RESEARCH ARTICLE

Subjective caregiver burden and anxiety in informal caregivers: A systematic review and meta-analysis

Rafael del-Pino-Casado1*, Emilia Priego-Cubero1, Catalina López-Martínez1, Vasiliki Orgeta2

1 Faculty of Health Sciences, Department of Nursing, University of Jaén, Jaén, Andalusia, Spain, 2 Division of Psychiatry, University College London, London, United Kingdom

* rdelpino@ujaen.es

Abstract

There is increasing evidence that subjective caregiver burden is an important determinant of clinically significant anxiety in family carers. This meta-analysis aims to synthesise this evidence and investigate the relationship between subjective caregiver burden and anxiety symptoms in informal caregivers. We searched PubMed, CINAHL and PsycINFO up to January 2020. Combined estimates were obtained using a random-effects model. After screening of 4,312 articles, 74 studies (with 75 independent samples) were included. There was a large, positive association between subjective caregiver burden and anxiety symptoms (r = 0.51; 95% CI = 0.47, 0.54; I² = 0.0%). No differences were found in subgroup analyses by type of study design (cross-sectional vs. longitudinal), sampling, control of confounders or care-recipient characteristics. Subjective caregiver burden is an important risk factor for anxiety in informal caregivers. Targeting subjective caregiver burden could be beneficial in preventing clinically significant anxiety for the increasing number of family carers worldwide.

Introduction

Research has consistently shown that informal family caregiving is often a burdensome role with negative consequences on carers’ physical and emotional health [1,2]. In contrast to formal caregivers, informal carers typically provide some form of unpaid, ongoing assistance with activities of daily living (ADLs) or instrumental activities of daily living (IADLs) to a person with a chronic illness or disability [3]. Due to increases in life expectancy and associated dependency, family carers will continue to be the main source of care for many people in both developed and developing countries [4]. As a result, caregiver burden will continue to be a significant public healthcare issue for many years to come affecting the quality of life of millions of people worldwide [5–7].

The negative health consequences of caregiving take place over many years affecting both the physical and emotional health of carers. Several studies have consistently reported that informal carers have an increased risk of experiencing psychiatric disorders [1,7,8]. Although anxiety disorders appear to be the most prevalent, they remain the least studied in the context
subjective caregiver burden is the most important correlate of carer anxiety. Despite several definitions in the literature, subjective caregiver burden is best conceptualised as a multidimensional concept that incorporates emotional, physical, social and economic aspects of the caregiving role, considered to be unique for each caregiver [14]. Several studies have examined the association between subjective caregiver burden and anxiety symptoms across several caregiving groups including carers of dependent older people [15], carers of people living with dementia [16], and those caring for cancer survivors [17]. Despite several reviews on the topic [18–20] there is currently no effect estimate on the association between subjective caregiver burden and anxiety symptoms in carers, and no systematic reviews combining evidence across all caregiving groups. As a result, the quality of evidence to date remains unknown and there are no reviews assessing the influence of potential moderators on the relationship between subjective caregiver burden and anxiety. Identifying moderators of this relationship is important for understanding mechanisms linking subjective caregiver burden and anxiety symptoms.

In this study our aim was to provide the first systematic review on the meta-analytic relationship between anxiety symptoms and subjective caregiver burden. We considered this analysis as very important in providing a quantitative estimate of the strength of the population effect size and a much-needed synthesis in the area. Therefore, the aim of this study was to conduct the first systematic review in the literature on the relationship between subjective caregiver burden and anxiety symptoms across all caregiving groups, determine the strength of the association and investigate the role of potential moderators to inform future research in the area.

Material and methods

Design

The present study is a systematic review and meta-analysis of original quantitative studies reporting on the relationship between subjective caregiver burden and anxiety symptoms across caregiving populations, in line with the recommendations of the COSMOS-E guide [21].

Search strategy

Unlimited time searches were performed using the following search terms: anxiety and burden (or strain or role overload) and caregivers (or carer”). We searched PubMed, CINAHL (EBSCO) and PsycINFO (ProQuest) up to 31 of January of 2020. An open search, without filters, was performed to maximize sensitivity. We performed additional hand searches of relevant reviews in the area and contacted authors for new studies. We requested data that did not appear in the original articles.

Eligibility criteria

Types of studies. Inclusion criteria of studies were: a) original studies on informal carers of dependent adults, carrying out caregiving duties at the home of the person they cared for, b)
assessing subjective caregiver burden and anxiety symptoms using a valid tool, and d) those providing data to calculate an appropriate effect size. Both cross-sectional and longitudinal studies were included. Study selection was made by two reviewers independently and disagreements were resolved by consensus with a third reviewer. Studies that did not report a correlation coefficient or another statistical metric that allowed calculation of a correlation coefficient were excluded.

**Types of participants.** Informal carers: Carers of dependent people, defined as those individuals who provided unpaid care to a “dependent person” or “care recipient”. Care recipients: individuals requiring support with at least one basic or instrumental activity of daily living.

**Methodological quality criteria**
Following the recommendations of Boyle [22] and Viswanathan et al. [23], we used the following criteria for assessing the methodological quality of individual studies: (1) sampling (use of probabilistic sampling or not), (2) reliability and validity of measures (content validity and internal consistency of measures in the target population or similar); (3) control for confounding factors (controlling for at least one measure of objective caregiver burden) and (4) for longitudinal studies: absence of attrition (≥ 80% follow-up rate of the original population taking part in the study). Criterion 2 was mandatory for a study to be included in the meta-analysis. Two reviewers (RdPC and EPC) assessed quality of studies independently and any disagreements were resolved by consensus with a third reviewer.

Controlling for objective caregiver burden was considered a necessary quality criterion for studies due to its association with subjective caregiver burden [24] and anxiety symptoms [25]. Measures of objective burden included in studies were functional capacity, cognitive impairment, behavioural problems experienced by the care recipient, and intensity of care provided [26]. Given that measures of objective burden are highly intercorrelated [27], we considered as high quality any study that controlled for at least one measure of objective burden in the design and/or analysis (e.g., through multivariate analysis) via allocation between groups (e.g., through stratification or matching) or studies controlling for confounding variables in the design and/or analysis (e.g. through multivariate analysis) [23]. If statistical adjustment was performed, we considered no confounding bias to be present if variation of the point estimate was less than 10% [28].

Based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) [29], we additionally evaluated imprecision, inconsistency and risk of publication bias. Imprecision was evaluated in line with guidelines [30], which comprise: a) number of included studies in a meta-analysis (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 through heterogeneity of findings in individual studies. Publication bias was assessed by a funnel plot and statistical tests.

**Data extraction**
Two reviewers (RdPC and EPC) extracted data independently using a standardized data extraction form, which included information on type of study design, sample size, health condition/illness of care recipients, quality criteria and effect sizes. Disagreements were resolved by consensus.

**Synthesis of information**
The estimated effect measure used was the correlation coefficient. Following the recommendations of Cooper et al. [31], a random effects model was used to calculate the combined effect,
in order to generalize findings across caregiving groups. For longitudinal studies with repeated measures reporting cross-sectional correlations in each time point, the first correlation was selected. We measured heterogeneity with the Cochran Q \cite{32}, considering p values above 0.10 indicative of no heterogeneity. We used the $I^2$ (Higgins et al. \cite{33}) to measure the proportion of heterogeneity due to the variability of effect estimates amongst individual studies, with values of 25, 50 and 75% indicative of mild, moderate and severe heterogeneity, respectively.

We assessed publication bias through evaluating asymmetry in a funnel plot, a p value above 0.10 on the Egger test \cite{34} and the Trim and Fill method which computes the combined effect in the context of absence of publication bias \cite{35}. We performed sensitivity analysis removing one study each time to evaluate the robustness of the results of the meta-analysis (leave-one-out method), and several subgroup analyses to investigate differences of the combined effect due to study design, methodological quality of individual studies and health condition of care recipients (i.e. frailty, dementia, cancer, stroke). We performed all analyses using Comprehensive Meta-analysis 3.3.

