The association between subjective caregiver burden and depressive symptoms in carers of older relatives: A systematic review and meta-analysis

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Abstract

Background

Family carers are an important source of care for older people. Although several studies have reported that subjective caregiver burden is related to depressive symptoms there are no systematic reviews quantifying this association.

Objective

To establish the extent to which subjective caregiver burden is associated with depressive symptoms and whether this association would vary by study or care characteristics.

Methods

We searched major databases such as PubMed, CINAHL, PsycINFO, Scopus and ISI Proceedings up to March 2018, and conducted a meta-analysis of included studies. Summary estimates of the association were obtained using a random-effects model to improve generalisation of findings.

Results

After screening of 4,688 articles, 55 studies were included providing a total of 56 independent comparisons with a total of 9,847 carers from data across 20 countries. There was a large, positive association between subjective caregiver burden and depressive symptoms (\(\hat{r} = 0.514; 95\% \text{ CI} = 0.486, 0.541\)), with very low heterogeneity amongst individual studies (\(I^2 = 8.6\%\)). Sensitivity analyses showed no differences between cross-sectional or repeated measures (\(\hat{r} = 0.521; 95\% \text{ CI} = 0.491, 0.550; 51 \text{ samples}\)) and longitudinal studies (\(\hat{r} = 0.454; 95\% \text{ CI} = 0.398, 0.508; 6 \text{ samples}\)). We found a higher effect size for those caring for people living with dementia compared to those caring for frail older people, and stroke survivors. Carer sex, age and kinship did not change the estimate of the effect.
Conclusions
Subjective caregiver burden is a significant risk factor for depressive symptoms in carers of older people and may precipitate clinical depression. Those caring for people with dementia experience greater burden. There is a need for longitudinal evaluations examining the effects of potential mediators of the association of subjective burden and depressive symptoms. Future interventions should test whether minimizing subjective burden may modify the risk of developing depression in carers of older relatives.

Introduction
Current trends in population aging in many countries mean that as the population of older people increases so does the need for provision of informal care by family members [1]. Increases in age-related morbidity and disability increase old age dependency which is projected to double by 2050 [2]. In fact family carers are the main source of support of older dependents [1]. Although this uncompensated support is an important societal asset, it is associated with substantial health burden for family carers representing a highly vulnerable population [3].

Caregiving is associated with negative consequences for family carers’ physical and mental health [3]. The emotional and psychological consequences of caring are mainly represented by subjective burden, anxiety and depressive symptoms [4–6]. Prevalence studies have shown that depressive symptoms in carers of older relatives is 40.2% for those caring for stroke survivors [5] and up to 34% for carers of people living with Alzheimer’s disease [6].

Theoretical models explaining the negative emotional consequences of caregiving have been largely based on Lazarus and Folkman’s Transactional Stress process model [7]. According to this model, stress consequences are mediated by the way carers’ perceive, evaluate and manage the caregiving process [8]. In this context, subjective caregiver burden is defined as a caregiving state, characterised by a negative reaction to the impact of providing care [9], whereby vulnerability to burden is due to several factors such as carers’ physical health, psychological well-being, finances, social support and relationship with the care-recipient [10]. Objective burden is considered to reflect daily and practical aspects of provision of care capturing quantitative dimensions of the caregiving role such as level of care needs and hours providing care [11].

Several studies have been conducted to explore the possible association of subjective burden and depressive symptoms in carers of older people [12–14]. To date, systematic reviews in the area have included only cross-sectional studies [14], or have provided a narrative [12,13] as opposed to a quantitative synthesis of the literature. In addition, no review has commented on the methodological quality of the evidence, or assessed for effects of publication bias or conducted sensitivity analyses of factors influencing this association. Consequently a meta-analysis that quantifies the effect of the association whilst also reporting on the quality of the evidence is very much needed. In this paper we describe a systematic review and meta-analysis of the published literature to date reporting on the association of subjective caregiver burden and depressive symptoms and comment on the quality of the evidence.

The objectives of the present review were to establish the extent to which subjective caregiver burden is associated with depressive symptoms and whether this association would vary by study design, methodological quality, carer or care recipient characteristics.
Material and methods

Design

We followed published guidelines on methodology of reviews [15], Cochrane Handbook guidelines [16] and reported findings using the PRISMA [17] and MOOSE statements [18].

Search strategy and selection criteria

Electronic databases (PubMed, CINAHL–EBSCO-, PsycINFO–ProQuest-, Scopus–Elsevier- and ISI Proceedings) were searched without time or language limits. We used search terms such as caregivers (MeSH term) or carer(s); burden, strain or role overload and depression (MeSH term), depressive symptom(s), depression or depressive (see S1 Appendix), up until March 2018. We conducted manual searches of relevant scientific journals (nursing, psychological and medical) and searched reference lists of included papers and reviews in the area [4,19,20] from January 1990 to March 2018.

Studies were included if they met the following criteria: (a) reported on an original quantitative investigation about informal carers of older care-recipients (≥ 65 years or more), (b) examined the association between subjective caregiver burden and depressive symptoms and (c) reported a correlation coefficient or another statistical metric that allowed calculation of a correlation coefficient.

To increase the validity of our eligibility criteria, we defined as “informal carers” someone who provided unpaid care (family members, friends, community members or volunteers) and those who cared both at home and in institutions [21]. We considered an “older care-recipient” any person over 65 years of age who scored as dependent in at least one activity of daily living (or instrumental activity of daily living). Depressive symptoms were defined as sad mood, loss of interest or joy in daily activities, fatigue, and excessive feelings of guilt and worthlessness [22,23]. In all studies subjective burden was defined as a caregiving state, reflecting the emotional, psychosocial and physical aspects of the caregiving role [10,11] measured by burden specific scales (i.e. the Zarit Burden Interview, Screen for Caregiver Burden, Caregiver Burden Inventory etc). Studies differed in the way they defined objective burden; this was measured by self-report measures of duration and/or hours of providing care, level of cognitive and/or functional impairment of the care recipient, disease severity or burden related to disease-specific symptoms.

Selection of studies was independently conducted by two reviewers (RdPC and MRC; Kappa: 0.78) and disagreements were resolved by consensus (discussion and agreement among the two reviewers).

Data extraction and synthesis

Two independent reviewers (RdPC and MRC) extracted data on sample characteristics, study design, effect estimates and quality criteria of each study using a standardised data extraction form (kappa: 0.79). Disagreements were resolved by consensus (discussion and agreement among the two reviewers). The effect size measure used to pool data was the correlation coefficient, adjusted by the inverse of the variance using a random effects model. We classified the effect size following Cohen’s criteria [24] as: 0.1–0.29 (small), 0.3–0.49 (moderate) and higher than 0.5 (large). In repeated measured studies with no relation between time points, the first measure was chosen.
Quality assessment

Following the recommendations of Boyle [25] and Viswanathan et al. [26], we used the following criteria for assessing methodological quality of individual studies: (1) sampling: probabilistic sampling, (2) measurement: i) details of the measurement process, ii) content validity and internal consistency of measures in the target or similar population, and iii) absence of information bias; (3) control for confounding factors: at least one measure of objective burden must be controlled for and (4) adequate reporting of statistical analysis. Criteria 2 and 4 were considered mandatory for a study to be included in the meta-analysis.

