare system is also common in Asian countries such as China, and as a consequence, families take over the significant caring role[6].

These suggest that unpaid family carers are an essential taskforce in caring for people with dementia worldwide. Therefore, this review focused on unpaid family carers (i.e. informal carers) who are characteristically different from formal carers (i.e., healthcare professionals) paid to provide essential care.

Caring for someone with dementia can be physically and emotionally demanding and it can seriously affect the social, psychological and physical wellbeing of the family carer[7, 8]. The previous literature demonstrates that poor carer quality of life (QoL) is likely to be associated with poorer QoL for the person with dementia[9] and with higher economic costs[10].

QoL is a term frequently used in the literature but, to date, there is no consensus about how to best define and assess QoL in family carers of people with dementia[11, 12]. The World Health Organization (WHO) defines it as the individual's perception of their position in life in relation to their goals, expectations, standards and concerns, according to the culture and value systems in which they live. General QoL includes several aspects such as psychological state, physical health, level of independence, personal beliefs and spirituality, social relationships and environment[13]. There is another important concept of QoL often used in the literature that is the Health-Related Quality of Life (HRQoL). HRQoL refers to the components of QoL that are directly and indirectly affected by health, disease, disorder, and injury and therefore, HRQoL often overlaps with the concept of health status[14, 15].

In the past ten years, there have been emerging studies which have developed more specific instruments to measure carer QoL[11, 16, 17]. Early carer studies predominately used general QoL and HRQoL measures. The use of general QoL and HRQoL instruments with older carers can be problematic as some aspects of these types of QoL (e.g., level of independence) could be affected by their age-related factors such as changes in physical conditions[18]. In this regard, these types of instruments have been criticised for lacking validity and not being sensitive enough to measure the psychological consequences and positive aspects of caring[11, 19]. In this meta-analysis, we defined the QoL of carers in a broader sense and included all types of QoL measures to provide a wider understanding of the potential impacts of different factors on carer QoL.

The national guidelines and policies such as the United Kingdom Government's action plan[20] emphasise the need for focusing on early interventions for carers to support them maintaining their QoL. For this reason, it is fundamental to identify the modifiable factors that may affect the family carers' QoL in order to guide the formulation and delivery of policy, treatment, care, and support to improve this crucial outcome[21].

Previously, there have been three review studies that have examined factors associated with the QoL of family carers of people with dementia. The first systematic review conducted by de Oliveira, Vass & Aubeeluck, which solely focused on examining the association of carers' advanced age with their QoL, demonstrated that carer's advanced age to be associated with low levels of their QoL[22].

The second study, an integrative review conducted by Pereira & Soares and published in Portuguese, found that both factors related to carers themselves (e.g., having depression, poor sleep quality, pre-existing health problems, social support received, leisure activities, having received interventions or training for carers) and people with dementia (e.g., dementia type, neuropsychiatric symptoms) can influence the QoL of family carers[23].

The most recent systematic review conducted by Farina et al. found that having better physical and mental health was the factor most strongly associated with having a better QoL. They also found that greater carer independence (e.g. activities and time not spent on caring duties) was positively associated with better QoL and that carers who lived with the care recipient had poorer QoL than those who did not. The health status of the people with dementia and their behavioural and psychological symptoms also seem to be detrimental to carer QoL[21].

These three reviews highlighted that both carer- and patient-characteristics could be potential predictors of carer QoL. However, these reviews have some methodological limitations. First, all reviews only included studies written in English which might have induced a bias in the findings. One of the reviews[22] only included studies that targeted carers aged 60 years or older and all included studies were carried out in developed countries and thus, the generalisability of the findings may be limited due to selection bias. When comparing the distribution of the total costs of dementia worldwide, 87% is currently spent in high-income countries despite the fact that the contribution of informal carers is expected to

be greatest in developing countries[2]. It is, therefore, important to explore the impact of dementia across countries with different economic development status. Another limitation is that the second review by Pereira & Soares did not employ a systematic approach, but it was rather an integrative review using purposive sampling. Therefore, the findings could be prone to researcher bias[23].

Large heterogeneity in the study designs was also evident across all three reviews. The authors combined correlational and regression studies[21-23] and included interventional and cross-sectional studies[23] or quantitative and qualitative studies[21] in their single purposive sampling review. As a result, the included studies were completely heterogeneous, making it difficult to draw a robust conclusion.

Moreover, although the most recent review by Farina et al. was published in 2017, the literature search was conducted in November 2015. Taking into consideration that in recent years, there has been an increasing interest in dementia care research[24], it is expected to find a larger number of articles over the last few years. As such, an updated review could address previous limitations and enhance our understanding of factors associated with carer QoL.

To overcome the aforementioned limitations and clarify the current state of the evidence base, an updated review using a meta-analytic approach was conducted with the following objectives:

1) To quantify the point estimate of effect size between carer QoL and different types of independent variables including those related to carers themselves (e.g., carer depression) and people with dementia (e.g., neuropsychiatric symptoms); and

2) To explore factors that may moderate the strength of such relationship including the development status of the country and types of tools used to assess the constructs of interest.

Methods

This meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [25]. The PRISMA checklist is included as a supplementary file (see Supplementary Table 1).

Eligibility Criteria

The review included quantitative articles published in peer-reviewed journals or academic reports (e.g. PhD thesis). Only cross-sectional and longitudinal studies were eligible for the review.

In order to be eligible for the current review, the study had to (a) recruit unpaid family carers of people with dementia; (b) use a validated measure of generic, health-related or care-related QoL to assess QoL in family carers as a dependent variable; (c) be published in English, Spanish, Portuguese or Japanese; and (d) report a Pearson correlation between the dependent variable (i.e., carer QoL) and independent variables. Any types of independent variables were eligible for the review including variables related to carers themselves (e.g., carer depression) and people with dementia (e.g., neuropsychiatric symptoms).

Information Sources

The databases of PubMed, PsycINFO and Scopus were searched to identify relevant published articles. ProQuest was used to search unpublished doctoral thesis and Lilacs and Scielo were used to search for studies from Spain and Latin America.

Search

The search was conducted by the first author (MC) using the keywords and search strategies outlined in Supplementary Table 2. Manual searches in the reference lists of relevant systematic reviews and articles were also completed to identify any potential missing articles. No date restriction was applied to the search for studies.

Study Selection

Search results were merged using EndNote software and duplicate articles were removed. All the titles and abstracts were screened for eligibility by the first author (MC), whereby clearly irrelevant articles were excluded. Following the initial screening, full-text articles were reviewed by two authors (MC and NK) independently using a structured checklist. The Kappa coefficient for the inter-rater agreement was .84, indicating almost perfect agreement[26]. Disagreements between two coders were resolved through discussions.

Data Collection Process

The first author (MC) developed an electronic data extraction sheet, which was pilot tested on a randomly selected study by two authors (MC and NK). Following this, the electronic form was refined accordingly. To minimize bias, data extraction was conducted on the first five selected studies by two authors (MC and NK) independently. No discrepancies were identified during this pilot phase. Following this, the first author (MC) and a research assistant independently extracted data from the remaining studies. The agreement rate between the two coders was 90.3%, indicating almost perfect agreement.

Data Items

For each included study, information was recorded on (a) study characteristics (the country where the study was conducted and study design); (b) sample characteristics (number of participants, age, gender, relationship with the person with dementia, the average length being a carer); (c) dementia type of the carer recipient; (d) measures used to assess carer QoL; (e) measures used to assess independent variables; and (f) correlation coefficient between carer QoL and the independent variables. If relevant information was not provided in the selected studies, it was considered as “not reported” and the authors did not contact researchers for further clarification.

Risk of Bias in Individual Studies

The Appraisal of Cross-sectional Studies[27] was used to assess the risk of bias in each included study. This tool consists of 20 items which assess different aspects of the methodological quality and reporting quality such as appropriateness of study design and target population, measurement validity and reliability, appropriateness of interpretation of results and justification of conclusion. The Appraisal of Cross-sectional Studies does not include a numerical scale that can be used to produce a quality assessment score; instead, it aims to measure the individual characteristics of a study cumulatively[28]. The first author and a research assistant assessed the risk of bias independently and disagreements were discussed. The Kappa coefficient for the inter-rater agreement was 0.56 indicating moderate agreement between the raters[26].

Summary of Measures and Synthesis of Results

The entire analysis was conducted using Comprehensive Meta-Analysis software version 3[29]. There are no simple criteria in terms of how many studies are needed to calculate the meaningful pooled effect size. However, the combination of very few studies with very different characteristics makes any kind of synthesis untenable in most cases[30]. In this study, the meta-analysis was conducted only when the correlation coefficient between carer QoL and the targeted independent variable was available from more than three studies (i.e., if only two studies reported the correlation coefficient between carer QoL and the targeted independent variable and then quantitative synthesis was not performed).

The correlation coefficient from included studies was transformed to corresponding Fisher's scores to estimate a pooled effect size and its 95% confidence intervals (CI) for each independent variable. A fixed-effect model was used to provide a pooled estimated effect for each independent variable and a test for heterogeneity was performed using the Q-statistic and the I^2 statistic. Where there was evidence of heterogeneity a random-effects model was used.

Estimated effect sizes of <0.09 were considered negligible, 0.10–0.29 small, 0.30–0.49 moderate and >0.50 large[31].

If the correlation coefficient for the same independent variable was reported from two or more independent samples within a single study, they were treated as separate studies for the purpose of analyses. For example, the correlation coefficient for the same independent variable was reported separately for female and male samples in one study[32] and for carers of people with mild, moderate and severe dementia in another study[33]. When the correlation coefficient for the same independent variable was reported for each subscale of the QoL measure rather the total QoL score within a single study[34], correlation coefficients were combined by calculating the mean of effect sizes across subscales to produce a single effect size[35]. The "total QoL score" was used when possible[36].

Risk of Bias Across Studies

To assess publication bias, the trim and fill method[37] was used to estimate how many studies could be missing from each meta-analysis and calculate adjusted effect-size estimates. Rosenthal's Fail-Safe N[38] was used to calculate the number of missing studies needed to be included in the analysis to reduce the overall effect size to a non-significant level. If only a few studies are required to nullify the observed effect, the observed overall effect may not be robust[35].

Additional Analyses

For those independent variables, which demonstrated a significant heterogeneity, a series of subgroup analyses were planned to examine the possible sources of variance. Initially, a series of subgroup analysis using the following moderators were planned: (a) the development status of the country as defined by the Human Development Index (HDI) category (low, medium, high, very high), which is a summary measure of a country's overall

achievement in its social and economic dimensions (i.e., health, education and standard living)[39]; (b) types of measures used to assess carer QoL; (c) types of measures used to assess the independent variable; (d) the relationship with the person with dementia; (e) dementia type of the care recipient; (f) carer's gender; and (g) average length being a carer. However, the latter four moderators (i.e., relationship, dementia type, gender, length as a carer) were not reported consistently in many of the included studies or seemed to be similar across the included studies that did report. Therefore, it was not possible to conduct the subgroup analyses using these four moderators.