**Results**

**Study characteristics**

A total of 4,304 references were retrieved from the search with a further eight additional articles identified via other sources. After removing duplicates, 3,365 records were screened, of which 2,938 were excluded as not relevant, leaving 427 articles to be assessed for eligibility. Of these 345 were excluded as not relevant or not meeting inclusion criteria, leaving a total of 82 full text articles assessed for quality appraisal (see Fig 1). Of these 82 studies, two studies were excluded as not meeting mandatory criteria for methodological quality \cite{36,37} and six studies \cite{38–43} reported secondary analyses of a primary study (samples already included). Finally, 74 studies with 75 independent samples, met inclusion criteria and were included in the review \cite{11–17,44–110}.

Characteristics of the included studies are presented in Table 1. Care recipients included people living with a diagnosis of dementia (24 studies), frail older people (11 studies with 12 samples), people living with cancer (12 studies) and stroke survivors (eight studies). All but nine studies employed a cross-sectional design. Those utilising a longitudinal design used repeated measures, with one study providing only cross-sectional correlations in each time point. Therefore, a total of 66 studies with 67 independent samples provided cross-sectional correlations and eight studies with eight independent samples contributed longitudinal correlations.

**Anxiety symptoms and subjective caregiver burden**

Results of the meta-analyses showed that the combined effect of the association between subjective caregiver burden and anxiety symptoms was $r = 0.51$ (95% confidence interval [CI] = 0.47; 0.54; 75 samples; Table 3), indicative of a large positive association. Fig 2 presents the results of the forest plot showing the effect of each individual study. All studies except one \cite{96} reported positive correlations and all studies except four \cite{47,77,96,104} reported a statistically significant association between subjective caregiver burden and anxiety symptoms. The total number of participants included in the meta-analysis was $n = 10,122$ and $n = 135$ was the mean number of participants per study. There was no heterogeneity amongst individual studies ($Q = 63.47$, degrees of freedom $= 74$, $p = 0.80$, $I^2 = 0.0\%$).

**Quality ratings.** Table 2 shows quality ratings of included studies. Most used non-probabilistic samples (70 studies with 71 samples), whereas all met criterion 2 reporting on a reliable and valid measure of subjective caregiver burden and anxiety symptoms. Only 20 studies
Fig 1. Flow diagram (PRISMA).

https://doi.org/10.1371/journal.pone.0247143.g001
Table 1. Description of the studies included in the review (I).

| Studies (author, year)                          | N   | Design        | Care recipients                  | Measure of burden | Measure of anxiety |
|------------------------------------------------|-----|---------------|----------------------------------|-------------------|-------------------|
| Adejumo et al., 2019 [44]                      | 57  | Cross-sectional | Chronic kidney failure           | ZBI               | HADS              |
| Alfaro-Ramirez del Castillo et al., 2008 [45]  | 100 | Cross-sectional | Cancer                          | ZBI               | MLSI              |
| Ar, 2017 [46]                                  | 190 | Cross-sectional | Dementia                        | ZBI               | STAI-S            |
| Bozkurt Zincir et al., 2014 [47]               | 138 | Cross-sectional | Other chronic conditions         | ZBI               | STAI-S            |
| Buscemi et al., 2010 [14]                      | 59  | Cross-sectional | Cancer                          | BCOS              | HADS              |
| Carod-Artal et al., 2009 [48]                  | 200 | Cross-sectional | Stroke                          | ZBI               | HADS              |
| Chan et al., 2018 [49]                         | 274 | Cross-sectional | Frail older people              | ZBI               | HADS              |
| Chattat et al., 2011 [50]                      | 273 | Cross-sectional | Dementia                        | ZBI               | HADS              |
| Coleman et al., 2015 [51]                     | 40  | Cross-sectional | Spinal cord injury               | ZBI               | STAI              |
| Cooper et al. 2008 [52]                        | 93  | Repeated measures | Dementia                      | ZBI               | HADS              |
| del-Pino-Casado et al., 2015 [53]             | 200 | Cross-sectional | Frail older people              | CSI               | Goldberg          |
| del-Pino-Casado et al., 2019 [54]             | 178 | Repeated measures | Frail older people              | CSI               | Goldberg          |
| Diike et al., 2018 [55]                        | 481 | Cross-sectional | Mental Illness                  | PFBS              | BAI               |
| Dos Santos et al., 2017 [56]                   | 36  | Cross-sectional | Mental Illness                  | ZBI               | BAI               |
| Edelstein et al., 2018 [15]                    | 107 | Cross-sectional | Frail older people              | ZBI               | HADS              |
| Efi et al., 2017 [57]                          | 150 | Cross-sectional | Stroke                         | BCOS              | HADS              |
| Fu et al., 2007 [58]                           | 42  | Cross-sectional | Dementia                        | ZBI               | SAS               |
| Galindo Vázquez et al., 2015 [59]             | 200 | Cross-sectional | Cancer                          | ZBI               | HADS              |
| Garand et al., 2005 [60]                       | 27  | Cross-sectional | Dementia                        | SBS               | STAI-S            |
| Garcia-Alberca et al., 2012 [11]               | 80  | Cross-sectional | Dementia                        | ZBI               | STAI-S            |
| Goetzinger et al., 2012 [61]                   | 610 | Cross-sectional | Other chronic conditions        | SCB               | STAI-S            |
| Gonzalez-Abrales et al., 2013 [62]            | 33  | Cross-sectional | Dementia                        | ZBI               | STAI-T            |
| Govina et al., 2015 [63]                       | 100 | Cross-sectional | Cancer                          | BCOS              | HADS              |
| Guedes and Pereira, 2013 [64]                  | 50  | Cross-sectional | Frail older people              | ZBI               | DASS              |
| Hu et al., 2018 [13]                           | 117 | Cross-sectional | Stroke                          | ZBI               | HARS              |
| Iavarone et al., 2014 [65]                     | 86  | Cross-sectional | Dementia                        | CBI               | STAI-T            |
| Jaracz et al., 2014 [66]                       | 150 | Cross-sectional | Frail older people              | CBS 1             | HADS              |
| Jones et al., 2015 [67]                        | 76  | Cross-sectional | Cancer                          | BASC              | DASS              |
| Karabekiroglu et al., 2018 [68]                | 60  | Cross-sectional | Cancer                          | ZBI               | BAI               |
| Kemp et al., 2018 [69]                         | 44  | Cross-sectional | Cancer                          | OCBS              | HADS              |
| Kruithof et al., 2016 [12]                     | 183 | Repeated measures | Stroke                      | CSI               | HADS              |
| Lee et al., 2010 [70]                          | 81  | Cross-sectional | Other chronic conditions        | CBS 2             | HADS              |
| Leibach et al., 2014 [71]                      | 90  | Cross-sectional | Traumatic brain injury          | ZBI               | STAI              |
| Liu et al., 2012 Liu et al. [72]                | 180 | Cross-sectional | Frail older people              | CBI               | SAS               |
| López Alonso and Moral Serrano, 2005 [73]      | 215 | Cross-sectional | Other chronic conditions        | CSI               | Goldberg          |
| López-Martinez, 2019 [74]                      | 81  | Repeated measures | Frail older people              | CSI               | Goldberg          |
| Macias-Delgado Yanet et al., 2014 [75]         | 35  | Cross-sectional | Multiple sclerosis              | ZBI               | ISRA              |
| Majestic and Eddington, 2019 [76]              | 102 | Cross-sectional | Cancer                          | ZBI               | DASS              |
| Manso Martinez et al., 2013 (men) [77]         | 14  | Cross-sectional | Frail older people              | ZBI               | HADS              |
| Manso Martinez et al., 2013 (women) [77]       | 74  | Cross-sectional | Frail older people              | ZBI               | HADS              |
| Mavardi et al., 2005 [78]                      | 419 | Cross-sectional | Dementia                        | CBI               | BSI               |
| McCullagh et al., 2005 [79]                    | 232 | Repeated measures | Stroke                      | CBS               | HADS              |
| Medrano et al., 2014 [80]                      | 67  | Cross-sectional | Dementia                        | ZBI               | HARS              |
| Mei et al., 2018 [81]                          | 145 | Cross-sectional | Stroke                          | CBI               | HADS              |
| Méndez et al., 2010 [82]                       | 14  | Cross-sectional | Dementia                        | ZBI               | STAI              |
| Molina Linde and Lainez Velasco 2006 [83]      | 46  | Cross-sectional | Dementia                        | ZBI               | STAI-s             |
| Morlet-Paredes, 2014 [84]                      | 102 | Cross-sectional | Mental Illness                 | ZBI               | GAD               |

(Continued)
(26.7%) reported controlling for several confounders which included function, behavioral and psychological symptoms, cognitive impairment, and intensity of care provided [17,48,53,60,71,74,77,86,88,91,92,100–104,106,107,111,112].