Regarding control of confounders, objective burden was considered necessary given its association with depression [4]. Objective burden encompasses functional capacity, cognitive impairment and behavioural problems [27]. Because measures of previous dimensions of objective burden are highly intercorrelated [20], we decided to control for at least one of these. We considered as high quality any study that controlled for confounding via allocation between groups (e.g., through stratification or matching) or controlling for confounding variables in the design and/or analysis (e.g. through multivariate analysis) [26]. If statistical adjustment was reported, we considered no confounding bias to be present if variation of the point estimate was less than 10% [28]. Two independent reviewers assessed quality (RdPC and CLP) and any disagreements were resolved by discussion with a third reviewer.

Following the recommendations of Meader et al. [29], based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) [30], imprecision, inconsistency and risk of publication bias were also assessed. Imprecision was evaluated through: a) number of included studies (large: >10 studies, moderate: 5–10 studies and small: <5 studies) and b) median sample size (high: >300 participants, intermediate: 100–300 and low: <100). Inconsistency was measured by heterogeneity of findings in individual studies. Publication bias was assessed by a funnel plot and statistical tests.

Analysis

Following recommendations of Cooper et al. [31], a random effects model was used for the meta-analysis in order to improve generalisation of findings. We further computed the relative risk reduction from the pooled correlation coefficient based on recommendations of Borenstein et al. [32] and Higgins and Green [33].

The Q test was used for quantifying heterogeneity alongside inconsistency (I²) [34]. We used several methods for evaluating publication bias (Guyatt et al. [35] such as a funnel plot, the Begg’s test [36], the Egger’s test [37] and the Trim and Fill method [38]. The Begg’s and Egger’s test evaluate asymmetry of the funnel plot with a p value less than 0.1 indicative of publication bias [31] whereas the Trim and Fill method computes the combined effect considering a possible publication bias [38].

We performed sensitivity analyses to assess the robustness of findings using the leave-one-out method and subgroup analyses. The leave-one-out method consists of performing k-1 meta-analyses removing one study and analysing the remaining k-1 studies each time. We used subgroup analyses and metaregression to analyse the influence of study design, methodological quality of individual studies, care recipient illness and carer characteristics (age [mean], sex [% of woman] and kinship [% of spouses]) on meta-analysis results. Analyses were carried out using Comprehensive Meta-Analysis 3.3 software.

Results

A total of 4,688 records were retrieved from searching databases and six further references were identified by manual search (Fig 1; Flow diagram of the search process). After removing
Fig 1. PRISMA flow diagram of the review process.

https://doi.org/10.1371/journal.pone.0217648.g001
duplicates, 2,859 records were screened, of which 2,603 were excluded as not relevant leaving 256 studies assessed for eligibility. Of these, 71 were excluded as not relevant and 130 not meeting inclusion criteria. We included a total of 55 studies all of which were assessed for quality and included in the meta-analysis [39–93]. All studies met both quality criterion 2 (measures) and 4 (adequate statistical analysis).

Characteristics of the 55 studies meeting inclusion criteria are presented in Table 1; there were 56 independent samples and 56 independent comparisons. Most studies were cross-sectional or repeated measures studies (with cross-sectional correlations) (n = 49); the majority (89%) reported on non-probabilistic samples (n = 47) and half of the studies did not report controlling for confounders (n = 28). The main care recipients were people with dementia (n = 31) and frail older people (n = 14). The included studies came from 20 different countries.

Meta-analysis indicated a large, positive pooled effect (\( \bar{r} = 0.513; 95\% \text{ CI} = 0.484, 0.541; N = 9,847; \) median sample size: 172.8) whereby high levels of subjective caregiver burden were associated with higher levels of depressive symptoms. The pooled effect is equivalent to an absolute risk reduction of 0.14; so if we eliminate or prevent subjective burden, risk of depressive symptoms would decrease by 14 percentage points.

The correlation coefficient was positive in all individual samples except in one (Fig 2). The leave-one-out method yielded variations in the combined estimate under 0.7% (from 0.509 to 0.517). Because of the width of confidence intervals (CIs), the number of studies and the median sample size we can be confident that results are precise. There was very low heterogeneity amongst individual studies (Q = 60.19, degree of freedom [df] = 55, p = 0.29, \( I^2 = 8.6\% \)) and inspection of the funnel plot indicated that publication bias was not present (Fig 3). The Egger’s test (\( p = 0.92 \)) and the Begg’s test (\( p = 0.98 \)) confirmed this. Statistical power for these tests was 83% [94] and the pooled effect calculated by the Trim and Fill method showed no variation (\( \bar{r} = 0.513 \)).

Regarding quality criteria, no differences were found between studies controlling for objective primary stressors (\( \bar{r} = 0.507; 95\% \text{ CI} = 0.467, 0.545; 26 \) samples) and those that did not (\( \bar{r} = 0.519; 95\% \text{ CI} = 0.477, 0.559; 31 \) samples). There was an effect however regarding differences between studies with probabilistic samples (\( \bar{r} = 0.446; 95\% \text{ CI} = 0.411, 0.479; 8 \) samples) and those without (\( \bar{r} = 0.524; 95\% \text{ CI} = 0.492, 0.554; 48 \) samples).

Additional meta-analyses found no effect of type of design with no differences between cross-sectional or repeated measures (\( \bar{r} = 0.520; 95\% \text{ CI} = 0.490, 0.550; 50 \) samples) versus longitudinal studies (\( \bar{r} = 0.454; 95\% \text{ CI} = 0.398, 0.508; 6 \) samples). When examining care recipient illness we found higher effect sizes for those caring for people living with dementia compared to those caring for frail older people and stroke survivors (Table 2).

Our metaregression showed that care recipient illness and type of sampling method accounted for 45% of heterogeneity. Sex (percentage of female; \( p = 0.80 \)), age (mean; \( p = 0.97 \)) and kinship (% of spouses; \( p = 0.30 \)) of carers did not contribute to the regression model.