Results

Study Selection

The search was conducted on 30th May 2018 and a total of 2458 articles were found. After deleting 1124 duplicated articles, 1334 titles and abstracts were examined by the first author (MC). One hundred and two studies were identified as relevant for the meta-analysis and the full text were reviewed by the two coders (MC and NK) independently. From the 102 full-text reviewed, 33 fulfilled the inclusion criteria and data was extracted from each study. However, only 27 were included in the final meta-analysis (See Figure 1). The remaining five studies did report correlations between QoL and some independent variables, but data for the same independent variable was not available from more than three studies. Thus, these five studies were not included in the quantitative synthesis.

Study Characteristics

Participants. The characteristics of included studies are presented in Table 1. The total number of carers was 6177. The majority of studies recruited carers from Europe (study *n*=12), North America (*n*=8) and South America (*n*=8). There were fewer studies which recruited carers from Asia (*n*=4) and Oceania (*n*=1). More than 65% of carers were females in

the majority (over 70%) of the studies included (*n*=24). Over 75% of the studies (*n*=26) recruited people over 55 years old and 78% of studies only recruited carers with Alzheimer's disease (*n*=26). This diagnosis was the most prevalent in the remaining studies. Eight studies did not report the type of dementia of the care recipient. These results suggest that carers recruited in the identified studies were predominantly females over 55 years old looking after a family member with Alzheimer's disease.

QoL measures. The most commonly used measure of carer QoL were Quality of Life in Alzheimer's disease for carers[40] (QoL-AD; *n*=7), 36-Item Short Form Survey[41] (SF-36; *n*=6) and WHO-QOL-BREF[13] (*n*=6). Over 60% of the included studies (*n*=20) used a general QoL measure (e.g., QoL-AD, WHO-QOL-BREF) and the rest used a health-related QoL measure (e.g., SF-36, EuroQol-5D[42]).

Independent variables. Most of the included studies reported correlations between carer QoL and carer subjective burden (*n*=11), carer depression (*n*=10), people with dementia's neuropsychiatric symptoms (*n*=11) and their level of independence in activities of daily living (ADL) (*n*=10). The majority of the studies used the Zarit Burden Interview (ZBI)[43] to measure subjective burden (*n*=10), the Beck Depression Inventory (BDI)[44] to measure depression (*n*=5), the Neuropsychiatric Inventory (NPI)[45] to measure neuropsychiatric symptoms (*n*=6) and the Katz Index of Activities of Daily Living[46] (*n*=3) to measure ADL.

Independent variables that were not included in the meta-analysis due to the number of studies identified were carer anxiety, satisfaction with life, coping strategies, social skills, frequency of nocturnal disruptions, relationship quality with the person with dementia, interpersonal support, some personality traits such as extraversion and neuroticism, physical health, number of hours providing care weekly, duration of caregiving in years (see Table 1).

Risk of bias within studies

The assessment of study quality and bias using the Appraisal of Cross-sectional Studies tool is presented in Table 2. All of the included studies clearly specified the aim of the study, used the appropriate study design, clearly defined the target population, measured carer QoL appropriately, used validated questionnaires, fully described the methods, and presented the results of all the analyses described in the methods. Overall, the methodological quality was adequate across the included studies. However, the majority of the included studies (*n*=25) did not justify the sample size and almost no studies reported information about non-responders.

Synthesis of results

Twenty-seven studies included in the meta-analysis demonstrated associations between carer QoL and different types of carer-related independent variables (subjective burden, depression, age, income, and distress) and people with dementia-related independent variables (neuropsychiatric symptoms, ADL, cognitive functioning and self-/proxy-rated QoL). A random model was used for carer depression and subjective burden, people with dementia's proxy-rated QoL, their neuropsychiatric symptoms and ADL due to significant heterogeneity.

Independent variables with a significant effect size (Figure 2)

Carer's depression (number of studies included in the analysis *n*=10). Ten studies reported the correlation coefficient between carer QoL and depression. The effect sizes varied from -0.30 to -0.82. Overall, the point estimate of effect size between carer QoL and depression was -0.58 (95% CI = -0.66 - -0.48, $p < 0.00$) suggesting a significant large effect. There was statistically significant high heterogeneity between study effect sizes ($I^2 = 80.77\%$, $Q = 57.29$).

Carer's subjective burden (*n*=11). The effect sizes varied from -0.03 to -0.66. The point estimate of effect size between carer QoL and subjective burden was -0.47 (95% CI = -0.51 - -0.21, $p < 0.00$), suggesting a significant moderate effect. The heterogeneity between study effect sizes was significantly high ($I^2 = 87.95\%$, $Q = 82.98$).

Carer's distress (*n*=3). The effect sizes varied from -0.15 to -0.34. The point estimate of effect size between carer QoL and care's distress was small -0.22 (95% CI = -0.33 - -0.11, $p < 0.00$). The heterogeneity between study effect sizes was not significant ($I^2 = 0.00\%$, $Q = 1.94$). However, this could be due to the limited number of studies included.

People with dementia's self-rated QoL (*n*=3). The effect sizes varied from 0.25 to 0.55. The point estimate of effect size between carer QoL and self-rated QoL was 0.37 (95% CI = 0.24 - 0.49, $p < 0.00$) suggesting a significant moderate effect. The heterogeneity between study effect sizes was not statistically significant ($I^2 = 41.07\%$, $Q = 5.09$).

People with dementias proxy-rated QoL (*n*=5). The effect sizes varied from -0.15 to 0.44. The point estimate of effect size between carer QoL and proxy-rated QoL was 0.27 (95% CI = -0.00 - 0.51, $p < 0.05$) suggesting a significant small effect. The heterogeneity between study effect sizes was significantly high ($I^2 = 89.69\%$, $Q = 38.79$).

People with dementia's neuropsychiatric symptoms (*n*=11). The effect sizes varied from -0.11 to -0.44. The point estimate of effect size between carer QoL and neuropsychiatric symptoms was -0.24 (95% CI = -0.31 - -0.17, $p < 0.00$) suggesting a significant small effect. There was statistically significant moderate heterogeneity between study effect sizes ($I^2 = 61.77\%$, $Q = 28.73$).

Independent variables with no significant effect size (Supplementary Figure 1)

Carer's income (*n*=4). The effect sizes varied from -0.06 to 0.30. The point estimate of effect size between carer QoL and care's income was 0.13 (95% CI = -0.00 - 0.26, *p*

=0.06). Both the overall effect size and the heterogeneity between study effect sizes were not statistically significant (I^2 = 42.23%, Q = 5.19).

Carer's age (*n*=10). The effect sizes varied from -0.10 to 0.10. Overall, the point estimate of effect size between carer QoL and carer's age was -0.03 (95% CI = -0.05 - 0.0, p = 0.13). Both the overall effect size and the heterogeneity between study effect sizes were not statistically significant (I^2 = 0.00%, Q = 2.58).

People with dementia's cognitive functioning (*n*=8). The effect sizes varied from -0.15 to 0.29. The point estimate of effect size between carer QoL and cognitive functioning was -0.04 (95% CI = -0.05 - 0.13, p = 0.40). Both the overall effect size and the heterogeneity between study effect sizes were not statistically significant (I^2 = 44.83%, Q = 14.50).

People with dementia's ADL (*n*=10). The effect sizes varied from -0.33 to 0.17. The point estimate of effect size between carer QoL and ADL was -0.01 (95% CI = -0.07 - 0.8, p = 0.79). Both the overall effect size and the heterogeneity between study effect sizes were not statistically significant (I^2 = 53.20%, Q = 21.37).

Risk of Bias Across Studies

The Duval & Tweedie trim-and-fill approach suggested that potentially no studies are missing for carer's depression, distress, income and age as well as people with dementia's neuropsychiatric symptoms and ADL. The results demonstrated that six studies are potentially missing for carer's subjective burden and three for people with dementia's cognitive functioning. If these missing studies were imputed, the point of estimate would decrease to -0.58 (95% CI = -0.69, -0.44) and -0.01 (95% CI = -0.07, 0.05) respectively. The results demonstrated that one study is potentially missing for people with dementia's self-rated and proxy-rated QoL. If these studies are imputed, the point of estimate would decrease to 0.30 (95% CI = 0.18, 0.41) and 0.23 (95% CI = -0.01, 0.44) respectively.

Rosenthal's Fail-safe N analysis suggested that more than 100 studies are required for the combined two-tailed p-value to exceed .05 for depression, subjective burden and people with dementia's neuropsychiatric symptoms, suggesting that the observed point of estimates are likely to be robust for these independent variables. Rosenthal's Fail-safe N analysis suggested that less than 50 studies are required for carer's distress people with dementia's self-rated QoL and proxy-rated QoL suggesting that the observed point of estimates are less likely to be robust for these two variables.

Subgroup Analyses

Subgroup analyses were conducted with independent variables which demonstrated a significant heterogeneity (i.e., people with dementia's neuropsychiatric symptoms, their proxy-rated QoL, carer's depression and carer's subjective burden). The possible sources of variance were tested using three moderators (i.e., the development status of the country, types of measures used to assess carer QoL and types of measures used to assess the independent variable).

People with dementia's neuropsychiatric symptoms. Subgroup analyses demonstrated that the point of estimate for neuropsychiatric symptoms differed according to the type of measure used to assess neuropsychiatric symptoms ($p<0.01$), but not according to the development status of the country ($p=0.79$) or the type of measures used to assess carer QoL ($p=0.47$). The subgroup of studies that used Revised Memory and Behaviour Problems Checklist (RMBPC)[47] reported the lowest effect estimate while the study that used the Baumgarten Dementia Behaviour Disturbance questionnaire (DBD)[48] reported the highest estimate of effect.

People with dementia's proxy-rated QoL. Subgroup analyses demonstrated that the point of estimate for people with dementia's proxy-rated QoL differed according to the type of

measure used to assess their QoL (p<.01) and the types of measures used to assess carer QoL (p<0.01) but not according to the development status of the country (p=0.48). The subgroup of studies that used EQ-5D to assess proxy-rated QoL as an independent variable reported the lowest effect estimate while the studies that used proxy-rated QoL-AD reported the highest estimate of effect. The subgroup of studies that used EQ-5D to assess carer QoL as a dependent variable reported the lowest effect estimate while the studies that used SF-12 reported the highest estimate of effect.