Publication bias and sensitivity analyses. Inspection of the funnel plot (see Fig 3) indicates asymmetry, even though there are no extreme values. Results of the Egger test showed that there is a low risk of publication bias overall (p = 0.13). We calculated additional analyses to investigate publication bias based on the Hedges and Pigott method [113] in order to calculate the power of the Egger test, obtaining 99%. The combined effect value using the Trim and Fill method [35] (r = 0.57) varied by 11.8% with respect to initial calculations (0.57), indicative of a small effect of publication bias. Sensitivity analyses eliminating one study at a time showed that the combined r-value differed less than 1.8% from the original combined effect (from 0.50 to 0.51), demonstrating the robustness of the findings.

Subgroup analyses. We performed several subgroup analyses to investigate the effect of several moderators in the association between subjective caregiver burden and anxiety.

| Studies (author, year) | N   | Design       | Care recipients          | Measure of burden | Measure of anxiety |
|------------------------|-----|--------------|--------------------------|-------------------|-------------------|
| Özyesil et al., 2014 [85] | 140 | Cross-sectional | Frail older people       | CBI               | STAI-S            |
| Pagnini et al., 2010 [86] | 40  | Cross-sectional | Multiple sclerosis       | ZBI               | STAI              |
| Palacio et al., 2018 [87] | 50  | Cross-sectional | Cancer                   | ZBI               | HADS              |
| Perez Cruz et al., 2019 [88] | 198 | Cross-sectional | Frail older people       | CSI               | HARS              |
| Pérez-Ordóñez et al., 2016 [17] | 50  | Cross-sectional | Cancer                   | CSI               | Goldberg          |
| Perpiña-Galván et al., 2019 [89] | 78  | Cross-sectional | Cancer                   | ZBI               | HADS              |
| Raveis et al., 2000 [90] | 164 | Cross-sectional | Cancer                   | CRA               | STAI-S            |
| Razani et al., 2014 [91] | 44  | Repeated measures | Dementia                | CBI               | BSI               |
| Romero-Moreno et al., 2011 [92] | 167 | Cross-sectional | Dementia                 | ZBI               | POMS              |
| Sadak et al., 2017 [93] | 227 | Cross-sectional | Dementia                 | KCSS              | GAD               |
| Sanyal et al., 2015 [94] | 150 | Cross-sectional | Parkinson                | ZBI               | HADS              |
| Shukri et al., 2020 [95] | 340 | Cross-sectional | Chronic kidney failure   | BPSFC             | HADS              |
| Stanley et al., 2017 [96] | 75  | Cross-sectional | Mental Illness           | ZBI               | DASS              |
| Stevens et al., 2013 [111] | 90  | Cross-sectional | Traumatic brain injury   | ZBI               | STAI-S            |
| Tang et al., 2011 [98] | 123 | Cross-sectional | Stroke                   | CBS 1             | HADS              |
| Torny et al., 2018 [99] | 38  | Cross-sectional | Parkinson                | ZBI               | HADS              |
| Trapp et al., 2015 [100] | 40  | Cross-sectional | Spinal cord injury       | ZBI               | STAI              |
| Tremont et al., 2006 [101] | 72  | Cross-sectional | Dementia                 | ZBI               | STAI              |
| Truzzi et al., 2008 [102] | 69  | Cross-sectional | Dementia                 | ZBI               | BAI               |
| Tsatali et al., 2019 [103] | 247 | Cross-sectional | Dementia                 | ZBI               | BAI               |
| Vérez Cotelo et al., 2015 [104] | 25  | Cross-sectional | Dementia                 | ZBI               | STAI-S            |
| Vitaliano et al., 1991 [105] | 79  | Repeated measures | Dementia                | SCB               | SCL               |
| Wang et al., 2008 [106] | 42  | Cross-sectional | Dementia                 | ZBI               | HARS              |
| Wang et al., 2018 [106] | 210 | Cross-sectional | Dementia                 | CBI               | SAS               |
| Winslow, 1997 [107] | 452 | Repeated measures | Dementia                | Study specific    | HSCL              |
| Yu et al., 2018 [108] | 327 | Cross-sectional | Mental Illness           | ZBI               | GAD               |
| Zawadzki et al., 2011 [109] | 51  | Cross-sectional | Dementia                 | ZBI               | Study specific    |
| Zhu and Jiang, 2018 [110] | 202 | Repeated measures (*) | Stroke                  | BCOS              | HARS              |

(* ) With cross-sectional correlations.

Note: Abbreviations of measures are presented in S1 Appendix.

https://doi.org/10.1371/journal.pone.0247143.t001
symptoms. As can be seen from Table 3, there were no differences between cross-sectional (r = 0.52; 95% CI = 0.48, 0.55; 67 samples) and longitudinal studies (r = 0.43; 95% CI = 0.36, 0.49; 8 samples), in terms of the estimate of the effect. We found no differences between studies using probabilistic samples (r = 0.49; 95% CI = 0.35, 0.60; 4 samples) versus those that did not (r = 0.51; 95% CI = 0.47, 0.54; 71 samples). Similarly, the effect estimate did not change between studies that controlled for several confounders (r = 0.50; 95% CI = 0.44, 0.56; 20 samples) versus those that did not (r = 0.51; 95% CI = 0.47, 0.55; 55 samples). We further investigated whether care recipient characteristics moderated the effect. As shown in Table 3 there were no differences between studies reporting on associations in carers of people with dementia, carers of frail older people, and carers of cancer or stroke survivors.

Discussion

Our study is the first systematic review and meta-analysis of the worldwide literature providing an estimate of the magnitude of the association between subjective caregiver burden and
Table 2. Quality assessment of the studies included in the review (I).