**Discussion**

To our knowledge, this is the first systematic review and meta-analysis examining the association of subjective caregiver burden and depressive symptoms in informal carers of older people. By including all available evidence to date we found that experiencing subjective caregiver burden was associated with a moderate increased risk of depression. Our meta-analysis is an important contribution to the literature as it is the first to assess the methodological quality of studies and the influence of parameters such as characteristics of care recipients. Our analyses in fact included many studies across 20 countries and a total of 9,847 carers of older relatives. We found that the association between subjective caregiver burden and depressive symptoms
Table 1. Description and quality criteria of the studies included in the meta-analysis.

| Author, year            | N  | Design          | Care recipients          | Probabilistic sampling | Appropriate measures | Control of confounders |
|-------------------------|----|-----------------|--------------------------|------------------------|----------------------|------------------------|
| Adams et al. 2008       | 428| Cross-sectional | Dementia                 | -                      | +                    | +                      |
| Alspaugh et al. 1999    | 188| Longitudinal    | Dementia                 | -                      | +                    | +                      |
| Ar 2017                 | 190| Cross-sectional | Dementia                 | -                      | +                    | +                      |
| Bachner 2016            | 125| Cross-sectional | Cancer                   | -                      | +                    | ?                      |
| Bianchi et al. 2016     | 121| Cross-sectional | Frail older people       | -                      | +                    | +                      |
| Brandão et al. 2017     | 43 | Cross-sectional | Frail older people       | -                      | +                    | ?                      |
| Buyn 2013               | 63 | Repeated measures| Stroke                   | -                      | +                    | +                      |
| Carter et al. 2008      | 219| Cross-sectional | Dementia                 | -                      | +                    | +                      |
| Cheng et al. 2013       | 142| Cross-sectional | Dementia                 | -                      | +                    | -                      |
| Chow & Ho 2012          | 158| Cross-sectional | Frail older people       | -                      | +                    | +                      |
| Clark et al. 2013       | 106| Cross-sectional | Frail older people       | -                      | +                    | +                      |
| Clyburn et al. 2000     | 613| Cross-sectional | Dementia                 | +                      | +                    | -                      |
| Cooper et al. 2008      | 83 | Cross-sectional | Dementia                 | -                      | +                    | +                      |
| Corazza et al. 2014     | 30 | Cross-sectional | Dementia                 | -                      | +                    | ?                      |
| D’Aoust et al. 2014     | 53 | Cross-sectional | Dementia                 | -                      | +                    | ?                      |
| Del-Pino-Casado et al. 2015 | 200 | Cross-sectional | Frail older people       | +                      | +                    | +                      |
| Del-Pino-Casado et al. 2017 | 200 | Cross-sectional | Frail older people       | +                      | +                    | +                      |
| Diehl-Schmid et al. 2013 | 104 | Cross-sectional | Dementia                 | -                      | +                    | -                      |
| Dos Santos et al. 2017  | 36 | Cross-sectional | Mental illness           | +                      | +                    | ?                      |
| Drinka et al. 1987      | 127| Cross-sectional | Frail older people       | -                      | +                    | +                      |
| Edelstein et al. 2017   | 107| Cross-sectional | Frail older people       | -                      | +                    | ?                      |
| Gallagher et al. 2011   | 84 | Cross-sectional | Dementia                 | -                      | +                    | +                      |
| Gonzalez-Abraides et al. 2013 | 33 | Cross-sectional | Dementia                 | -                      | +                    | ?                      |
| Graf et al. 2017        | 72 | Longitudinal    | Stroke                   | -                      | +                    | +                      |
| Grano et al. 2017       | 170| Longitudinal    | Dementia                 | -                      | +                    | ?                      |
| Heo & Koeske 2013       | 642| Cross-sectional | Dementia                 | -                      | +                    | ?                      |
| Hirschman et al. 2004   | 251| Cross-sectional | Dementia                 | -                      | +                    | ?                      |
| Jaracz et al. 2012      | 150| Cross-sectional | Stroke                   | -                      | +                    | +                      |
| Jones et al. 2015       | 76 | Cross-sectional | Cancer                   | -                      | +                    | ?                      |
| Karabekiroğlu et al. 2018 | 69 | Cross-sectional | Cancer                   | -                      | +                    | ?                      |
| Khalaila & Litwin 2011  | 250| Cross-sectional | Frail older people       | +                      | +                    | +                      |
| Kim et al. 2016         | 476| Cross-sectional | Dementia                 | -                      | +                    | ?                      |
| Kowalska et al. 2017    | 58 | Cross-sectional | Dementia                 | -                      | +                    | ?                      |
| Kruthoff et al. 2016    | 183| Longitudinal    | Stroke                   | -                      | +                    | +                      |
| Lai 2009                | 339| Cross-sectional | Frail older people       | +                      | +                    | +                      |
| Lawton et al. 1991      | 285 | Cross-sectional | Dementia                 | -                      | +                    | +                      |
| Li & Lewis 2013         | 65 | Cross-sectional | Dementia                 | -                      | +                    | ?                      |
| Liu et al. 2012         | 180| Cross-sectional | Dementia                 | -                      | +                    | ?                      |
| Liu et al. 2017         | 120| Cross-sectional | Dementia                 | -                      | +                    | +                      |
| Lopez-Martinez et al. 2017 | 132 | Cross-sectional | Frail older people       | +                      | +                    | +                      |
| Luther 2014             | 150| Cross-sectional | Dementia                 | -                      | +                    | +                      |
| Mausbach et al. 2012    | 126| Cross-sectional | Dementia                 | -                      | +                    | -                      |
| McCullag et al. 2005    | 232| Longitudinal    | Stroke                   | -                      | +                    | ?                      |
| Medrano et al. 2014     | 67 | Cross-sectional | Dementia                 | -                      | +                    | ?                      |
| Mohamed et al. 2010     | 421| Cross-sectional | Dementia                 | -                      | +                    | +                      |

(Continued)
represents a large effect. We can be confident that our findings are relatively robust given the low heterogeneity observed. Our conclusions can be further strengthened by the fact that effects were consistent across studies and there was no evidence of publication bias.

We have been able to include recent studies compared to previous meta-analyses [20] and provide an estimate of the effect. Regarding the methodological quality of research conducted to date we found limitations in the design, sampling methods and control of confounders. Given therefore limitations in the current literature, we can conclude that evidence to date is of moderate quality. We also report that type of sampling method influenced our results.

An important concern in systematic reviews of observational studies is controlling for the effect of confounders [26]. In the present study, we applied several strategies for addressing this issue and we found that controlling for levels of subjective burden experienced by carers in individual studies did not influence the pooled estimate. Our findings are consistent with previous reviews [12–14] but additionally expand the evidence by demonstrating that the association of subjective caregiver burden and depressive symptoms is a robust one, based on moderate quality evidence, and generally represents a large effect. An important strength of our review is that studies were consistent in their definition and measurement of subjective caregiver burden as a psychological construct [95].

In previous reviews [12–14], most of the studies employed cross-sectional designs, which prevents conclusions about causality. In the present review, we included six longitudinal studies and have demonstrated no statistical differences between the pooled effect of cross-sectional versus longitudinal studies; our findings therefore provide evidence that subjective caregiver burden is an important risk factor for psychiatric morbidity in carers. Depressive symptoms originate from stress responses and are associated with high levels of psychological distress [4]; however stressors do not cause depressive symptoms directly [19]. They can be conceptualised as the consequences of appraising the caregiving situation as highly stressful whereby high levels of subjective caregiver burden are associated with increased risk of experiencing psychiatric distress [96].

