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

Rafael del-Pino-Casado[1*], Marta Rodríguez Cardosa[1], Catalina López-Martínez[1], Vasiliki Orgeta[2]

[1] Department of Nursing, School of Health Sciences, University of Jaén, Jaén, Spain.

[2] Division of Psychiatry, Faculty of Brain Sciences, University College London, UK.

* Corresponding author

rdelpino@ujaen.es (RdPC)

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 ($\bar{r}$ = 0.514; 95% 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 ($\bar{r}$ = 0.521; 95% CI = 0.491, 0.550; 51 samples) and longitudinal studies ($\bar{r}$ = 0.454; 95% CI = 0.398, 0.508; 6 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.

Keywords: family carers; subjective caregiver burden; depressive symptoms.

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 (I^2) [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 0.10 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 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).

Figure 1. PRISMA flow diagram of the review process.

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.

Table 1. Description and quality criteria of the studies included in the meta-analysis.

Author, year	N	Design	Care recipients	Sampling	Measures	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'Aoutst 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	-	+	?
Gallager et al. 2011	84	Cross-sectional	Dementia	-	+	+
González-Abraldes 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	-	+	?
Jarazc 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	-	+	?
Kruithof et al 2016	183	Longitudinal	Stroke	-	+	+
Lai 2009	339	Cross-sectional	Frail older people	+	+	+

Table 1. Description and quality criteria of the studies included in the meta-analysis (continues).

Author, year	N	Design	Care recipients	Sampling	Measures	Confounders
Lawton et al. 1991	285 (1)	Cross-sectional	Dementia	-	+	+
	244 (2)	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-Martínez 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	-	+	+
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	-	+	+

Meta-analysis indicated a large, positive pooled effect ($\bar{r}$ = 0.513; 95% 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).

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

Figure 3. Funnel plot for subjective caregiver burden and depressive symptoms.

Regarding quality criteria, no differences were found between studies controlling for objective primary stressors ($\bar{r}$ = 0.507; 95% CI = 0.467, 0.545; 26 samples) and those that did not ($\bar{r}$ = 0.519; 95% CI = 0.477, 0.559; 31 samples). There was an effect however regarding differences between studies with probabilistic samples ($\bar{r}$ = 0.446; 95% CI = 0.411, 0.479; 8 samples) and those without ($\bar{r}$ = 0.524; 95% 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% CI = 0.490, 0.550; 50 samples) versus longitudinal studies ($\bar{r}$ = 0.454; 95% 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).

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

Care recipient	**k**	$\bar{r}$	**95% CI of** $\bar{r}$	**P-value**	I^2	$\bar{r}$ **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

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 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 (Viswanathan et al., 2013). In the present study, we applied several strategies for addressing this issue and we found that controlling for levels of objective burden experienced by carers in individual studies did not influence the pooled estimate. Our findings are consistent with previous reviews[2, 10] 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[2, 10], 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 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.

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.

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. doi: 10.1007/s11606-007-0322-1

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. doi: 10.1017/s0033291718002222

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. doi: 10.1016/j.arr.2014.03.003

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. doi: 10.1016/j.jamda.2016.08.014

6. Sallim AB, Sayampanathan AA, Cuttilan A, Chun-Man Ho R (2015) Prevalence of Mental Health Disorders Among Caregivers of Patients With Alzheimer Disease. J Am Med Dir Assoc 16: 1034-1041. doi: 10.1016/j.jamda.2015.09.007

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. doi: 10.1371/journal.pone.0189874

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.

10. Zarit SH, Reever KE, Bach-Peterson J (1980) Relatives of the impaired elderly: Correlates of feelings of burden. Gerontologist 20: 649-654.

11. Domingues NS, Verreault P, Hudon C (2018) Reducing Burden for Caregivers of Older Adults With Mild Cognitive Impairment: A Systematic Review. Am J Alzheimers Dis Other Demen 33: 401-414. doi: 10.1177/1533317518788151

12. Geng HM, Chuang 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. doi: 10.1097/md.0000000000011863

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. doi: 10.1016/j.jstrokecerebrovasdis.2018.08.037

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. doi: 10.1016/j.jclinepi.2009.06.006

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.

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. doi: 10.1016/j.maturitas.2010.02.009

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. doi: 10.1111/j.1365-2648.2011.05725.x

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.

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.

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 Rsearch 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. Meader 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. doi: 10.1186/2046-4053-3-82

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. doi: 10.1136/bmj.328.7454.1490

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. doi: 10.1016/j.jclinepi.2011.01.011

36. Begg CB, Mazumdar M (1994) Operating characteristics of a rank correlation test for publication bias. Biometrics 50: 1088-1101.

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.

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.

39. Adams KB, McClendon MJ, Smyth KA (2008) Personal losses and relationship quality in dementia caregiving. Dementia 7: 301-319.