| Studies                                      | Probabilistic sampling | Reliability and validity of measures | Control of confounders | Absence of attrition |
|----------------------------------------------|------------------------|--------------------------------------|-------------------------|----------------------|
| Adejumo et al., 2019 [44]                   | -                      | +                                    | ?                       | N/A                  |
| Alfaro-Ramirez del Castillo et al., 2008 [45]| -                      | +                                    | ?                       | N/A                  |
| Ar, 2017 [46]                                | -                      | +                                    | ?                       | N/A                  |
| Bozkurt Zincir et al., 2014 [47]            | -                      | +                                    | ?                       | N/A                  |
| Buscemi et al., 2010 [14]                   | -                      | +                                    | -                       | N/A                  |
| Carod-Artal et al., 2009 [48]               | -                      | +                                    | +                       | N/A                  |
| Chan et al., 2018 [49]                      | -                      | +                                    | ?                       | N/A                  |
| Chattat et al., 2011 [50]                   | -                      | +                                    | ?                       | N/A                  |
| Coleman et al., 2015 [51]                  | -                      | +                                    | ?                       | N/A                  |
| Cooper et al., 2008 [52]                    | -                      | +                                    | ?                       | -                    |
| del-Pino-Casado et al., 2015 [53]           | +                      | +                                    | +                       | N/A                  |
| del-Pino-Casado et al., 2019 [54]           | +                      | +                                    | +                       | +                    |
| Diikeç et al., 2018 [55]                    | -                      | +                                    | ?                       | N/A                  |
| Dos Santos et al., 2017 [56]                | -                      | +                                    | ?                       | N/A                  |
| Edelstein et al., 2018 [15]                 | -                      | +                                    | ?                       | N/A                  |
| Efi et al., 2017 [57]                       | -                      | +                                    | ?                       | N/A                  |
| Fu et al., 2007 [58]                        | -                      | +                                    | ?                       | N/A                  |
| Galindo Vázquez et al., 2015 [59]           | -                      | +                                    | ?                       | N/A                  |
| Garand et al., 2005 [60]                    | -                      | +                                    | +                       | N/A                  |
| Garcia-Alberca et al., 2012 [11]            | -                      | +                                    | ?                       | N/A                  |
| Goetzinger et al., 2012 [61]                | -                      | +                                    | ?                       | N/A                  |
| Gonzalez-Abraldes et al., 2013 [62]         | -                      | +                                    | ?                       | N/A                  |
| Govina et al., 2015 [63]                    | -                      | +                                    | ?                       | N/A                  |
| Guedes and Pereira, 2013 [64]               | -                      | +                                    | ?                       | N/A                  |
| Hu et al., 2018 [13]                        | -                      | +                                    | ?                       | N/A                  |
| Iavarone et al., 2014 [65]                  | -                      | +                                    | ?                       | N/A                  |
| Jaracz et al., 2014 [66]                    | -                      | +                                    | ?                       | N/A                  |
| Jones et al., 2015 [67]                     | -                      | +                                    | ?                       | N/A                  |
| Karabekiroglu et al., 2018 [68]             | -                      | +                                    | ?                       | N/A                  |
| Kemp et al., 2018 [69]                      | -                      | +                                    | ?                       | N/A                  |
| Kruihof et al., 2016 [12]                   | -                      | +                                    | ?                       | +                    |
| Lee et al., 2010 [70]                       | -                      | +                                    | ?                       | N/A                  |
| Leibach et al., 2014 [71]                   | -                      | +                                    | +                       | N/A                  |
| Liu et al., 2012 Liu et al. [72]            | -                      | +                                    | ?                       | N/A                  |
| López Alonso and Moral Serrano, 2005 [73]   | +                      | +                                    | ?                       | N/A                  |
| López-Martinez, 2019 [74]                   | +                      | +                                    | +                       | -                    |
| Macias-Delgado Yanet et al., 2014 [75]      | -                      | +                                    | ?                       | N/A                  |
| Majestic and Eddington, 2019 [76]           | -                      | +                                    | ?                       | N/A                  |
| Manso Martinez et al., 2013 (men) [77]      | -                      | +                                    | -                       | N/A                  |
| Manso Martinez et al., 2013 (women) [77]    | -                      | +                                    | +                       | N/A                  |
| Mavardi et al., 2005 [78]                   | -                      | +                                    | ?                       | N/A                  |
| McCullagh et al., 2005 [79]                 | -                      | +                                    | ?                       | -                    |
| Medrano et al., 2014 [80]                   | -                      | +                                    | ?                       | N/A                  |
| Mei et al., 2018 [81]                       | -                      | +                                    | ?                       | N/A                  |
| Méndez et al., 2010 [82]                    | -                      | +                                    | ?                       | N/A                  |
| Molina Linde and Iañez Velasco 2006 [83]    | -                      | +                                    | -                       | N/A                  |
| Morlett Paredes, 2014 [84]                  | -                      | +                                    | ?                       | N/A                  |

(Continued)
anxiety symptoms in informal carers. Results of our meta-analyses found a large positive association between subjective caregiver burden and anxiety symptoms as predicted by theory [10] and empirical work in the area [11–13]. The results showed robustness to the effects of several modifiers such as study design (cross-sectional vs. longitudinal), sampling methods used (probabilistic or non-probabilistic), control of confounders, and care-recipient characteristics. An important strength of this study was quantifying the relationship between subjective caregiver burden and anxiety in informal carers across all caregiving groups. Our findings that the estimate of the association was similar across different groups of caregivers supports the wider applicability of our findings.

Our review provides important new knowledge in the area by rigorously evaluating the methodological quality of evidence to date and assessing the influence of important confounders such as objective burden and the potential effect of publication bias. Our findings have

| Studies                        | Probabilistic sampling | Reliability and validity of measures | Control of confounders | Absence of attrition |
|--------------------------------|------------------------|-------------------------------------|------------------------|----------------------|
| Özyesil et al., 2014 [85]     | -                      | +                                   | ?                      | N/A                  |
| Pagnini et al., 2010 [86]     | -                      | +                                   | +                      | N/A                  |
| Palacio et al., 2018 [87]     | -                      | +                                   | +                      | N/A                  |
| Perez Cruz et al., 2019 [88]  | -                      | +                                   | N/A                    |
| Pérez-Ordóñez et al., 2016 [17]| -                      | +                                   | N/A                    |
| Perpiñá-Galvañ et al., 2019 [89]| -                      | +                                   | N/A                    |
| Reavis et al., 2000 [90]      | -                      | +                                   | -                      | N/A                  |
| Razani et al., 2014 [91]      | -                      | +                                   | ?                      |
| Romero-Moreno et al., 2011 [92]| -                      | +                                   | N/A                    |
| Sanyal et al., 2015 [94]      | -                      | +                                   | N/A                    |
| Shukri et al., 2020 [95]      | -                      | +                                   | N/A                    |
| Stanley et al., 2017 [96]     | -                      | +                                   | N/A                    |
| Stevens et al., 2013 [111]    | -                      | +                                   | N/A                    |
| Tang et al., 2011 [98]        | -                      | +                                   | N/A                    |
| Torny et al., 2018 [99]       | -                      | +                                   | N/A                    |
| Trapp et al., 2015 [100]      | -                      | +                                   | N/A                    |
| Tremont et al., 2006 [101]    | -                      | +                                   | N/A                    |
| Truzzi et al., 2008 [102]     | -                      | +                                   | N/A                    |
| Tsatali et al., 2019 [103]    | -                      | +                                   | N/A                    |
| Vérez Cotelo et al., 2015 [104]| -                      | +                                   | N/A                    |
| Vitaliano et al., 1991 [105]  | -                      | +                                   | N/A                    |
| Wang et al., 2008 [106]       | -                      | +                                   | N/A                    |
| Wang et al., 2018 [10]        | -                      | +                                   | N/A                    |
| Winslow, 1997 [107]           | -                      | +                                   | N/A                    |
| Yu et al., 2018 [108]         | -                      | +                                   | N/A                    |
| Zawadzki et al., 2011 [109]   | -                      | +                                   | N/A                    |
| Zhu and Jiang, 2018 [110]     | -                      | +                                   | N/A                    |

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

https://doi.org/10.1371/journal.pone.0247143.t002
high consistency and precision overall, given that the risk of publication bias was small, and sensitivity analyses showed no substantial variation in the combined effect. There were no differences in the combined effect between cross-sectional and longitudinal studies providing further support for the robustness and precision of our results. However, the observed differences in the point estimates and the slight overlap of the confidence intervals indicate a possible overestimation of the effect in cross-sectional studies.

As predicted by individual studies subjective caregiver burden was associated with high levels of clinically significant anxiety in carers [11–13]. The strength of the association observed in our meta-analysis suggests that subjective caregiver burden is an important determinant of anxiety-related psychological distress in carers. This finding indicates that alleviating subjective caregiver burden will protect carers from experiencing high levels of anxiety symptoms. Therefore, interventions aimed at early detection and prevention of subjective caregiver burden and anxiety symptoms such as psychoeducation and skills building interventions and access to respite care should be routinely offered to family carers [114,115]. Interestingly our analyses indicated that this association was not influenced by objective burden parameters such as levels of every-day function, behavioural and psychological symptoms or presence of cognitive impairment in the care recipient.
Implications for clinical practice and research

Within the caregiving context, our finding that carers reporting high levels of subjective caregiver burden are more likely to experience clinically significant anxiety is important. Anxiety is a highly distressing condition, increasing risk of cardiovascular disease, compromising carers’ physical health, and lowering their quality of life [116]. Screening for, and addressing high caregiver burden therefore may improve psychiatric and physical health outcomes for carers [112]. More widely, interventions that prevent caregiver burden supporting carers to cope with the demands of caregiving duties such as access to day care services [115] and psychotherapeutic support [114] would be an important investment for clinical services worldwide. Future research however is needed to explore some of the issues raised by our meta-analysis. For example, future studies are required to identify other individual and environmental factors that may moderate the association between subjective caregiver burden and anxiety.