We tested several hypotheses in relation to sources of heterogeneity between studies. Our sensitivity analyses showed that the pooled effect of subjective caregiver burden on depressive symptoms was higher in dementia caregivers compared to those caring for frail older people, or stroke survivors similar to the Pinquart and Sorensen [20] review. Type of care recipient illness therefore was an important source of heterogeneity. Our findings add new evidence that

Table 1. (Continued)

| Author, year       | N   | Design     | Care recipients | Probabilistic sampling | Appropriate measures | Control of confounders |
|--------------------|-----|------------|-----------------|------------------------|----------------------|------------------------|
| Morlett Paredes 2014 | 103 | Cross-sectional | Dementia        | -                      | +                    | ?                      |
| Parker 2007        | 40  | Cross-sectional | Dementia        | -                      | +                    | ?                      |
| Powers 2014        | 83  | Cross-sectional | Frail older people | -                     | +                    | +                      |
| Raveis et al. 1998 | 164 | Cross-sectional | Cancer          | -                      | +                    | ?                      |
| Robison-Surgot & Knight 2005 | 48  | Cross-sectional | Dementia        | -                      | +                    | ?                      |
| Romero Moreno et al. 2011 | 167 | Cross-sectional | Dementia        | -                      | +                    | +                      |
| Sutter et al. 2016 | 127 | Cross-sectional | Dementia        | -                      | +                    | ?                      |
| Vitaliano et al. 1991 | 79  | Longitudinal | Dementia        | -                      | +                    | ?                      |
| Wang et al. 2017   | 621 | Cross-sectional | Frail older people | +                     | +                    | +                      |
| Yates et al. 1999  | 204 | Cross-sectional | Frail older people | -                     | +                    | +                      |

Notes: (+) characteristic is present; (-) characteristic is absent; (?) there is not enough information to assess.

https://doi.org/10.1371/journal.pone.0217648.1001
### Subjective caregiver burden and depressive symptoms in carers of older relatives

| Study name                | Correlation | Lower limit | Upper limit | p-Value |
|---------------------------|-------------|-------------|-------------|---------|
| Adams et al.2008          | 0.520       | 0.447       | 0.596       | 0.000   |
| Alsopauh et al.1999       | 0.450       | 0.328       | 0.557       | 0.000   |
| Ar 2017                   | 0.470       | 0.351       | 0.574       | 0.000   |
| Bachner 2016              | 0.300       | 0.131       | 0.452       | 0.001   |
| Bianchi et al.2016        | 0.460       | 0.307       | 0.550       | 0.000   |
| Brandão et al.2017        | 0.370       | 0.078       | 0.693       | 0.014   |
| Buyyn 2013                | 0.470       | 0.252       | 0.643       | 0.000   |
| Carter et al.2008         | 0.550       | 0.450       | 0.636       | 0.000   |
| Cheng et al.2013          | 0.570       | 0.447       | 0.672       | 0.000   |
| Chow & Ho 2012            | 0.450       | 0.316       | 0.566       | 0.000   |
| Clark et al 2013          | 0.590       | 0.450       | 0.702       | 0.000   |
| Clyburn et al 2000        | 0.460       | 0.247       | 0.586       | 0.000   |
| Cooper et al.2008         | 0.290       | 0.047       | 0.430       | 0.017   |
| Corza et al.2014          | 0.600       | 0.306       | 0.790       | 0.000   |
| D’Anust et al.2014        | 0.720       | 0.558       | 0.829       | 0.000   |
| del-Pino-Casado et al.2015| 0.450       | 0.332       | 0.554       | 0.000   |
| del-Pino-Casado et al.2017| 0.440       | 0.321       | 0.545       | 0.000   |
| Diehl-Schmidt et al.2013  | 0.340       | 0.158       | 0.500       | 0.000   |
| Dos Santos et al.2017     | 0.580       | 0.311       | 0.763       | 0.000   |
| Dirinka et al.1987        | 0.620       | 0.500       | 0.717       | 0.000   |
| Edelstein et al.2017      | 0.450       | 0.284       | 0.589       | 0.000   |
| Gallage et al.2011        | 0.700       | 0.571       | 0.795       | 0.000   |
| González-Abaladas et al.2013| 0.530     | 0.228       | 0.730       | 0.001   |
| Graf et al.2017           | 0.470       | 0.267       | 0.633       | 0.000   |
| Grano et al.2017          | 0.520       | 0.401       | 0.622       | 0.000   |
| Heo & Koekse 2013         | 0.590       | 0.457       | 0.638       | 0.000   |
| Hirschman et al.2004      | 0.640       | 0.511       | 0.708       | 0.000   |
| Jaracz et al.2012         | 0.320       | 0.168       | 0.457       | 0.000   |
| Jones et al.2015          | 0.670       | 0.524       | 0.778       | 0.000   |
| Karabekiroglu et al.2016  | 0.400       | 0.180       | 0.562       | 0.001   |
| Khalil & Liwir 2011       | 0.440       | 0.334       | 0.535       | 0.000   |
| Kim et al.2016            | 0.570       | 0.392       | 0.748       | 0.001   |
| Kowalska et al.2017       | 0.640       | 0.457       | 0.771       | 0.000   |
| Kruthof et al.2016        | 0.340       | 0.205       | 0.462       | 0.000   |
| Lai 2009                  | 0.420       | 0.328       | 0.504       | 0.000   |
| Lawton et al.1991 (1)     | 0.630       | 0.554       | 0.695       | 0.000   |
| Lawton et al.1991 (2)     | 0.630       | 0.548       | 0.700       | 0.000   |
| Li & Lewis 2013           | 0.710       | 0.564       | 0.813       | 0.000   |
| Liu et al.2012            | 0.640       | 0.545       | 0.719       | 0.000   |
| Liu et al.2017            | 0.590       | 0.459       | 0.698       | 0.000   |
| Lopez-Martinez et al.2017 | 0.520       | 0.363       | 0.634       | 0.000   |
| Luther 2014               | 0.700       | 0.508       | 0.773       | 0.000   |
| Mausbach et al.2012       | 0.460       | 0.310       | 0.598       | 0.000   |
| McCullagh et al.2005      | 0.500       | 0.367       | 0.591       | 0.000   |
| Medrano et al.2014        | 0.350       | 0.120       | 0.544       | 0.003   |
| Mohamed et al.2010        | 0.670       | 0.531       | 0.640       | 0.000   |
| Morletti Paredes 2014     | 0.440       | 0.269       | 0.594       | 0.000   |
| Parker 2007               | 0.240       | -0.077      | 0.513       | 0.137   |
| Powers 2014               | 0.650       | 0.505       | 0.795       | 0.000   |
| Ravits et al.1998         | 0.480       | 0.253       | 0.550       | 0.000   |
| Robison-Surgot & Knight 2005| 0.650     | 0.315       | 0.721       | 0.000   |
| Romero Moreno et al.2011  | 0.490       | 0.365       | 0.617       | 0.000   |
| Sutter et al.2016         | 0.450       | 0.299       | 0.579       | 0.000   |
| Vitaliano et al.1991      | 0.420       | 0.219       | 0.587       | 0.000   |
| Wang et al.2017           | 0.390       | 0.321       | 0.455       | 0.000   |
| Yates et al.1999          | 0.440       | 0.322       | 0.444       | 0.000   |

Fig 2. Forest plot for subjective caregiver burden and depressive symptoms.