Carer's depression. The test for subgroup differences indicated that the point of estimate for carer's depression did not differ according to any of moderators (measures used to assess depression p=0.72; measures used to assess carer QoL p=0.94; development status of the country p=0.69).

Carer's subjective burden. Subgroup analyses demonstrated that the point of estimate for carer's subjective burden did not differ according to any of moderators (measures used to assess subjective burden p=0.68; measures used to assess carer QoL p=4.00; development status of the country p=0.48).

Discussion

The current meta-analysis had two purposes, mainly to quantify the point estimate of effect size between carer QoL and different types of independent variables related to carers themselves and people with dementia. Secondly, it aimed to explore factors that may moderate the strength of such relationships, including the development status of the country and types of tools used to assess the measures of interest. To our knowledge, this was the first meta-analysis to quantitatively synthesise the factors associated with carer QoL. Thirty-three

cross-sectional studies providing data from 6177 family carers were included, however, only 27 studies were included in the final meta-analysis.

The current meta-analysis found that the pooled correlations with carer QoL (i.e., effect size) were significantly large for depression and significantly moderate for carer subjective burden, while the effect size for people with dementia's neuropsychiatric symptoms was significant but small. These results were indicated to be robust in the context of publication bias. The effect size for people with dementia's self-rated QoL was also significantly moderate. Furthermore, the effect size was significantly small for people with dementia's proxy-rated QoL and carer's distress. However, these results were less likely to be robust in the context of publication bias, therefore, the findings need to be interpreted with caution.

The results of this meta-analysis support evidence from the previous review[21] that suggested that carer's mental health and people with dementia's behavioural and psychological symptoms were strongly associated with carer QoL. On the other hand, the findings differed from those of de Oliveira, Vass & Aubeeluck, which included only studies that targeted carers aged 60 and over [22]. While the previous review suggested that carer's increased age was associated with lower levels of QoL, the results of the current meta-analysis without any age restriction did not support this association. This could be due to the differences in methodological approaches. De Oliveira, Vass & Aubeeluck included both regression and correlational studies in the systematic review and did not conduct a quantitative synthesis[22]. The current study also included four studies that were not considered in the review conducted by de Oliveira, Vass & Aubeeluck and the findings of the current study were similar to those from a more recent review conducted by Farina et al., which concluded that the associations between carer QOL and carer age to be less clear[21].

The results of subgroup analyses demonstrated the moderating effect of the country development status (i.e., high versus very high developed countries) was not significant for any of the independent variables. The results of subgroup analyses suggest that independent variables which are considered to be a critical predictor of carer QoL (i.e., carer depression, carer subjective burden and neuropsychiatric symptoms) may be important variables for intervention regardless of the opportunities offered for better health, education and living conditions across different high and very high developed countries.

This finding is particularly important as, in the recent years, there has been an increase in the number of interventions developed for family carers of people with dementia, but the majority of well-established interventions have only been tested in the most economically developed countries[49, 50]. Interventions that can be accessed globally and can support carers worldwide are urgently needed considering that a greater number of people with dementia are currently living in low and middle-income countries and this trend is expected to be more profound in the future[51].

The well-established multi-component interventions that can tackle some of the critical predictors such as START[52] could be beneficial for carers from countries with the lower development status if the intervention materials could be translated into multiple languages. However, there are other factors that should be considered apart from the language translation such as differences in culture, health and social care systems and the availability of resources including skilled therapists. To address such challenges, the 10/66 Dementia Research Group developed a programme called Helping Carers to Care, which is a psychoeducational intervention especially designed for use in low and middle-income countries and this programme has already been tested in India, Peru and Russia[53].

The results of subgroup analyses also demonstrated that the type of measure used to assess independent variables such as neuropsychiatric symptoms and people with dementia's proxy-rated QoL may moderate the relationship between these variables and carer QoL. It is not possible to make direct recommendations on which measures to be used to assess these types of variables based on the current review due to a large variability across included studies. The future studies are required to carefully make a choice of measures guided by several considerations such as the setting in which the assessment will occur and their reliability and validity. For example, previous studies have found that the Neuropsychiatric Inventory (NPI) seems to be one of the most efficient measures of people with dementia's neuropsychiatric symptoms, as it includes multiple behavioural domains at a general level as well as targets specific behaviours within domains and can be used in multiple clinical settings[54]. A recent systematic review, which identified 16 different types of QoL measures specifically designed for people with dementia, concluded that many measures still have limited evidence supporting their reliability and validity and thus more research is needed to have complete confidence in their utility[55].

Limitations

This meta-analysis has some methodological limitations. Firstly, although we made every effort to minimise missing studies, all the identified studies were from high or very high developed countries as indicated by the HDI category. Regardless of the inclusion of non-English articles, the current meta-analysis was not able to identify any studies from low developed countries (e.g., countries from Africa, Central America, Caribbean islands and some areas of Asia). However, it is worth mentioning that the current meta-analysis included seven studies conducted in countries that are defined as high developed countries by the HDI (e.g., Colombia and Brazil), but are also considered middle-income countries according to the World Bank classification by income per capita[56]. Thus, the results of the subgroup analysis

by the HDI category still provide an important implication. Although, it is recommended future cross-sectional studies focus on researching the impact of caring on carer QoL in low developed countries as a great number of people with dementia are expected to be living in these countries[57].

Secondly, due to a large variation in the existing assessment tools, it was not possible to have enough studies in each subcategory when conducting subgroup analyses for some independent variables such as people with dementia's proxy-rated QoL and their neuropsychiatric symptoms. For example, 11 studies with four different types of measures were included in the analysis of neuropsychiatric symptoms. Of these 11 studies, there was only one study that used the DBD. Consequently, these results could potentially change if more studies are included.

Furthermore, subgroup analyses were also challenging as characteristics of the sample (e.g., relationship with the person with dementia, hours of caring per day) were not fully reported across the included studies. Therefore, only three moderating factors were explored in the current study. In order to conduct a robust moderation analysis, we encourage future cross-sectional studies to fully report data on sample characteristics for both carers and people with dementia.

Thirdly, similarly to previous reviews[21-23], all included studies employed a generic QoL or HRQoL measures to assess carer QoL and no studies used care-related QoL measures. This is problematic as generic measures of QoL may not capture caring-specific components that can affect QoL and might not be sensitive enough for detecting changes in the progression of dementia[21, 58, 59]. Therefore, it is recommended that future studies use carer-related QoL instruments.

Fourthly, some independent variables that reported a statistically significant correlation with carer QoL were not included in the meta-analysis due to the small number of studies identified (i.e., fewer than three studies). These independent variables included carer anxiety, satisfaction with life, coping strategies, social skills, frequency of nocturnal disruptions, relationship quality with the person with dementia, interpersonal support, some personality traits such as extraversion and neuroticism, physical health, number of hours providing care weekly, and duration of caregiving in years. Future studies should continue exploring the association of carer QoL with these variables in order to be included in future meta-analyses, especially with anxiety as the correlation was reported to be strong in two studies[60, 61]. A recent systematic review also highlighted that although anxiety is a prevalent psychological difficulty experienced by family carers of people with dementia, it is somewhat neglected compared to other carer outcomes (e.g., care burden, depression) in the current literature and therefore requires more attention[62].

Previous studies also have demonstrated that carer's race and ethnicity can have an impact on carer outcomes such as depression and burden[63-65]. Ethnicity was not included in the current meta-analysis as in most of the included studies the data was collected mainly from white carers and there was a lack of diversity in the study samples. Future cross-sectional studies should look at other ethnicities and races to understand how it might affect the caring experience.

Finally, the current meta-analysis was based on correlational studies, and thus the causality in the relationship between independent and dependent variables may not be entirely one-way. It is possible that poorer carer QoL could lead to higher depression or worse neuropsychiatric symptoms. Future longitudinal studies should explore how these variables change over time as dementia progresses.

Conclusion and Implications

In summary, this meta-analysis revealed that carer depression, carer subjective burden and people with dementia's neuropsychiatric symptoms are critical predictors of carer QoL. Therefore, carer interventions that can target multiple outcomes, such as these three variables, seem important for improving carer QoL. Most of the included participants were female, over fifty-five years old and from developed countries, thus the findings may not be able to generalise to the groups of carers who do not fall into this category.

It is highly recommended for future studies to target a wider population, including those from low or moderately developed countries, to use instruments specifically designed for carers to measure carer QoL and to explore the relationship between carer QoL and those independent variables that seem to have a strong correlation with carer QoL but have been less studied such as carer anxiety.

Acknowledgement

The authors would like to thank Natali Sofroniou for her assistance with the data extraction and the assessment of the methodological quality of the included studies.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