Furthermore, research has shown that spousal and adult-child caregivers differ on several dimensions of subjective caregiver burden [117], and on the objective stressors that influence levels of burden experienced [118]. For example, behavioral and psychological symptoms are more strongly associated with subjective burden in spousal as opposed to adult-child caregivers [27]. A better understanding of these associations and how interventions can better address the needs of spousal versus adult-child caregivers, will increase their effectiveness, and should be a focus of future work in the area.

Prospective studies investigating prognosis and long-term outcomes for carers experiencing high levels of anxiety and subjective caregiver burden are currently lacking. Further longitudinal studies are required that evaluate how subjective caregiver burden and anxiety symptoms may change over time.

Limitations

Despite the rigour of our meta-analysis the results of our review should be interpreted with caution. First, the design of the longitudinal studies included in our review does not allow us to conclude whether reverse causation between subjective caregiver burden and anxiety symptoms is present or absent. An important potential bias could be that higher levels of subjective
caregiver burden reported by carers may not be burden attributed to the caregiving experience per se but may instead reflect high levels of anxiety symptoms experienced by carers. Second, we were not able to control for confounders other than objective caregiver burden, such as stressful life events, social support, coping or socio-economic factors that are related to anxiety symptoms [18] and our meta-analysis was not registered online. Moreover, some of the studies included in our meta-analysis did not primarily investigate the association between subjective caregiver burden and anxiety symptoms, and this may have influenced the accuracy of the effect observed in our meta-analyses. Lastly, we were not able to examine how being a spousal versus an adult-child caregiver influences the association between subjective caregiver burden and anxiety and the differential impact of moderators of this association amongst spousal versus adult-child caregivers.

Conclusion

Despite limitations, this is an important study providing the first quantitative estimate of the association of subjective caregiver burden and anxiety symptoms in informal caregivers. This meta-analysis suggests that subjective caregiver burden has a large association with anxiety symptoms, and this relationship is found across all caregiving groups. It does not appear to be affected by study design (cross-sectional vs. longitudinal), sampling, control for confounders or care-recipient characteristics. Results provide support for a newly focus on interventions to detect subjective caregiver burden and prevent clinically significant anxiety symptoms for the increasing number of informal caregivers worldwide.

Supporting information

S1 Checklist. PRISMA checklist.
(DOC)

S1 Appendix. Abbreviations of measures.
(DOCX)

Author Contributions

Conceptualization: Rafael del-Pino-Casado, Vasiliki Orgeta.

Data curation: Rafael del-Pino-Casado, Emilia Priego-Cubero, Catalina López-Martinez, Vasiliki Orgeta.

Formal analysis: Rafael del-Pino-Casado, Emilia Priego-Cubero, Vasiliki Orgeta.

Investigation: Rafael del-Pino-Casado, Emilia Priego-Cubero, Catalina López-Martinez, Vasiliki Orgeta.

Project administration: Rafael del-Pino-Casado, Vasiliki Orgeta.

Supervision: Rafael del-Pino-Casado, Vasiliki Orgeta.

Visualization: Rafael del-Pino-Casado, Emilia Priego-Cubero, Catalina López-Martinez, Vasiliki Orgeta.

Writing – original draft: Rafael del-Pino-Casado, Emilia Priego-Cubero, Catalina López-Martinez, Vasiliki Orgeta.

Writing – review & editing: Rafael del-Pino-Casado, Emilia Priego-Cubero, Catalina López-Martinez, Vasiliki Orgeta.
References

1. Sallim AB, Sayyamanthan 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. https://doi.org/10.1016/j.jamda.2015.09.007 PMID: 26593303

2. Lee S, Colditz GA, Berkman LF, Kawachi I (2003) Caregiving and risk of coronary heart disease in U. S. women: a prospective study. Am J Prev Med 24: 115–119. https://doi.org/10.1016/s0749-3797(02)00582-2 PMID: 12568816

3. Roth DL, Fredman L, Haley WE (2015) Informal caregiving and its impact on health: a reappraisal from population-based studies. Gerontologist 55: 309–319. https://doi.org/10.1093/geront/gnu177 PMID: 26035608

4. Organisation for Economic Co-operation and Development (2019) Health at a Glance 2019: OECD indicators. Paris: OECD Publishing.

5. Organisation for Economic Co-operation and Development (2018) Care needed: Improving the lives of people with dementia. Paris: OECD Publishing.

6. Kent EE, Rowland JH, Northouse L, Litzelman K, Chou WY, Shelburne N, et al. (2016) Caring for caregivers and patients: Research and clinical priorities for informal cancer caregiving. Cancer 122: 1987–1995. https://doi.org/10.1002/cncr.29939 PMID: 26991807

7. 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

8. 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. https://doi.org/10.1097/MD.0000000000011863 PMID: 30278483

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

10. Pearlin LI, Mullan JT, Semple SJ, Skaff MM (1990) Caregiving and the stress process: An overview of concepts and their measures. Gerontologist 30: 583–594. https://doi.org/10.1093/geront/30.5.583 PMID: 2276631

11. Garcia-Alberca JM, Cruz B, Lara JP, Garrido V, Gris E, Lara A, et al. (2012) Disengagement coping partially mediates the relationship between caregiver burden and anxiety and depression in caregivers of people with Alzheimer’s disease. Results from the MALAGA-AD study. Journal of Affective Disorders 136: 848–856. https://doi.org/10.1016/j.jad.2011.09.026 PMID: 22030129

12. 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. https://doi.org/10.1016/j.pec.2016.04.007 PMID: 27103190

13. Hu P, Yang Q, Kong L, Hu L, Zeng L (2018) Relationship between the anxiety/depression and care burden of the major caregiver of stroke patients. Medicine (Baltimore) 97: e12638. https://doi.org/10.1097/MD.0000000000012638 PMID: 30290641

14. Buscemi V, Font A, Viladrich C (2010) Focus on relationship between the caregivers unmet needs and other caregiving outcomes in cancer palliative care. Psicooncología 7: 109–125.

15. 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. https://doi.org/10.1080/13607863.2017.1289365 PMID: 28828731

16. Wang Z, Ma C, Han H, He R, Zhou L, Liang R, et al. (2018) Caregiver burden in Alzheimer’s disease: Moderation effects of social support and mediating effects of positive aspects of caregiving. International Journal of Geriatric Psychiatry. https://doi.org/10.1002/gps.4910 PMID: 28856091

17. Pérez-Ordóñez F, Frías-Osuna A, Romero-Rodriguez Y, del-Pino-Casado R (2016) Coping strategies and anxiety in caregivers of palliative cancer patients. European Journal of Cancer Care 25: 600–607. https://doi.org/10.1111/ecc.12507 PMID: 27099167

18. Cooper C, Balamurall TB, Livingston G (2007) A systematic review of the prevalence and covariates of anxiety in caregivers of people with dementia. International Psychogeriatrics 19: 175–195. https://doi.org/10.1017/s1041610207000429 PMID: 17035066

19. Jansen L, Dauphin S, van den Akker M, De Burghgrave T, Schoenmakers B, Buntinx F (2018) Prevalence and predictors of psychosocial problems in informal caregivers of older cancer survivors—A systematic review: Still major gaps in current research. Eur J Cancer Care (Engl): e12899. https://doi.org/10.1111/ecc.12899 PMID: 30168877
20. 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

21. Dekkers OM, Vandenbroucke JP, Cevallos M, Renehan AG, Altman DG, Egger M (2019) COSMOS-E: Guidance on conducting systematic reviews and meta-analyses of observational studies of etiology. PLoS Med 16: e1002742. https://doi.org/10.1371/journal.pmed.1002742 PMID: 30789892

22. Boyle MH (1998) Guidelines for evaluating prevalence studies. Evidence Based Mental Health 1: 37–39.

23. 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.