40. Alspaugh 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.

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. doi: 10.1177/1078390316629959

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. doi: 10.1016/j.jamda.2016.10.009

10.1590/1518-8345.1379.2835

44. Brandão D, Ribeiro O, Oliveira M, Paúl C (2017) Caring for a centenarian parent: an exploratory study on role strains and psychological distress. Scandinavian Journal of Caring Sciences 31: 984-994. doi: 10.1111/scs.12423

45. Byun E (2013) Effects of uncertainty on perceived and physiological stress and psychological outcomes in stroke-survivor caregivers [Doctoral dissertation]. Philadelphia, Pensylvania: University of Pennsylvania.

46. Carter JH, Stewart BJ, Lyons KS, Archbold PG (2008) Do motor and nonmotor symptoms in PD patients predict caregiver strain and depression? Movement Disorders 23: 1211-1216.

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. doi: 10.1016/j.jagp.2013.01.041

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. doi: 10.1080/13607863.2012.692769 [doi]

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. doi: 10.1177/1099800411414872

50. Clyburn 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, Livingston 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: S104161020700645X [pii]

10.1017/S104161020700645X [doi]

52. Corazza DI, Pedroso RV, Andreatto CA, Scarpari L, Garuffi 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. doi: 10.1016/j.regg.2014.03.007

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. doi: 10.1111/opn.12043

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. doi: 10.1002/nur.21671 [doi]

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. doi: 10.1186/s12877-017-0667-1

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. doi: 10.1177/0891988713498467

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. doi: 10.1111/ijn.12521

10.1111/psyg.12241

58. Drinka TJ, 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.

59. Edelstein 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. doi: 10.1080/13607863.2017.1289363

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. doi: 10.1080/13607863.2011.562179

61. González-Abraldes I, Millán-Calenti 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.

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: 488-495. doi: 10.1080/10749357.2017.1338371

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

64. Heo GJ, Koeske G (2013) The role of religious coping and race in Alzheimer's disease caregiving. Journal of Applied Gerontology 32: 582-604. doi: 10.1177/0733464811433484

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. doi: 10.1111/j.1532-5415.2004.52468.x [doi]

JGS52468 [pii]

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

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. doi: 10.1080/07347332.2014.1002657

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. doi: 10.11622/smedj.2018066

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

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. doi: 10.1017/s1041610216001770

71. Kowalska J, Goraczko A, Jaworska L, Szczepanska-Gieracha 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. doi: 10.1177/1533317517734350

72. Kruithof WJ, Post MWM, van Mierlo ML, van den Bos GAM, de Man-van Ginkel JM, Visser-Meily JMA (2016) Caregiver burden and emotional problems in partners of stroke patients at two months and one year post-stroke: Determinants and prediction. Patient Education & Counseling 99: 1632-1640. doi: 10.1016/j.pec.2016.04.007

73. 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. doi: 10.1080/00981380802591759

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.

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. doi: 10.1080/13607863.2013.814098

76. Liu H-Y, Yang C-T, Wang Y-N, Hsu W-C, Huang T-H, Lin Y-E, et al. (2017) Balancing competing needs mediates the association of caregiving demand with caregiver role strain and depressive symptoms of dementia caregivers: A cross-sectional study. Journal of Advanced Nursing 73: 2962-2972. doi: 10.1111/jan.13379

77. 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. doi: 10.1016/j.archger.2012.05.014

78. López-Martínez C, Frías-Osuna A, Del-Pino-Casado R (2019) Sentido de coherencia y sobrecarga subjetiva, ansiedad y depresion 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. doi: 10.1016/j.gaceta.2017.09.005

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. doi: 10.1080/13607863.2011.615738

81. McCullagh E, Brigstocke G, Donaldson N, Kalra L (2005) Determinants of caregiving burden and quality of life in caregivers of stroke patients. Stroke 36: 2181-2186.

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. doi: 10.1590/s1980-57642014dn84000013

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

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. doi: 10.1002/(SICI)1097-0142(19981015)83:8<1652::AID-CNCR22>3.0.CO;2-Q [pii]

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-Moreno 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. doi: 10.1080/13607863.2010.505231

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. doi: 10.1177/1043659615573081

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.

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: 10.1161/circoutcomes.116.003160

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.

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. doi: 10.1017/s1041610216000922

96. Roche DL, Croot K, MacCann C, Cramer B, Diehl-Schmid J (2015) The Role of Coping Strategies in Psychological Outcomes for Frontotemporal Dementia Caregivers. J Geriatr Psychiatry Neurol 28: 218-228. doi: 10.1177/0891988715588830

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]

10.1017/S1041610212000737 [doi]

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. doi: 10.1016/j.jad.2018.08.002

S1 Appendix. Syntax used in each database.