[https://doi.org/10.1371/journal.pone.0217648.g002](https://doi.org/10.1371/journal.pone.0217648.g002)
dementia may differentially affect caregiver burden and risk of experiencing depressive symptoms for carers [20]. Carer age, sex and relationship to care recipient on the other hand did not explain heterogeneity between studies. Studies that employed non-probabilistic sampling showed a higher pooled effect estimate compared to those using probabilistic sampling; this indicates that non-probabilistic sampling overestimates the effect of subjective caregiver burden on depressive symptoms.

![Funnel Plot of Precision by Fisher's Z](https://doi.org/10.1371/journal.pone.0217648.g003)

**Table 2.** Pooled effect of subjective caregiver burden on depressive symptoms by care recipient illness.

| Care recipient   | k  | \( r \) | 95% CI of \( r \) | P-value | \( I^2 \) | \( r \) corrected by Trim & Fill |
|------------------|----|--------|-------------------|---------|--------|-----------------------------|
| Mental illness   | 1  | 0.580  | 0.311; 0.763      | 0.0001  |        |                             |
| Dementia         | 32 | 0.547  | 0.513; 0.579      | < 0.0001| 24.8%  | 0.547                      |
| Cancer           | 4  | 0.471  | 0.305; 0.609      | < 0.0001| 9.8%   | 0.471                      |
| Frail older people | 14 | 0.470  | 0.427; 0.511      | < 0.0001| 5.2%   | 0.472                      |
| Stroke           | 5  | 0.416  | 0.331; 0.494      | < 0.0001| 0.0%   | 0.416                      |

[https://doi.org/10.1371/journal.pone.0217648.t002](https://doi.org/10.1371/journal.pone.0217648.t002)
Although our study is the first comprehensive meta-analysis in the literature, it has several limitations. Our meta-analysis has not been registered online and it was not possible to control for several confounders such as prior history of depression, influence of individual patient behavioural and psychological symptoms [97] and time-varying characteristics of subjective caregiver burden, which may have influenced our results. Studies used different scales to measure subjective caregiver burden and this may have added to heterogeneity. Further longitudinal epidemiological research is warranted to establish significant mediators of the association of subjective burden and depressive symptoms.

Despite limitations the results of our review have significant clinical implications. We have been able to demonstrate that subjective caregiver burden may signal clinical depression in family carers of frail older people. Screening questions by clinicians will be useful in identifying carers at increased risk of psychological distress. Our findings support the use of interventions aimed at alleviating subjective caregiver burden to prevent depressive symptoms and psychiatric morbidity in this population. Interventions for example that target cognitive reappraisals, teach coping strategies and provide emotional support, are effective in reducing caregiver burden [98] and may protect carers’ mental health via reinforcing protective psychological mechanisms [99]. More research is needed in order to strengthen the evidence and understand which factors associated with caregiver burden may be responsive to change by psychological interventions.

Supporting information
S1 Appendix. Syntax used in each database. (DOCX)
S1 Checklist. PRISMA checklist for systematic reviews. (DOCX)

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References
1. OECD (2017) Health at a Glance 2017: OECD indicators. Paris: OECD Publishing.
2. Vogeli C, Shields AE, Lee TA, Gibson TB, Marder WD, Weiss KB, et al. (2007) Multiple chronic conditions: prevalence, health consequences, and implications for quality, care management, and costs. J Gen Intern Med 22 Suppl 3: 391–395. https://doi.org/10.1007/s11606-007-0322-1 PMID: 18026807
3. Lacey RE, McMunn A, Webb E (2018) Informal caregiving patterns and trajectories of psychological distress in the UK Household Longitudinal Study. Psychol Med: 1–9. https://doi.org/10.1017/s0033291718002222 PMID: 30205848

4. van der Lee J, Bakker TJ, Duivenvoorden HJ, Droes RM (2014) Multivariate models of subjective caregiver burden in dementia; a systematic review. Ageing Res Rev. https://doi.org/10.1016/j.arr.2014.03.008 PMID: 24675045

5. Loh AZ, Tan JS, Zhang MW, Ho RC (2017) The Global Prevalence of Anxiety and Depressive Symptoms Among Caregivers of Stroke Survivors. J Am Med Dir Assoc 18: 111–116. https://doi.org/10.1016/j.jamda.2016.08.014 PMID: 27742585

6. Salim AB, Sayampanathan AA, Cuttilan A, Chun-Man Ho R (2015) Prevalence of Mental Health Disorders Among Caregivers of Patients With Alzheimer Disease. J Alzheimer Dis 16: 1034–1041. https://doi.org/10.1016/j.jamda.2015.09.007 PMID: 26593303

7. Lazarus RS, Folkman S (1984) Stress, appraisal and coping. New York, NY: Springer.

8. Del-Pino-Casado R, Frias-Osuna A, Palomino-Moral PA, Ruzafa-Martinez M, Ramos-Morcillo AJ (2018) Social support and subjective burden in caregivers of adults and older adults: A meta-analysis. PLoS One 13: e0189874. https://doi.org/10.1371/journal.pone.0189874 PMID: 29293522

9. Sherwood PR, Given CW, Given BA, von Eye A (2005) Caregiver burden and depressive symptoms: analysis of common outcomes in caregivers of elderly patients. Journal of Aging and Health 17: 125–147. https://doi.org/10.1177/0898264304274179 PMID: 15750048

10. Zarit SH, Reever KE, Bach-Peterson J (1980) Relatives of the impaired elderly: Correlates of feelings of burden. Gerontologist 20: 649–654. https://doi.org/10.1093/geront/20.6.649 PMID: 7203086

11. Domingues NS, Verreault P, Hudon C (2018) Reducing Burden for Caregivers of Older Adults With Mild Cognitive Impairment: A Systematic Review. Am J Alzheimer Dis Other Dement 33: 401–414. https://doi.org/10.1177/1533317517788151 PMID: 30041535

12. Geng HM, Chiang DM, Yang F, Yang Y, Liu WM, Liu LH, et al. (2018) Prevalence and determinants of depression in caregivers of cancer patients: A systematic review and meta-analysis. Medicine (Baltimore) 97: e11863. https://doi.org/10.1097/md.00000000000011863 PMID: 30278483

13. Watson B, Tatangelo G, McCabe M (2018) Depression and Anxiety Among Partner and Offspring Carers of People With Dementia: A Systematic Review. Gerontologist.

14. Zhu W, Jiang Y (2018) A Meta-analytic Study of Predictors for Informal Caregiver Burden in Patients With Stroke. J Stroke Cerebrovasc Dis 27: 3636–3646. https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.08.037 PMID: 30268368

15. Roe B (2007) Key stages and considerations when undertaking a systematic review: bladder training for the management of urinary incontinence. In: Webb C, Roe B, editors. Reviewing research evidence for nursing practice: systematic reviews. Oxford: Blackwell. pp. 9–22.