References

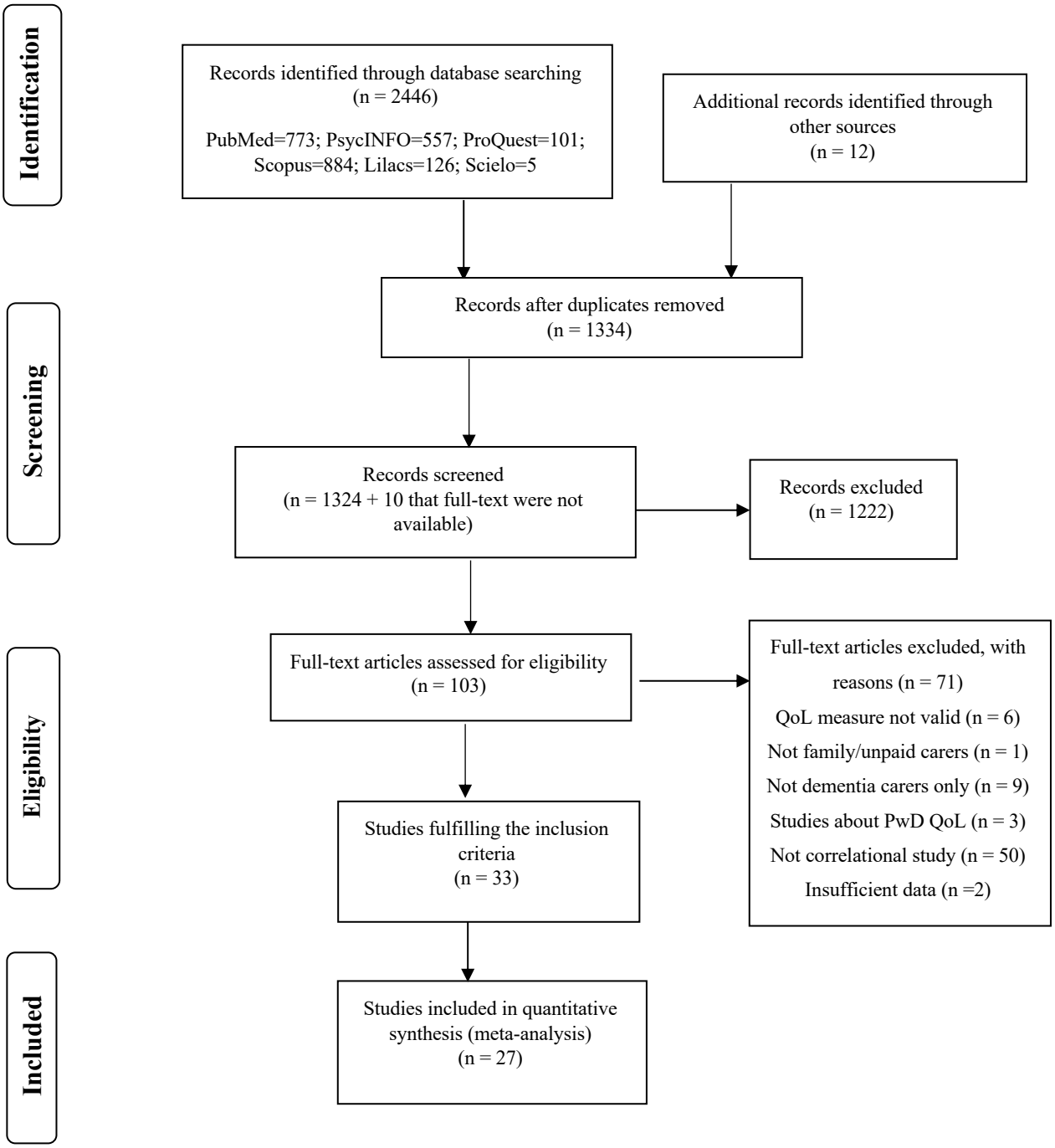
1. Wortmann M. Dementia: a global health priority - highlights from an ADI and World Health Organization report. *Alzheimer's research & therapy* 2012; 4: 40. DOI: 10.1186/alzrt143.
2. Wimo A, Gauthier S and Prince M. *Global estimates of informal care*. 2018. London: Alzheimer's Disease International.
3. Alzheimer's Society. *The dementia guide: living well after diagnosis*. London, England: Alzheimer's Society, 2013.
4. Society As. *Dementia-the true cost: Fixing the care crisis*. 2018. London: Alzheimer's Society.
5. Santos RL, Sousa MFBd, Ganem AC, et al. Cultural aspects in dementia: differences in the awareness of Brazilian caregivers. *Trends in psychiatry and psychotherapy* 2013; 35: 191-197.
6. Wang J, Xiao LD, He G-P, et al. Family caregiver challenges in dementia care in a country with undeveloped dementia services. *Journal of advanced nursing* 2014; 70: 1369-1380. DOI: 10.1111/jan.12299.
7. Ferrara M, Langiano E, Di Brango T, et al. Prevalence of stress, anxiety and depression in with Alzheimer caregivers. *Health and quality of life outcomes* 2008; 6. Article. DOI: 10.1186/1477-7525-6-93.
8. Richardson TJ, Lee SJ, Berg-Weger M, et al. Caregiver health: Health of caregivers of Alzheimer's and other dementia patients topical collection on geriatric disorders. *Current psychiatry reports* 2013; 15. Article. DOI: 10.1007/s11920-013-0367-2.
9. Bruvik FK, Ulstein ID, Ranhoff AH, et al. The quality of life of people with dementia and their family carers. *Dementia and geriatric cognitive disorders* 2012; 34: 7-14. DOI: 10.1159/000341584.
10. Prince M, Wimo AGM, Ali GC, et al. *World Alzheimer Report 2015: the global impact of dementia: an analysis of prevalence, incidence, cost and trends*. 2015. London, England: Alzheimer's Disease International.
11. Dow J, Robinson J, Robalino S, et al. How best to assess quality of life in informal carers of people with dementia; A systematic review of existing outcome measures. *PloS one* 2018; 13. Review. DOI: 10.1371/journal.pone.0193398.
12. Langenhoff BS, Krabbe PF, Wobbes T, et al. Quality of life as an outcome measure in surgical oncology. *The British journal of surgery* 2001; 88: 643-652. 2001/05/15. DOI: 10.1046/j.1365-2168.2001.01755.x.
13. WHO. The World Health Organization quality of life assessment (WHOQOL): Position paper from the World Health Organization. *Social Science & Medicine* 1995; 41: 1403-1409. DOI: https://doi.org/10.1016/0277-9536(95)00112-K.
14. Dijkers M. Quality of life after spinal cord injury: a meta analysis of the effects of disablement components. *Spinal cord* 1997; 35: 829-840. 1998/01/16.
15. Post MW. Definitions of quality of life: what has happened and how to move on. *Topics in spinal cord injury rehabilitation* 2014; 20: 167-180. 2014/12/09. DOI: 10.1310/sci2003-167.
16. Al-Janabi H, Coast J and Flynn TN. What do people value when they provide unpaid care for an older person? A meta-ethnography with interview follow-up. *Social science & medicine (1982)* 2008; 67: 111-121. 2008/04/26. DOI: 10.1016/j.socscimed.2008.03.032.
17. Quirk A, Smith S, Hamilton S, et al. Development of the carer well‐being and support (CWS) questionnaire. *Mental Health Review Journal* 2012; 17: 128-138. DOI: 10.1108/13619321211287184.

18. Grewal I, Lewis J, Flynn T, et al. Developing attributes for a generic quality of life measure for older people: Preferences or capabilities? *Social Science & Medicine* 2006; 62: 1891-1901. DOI: https://doi.org/10.1016/j.socscimed.2005.08.023.
19. Al-Janabi H, Flynn TN and Coast J. Estimation of a preference-based carer experience scale. *Medical decision making : an international journal of the Society for Medical Decision Making* 2011; 31: 458-468. 2010/10/07. DOI: 10.1177/0272989x10381280.
20. HMGovernment. *Recognised, Valued and Supported: Next Steps for the Carers Strategy*. 2010. London, England: Department of Health and Social Care.
21. Farina N, Page TE, Daley S, et al. Factors associated with the quality of life of family carers of people with dementia: A systematic review. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association* 2017; 13: 572-581. DOI: 10.1016/j.jalz.2016.12.010.
22. de Oliveira DC, Vass C and Aubeeluck A. Ageing and quality of life in family carers of people with dementia being cared for at home: a literature review. *Quality in primary care* 2015; 23: 13.
23. Pereira LSM and Soares SM. Factors influencing the quality of life of family caregivers of the elderly with dementia. *Cienc Saude Coletiva* 2015; 20: 3839-3851. Article. DOI: 10.1590/1413-812320152012.15632014.
24. Manthrope J and Bowling A. Quality of life measures for carers for people with dementia: measurement issues, gaps in research and promising paths. *Research, Policy and Planning* 2016; 31: 15.
25. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS medicine* 2009; 6: e1000097. 2009/07/22. DOI: 10.1371/journal.pmed.1000097.
26. Cohen J. A coefficient of agreement for nominal scales. *Educational and Psychological Measurement* 1960; 20: 37-46. DOI: 10.1177/001316446002000104.
27. Downes MJ, Brennan ML, Williams HC, et al. Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS). *BMJ open* 2016; 6: e011458. 2016/12/10. DOI: 10.1136/bmjopen-2016-011458.
28. Wong JN, McAuley E and Trinh L. Physical activity programming and counseling preferences among cancer survivors: a systematic review. *Int J Behav Nutr Phys Act* 2018; 15: 48. 2018/06/09. DOI: 10.1186/s12966-018-0680-6.
29. Borenstein M, Hedges LV, Higgins JPT, et al. Comprehensive Meta-analysis 3ed. Englewood, NJ: Biostat, 2005.
30. Valentine JC, Pigott TD and Rothstein HR. How Many Studies Do You Need?: A Primer on Statistical Power for Meta-Analysis. *Journal of Educational and Behavioral Statistics* 2010; 35: 215-247. DOI: 10.3102/1076998609346961.
31. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. New York: Routledge, 1988.
32. Thompson RL, Lewis SL, Murphy MR, et al. Are there sex differences in emotional and biological responses in spousal caregivers of patients with Alzheimer's disease? *Biological research for nursing* 2004; 5: 319-330. Article. DOI: 10.1177/1099800404263288.
33. Novelli MMPC and Caramelli P. The influence of neuropsychiatric and functional changes on quality of life in Alzheimer's disease. *Dementia Neuropsychologia* 2010; 4: 47-53. Article. DOI: 10.1590/S1980-57642010DN40100008.
34. Moreno JA, Nicholls E, Ojeda N, et al. Caregiving in dementia and its impact on psychological functioning and health-related quality of life: Findings from a Colombian sample. *Journal of cross-cultural gerontology* 2015; 30: 393-408. DOI: 10.1007/s10823-015-9270-0.
35. Borenstein M, Hedges LV, Higgins JPT, et al. *Introduction to Meta-Analysis*. Chichester, UK: John Wiley & Sons, Ltd, 2009.