24. 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 15: 76–93. https://doi.org/10.1016/j.arr.2014.03.003 PMID: 24675045

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

26. Aneshensel CS, Pearlin LI, Mullan JT, Zarit SH, Whitlatch CJ (1995) Profiles in Caregiving. San Diego, CA: Academic Press.

27. 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. https://doi.org/10.1093/geronb/58.2.p112 PMID: 12646594

28. Rothman KJ, Greenland S, Lash TL (2008) Modern epidemiology. Philadelphia: Lippincott Williams & Wilkins.

29. 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

30. 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. https://doi.org/10.1186/2046-4053-3-82 PMID: 25056145

31. Cooper HM, Hedges LV, Valentine JC (2009) The handbook of research synthesis and meta-analysis. New York, NY: Russell Sage Foundation Publications.

32. Cochran WG (1954) The combination of estimates from different experiments. Biometrics 10: 101–129.

33. Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. BMJ: British Medical Journal 327: 557. https://doi.org/10.1136/bmj.327.7414.557 PMID: 12958120

34. 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

35. 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. https://doi.org/10.1111/j.0006-341x.2000.00455.x PMID: 10877304

36. Beach SR, Schulz R, Yee JL, Jackson S (2000) Negative and positive health effects of caring for a disabled spouse: longitudinal findings from the caregiver health effects study. Psychol Aging 15: 259–271. https://doi.org/10.1037//0882-7974.15.2.259 PMID: 10879581

37. Schuz B, Czernecki A, Davie N, Miller L, Quinn MG, King C, et al. (2015) Leisure Time Activities and Mental Health in Informal Dementia Caregivers. Appl Psychol Health Well Being 7: 230–248. https://doi.org/10.1111/apwh.12046 PMID: 26097155

38. Cooper C, Katona C, Orrell M, Livingston G (2006) Coping strategies and anxiety in caregivers of people with Alzheimer’s disease: the LASER-AD study. Journal of Affective Disorders 90: 15–20. https://doi.org/10.1016/j.jad.2005.08.017 PMID: 16337688

39. 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. https://doi.org/10.1017/S104161020700645X PMID: 18053290

40. Garcia-Alberca JM, Cruz B, Lara JP, Garrido V, Lara A, Gris E (2012) Anxiety and depression are associated with coping strategies in caregivers of Alzheimer’s disease patients: results from the MALAGA-AD study. Int Psychogeriatr 24: 1325–1334. https://doi.org/10.1017/S1041610211002948 PMID: 22340759
41. Govina O, Vlachou E, Kalemirkakis I, Papageorgiou D, Kavga A, Konstantinidis T (2019) Factors Associated with Anxiety and Depression among Family Caregivers of Patients Undergoing Palliative Radiotherapy. Asia Pac J Oncol Nurs 6: 283–291. https://doi.org/10.4103/apjon.apjon_74_18 PMID: 31259225

42. Govina O, Vlachou E, Kavga-Paltoglou A, Kalemirkakis I, Papageorgiou D, Fasoi G, et al. (2014) Exploring the factors influencing time and difficulty of tasks provided by family caregivers of patients with advanced cancer in Greece. Health Science Journal 8: 438.

43. Jaracz K, Grabowska-Fudala B, Kozubek 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

44. Adejumo OA, Iyawe IO, Akinbodewa AA, Abolarin OS, Alli EO (2019) Burden, psychological well-being and quality of life of caregivers of end stage renal disease patients. Ghana Med J 53: 190–196. https://doi.org/10.4341/gmj.v53i3.2 PMID: 31741490

45. Alfaroe-Ramirez del Castillo Ol, Morales-Vigil T, Vazquez-Pineda F, Sanchez-Roman S, Ramos-del Rio B, Guevara-Lopez U (2008) Sobrecarga, ansiedad y depresión en cuidadores primarios de pacientes con dolor crónico y terminales [Overload, anxiety and depression in caregivers of patients included in the home care program]. Rev Med Inst Mex Seguro Soc 46: 485–494.

46. 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 [PhD]. Ankara: Middle East Technical University.

47. Bozkurt Zincir S, Sunbul M, Zincir S, Aydin Sunbul E, Oguz M, Feriha Cengiz F, et al. (2014) Burden and depressive symptoms associated with adult-child caregiving for individuals with heart failure. ScientificWorldJournal 2014: 641817. https://doi.org/10.1155/2014/641817 PMID: 25431793

48. Carod-Artal FJ, Ferreira Coral L, Trizotto DS, Menezes Moreira C (2009) Burden and perceived health status among caregivers of stroke patients. Cerebrovascular diseases (Basel, Switzerland) 28: 472–480. https://doi.org/10.1159/000263525 PMID: 19752548

49. Chan EY, Glass G, Chua KC, Ali N, Lim WS (2018) Relationship between Mastery and Caregiving Competence in Protecting against Burden, Anxiety and Depression among Caregivers of Frail Older Adults. J Nutr Health Aging 22: 1238–1246. https://doi.org/10.1007/s12603-018-1098-1 PMID: 30498832

50. Chattat R, Cortesi V, Izzicupo F, Del Re ML, Sgarbi C, Fabbo A, et al. (2011) The Italian version of the Zarit Burden interview: a validation study. Int Psychogeriatr 23: 797–805. https://doi.org/10.1017/S1041610210000221 PMID: 21205379

51. Coleman JA, Harper LA, Perrin PB, Olabanrieta Landa L, Leonor Olvera S, Libardo Perdomo J, et al. (2015) Mind and body: Mental health and health related quality of life in SCI caregivers from Neiva, Colombia. NeuroRehabilitation 36: 223–232. https://doi.org/10.3233/NRE-151216 PMID: 25882203

52. Cooper C, Katona C, Orrell M, Livingston G (2008) Coping strategies, anxiety and depression in caregivers of people with Alzheimer’s disease. International Journal of Geriatric Psychiatry 23: 929–936. https://doi.org/10.1002/gps.2007 PMID: 18383189

53. 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

54. del-Pino-Casado R, Serrano-Ortega N, Lopez-Martinez C, Orgeta V (2019) Coping strategies and psychological distress in family carers of frail older people: A longitudinal study. J Affect Disord 256: 517–523. https://doi.org/10.1016/j.jad.2019.06.038 PMID: 31280075

55. Dikeç G, Ergün G, Gumus F (2018) Relation Among Anxiety and Family Burden in Primary First-Degree Caregivers of Outpatients with Mental Disorders in Turkey. Issues in Mental Health Nursing 39: 142–150. https://doi.org/10.1080/01612840.2017.1373174 PMID: 29193998

56. 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/psyg.12241 PMID: 28130857

57. Efi P, Fani K, Eleni T, Stylianos K, Vassilios K, Konstantinos B, et al. (2017) Quality of Life and Psychological Distress of Caregivers’ of Stroke People. Acta Neurol Taiwan 26: 154–166. PMID: 30335561

58. Fu Y, Yue P, Liu Q-S (2007) Burdens of spouse caregivers of patients with dementia at home. Chinese Mental Health Journal 21: 267–270.

59. Galindo Vázquez O, Meneses García A, Herrera Gómez A, Caballero Tinoco MdR, Aguilar Ponce JL (2015) Escala hospitalaria de ansiedad y depresión (HADS) en cuidadores primarios informales de pacientes con cáncer: propiedades psicométricas [Hospital anxiety and depression scale (HADS) in hospitalised caregivers: psychometric properties]. Radiotherapy. Asia Pac J Oncol Nurs 6: 283–291. https://doi.org/10.4103/apjon.apjon_74_18 PMID: 31259225
informal primary Caregivers of cancer patients: psychometric properties]. Psicooncologia 12: 383–392.