16. Higgins JP, Green S (2011) Cochrane handbook for systematic reviews of interventions: John Wiley & Sons.

17. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemiol 62: 1006–1012. https://doi.org/10.1016/j.jclinepi.2009.06.005 PMID: 19631508

18. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 283: 2008–2012. PMID: 10789670

19. Schoenmakers B, Buntinx F, Delepeleire J (2010) Factors determining the impact of care-giving on caregivers of elderly patients with dementia. A systematic literature review. Maturitas 66: 191–200. https://doi.org/10.1016/j.maturitas.2010.02.009 PMID: 20307942

20. Pinquart M, Sorensen S (2003) Associations of stressors and uplifts of caregiving with caregiver burden and depressive mood: a meta-analysis. Journals of Gerontology Series B: Psychological Sciences and Social Sciences 58: P112–128.

21. Del-Pino-Casado R, Frias-Osuna A, Palomino-Moral PA, Pancorbo-Hidalgo PL (2011) Coping and subjective burden in caregivers of older relatives: a quantitative systematic review. Journal of Advanced Nursing 67: 2311–2322. https://doi.org/10.1111/j.1365-2648.2011.05725.x PMID: 21658096

22. Goldberg D, Bridges K, Duncan-Jones P, Grayson D (1988) Detecting anxiety and depression in general medical settings. British Medical Journal 297: 897–899. https://doi.org/10.1136/bmj.297.6653.897 PMID: 3140969

23. American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders. Washington, DC: Author.

24. Cohen J (1992) A power primer. Psychological Bulletin: 155–159. PMID: 19565683
25. Boyle MH (1998) Guidelines for evaluating prevalence studies. Evidence Based Mental Health 1: 37–39.
26. Viswanathan M, Berkman ND, Dryden DM, Hartling L (2013) Assessing risk of bias and confounding in observational studies of interventions or exposures: further development of the RTI Item Bank. Rockville, MD: Agency for Healthcare Research and Quality.
27. Aneshensel CS, Pearlin LI, Mullan JT, Zarit SH, Whitlatch CJ (1995) Profiles in Caregiving. San Diego, CA: Academic Press.
28. Rothman KJ, Greenland S, Lash TL (2008) Modern epidemiology: Lippincott Williams & Wilkins.
29. Meander N, King K, Llewellyn A, Norman G, Brown J, Rodgers M, et al. (2014) A checklist designed to aid consistency and reproducibility of GRADE assessments: development and pilot validation. Syst Rev 3: 82. https://doi.org/10.1186/2046-4053-3-82 PMID: 25056145
30. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. (2004) Grading quality of evidence and strength of recommendations. BMJ 328: 1490–1494. https://doi.org/10.1136/bmj.328.7454.1490 PMID: 15205295
31. Cooper HM, Hedges LV, Valentine JC (2009) The handbook of research synthesis and meta-analysis. New York, NY: Russell Sage Foundation Publications.
32. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR (2009) Converting among effect sizes. Introduction to Meta-Analysis. Chichester, UK: John Wiley & Sons, Ltd. pp. 45–49.
33. Higgins J, Green S (2008) Cochrane handbook for systematic reviews of interventions, version 5.0.1. Chichester: Wiley Online Library.
34. Higgins J, Thompson S, Deeks J, Altman D (2002) Statistical heterogeneity in systematic reviews of clinical trials: a critical appraisal of guidelines and practice. Journal of health services research & policy 7: 51–61.
35. Guyatt GH, Oxman AD, Montori V, Vist G, Kunz R, Brozek J, et al. (2011) GRADE guidelines: 5. Rating the quality of evidence—publication bias. J Clin Epidemiol 64: 1277–1282. https://doi.org/10.1016/j.jclinepi.2011.01.011 PMID: 21802904
36. Begg CB, Mazumdar M (1994) Operating characteristics of a rank correlation test for publication bias. Biometrics 50: 1088–1101. PMID: 7786990
37. Egger M, Davey Smith G, Schneider M, Minder C (1997) Bias in meta-analysis detected by a simple, graphical test. British Medical Journal 315: 629–634. https://doi.org/10.1136/bmj.315.7109.629 PMID: 9310563
38. Duval S, Tweedie R (2000) Trim and Fill: A Simple Funnel Plot-Based Method of Testing and Adjusting for Publication Bias in Meta-Analysis. Biometrics 56: 455–463. PMID: 10877304
39. Adams KB, McIclenond MJ, Smyth KA (2008) Personal losses and relationship quality in dementia caregiving. Dementia 7: 301–319.
40. Alsophaugh ME, Stephens MA, Townsend AL, Zarit SH, Greene R (1999) Longitudinal patterns of risk for depression in dementia caregivers: objective and subjective primary stress as predictors. Psychol Aging 14: 34–43. PMID: 10224630
41. Ar Y (2017) Predictors of depression, anxiety, grief and growth among Turkish offspring as caregivers of parents with Alzheimer’s disease: a multi-method study [Doctoral dissertation]. Ankara: Middle East Technical University.
42. Bachner YG (2016) Psychometric Properties of Responses to an Arabic Version of the Hamilton Depression Rating Scale (HAM-D6). Journal of the American Psychiatric Nurses Association 22: 27–30. https://doi.org/10.1177/1078390316629959 PMID: 26929229
43. Bianchi M, Flesch LD, Alves EV, Batistoni SS, Neri AL (2016) Zarit Burden Interview Psychometric Indicators Applied in Older People Caregivers of Other Elderly. Rev Lat Am Enfermagem 24: e2835. https://doi.org/10.1590/1518-8345.1379.2835 PMID: 27901220
44. Brandão D, Ribeiro O, Oliveira M, Paul C (2017) Caring for a centenarian parent: an exploratory study on role strains and psychological distress. Scandinavian Journal of Caring Sciences 31: 984–994. https://doi.org/10.1111/scs.12423 PMID: 28475220
45. Byun E (2013) Effects of uncertainty on perceived and physiological stress and psychological outcomes in stroke-survivor caregivers [Doctoral dissertation]. Philadelphia, Pennsylvania: University of Pennsylvania.
46. Carter JH, Steward BJ, Lyons KS, Archbold PG (2008) Do motor and nonmotor symptoms in PD patients predict caregiver strain and depression? Movement Disorders 23: 1211–1216. https://doi.org/10.1002/mds.21686 PMID: 18528898
47. Cheng S-T, Lam LCW, Kwok T (2013) Neuropsychiatric Symptom Clusters of Alzheimer Disease in Hong Kong Chinese: Correlates with Caregiver Burden and Depression. American Journal of Geriatric Psychiatry 21: 1029–1037. https://doi.org/10.1016/j.jagp.2013.01.041 PMID: 23567373
48. Chow EO, Ho HC (2012) The relationship between psychological resources, social resources, and depression: results from older spousal caregivers in Hong Kong. Aging Ment Health 16: 1016–1027. https://doi.org/10.1080/13607863.2012.692769 PMID: 22690796

49. Clark MC, Nicholas JM, Wassira LN, Gutierrez AP (2013) Psychosocial and biological indicators of depression in the caregiving population. Biol Res Nurs 15: 112–121. https://doi.org/10.1177/1099800411414872 PMID: 21765116

50. Cyburn LD, Stones MJ, Hadjistavropoulos T, Tuokko H (2000) Predicting caregiver burden and depression in Alzheimer’s disease. Journals of Gerontology Series B, Psychological Sciences and Social Sciences 55: S2–13.