36. Amorim FAd, Giorgion MdCP and Forlenza OV. Social skills and well-being among family caregivers to patients with Alzheimer s disease. *Archives of Clinical Psychiatry (São Paulo)* 2017; 44: 159-161.
37. Duval S and Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000; 56: 455-463. 2000/07/06.
38. Rosenthal R. The file drawer problem and tolerance for null results. *Psychological Bulletin* 1979; 86: 638-641. DOI: 10.1037/0033-2909.86.3.638.
39. UNDP. *Human Development Indices and Indicators 2018 Statistical Update*. 2018. New York: United Nations Development Programme.
40. Logsdon RG, Gibbons LE, McCurry SM, et al. Quality of life in Alzheimer's disease: Patient and caregiver reports. *Journal of Mental Health and Aging* 1999; 5: 21-32.
41. Ware JE, Jr. and Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; 30: 473-483. 1992/06/11.
42. Group TE. EuroQol--a new facility for the measurement of health-related quality of life. *Health policy (Amsterdam, Netherlands)* 1990; 16: 199-208. 1990/11/05. DOI: 10.1016/0168-8510(90)90421-9.
43. Zarit S, Orr NK and Zarit JM. *The Hidden Victims of Alzheimer's Disease: Families Under Stress*. NYU Press, 1985.
44. Beck AT, Steer RA and Carbin MG. Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. *Clinical psychology review* 1988; 8: 77-100. DOI: https://doi.org/10.1016/0272-7358(88)90050-5.
45. Cummings JL, Mega M, Gray K, et al. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology* 1994; 44: 2308-2308.
46. Katz S, Ford AB, Moskowitz RW, et al. Studies of illness in the aged. The index of ADL: A standardized measure of biological and psychosocial function. *Jama* 1963; 185: 914-919. 1963/09/21. DOI: 10.1001/jama.1963.03060120024016.
47. Teri L, Truax P, Logsdon R, et al. Assessment of behavioral problems in dementia: the revised memory and behavior problems checklist. *Psychology and aging* 1992; 7: 622.
48. Baumgarten M, Becker R and Gauthier S. Validity and reliability of the dementia behavior disturbance scale. *Journal of the American Geriatrics Society* 1990; 38: 221-226.
49. Nickel F, Barth J and Kolominsky-Rabas PL. Health economic evaluations of non-pharmacological interventions for persons with dementia and their informal caregivers: a systematic review. *BMC geriatrics* 2018; 18: 69. DOI: 10.1186/s12877-018-0751-1.
50. Jones C, Edwards RT and Hounsome B. A systematic review of the cost-effectiveness of interventions for supporting informal caregivers of people with dementia residing in the community. *International psychogeriatrics* 2011; 24: 6-18. 08/04. DOI: 10.1017/S1041610211001207.
51. Pot AM, Gallagher-Thompson D, Xiao LD, et al. iSupport: a WHO global online intervention for informal caregivers of people with dementia. *World Psychiatry* 2019; 18: 365-366. DOI: 10.1002/wps.20684.
52. Livingston G, Barber J, Rapaport P, et al. Clinical effectiveness of a manual based coping strategy programme (START, STrAtegies for RelaTives) in promoting the mental health of carers of family members with dementia: Pragmatic randomised controlled trial. *BMJ: British Medical Journal* 2013; 347.
53. Prina AM, Mayston R, Wu Y-T, et al. A review of the 10/66 dementia research group. *Social psychiatry and psychiatric epidemiology* 2019; 54: 1-10. 2018/11/22. DOI: 10.1007/s00127-018-1626-7.

54. Gitlin LN, Marx KA, Stanley IH, et al. Assessing neuropsychiatric symptoms in people with dementia: a systematic review of measures. *International psychogeriatrics* 2014; 26: 1805-1848. 08/06. DOI: 10.1017/S1041610214001537.
55. Bowling A, Rowe G, Adams S, et al. Quality of life in dementia: a systematically conducted narrative review of dementia-specific measurement scales. *Aging & mental health* 2015; 19: 13-31. DOI: 10.1080/13607863.2014.915923.
56. Bank TW. World Bank Country and Lending Groups, https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups (2020, accessed March 24th 2020).
57. Prince M, Graham N, Brodaty H, et al. Alzheimer Disease International's 10/66 Dementia Research Group - one model for action research in developing countries. *International journal of geriatric psychiatry* 2004; 19: 178-181. 2004/02/06. DOI: 10.1002/gps.1059.
58. Reed C, Barrett A, Lebrec J, et al. How useful is the EQ-5D in assessing the impact of caring for people with Alzheimer's disease? *Health and quality of life outcomes* 2017; 15.
59. Kishita N, Hammond L, Dietrich CM, et al. Which interventions work for dementia family carers?: an updated systematic review of randomized controlled trials of carer interventions. *International psychogeriatrics* 2018; 30: 1679-1696. 2018/07/19. DOI: 10.1017/s1041610218000947.
60. Santos RL, de Sousa MFB, Simões-Neto JP, et al. Caregivers' quality of life in mild and moderate dementia. *Arquivos de neuro-psiquiatria* 2014; 72: 931-937. DOI: 10.1590/0004-282X20140155.
61. Zawadzki L, Mondon K, Peru N, et al. Attitudes towards Alzheimer's disease as a risk factor for caregiver burden. *International psychogeriatrics* 2011; 23: 1451-1461. DOI: 10.1017/S1041610211000640.
62. Kaddour L and Kishita N. Anxiety in Informal Dementia Carers: A Meta-Analysis of Prevalence. *Journal of geriatric psychiatry and neurology* 2019: 891988719868313. 2019/08/15. DOI: 10.1177/0891988719868313.
63. Connell CM and Gibson GD. Racial, ethnic, and cultural differences in dementia caregiving: review and analysis. *The Gerontologist* 1997; 37: 355-364. 1997/06/01. DOI: 10.1093/geront/37.3.355.
64. Janevic MR and Connell CM. Racial, ethnic, and cultural differences in the dementia caregiving experience: recent findings. *The Gerontologist* 2001; 41: 334-347. 2001/06/19. DOI: 10.1093/geront/41.3.334.
65. Sun F, Ong R and Burnette D. The influence of ethnicity and culture on dementia caregiving: a review of empirical studies on Chinese Americans. *American journal of Alzheimer's disease and other dementias* 2012; 27: 13-22. 2012/04/03. DOI: 10.1177/1533317512438224.

Figure 1: PRISMA flowchart of the selection of studies.



Note: QoL= quality of life; PwD= people with dementia155

Table 1: Characteristics of included studies.

Authors	Country	Sample	Relationship to patient (%)	Average length being carer in years	Care Recipient Characteristics (Diagnosis, severity %)	Carer QoL measures	Variables correlated with QoL
1. Andreakou (2016)	Greece	155 carers Female %: NR Mean age (SD): 58.1 (13.4)	Spouse: 38.00 Daughter/son: 48.40 Sibilings: 2.60 Other: 11.60	4.6	Diagnosis: Alzheimer's Mild: 22.6 Moderate: 54.8 Severe: 22.6	SF-36 (mental and physical components)	**Depression (ZDRS)**
2. Araujo de Amorim (2017)	Brazil	41 carers Female %: 87.8 Mean age (SD): 61.09 (13.4)	Spouse: 34.10 Daughter/son: 56.09 Other: 9.81	4.8	Diagnosis: Alzheimer's Severity: NR	WHOQOL-BREF	**Social Skills**
3. Borghi (2011)	Brazil	50 carers Female %: 82.0 Mean age (SD): 53.83 (14.52)	Spouse: 16.00 Daughter: 60.0 Other: 24.00	4.63	Diagnosis: Alzheimer's Severity: NR	QoL-AD	**Carer-rated PwD QoL (QoL-AD)**
4. Coen (1999)	Ireland	50 carers Female %: 72.0 Mean age: 56.5	Spouse: 46.00 Daughter/son: 44.00 Sibilings: 2.00 Other: 8.00	2 (Median)	Diagnosis: Alzheimer's Mild: 66.0 Moderate: 22.0 Severe: 12.0	Evaluation of Individual Quality of Life – Direct Weighting (SEIQoL-DW)	**Perceived Burden (ZBI); Well-being;** Social support; Behaviour disturbance (DBD); Cognitive functioning; Functional status; Carer-rated patient QoL (QoL-AD)
5. Conde-Sala (2010)	Spain	251 carers Female %: 66.1 Mean age (SD): Spouse: 75.3(7.3); Child: 79.5(5.7)	Spouse: 44.60 Daughter/son: 55.30	NR	Diagnosis: Alzheimer's Mild: 10.36 Moderate: 68.92 Severe: 20.72	SF-12 (mental component)	**Daughter-rated patient QoL (QoL-AD)**; Wives-rated patient QoL (QoL-AD); Husbands-rated patient QoL (QoL-AD); Son-rated patient QoL (QoL-AD)
6. Creese (2008)	Canada	60 carers Female %: 68 Mean age (SD): 73.65 (9.26)	Spouse: 100	4.61	Diagnosis: Alzheimer's Severity: NR	SF-36 (mental and physical components)	Current sleep quality; Change in sleep quality; Frequency of nocturnal disruptions; Current sleep quality; Change in sleep quality; **Frequency of nocturnal disruptions**
7. Crellin (2015)	UK	289 carers Female %: 68.2 Mean age (SD): 66.7 (12.3)	Spouse: 63.3 Adult child/other family: 34.9 Other: 1.7	4.4	Alzheimer's: 51.0 Vascular: 18.6 Others: 30.4 Mild: 63.0 Moderate: 27.0 Severe: 10.0	SF-12 (mental and physical components)	**Positive impact; QoL physical component score (SF-12); Self-efficacy for obtaining respite; Self-efficacy for responding to disruptive behaviours; Self-efficacy for controlling upsetting thoughts; Self-efficacy for managing neuropsychiatric symptoms; Quality of support,** Emotion-focused coping**; Problem focused coping; Dysfunctional coping; PwD neuropsychiatric symptoms (NPI);** PwD Cognitive funtioning**; PwD activities of daily living**

*Note:*NR= Not reported; QoL= quality of life; PwD= people with dementia, AD= Alzheimer's Disease. SF= Short form; ZDRS= Zung Depression Rating Scale; ZBI= Zarit Burden Interview; DBD= Dementia Behaviour Disturbance. Variables in bold are those ones that presented statistically significant correlations with carer QoL.

Authors	Country	Sample	Relationship to patient (%)	Average length being carer in years	Care Recipient Characteristics (Diagnosis, severity %)	Carer QoL measures	Variables correlated with QoL
8. Feast (2017)	UK	157 carers Female %: 70.96 Mean age: 66.34	Spouse: 53.55	NR	Diagnosis: NR Severity: NR	EQ-5D	BPSD-related distress; Frequency of BPSD; **Relationship quality**; Carer competence; **Carer guilt;** Carer-rated patient QoL (EQ-5D); **Burden (The relative stress scale)**; Reactivity to BPSD
9. Häusler (2016)	Germany	82 carers Female %: 60.97 Mean age (SD): 73.02 (6.68)	Spouse: 100	NR	Alzheimer's: 78.05 Vascular: 18.6 Lewy bodies: Others: 30.4 Severity: NR	WHOQOL-BREF	**Perceived Stress**
10. Jackson (2009)	UK	132 carers Female %: 72.0 Mean age (SD): 62 (13.4)	Spouse: 36.00 Offspring (or son or daughter in law) : 44.00 Siblings: 4.00 Other: 16.00	NR	Diagnosis: Alzheimer's Severity: NR	WHOQOL-BREF Physical Psychological Social Environmental	Activities of Daily Living; **Memory and Behaviour Problems (MBPC-1990R)**
11. Kaufman (2010)	United States	141 carers Female %: 85.1 Mean age: 52	Spouse: 9.9 Daughter/son: 58.9 Other: 31.2	NR	Diagnosis: NR Severity: NR	Quality of Life Inventory (QOLI)	**Interpersonal Support tangible component; Interpersonal Support appraisal component; Interpersonal Support belonging component; Interpersonal Support self-esteem component**
12. kim (2016)	South Korea	476 carers Female %: 67.7 Mean age (SD): 57.4 (13.1)	Spouse: 67.7 Daughter/son: 37.9 Other: 42.5	4.3 +/- 4.6	Diagnosis: NR Severity: NR	SF-36 (mental and physical components)	**QoL Mental component & Physical component (SF-36); Depression (BDI); Burden (ZBI) Extraversion;** Agreeableness; Conscientiousness; **Neuroticism**, Openness
13. Kramer (1993)	United States	72 carers Female %: 100.0 Mean age: 70.0	Spouse: 100	4.75	Diagnosis: Alzheimer's Severity: NR	The Quality of Life Index	PwD functional status ADL; PwD functional status instrumental ADL; **PwD Memory and behavior problems (MBPC)**; Caregiver age; Duration of caregiving; **Quality of prior relationship**; **Physical health**; Family income; **Social involvement satisfaction**; Appraisal of the stressfulness of ADL; **Appraisal of the stressfulness of IADL**; **Appraisal of the stressfulness of MBP**
14. Markowitz (2003)	United States	2477 carers Female %: 77.7 Mean age (SD): 58.8 (10.1)	Spouse: 67.7 Daughter/son: 37.9 Other: 42.5	NR	Diagnosis: Alzheimer's Severity: NR	SF-12 (mental and physical components)	**PwD disruptive behaviour (MBPC-R); PwD feelings of depression (MBPC-R); PwD Memory (MBPC-R);** PwD instrumental funtioning; PwD personal funtioning; **No hours per week providing care**; Caregiver's age