60. Garand L, Dew MA, Eazor LR, DeKosky ST, Reynolds CF (2005) Caregiving burden and psychiatric morbidity in spouses of persons with mild cognitive impairment. International Journal of Geriatric Psychiatry 20: 512–522. https://doi.org/10.1002/gps.1318 PMID: 15920711

61. Goetzinger AM, Blumenthal JA, O’Hayer CV, Babyak MA, Hoffman BM, Ong L, et al. (2012) Stress and coping in caregivers of patients awaiting solid organ transplantation. Clinical Transplantation 26: 97–104. https://doi.org/10.1111/j.1399-0012.2011.01431.x PMID: 21395692

62. González-Aburales I, Millan-Calenti JC, Lorenzo-Lopez 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

63. Govina O, Kotronoulas G, Mystakidou K, Katzaragakis S, Vlachou E, Patiraki E (2015) Effects of patient and personal demographic, clinical and psychosocial characteristics on the burden of family members caring for patients with advanced cancer in Greece. Eur J Oncol Nurs 19: 81–88. https://doi.org/10.1016/j.ejogn.2014.06.009 PMID: 25442373

64. Guedes AC, Pereira MG (2013) Burden, coping, physical symptoms and psychological morbidity in caregivers of functionally dependent family members. Rev Lat Am Enfermagem 21: 935–940. https://doi.org/10.1590/S0104-11692012000400015 PMID: 23970231

65. Iavarone A, Ziello AR, Pastore F, Fasanaro AM, Poderico C (2014) Caregiver burden and coping strategies in caregivers of patients with Alzheimer’s disease. Neuropsychiatr Dis Treat 10: 1407–1413. https://doi.org/10.2147/NDT.S58063 PMID: 25114532

66. Jaracz K, Grabowska-Fudala B, Gornk K, Kozubski W (2014) Caregiving burden and its determinants in Polish caregivers of stroke survivors. Arch Med Sci 10: 941–950. https://doi.org/10.5114/aoms.2014.46214 PMID: 25395945

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

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. Kemp E, Prior K, Beatty L, Lambert SD, Brown C, Koczwara B (2018) Relationships between supportive care needs and perceived burden in breast cancer survivor-caregiver dyads. European Journal of Cancer Care 27: 1–12. https://doi.org/10.1111/ecc.12875 PMID: 30015995

70. Lee E, Lum CM, Xiang YT, Ungvari GS, Tang WK (2010) Psychosocial condition of family caregivers of patients with chronic obstructive pulmonary disease in Hong Kong. East Asian Arch Psychiatry 20: 180–185. PMID: 22348927

71. Leibach GG, Trapp SK, Perrin PB, Everhart RS, Cabrera TV, Jimenez-Maldonado M, et al. (2014) Family needs and TBI caregiver mental health in Guadalajara, Mexico. NeuroRehabilitation 34: 167–175. https://doi.org/10.3233/NRE-131013 PMID: 24284459

72. 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. Archives of Gerontology and Geriatrics 55: 560–563. https://doi.org/10.1016/j.archger.2012.05.014 PMID: 22749403

73. López Alonso SR, Moral Serrano MS (2005) Validación del Índice de Esfuerzo del Cuidador en la población española [Validation of the Caregiver Strain Index in a Spanish population]. Enfermería Comunitaria 1: 12–17.

74. López-Martínez C (2019) Sentido de coherencia, sobrecarga subjetiva, ansiedad y síntomas depresivos en personas cuidadoras de familiares mayores dependientes [PhD]. Jaén: Universidad de Jaén.

75. Macías-Delgado Y, Pedraza-Núñez H, Jiménez-Morales R, Pérez-Rodríguez M, Valle-Solano RDiC, Fundara-Díaz R (2014) Sobrecarga en los cuidadores primarios de pacientes con esclerosis múltiple: Su relación con la depresión y ansiedad [Burden in primary caregivers of patients with multiple sclerosis: Their relationship with depression and anxiety]. Rev Mex Neuroci 15: 81–86.

76. Majestic C, Eddington KM (2019) The impact of goal adjustment and caregiver burden on psychological distress among caregivers of cancer patients. Psychooncology 28: 1283–1300. https://doi.org/10.1002/pon.5081 PMID: 30946499

77. Manso Martínez ME, Sánchez López MdP, Cuellar Flores I (2013) Salud y sobrecarga percibida en personas cuidadoras familiares de una zona rural [Health and perceived overload in people involved in family care in a rural area]. Clínica y Salud 24: 37–45.
78. Marvardi M, Mattioli P, Spazzafumo L, Mastriforti R, Rinaldi P, Poldori MC, et al. (2005) The Caregiver Burden Inventory in evaluating the burden of caregivers of elderly demented patients: results from a multicenter study. Aging Clinical and Experimental Research 17: 46–53. https://doi.org/10.1007/BF03337720 PMID: 15847122

79. 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. https://doi.org/10.1161/01.STR.000018755.23914.53 PMID: 16151029

80. Medrano M, Rosario RL, Payano AN, Capellán NR (2014) Burden, anxiety, and depression in caregivers of Alzheimer patients in the Republic of Mexico. Dementia & Neuropsychologia 8: 384–388. https://doi.org/10.1590/S1980-57642014DN84000013 PMID: 29213930

81. Mei Y, Wilson S, Lin B, Li Y, Zhang Z (2018) Benefit finding for Chinese family caregivers of community-dwelling stroke survivors: A cross-sectional study. J Clin Nurs 27: e1419–e1428. https://doi.org/10.1111/jocn.14249 PMID: 29288499

82. Méndez L, Giraldo O, Aguirre-Acevedo D, Lopera F (2010) Relación entre ansiedad, depresión, estrés y sobrecarga en cuidadores familiares de personas con demencia tipo alzheimer por mutación e280a en presenilina 1 [Relation among anxiety, depression, stress and overload on relative caregivers of patients with Alzheimer’s dementia by mutation e280a in presenilin]. Revista Chilena de Neuropsicología 5: 137–145.

83. Molina Linde JM, Iañez Velasco MA (2006) Cuidadores informales de enfermos de Alzheimer: factores influyentes en la sobrecarga. Anales de Psiquiatría 22: 234–242.

84. Morlett Paredes A (2014) The influence of dementia caregiver mental health on quality of care in Argentina [MSc]. Richmond, Virginia: Virginia Commonwealth University.

85. Özyesil Z, Oluik A, Çakmak D (2014) Yaşlı hastalara bakım verme yükünün durumluksürekli kaygıyı yordama düzeyi [The level of predicting anxiety-state anxiety of the burden of care for elderly patients]. Anatolian Journal of Psychiatry/Anadolu Psikiyatri Dergisi 15: 39–44.

86. Pagnini F, Rossi G, Lunetta C, Banfi P, Castelnuovo G, Corbo M, et al. (2010) Burden, depression, and anxiety in caregivers of people with amyotrophic lateral sclerosis. Psychol Health Med 15: 685–693. https://doi.org/10.1080/13548506.2010.507773 PMID: 21154021

87. Palacio C, Krikorian A, Limonero JT (2018) The influence of psychological factors on the burden of caregivers of patients with advanced cancer: Resiliency and caregiver burden. Palliat Support Care 16: 269–277. https://doi.org/10.1017/S1478951517000268 PMID: 28464972

88. Perez-Cruz M, Parra-Anguita L, Lopez-Martinez C, Moreno-Camara S, del-Pino-Casado R (2019) Coping and Anxiety in Caregivers of Dependent Older Relatives. Int J Environ Res Public Health 16: 1565. https://doi.org/10.3390/ijerph16091651 PMID: 31083624

89. Perpiñá-Galvan J, Orts-Beneito N, Fernandez-Alcantara M, Garcia-Sanjuan S, Garcia-Caro MP, Cabanero-Martinez MJ (2019) Level of Burden and Health-Related Quality of Life in Caregivers of Palliative Care Patients. Int J Environ Res Public Health 16. https://doi.org/10.3390/ijerph16234806 PMID: 31795461

90. Raveis VH, Karus D, Pretter S (2000) Correlates of anxiety among adult daughter caregivers to a parent with cancer. Journal of Psychosocial Oncology 17: 1–26.