51. Cooper C, Owens C, Katona C, Livingstone G (2008) Attachment style and anxiety in carers of people with Alzheimer’s disease: results from the LASER-AD study. Int Psychogeriatr 20: 494–507. doi: 10.1017/S104161020800015X PMID: 18053290

52. Corazza DI, Pedrosa RV, Andreatto CA, Scarpari L, Garufi M, Costa JL, et al. (2014) [Psychoneuroimmunological predictors for burden in older caregivers of patients with Alzheimer’s disease]. Revista espanola de geriatria y gerontologia 49: 173–178. https://doi.org/10.1016/j.regg.2014.03.007 PMID: 24837199

53. D’Aoust RF, Brewster G, Rowe MA (2015) Depression in informal caregivers of persons with dementia. International Journal of Older People Nursing 10: 14–26. https://doi.org/10.1111/opn.12043 PMID: 24433320

54. Del-Pino-Casado R, Palomino-Moral PA, Frias-Osuna A (2015) The Association of Satisfaction and Perceived Burden With Anxiety and Depression in Primary Caregivers of Dependent Elderly Relatives. Research in Nursing and Health 38: 384–391. https://doi.org/10.1002/nur.21671 PMID: 26132463

55. Del-Pino-Casado R, Palomino-Moral PA, Pastor-Bravo MDM, Frias-Osuna A (2017) Determinants of depression in primary caregivers of disabled older relatives: a path analysis. BMC Geriatr 17: 274. https://doi.org/10.1186/s12877-017-0667-1 PMID: 29169326

56. Diehl-Schmid J, Schmidt EM, Nunnemann S, Riedl L, Kurz A, Forstl H, et al. (2013) Caregiver burden and needs in frontotemporal dementia. J Geriatr Psychiatry Neurol 26: 221–229. https://doi.org/10.1177/0891988713498467 PMID: 23904354

57. Dos Santos GD, Forlenza OV, Ladeira RB, Aprahamian I, Almeida JG, Lafer B, et al. (2017) Caregiver burden in older adults with bipolar disorder: relationship to functionality and neuropsychiatric symptoms. Psychogeriatrics: the official journal of the Japanese Psychogeriatric Society 17: 317–323. https://doi.org/10.1111/ijnp.12521

58. Drinka T J, Smith JC, Drinka PJ (1987) Correlates of depression and burden for informal caregivers of patients in a geriatrics referral clinic. J Am Geriatr Soc 35: 522–525. PMID: 3553288

59. Edelestein OE, Band-Winterstein T, Bachner YG (2018) Profile and burden of care among caregivers of Ultra-Orthodox Frail Elders. Aging Ment Health 22: 639–645. https://doi.org/10.1080/13607863.2017.1289363 PMID: 28282731

60. Gallagher D, Ni Mhaolain A, Crosby L, Ryan D, Lacey L, Coen RF, et al. (2011) Self-efficacy for managing dementia may protect against burden and depression in Alzheimer’s caregivers. Aging Ment Health 15: 663–670. https://doi.org/10.1080/13607863.2011.562179 PMID: 21547745

61. González-Abraldes I, Milián-Calelín JC, Lorenzo-López L, Maseda A (2013) The influence of neuroticism and extraversion on the perceived burden of dementia caregivers: An exploratory study. Archives of gerontology and geriatrics 56: 91–95. https://doi.org/10.1016/j.archger.2012.07.011 PMID: 22906469

62. Graf R, LeLaurin J, Schmitzberger M, Freytes IM, Orozco T, Dang S, et al. (2017) The stroke caregiving trajectory in relation to caregiver depressive symptoms, burden, and intervention outcomes. Top Stroke Rehabil 24: 486–495. https://doi.org/10.1080/10749357.2017.1338371 PMID: 28618848

63. Grano C, Lucidi F, Violani C (2017) The relationship between caregiver self-efficacy and depressive symptoms in family caregivers of patients with Alzheimer disease: a longitudinal study. Int Psychogeriatr 29: 1095–1103. https://doi.org/10.1017/S1041610217000059 PMID: 28162131

64. Heo GJ, Koess G (2013) The role of religious coping and race in Alzheimer’s disease caregiving. Journal of Applied Gerontology 32: 582–604. https://doi.org/10.1177/0733464811433484 PMID: 25474763

65. Hirschman KB, Shea JA, Xie SX, Karlawish JH (2004) The development of a rapid screen for caregiver burden. J Am Geriatr Soc 52: 1724–1729. https://doi.org/10.1111/j.1532-5415.2004.52468.x [doi] JGSS52468 [pii] PMID: 15450052

66. Jaracz K, Grabowska-Fudala B, Kozubiak W (2012) Caregiver burden after stroke: towards a structural model. Neurol Neurochir Pol 46: 224–232. https://doi.org/10.5114/ninp.2012.29130 PMID: 22773508

67. Jones SB, Whitford HS, Bond MJ (2015) Burden on informal caregivers of elderly cancer survivors: risk versus resilience. J Psychosoc Oncol 33: 178–198. https://doi.org/10.1080/07347332.2014.1002657 PMID: 25658457
Subjective caregiver burden and depressive symptoms in carers of older relatives

68. Karabekiroglu A, Demir EY, Aker S, Kocamanoglu B, Karabulut GS (2018) Predictors of depression and anxiety among caregivers of hospitalised advanced cancer patients. Singapore Med J 59: 572–577. https://doi.org/10.11622/smedj.2018066 PMID: 29876580

69. Khalaila R, Litwin H (2011) Does filial piety decrease depression among family caregivers? Aging Ment Health 15: 679–686. https://doi.org/10.1080/13607863.2011.569479 PMID: 21562983

70. Kim SK, Park M, Lee Y, Choi SH, Moon SY, Seo SW, et al. (2017) Influence of personality on depression, burden, and health-related quality of life in family caregivers of persons with dementia. International Psychogeriatrics 29: 227–237. https://doi.org/10.1017/S1041610216001770 PMID: 27780493

71. Kowalska J, Goraczko A, Jaworska L, Szczepanska-Gierach J (2017) An Assessment of the Burden on Polish Caregivers of Patients With Dementia: A Preliminary Study. Am J Alzheimers Dis Other Demen 32: 509–515. https://doi.org/10.1177/1533317517734350 PMID: 28990393

72. Kruithof WJ, Post MWM, van Mierlo ML, van den Bos GAM, de Man-van Ginkel JM, Visser-Meyl JMA (2018) Symptoms of depression in caregivers of dementia patients: A qualitative study. Dementia & Neuropsychologia 32: 509–515. https://doi.org/10.1177/1533317517734350 PMID: 28990393

73. Liu H-Y, Yang C-T, Wang Y-N, Hsu W-C, Huang T-H, Lin Y-E, et al. (2017) Balancing competing needs and resources in family caregivers of persons with dementia: A cross-sectional study. Journal of Advanced Nursing 73: 2962–2972. https://doi.org/10.1111/jan.13379 PMID: 28816364