*Note:*NR= Not reported; QoL= quality of life; PwD= people with dementia. BPSD= Behavioural and psychological symptoms of dementia; MBPC= Memory and Behaviour Problems Checklist; SF= Short form; BDI= Bender Depression Inventory; ZBI= Zarit Burden Interview; ADL= Activities of daily living; IADL= Instrumental activities of daily living; MBPC-R= Memory and Behaviour Problems Checklist-revised. Variables in bold are those ones that presented statistically significant correlations with carer QoL.

Authors	Country	Sample	Relationship to patient (%)	Average length being carer in years	Care Recipient Characteristics (Diagnosis, severity %)	Carer QoL measures	Variables correlated with QoL
15. McConaghy (2005)	Australia	42 carers Female %: 76.2 Mean age (SD): 62 (13.2)	Spouse: 54.76 Daughter/son: 34.8 Other: 9.5	5.45	Diagnosis: NR Mild: 40.9 Moderate: 18.18 Severe: 40.9	SF-12 v2 Physical component	Coping; Burden (ZBI); Satisfaction with life
16. McLennon (2011)	United States	84 carers Female %: 59.5 Mean age (SD): 73.3 (10.5)	Spouse: 100	4.6	Diagnosis: NR Severity: NR	SF-36 v2 (mental and physical components)	**Income; Duration of caregiving; Burden (ZBI); Finding meaning;** Education;
17. Moreno (2015)	Colombia	102 carers Female %: 81.4 Mean age (SD): 58.4 (13.3)	NR	3.9	Diagnosis: NR Severity: NR	SF-36 Physical functioning, Role-Physical, Vitality, Social functioning, Bodily pain and General Health components	**Satisfaction with life; Depression (PHQ-9); Burden (ZBI)**
18. Nogueira (2015)	Brazil	54 carers Female %: 66.7 Mean age (SD): Males: 72 (13.6); Females:67.6 (8.2)	Spouse: 100	NR	Diagnosis: Alzheimer's Moderate: 62.96 Severe: 37.04	QoL-AD	**PwD QoL (QoL-AD); Burden (ZBI); PWD functional status; PwD awareness of disease**
19. Novelli (2010)	Brazil	60 carers Female %: 73.3 Mean age (SD): Mild dementia: 59.5 (15.4) Moderate: 60.1(14.5)	Spouse: 41.67 Daughter/son: 41.67 Sibilings: 13.33 Other: 3.3	NR	Diagnosis: Alzheimer's Mild: 50.0 Moderate: 50.0	QoL-AD (mild dementia and moderate dementia)	PwD cognitive function; PwD depression/mood; **PwD Insturmental ADL; PwD ADL; PwD behavioral disturbances (NPI); Carer depression/mood (GDS); PwD QoL self-reported; Carer-rated PwD QoL (QoL-AD)**
20. Papastavrou (2014)	Cyprus	76 carers Female %: 75.0 Age%: <50: 18.0; 51-60: 25.0; 61-70: 29.0; >71: 21.0	Spouse: 53.0 Other:47.0	1-2: 33.3 3-4: 28 >5: 38.7	Diagnosis: NR Severity: NR	QoL-AD	**Burden (ZBI); Depression (CES-D);** ADL
21. Perrin (2014)	Colombia	90 carers Female %: 64.4 Mean age (SD): 54.1 (11.5)	Spouse: 17.8 Daughter/son: 22.2 Sibilings: 60.0	3.7	Alzheimer's: 91.11 Vascular: 4.44 Mixed: 2.22 Others: 2.22	SF-36 (Values not available to conduct meta-analysis)	**Satisfaction with life;** Depression (PHQ-9)**; Burden (ZBI)**

*Note:*NR= Not reported; QoL= quality of life; PwD= people with dementia; AD= Alzheimer's Disease. SF= Short form; ZBI= Zarit Burden Interview; PHQ-9= Patient health questionnaire; ADL= Activities of daily living; IADL= Instrumental activities of daily living; CES-D= Center for Epidemiologic Studies Depression Scale. Variables in bold are those ones that presented statistically significant correlations with carer QoL.

Authors	Country	Sample	Relationship to patient (%)	Average length being carer in years	Care Recipient Characteristics (Diagnosis, severity %)	Carer QoL measures	Variables correlated with QoL
22. Santos (2014)	Brazil	88 carers Female %: 76.1 Mean age (SD): 59.22 (13.8)	Spouse: 31.8 Daughter/son: 48.9 Other: 19.3	4.4	Diagnosis: Alzheimer's Mild: 48.9 Moderate: 51.1	QoL-AD	Carer's gender; Carer's age; Carer's schooling; **Burden (ZBI); Mood (BDI); Anxiety;** PwD gender; PwD age; PwD schooling; PwD marital status; **PwD age of onset; PwD duration of disease; PwD self-rated QoL (QoL-AD); PwD carer-rated (QoL-AD); PwD cognition; PwD depression; PwD funtional activities; PwD Neuropsychiatric symptoms (NPI)**
23. Schiffczyk (2013)	Germany	194 carers Female %: 72.2 Mean age (SD): 69 (7.7)	NR	NR	Diagnosis: Alzheimer's (most of them) Severity: NR	QoL-AD	PwD cognitive symptoms; **Non-cognitive symptoms of the PwD (Behave-AD)**
24. Scholzel-Dorenbos (2009)	The Netherlands	87 carers Female %: 47.0 Mean age (SD): 72.2 (7.3)	NR	NR	Diagnosis: Alzheimer's Severity: NR	SEIQoL	**PwD cognitive symptoms; Burden (ZBI)**
25. Shin (2005)	United States	62 carers Female %: NR Mean age (SD):NR	Spouse: 51.6 Daughter/son: 33.9 Other: 14.5	NR	Diagnosis: Alzheimer's Severity: NR	QoL-AD	**PwD Neuropsychiatric symptoms (NPI); Caregiver distress**
26. Takahashi (2005)	Japan	23 carers Female %: 78.27 Mean age (SD): 61.1 (13.0)	Spouse: 78.3 Daughter/son: 60.9 Other: 17.4	3	Alzheimer's: 73.9 Vascular: 4.3 Lewy bodies: 8.7 Frontotemporal: 8.7 Others: 4.4 Mild: 30.4 Moderate: 30.4 Severe: 3.1	WHO-QOL26	**Depression**
27. Takai (2011)	Japan	118 carers Female %: 59.3 Mean age (SD): 60.9 (14.0)	Spouse: 55.1 Daughter/son: 37.3 Other: 7.6	NR	Alzheimer's: 77.9 Vascular: 11.0 Lewy bodies: 2.5 Frontotemporal: 4.2 Mixed: 4.2 Severity: NR	WHO-QOL26	PwD Cognitive function; PwD Cognitive and functional performance; **PwD Neuropsychiatric symptoms (NPI); Burnout; Depression (BDI-II)**

*Note:*NR= Not reported; QoL= quality of life; PwD= people with dementia AD= Alzheimer's Disease;. ZBI= Zarit Burden Interview; BDI= Bender Depression Inventory; NPI= Neuropsychiatric Inventory. Variables in bold are those ones that presented statistically significant correlations with carer QoL.

Authors	Country	Sample	Relationship to patient (%)	Average length being carer in years	Care Recipient Characteristics (Diagnosis, severity %)	Carer QoL measures	Variables correlated with QoL
28. Tay (2016)	Singapore	84 carers Female %: 69.0 Mean age (SD): 50.89 (10.6)	Spouse: 7.1 Daughter/son: 83.3 Other: 9.6	NR	Alzheimer's: 36.9 Vascular: 27.4 Mixed: 35.7 Mild: 59.5 Moderate: 40.5	WHOQoL-BREF	**Family burden (FBIS); Coping strategies Total; General perceived** self-efficacy**; Caregiver's age; Patient's age; Income**
29. Thompson (2004)	United States	61 carers Female %: 73.80 Mean age: Female: 69.7 Male: 71.4	Spouse: 100	5.3	Diagnosis: Alzheimer's Severity: NR	SF-36 (Mental component)	**Natural killer cell number; Male Sense of coherence; Male Depression (CES-D); Male Stress; Female Sense of coherence; Female Depression (CES-D); Female Stress**
30. Valimaki (2009)	Finland	170 carers Female %: 62.9 Mean age (SD): 71.6 (7.2)	Spouse: 100	NR	Diagnosis: Alzheimer's Severity: Only Mild	15D + 15D VAS	**PwD Cognitive function; PwD Neuropsychiatric symptoms (NPI);** PwD Cognitive function; Caregiver's age; PwD age; **HRQoL VAS; Sense of Coherence; Distress; Depression (BDI);** Income**; Total amount of medication;** Years of education
31. Vargas Escobar (2010)	Colombia	192 carers Gender: most of them women Age: 36-59 years old	Daughter/son: most of them	NR, between 10-36 months	Diagnosis: Alzheimer's Mild: 25.5 Moderate: 45.8 Severe: 28.6	QOL (Betty Ferrell)	PwD functional dependency
32. Weisman de Mamani (2017)	United States	106 carers Female %: 81.1 Mean age (SD): 50.73 (12.7)	Spouse: 14.2 Daughter/son: 51.9 Sibilings: 1.9 Other: 32.1	NR	Diagnosis: Alzheimer's Severity: NR	Quality of Life Inventory (QOLI)	**Expressed Emotion (EE) total; EE Emotional Overinvolvement; EE Criticism**
33. Zawadzki (2011)	France	51 carers Female %: 66.67 Mean age (SD) Female: 64.3(10.2) Male: 74.5(14.7)	Spouse: 57.0 Daughter/son: 37.0 Sibilings: 2.0 Other: 10.0	3.5	Diagnosis: Alzheimer's Severity: NR	PIXEL Study	**Authoritarianism; Benevolence; Social restrictiveness; Community mental health ideology; Emotional Reaction Rejection; Emotional Reaction Anxiety; Emotional Reaction Agressiveness;** Emotional Reaction Prosocial Reactions; Perceived overall incompetence; Perceived susceptibility of having AD during one day

*Note:*NR= Not reported; QoL= quality of life; PwD= people with dementia AD= Alzheimer's Disease; FBIS= Family Burden Interview Schedule; CES-D= Center for Epidemiologic Studies Depression Scale; NPI= Neuropsychiatric Inventory; HRQoL VAS= Visual analogue rating scale of health-related quality of life BDI= Bender Depression Inventory;. Variables in bold are those ones that presented statistically significant correlations with carer QoL.