91. Razani J, Corona R, Quillici J, Matevosyan AA, Funes C, Larco A, et al. (2014) The Effects of Declining Functional Abilities in Dementia Patients and Increases Psychological Distress on Caregiver Burden Over a One-Year Period. Clin Gerontol 37: 235–252. https://doi.org/10.1080/07317115.2014.885920 PMID: 24839349

92. 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. https://doi.org/10.1080/13607863.2010.505231 PMID: 20924819

93. Sadak T, Korpak A, Wright JD, Lee MK, Noel M, Buckwalter K, et al. (2017) Psychometric Evaluation of Kingston Caregiver Stress Scale. Clinical Gerontologist 40: 268–280. https://doi.org/10.1080/07317115.2017.1313349 PMID: 28459351

94. Sanyal J, Das S, Ghosh E, Banerjee TK, Bhaskar LV, Rao VR (2015) Burden among Parkinson’s disease care givers for a community based study from India. J Neurol Sci 358: 276–281. https://doi.org/10.1016/j.jns.2015.09.009 PMID: 26382831

95. Shukri M, Mustofai MA, Md Yasin MAS, Tuan Hadi TS (2020) Burden, quality of life, anxiety, and depressive symptoms among caregivers of hemodialysis patients: The role of social support. Int J Psychiatry Med: 91217420913388. https://doi.org/10.1177/0091217420913388 PMID: 32216495

96. Stanley S, Balakrishnan S, Ilangovan S (2017) Psychological distress, perceived burden and quality of life in caregivers of persons with schizophrenia. J Ment Health 26: 134–141. https://doi.org/10.1080/09638237.2016.1276537 PMID: 28385096
97. Stevens LF, Perrin PB, Guin S, Rogers HL, Villasenor Cabrera T, Jimenez-Maldonado M, et al. (2013) Examining the influence of three types of social support on the mental health of Mexican caregivers of individuals with traumatic brain injury. Am J Phys Med Rehabil 92: 959–967. https://doi.org/10.1097/PHM.0b013e31828cd549 PMID: 23552337

98. Tang WK, Lau CG, Mok V, Ungvari GS, Wong KS (2011) Burden of Chinese stroke family caregivers: the Hong Kong experience. Arch Phys Med Rehabil 92: 1462–1467. https://doi.org/10.1016/j.apmr.2011.03.027 PMID: 21678218

99. Torny F, Videaud H, Chatainer P, Tarrade C, Meissner WG, Couratier P (2018) Factors associated with spousal burden in Parkinson’s disease. Rev Neurol (Paris) 174: 711–715. https://doi.org/10.1016/j.neuro.2018.01.372 PMID: 30032927

100. Trapp SK, Leibach GG, Perrin PB, Morlett A, Olivera SL, Perdomo JL, et al. (2015) Spinal cord injury functional impairment and caregiver mental health in a Colombian sample: an exploratory study. Psicologia desde el Caribe 32: 380–392.

101. Tremont G, Davis JD, Bishop DS (2006) Unique contribution of family functioning in caregivers of patients with mild to moderate dementia. Dement Geriatr Cogn Disord 21: 170–174. https://doi.org/10.1159/000090699 PMID: 16397397

102. Truzzi A, Souza W, Bucasio E, Berger W, Figueira I, Engelhardt E, et al. (2008) Burnout in a sample of Alzheimer’s disease caregivers in Brazil. The European Journal of Psychiatry 22: 151–160. https://doi.org/10.4321/S0213-61632008000300004

103. Tsatali M, Egkiazarova M, Troupaidou M, Karagioukis K, Margaridou P, Tsolak M (2019) Greek Adaptation of the Positive Aspects of Caregiving (PAC) Scale in Dementia Caregivers. Clin Gerontol: 1–10. https://doi.org/10.1080/07317115.2019.1685047 PMID: 31684839

104. Vérez Cotelo N, Andrés Rodríguez NF, Fornós Perez JA, Andrés Iglesias JC, Rios Lago M (2015) Burden and associated pathologies in family caregivers of Alzheimer’s disease patients in Spain. Pharm Pract (Granada) 13: 521.

105. 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. https://doi.org/10.1037//0882-7974.6.3.392 PMID: 18978599

106. Wang G, Cheng Q, Wang Y, Deng YL, Ren RJ, Xu W, et al. (2008) The metric properties of Zarit caregiver burden scale: validation study of a Chinese version. Alzheimer Dis Assoc Disord 22: 321–326. https://doi.org/10.1097/WAD.0b013e3181902334 PMID: 18978599

107. Winslow BW (1997) Effects of formal supports on stress outcomes in family caregivers of Alzheimer’s patients. Research in Nursing and Health 20: 27–37. PMID: 9024475

108. Yu Y, Liu ZW, Zhou W, Chen XC, Zhang XY, Hu M, et al. (2018) Assessment of Burden Among Family Caregivers of Schizophrenia: Psychometric Testing for Short-Form Zarit Burden Interviews. Front Psychol 9: 2539. https://doi.org/10.3389/fpsyg.2018.02539 PMID: 30618690

109. Zawadzki L, Mondon K, Peru N, Hommet C, Constan T, Caillard P, et al. (2011) Attitudes towards Alzheimer’s disease as a risk factor for caregiver burden. International Psychogeriatrics 23: 1451–1461. https://doi.org/10.1017/S1041610211000640 PMID: 21554792

110. Zhu W, Jiang Y (2018) Determinants of caregiver burden of patients with haemorrhagic stroke in China. Int J Nurs Pract: e12719. https://doi.org/10.1111/inj.12719 PMID: 30561838

111. Stevens LF, Perrin PB, Guin S, Rogers HL, Villasenor Cabrera T, Jimenez-Maldonado M, et al. (2013) Examining the Influence of Three Types of Social Support on the Mental Health of Mexican Caregivers of Individuals with Traumatic Brain Injury. Am J Phys Med Rehabil. https://doi.org/10.1097/PHM.0b013e31828cd549 PMID: 23552337

112. del-Pino-Casado R, Rodriguez Cardosa M, Lopez-Martinez C, Ortega V (2019) The association between subjective caregiver burden and depressive symptoms in carers of older relatives: A systematic review and meta-analysis. PLoS One 14: e0217648. https://doi.org/10.1371/journal.pone.0217648 PMID: 3114556

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

114. Kishita N, Hammond L, Dietrich CM, Mioshi E (2018) Which interventions work for dementia family carers?: an updated systematic review of randomized controlled trials of carer interventions. Int Psychogeriatr 30: 1679–1696. https://doi.org/10.1017/S1041610218000947 PMID: 30017008

115. Vandepitte S, Van Den Noortgate N, Putman K, Verhaeghe S, Verdonck C, Annemans L (2016) Effectiveness of respite care in supporting informal caregivers of persons with dementia: a systematic review. Int J Geriatr Psychiatry 31: 1277–1288. https://doi.org/10.1002/gps.4504 PMID: 27245986
116. Emdin CA, Odutayo A, Wong CX, Tran J, Hsiao AJ, Hunn BH (2016) Meta-Analysis of Anxiety as a Risk Factor for Cardiovascular Disease. Am J Cardiol 118: 511–519. https://doi.org/10.1016/j.amjcard.2016.05.041 PMID: 27324160

117. Pinquart M, Sorensen S (2011) Spouses, adult children, and children-in-law as caregivers of older adults: A meta-analytic comparison. Psychology and Aging 26: 1–14. https://doi.org/10.1037/a0021863 PMID: 21417538

118. Broese van Groenou MI, Boer A, Iedema J (2013) Positive and negative evaluation of caregiving among three different types of informal care relationships. European Journal of Ageing 10: 301–311. https://doi.org/10.1007/s10433-013-0276-6 PMID: 28804305