74. Lawton MP, Moss M, Kleban MH, Glicksman A, Rovine M (1991) A two-factor model of caregiving appraisal and psychological well-being. J Gerontol 46: P181–189. PMID: 2071844

75. Li CY, Lewis FM (2013) Expressed emotion and depression in caregivers of older adults with dementia: results from Taiwan. Aging & mental health 17: 924–929. https://doi.org/10.1080/13607863.2013.814098 PMID: 23826863

76. Liu J, Wang LN, Tan JP, Ji P, Gauthier S, Zhang YL, et al. (2012) Burden, anxiety and depression in caregivers of veterans with dementia in Beijing. Arch Gerontol Geriatr 55: 560–563. https://doi.org/10.1016/j.archger.2012.05.014 PMID: 22749403

77. Lai DW (2009) From burden to depressive symptoms: the case of Chinese-Canadian family caregivers for the elderly. Soc Work Health Care 48: 432–449. https://doi.org/10.1080/00981380802591759 PMID: 19396711

78. López-Martínez C, Frías-Osuna A, Del-Pino-Casado R (2019) Sentido de coherencia y sobrecarga subjetiva, ansiedad y depresión en personas cuidadoras de familiares mayores [Sense of coherence and subjective overload, anxiety and depression in caregivers of elderly relatives]. Gac Sanit 33: 185–190. https://doi.org/10.1016/j.gaceta.2017.09.005 PMID: 29174275

79. Luther K (2014) The Association of Attachment Style and Perceptions of Caregiver Experience [doctoral dissertation]. Orlando, FL: University of Central Florida.

80. Mausbach BT, Roepke SK, Chattillion EA, Harmell AL, Moore R, Romero-Moreno R, et al. (2012) Multiple mediators of the relations between caregiving stress and depressive symptoms. Aging & Mental Health 16: 27–38. https://doi.org/10.1080/13607863.2011.615738 PMID: 22224706

81. McCullagh E, Brigitstocke G, Donaldson N, Kalra L (2005) Determinants of caregiver burden and quality of life in caregivers of stroke patients. Stroke 36: 2181–2186. https://doi.org/10.1161/01.STR.0000181755.23914.53 PMID: 16151029

82. Medrano M, Rosario RL, Payano AN, Capellán NR (2014) Burden, anxiety and depression in caregivers of Alzheimer patients in the Dominican Republic. Dementia & Neuropsychologia 8: 384–388. https://doi.org/10.1590/s1980-57642014dn840000013 PMID: 29213930

83. Mohamed S, Rosenheack R, Lyketsos CG, Schneider LS (2010) Caregiver burden in Alzheimer disease: cross-sectional and longitudinal patient correlates. Am J Geriatr Psychiatry 18: 917–927. https://doi.org/10.1097/JGP.0b013e3181d5745d PMID: 20808108

84. Morlett Paredes A (2014) The influence of dementia caregiver mental health on quality of care in argentina [Master’s thesis]. Richmond, Virginia: Virginia Commonwealth University.

85. Parker LD (2007) A study about older African American spousal caregivers of persons with Alzheimer’s disease [doctoral dissertation]: Georgia State University. 94 p-94 p p.

86. Powers SM (2014) The Influence of Cultural Values on the Informal Caregiving Experience of Dependent Older Adults [doctoral dissertation]. Akron, OH: The University of Akron.

87. Raveis VH, Karus DG, Siegel K (1998) Correlates of depressive symptomatology among adult daughter caregivers of a parent with cancer. Cancer 83: 1652–1663. https://doi.org/10.1002/(SICI)1097-0142(19981015)83:8<1652::AID-CNCR22>3.0.CO;2-Q [pii] PMID: 9781961
88. Robinson Shurgot GS, Knight BG (2005) Preliminary study investigating acculturation, cultural values, and psychological distress in Latino caregivers of dementia patients. Hispanic Health Care International 3: 37–44.

89. Romero-Morenro R, Losada A, Mausbach BT, Marquez-Gonzalez M, Patterson TL, Lopez J (2011) Analysis of the moderating effect of self-efficacy domains in different points of the dementia caregiving process. Aging and mental health 15: 221–231. https://doi.org/10.1080/13607863.2010.505231 PMID: 20924819

90. Sutter M, Perrin PB, Peralta SV, Stolfi ME, Morelli E, Pena Obeso LA, et al. (2016) Beyond Strain: Personal Strengths and Mental Health of Mexican and Argentinean Dementia Caregivers. Journal of Transcultural Nursing 27: 376–384. https://doi.org/10.1177/1043659615573081 PMID: 25712148

91. Vitaliano PP, Russo J, Young HM, Teri L, Maiuro RD (1991) Predictors of burden in spouse caregivers of individuals with Alzheimer’s disease. Psychology and Aging 6: 392–402. PMID: 1930756

92. Wang WT, He B, Wang YH, Wang MY, Chen XF, Wu FC, et al. (2017) The relationships among Muslim Uyghur and Kazakh disabled elders’ life satisfaction, activity of daily living, and informal family caregiver’s burden, depression, and life satisfaction in far western China: A structural equation model. Int J Nurs Pract 23. doi:10.1111/ijn.12521

93. Yates ME, Tennstedt S, Chang BH (1999) Contributors to and mediators of psychological well-being for informal caregivers. Journals of gerontology Series B, Psychological sciences and social sciences 54: P12–22.

94. Hedges LV, Pigott TD (2001) The power of statistical tests in meta-analysis. Psychological methods 6: 203. PMID: 11570228

95. Feast A, Moniz-Cook E, Stoner C, Charlesworth G, Orrell M (2016) A systematic review of the relationship between behavioral and psychological symptoms (BPSD) and caregiver well-being. Int Psychogeriatr 28: 1761–1774. https://doi.org/10.1017/S1041610216000922 PMID: 27345942

96. Roche DL, Croft K, MacCann C, Cramer B, Diehl-Schmidt J (2015) The Role of Coping Strategies in Psychological Outcomes for Frontotemporal Dementia Caregivers. J Geriatr Psychiatry Neurol 28: 218–228. https://doi.org/10.1177/0891988715558830 PMID: 26072312

97. Ornstein K, Gaugler JE (2012) The problem with “problem behaviors”: a systematic review of the association between individual patient behavioral and psychological symptoms and caregiver depression and burden within the dementia patient-caregiver dyad. Int Psychogeriatr 24: 1536–1552. doi: S1041610212000737 [pii] https://doi.org/10.1017/S1041610212000737 PMID: 22812881

98. Williams F, Moghaddam N, Ramsden S, De Boos D (2018) Interventions for reducing levels of burden amongst informal carers of persons with dementia in the community: A systematic review and meta-analysis of randomised controlled trials. Aging Ment Health. 2018/11/20 ed. pp. 1–14.

99. del-Pino-Casado R, Espinosa-Medina A, López-Martínez C, Orgeta V (2019) Sense of coherence, burden and mental health in caregiving: A systematic review and meta-analysis. Journal of Affective Disorders 242: 14–21. https://doi.org/10.1016/j.jad.2018.08.002 PMID: 30170234