Table 2: Assessment of study quality using the Appraisal of Cross-sectional Studies tool.

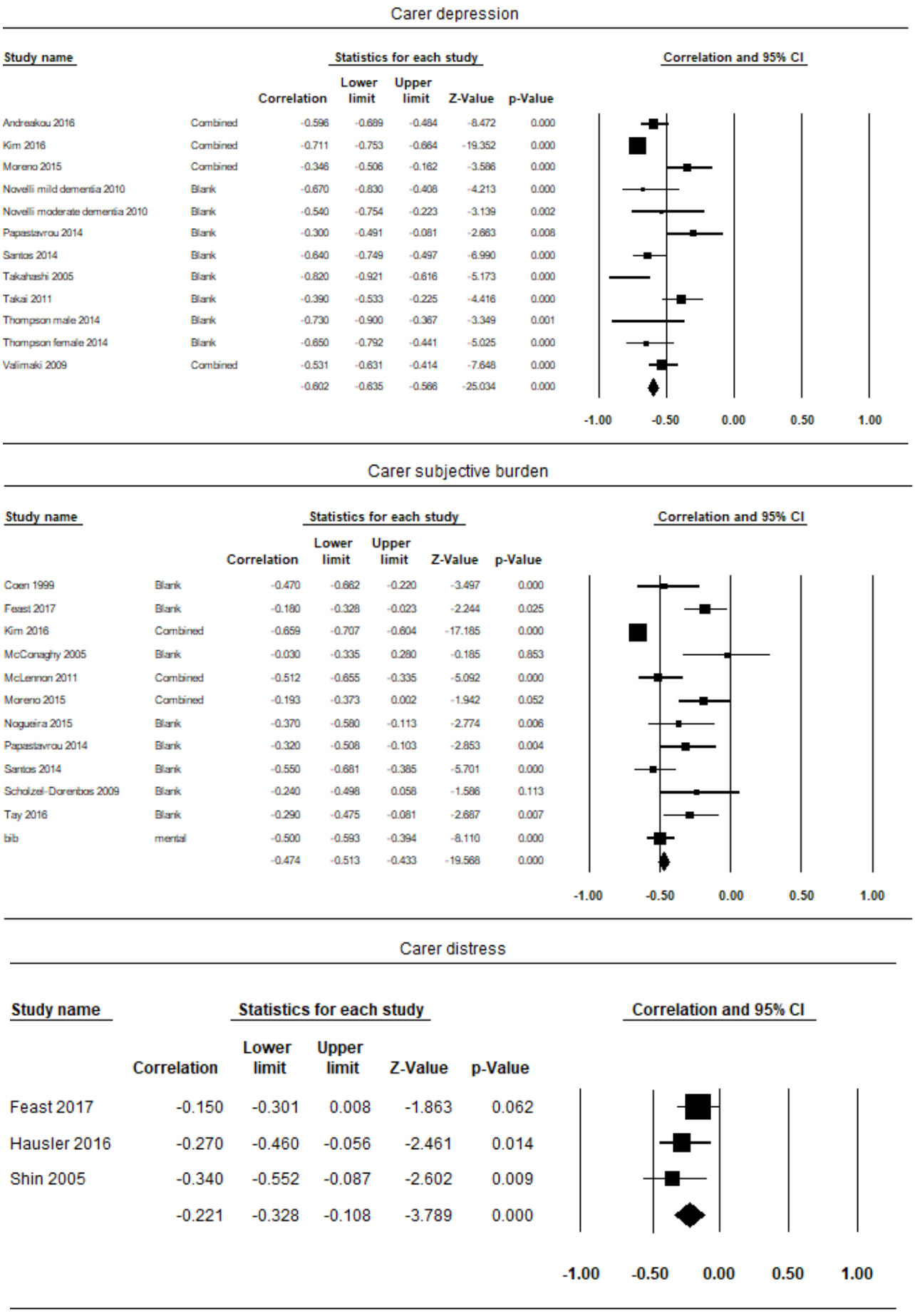
	Study number according to table 1																																
Introduction	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33
Were the aims/objectives of the study clear?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the study design appropriate for the stated aim(s)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the sample size justified?	Y	N	N	N	N	N	Y	N	N	Y	Y	Y	N	N	N	Y	N	N	N	N	Y	N	N	N	N	N	N	Y	N	N	N	N	N
Was the target/reference population clearly defined? (Is it clear who the research was about?)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the sample frame taken from an appropriate population base so that it closely represented the target/ reference population under investigation?	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	N
Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y	N	N	N	Y	Y	N	Y	N	Y	Y	N	Y	Y
Were measures undertaken to address and categorise non-responders?	Y	N	N	Y	Y	N	Y	N	Y	Y	N	N	N	Y	Y	Y	N	N	N	Y	Y	N	Y	Y	N	N	Y	N	N	N	N	N	N
Were the risk factor and outcome variables measured appropriate to the aims of the study?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the risk factor and outcome variables measured correctly using instruments/ measurements that had been trialled, piloted or published previously?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Is it clear what was used to determined statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Note: Y= Yes, (the study clearly demonstrated the information regarding the question); N= No, (no clear information was provided in the study to record the item as yes)

	Study number according to table 1																																
Results	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33
Were the basic data adequately described?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y
Does the response rate raise concerns about non-response bias?	Y	N	N	Y	Y	N	Y	N	Y	N	N	N	N	Y	Y	Y	N	N	N	Y	N	N	Y	Y	N	N	Y	N	N	N	N	N	N
If appropriate, was information about non-responders described?	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Were the results internally consistent?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the results presented for all the analyses described in the methods?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Discussions																																	
Were the authors' discussions and conclusions justified by the results?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the limitations of the study discussed?	Y	N	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	N	Y	Y	N	N	N	Y	Y
Other																																	
Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	Y	N	N	Y	N	Y	Y	Y	Y	Y	N	Y	N	N	N	N	N	Y	Y	Y	Y	N	Y	N	Y	N	Y	Y	N	Y	Y	N	Y
Was ethical approval or consent of participants attained?	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
Total number of items rated as yes	**19**	**14**	**13**	**16**	**16**	**15**	**20**	**15**	**18**	**18**	**15**	**15**	**14**	**14**	**16**	**18**	**14**	**15**	**15**	**18**	**17**	**14**	**15**	**17**	**16**	**12**	**17**	**16**	**14**	**15**	**13**	**15**	**14**

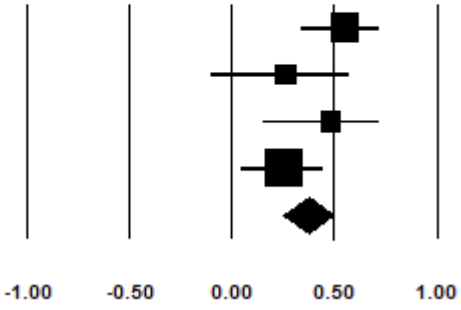
Note: Y= Yes, (the study clearly demonstrated the information regarding the question); N= No, (no clear information was provided in the study to record the item as yes)

Figure 2: Forest plot for independent variables with a significant effect.



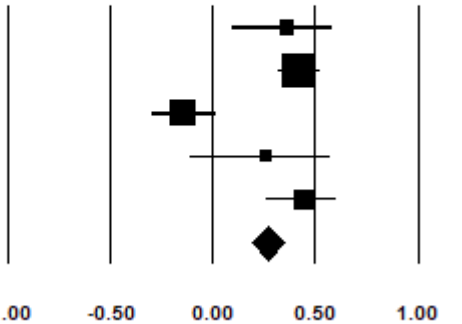
PwD self-rated QoL

Study name		Correlation	Lower limit	Upper limit	Z-Value	p-Value
Nogueira 2015	Blank	0.550	0.331	0.713	4.416	0.000
Novelli 2010	mild	0.260	-0.111	0.567	1.383	0.167
Novelli 2010	moderate	0.480	0.145	0.716	2.718	0.007
Santos 2014	Blank	0.250	0.043	0.437	2.355	0.019
		0.373	0.245	0.489	5.409	0.000



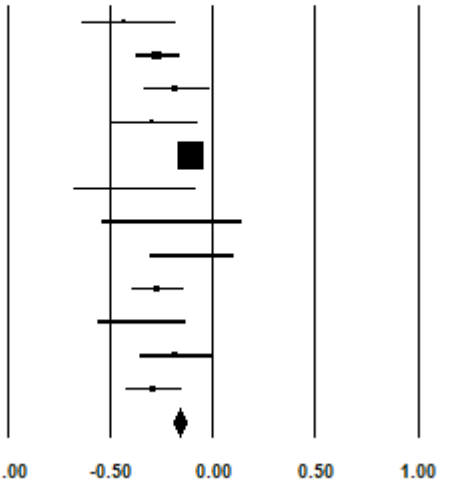
PwD proxy-rated QoL

Study name	Outcome	Correlation	Lower limit	Upper limit	Z-Value	p-Value
Borghi 2011	Blank	0.360	0.091	0.580	2.584	0.010
Conde-Sala 2010	daughters	0.420	0.312	0.517	7.050	0.000
Feast 2017	Blank	-0.150	-0.301	0.008	-1.863	0.062
Novelli 2010	mild	0.260	-0.111	0.567	1.383	0.167
Santos 2014	Blank	0.440	0.254	0.595	4.354	0.000
		0.267	0.189	0.342	6.475	0.000



PwD neuropsychiatric symptoms

Study name		Correlation	Lower limit	Upper limit	Z-Value	p-Value
Coen 1999	Blank	-0.440	-0.640	-0.184	-3.237	0.001
Crellin 2015	Combined	-0.276	-0.379	-0.166	-4.790	0.000
Jackson 2009	Combined	-0.183	-0.343	-0.013	-2.107	0.035
Kramer 1993	Blank	-0.300	-0.497	-0.073	-2.571	0.010
Markowitz 2003	Combined	-0.111	-0.149	-0.072	-5.529	0.000
Novelli 2010 mild	Blank	-0.430	-0.684	-0.083	-2.390	0.017
Novelli 2010 moderate	Blank	-0.230	-0.545	0.142	-1.217	0.224
Santos 2014	Blank	-0.110	-0.312	0.102	-1.018	0.309
Schiffczyk 2013	Blank	-0.275	-0.400	-0.140	-3.901	0.000
Shin 2005	Blank	-0.370	-0.567	-0.132	-2.984	0.003
Takai 2011	Blank	-0.190	-0.358	-0.010	-2.083	0.039
Valimaki 2009	Combined	-0.295	-0.427	-0.152	-3.935	0.000
		-0.162	-0.193	-0.131	-9.919	0.000



Supplementary table 1: PRISMA checklist.

	#	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.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4–6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
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.	8
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.	8
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.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	8
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).	9
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.	9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	9
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.	10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	10-11
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.	10-11

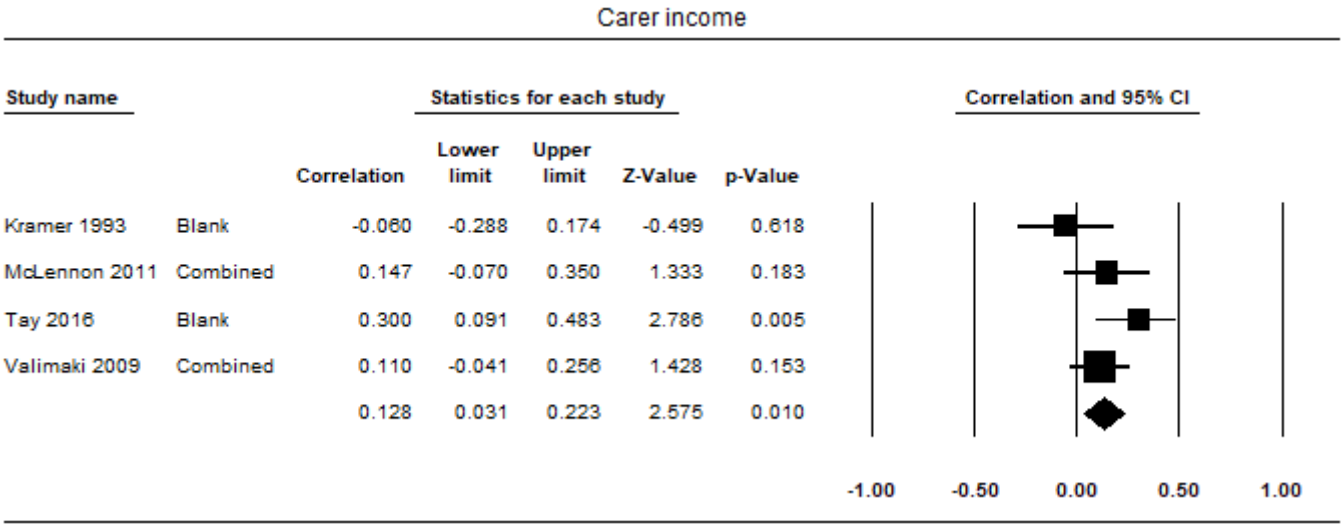
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	11
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	12
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	12
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	13-14
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	14
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	14
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	14-16
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	16-17
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	17-18
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	18-19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	19-21
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	21-22
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	2

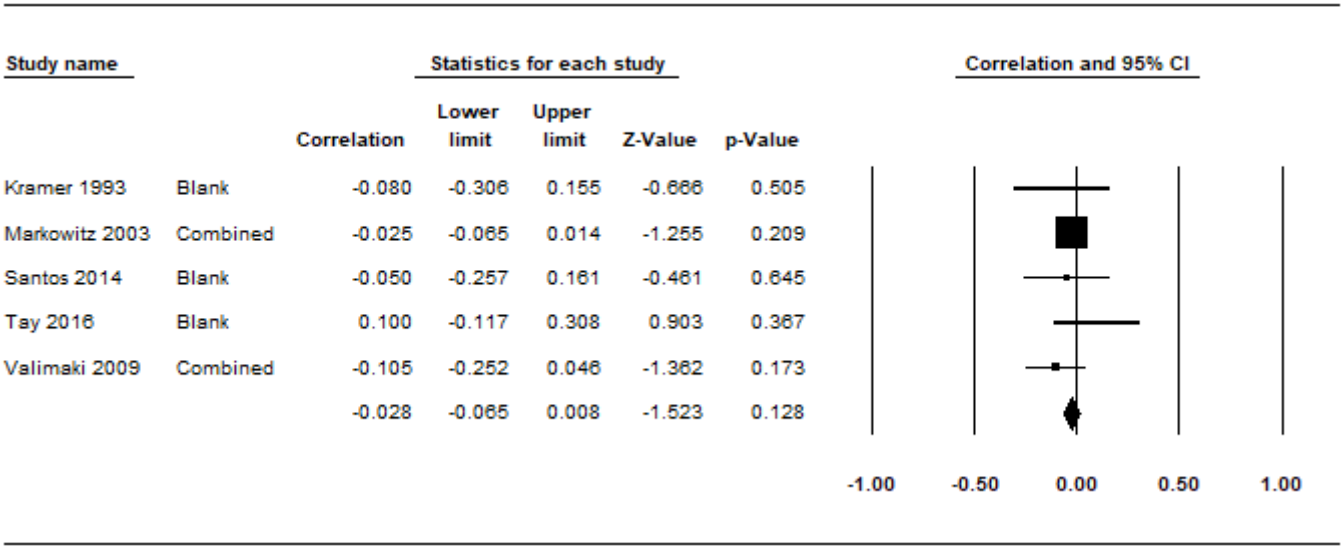
From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

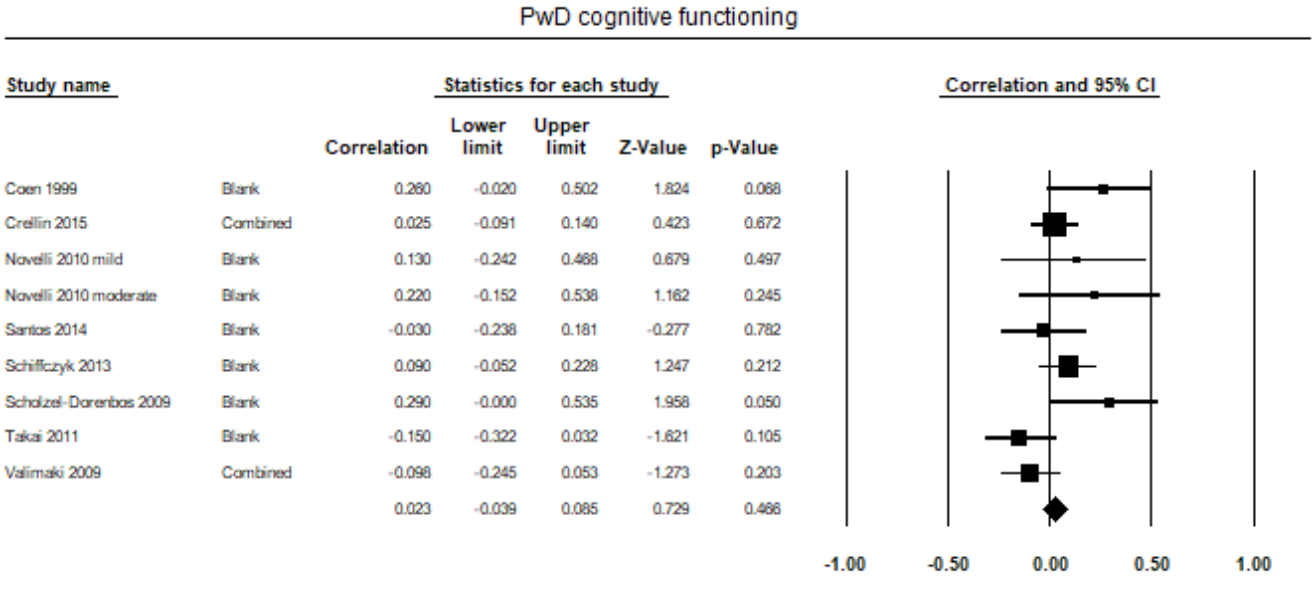
Supplementary table 2: Search strategy.

Search terms		
#1 demen*	#8 "quality of life"	#19 informal*
#2 alzheimer*	#9 QOL	#20 unpaid
#3 (#1 OR #2)	#10 QL	#21 spous*
#4 carer*	#11 HRQOL	#22 espos*
#5 caregiver*	#12 HRQL	#23 famil*
#6 cuidador*	#13 "calidad de vida"	#24 (#19 OR #20 OR #21 OR #22 OR #23)
#7 (#4 OR #5 OR #6)	#14 "qualidade de vida"	#25 (#3 AND #7 AND #18 AND #24)
	#15 wellbeing	
	#16 bienestar	
	#17 "bem-estar"	
	#18 (#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17)	

Supplementary Figure 1: Forest plot for independent variables with non-significant effect.







PwD functionality (ADL)

Study name		Correlation	Lower limit	Upper limit	Z-Value	p-Value
Coen 1999	Blank	-0.190	-0.445	0.093	-1.319	0.187
Crellin 2015	Combined	0.175	0.061	0.285	2.992	0.003
Jackson 2009	Combined	-0.000	-0.171	0.171	-0.000	1.000
Kramer 1993	Combined	-0.025	-0.255	0.208	-0.210	0.834
Markowirtz 2003	Combined	0.015	-0.024	0.054	0.747	0.455
Nogueira 2015	Blank	-0.270	-0.502	-0.002	-1.977	0.048
Novelli 2010 mild	Combined	-0.190	-0.515	0.182	-1.001	0.317
Novelli 2010 moderate	Combined	-0.331	-0.618	0.033	-1.787	0.074
Papastavrou 2014	Blank	0.170	-0.056	0.380	1.477	0.140
Santos 2014	Blank	0.050	-0.161	0.257	0.461	0.645
Vargas Escobar 2010	Blank	0.090	-0.052	0.229	1.241	0.215
		0.024	-0.010	0.057	1.401	0.161