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Non-pharmacological interventions for caregivers with depression and caregivers of care recipients with co-morbid depression: Systematic review and meta-analysis

A systematic review of non-pharmacological intervention for caregivers with depression

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Non-pharmacological interventions for caregivers with depression and caregivers of care recipients with co-morbid depression: Systematic review and meta- analysis

Background

Caregivers experiencing depression or caring for people experiencing depression are at risk of high burden. This systematic review examined the effect of non-pharmacological interventions for caregivers that a) target improving caregivers' depressive symptoms, b) help caregivers manage the depressive symptoms of the person for whom they provide care, or c) both (a) and (b).

Methods

Eligible trials published between January 1st, 1985 and May 30th, 2019 were retrieved from five electronic databases. Studies' methodological quality was assessed against 15 criteria. Pooled effect sizes (ESs) were calculated, and heterogeneity assessed using the Higgin's I² statistic. Meta-regressions were also conducted to identify significant moderators (participant sub-group analysis) and mediators (identify how the interventions worked).

Results

Sixteen studies evaluating 18 interventions were included for review. These studies included a total of 2178 participants (mean=94, SD=129.18, range 25-518). The most common condition (n = 10/16) of the care recipient was dementia. The average methodological score was in the moderate range ((8.76/15)). Interventions had a moderate effect on caregivers' depression in the short-term (ES = -0.62, CI -0.81, -0.44), but the effect dissipated over time (ES = -0.19; CI -0.29, -0.09). A similar pattern was noted for anxiety. The moderator analysis was not significant, and of the mediators examined significant ones were self-management skills of taking action, problem solving, and decision making.

Discussion

Non-pharmacological interventions are associated with improvement of depression and anxiety in caregivers, particularly in the short-term. The main recommendation for future interventions is to include self-management skills taking action, problem-solving, and decision-making. Enhancing the effect of these interventions will need to be the focus of future studies, particularly examining the impact of booster sessions. More research is needed on non-dementia caregiving and dyadic approaches.

Background

Approximately 50 million caregivers in North America provide care to a family member or friend for issues related to chronic illness, disability, or aging (1, 2). The annual economic value of caregivers' unpaid care (on average 10-30 hours per week (3-5)) is estimated to be \$450 billion in the United States and at least \$26 billion in Canada (6, 7). With the confluence of increasing life expectancy, an aging population, and increasing prevalence of chronic illness, the need for caregivers continues to grow (4) and supporting caregivers in maintaining their critical roles is imperative.

Although caregivers may feel rewarded by the experience (3, 7), they nonetheless develop psychological or mental health symptoms from the challenges and additional roles imposed on them (4, 8, 9). It is estimated that between 30% and 70% of caregivers experience clinically significant symptoms of depression and approximately 10-25% meet the diagnostic criteria of major depression (4, 8-10). The impact of depression is significant and is associated with reduced physical health, psychiatric morbidity, and reduced quality of life, which all may lead to lower quality of caregiving (11, 12).

Caregivers caring for someone experiencing depressive symptoms are a particularly vulnerable sub-group, reporting increased time spent caregiving, increased caregiver burden, and worse caregiver mental health symptoms (potentially persisting for years) as compared to those caring for someone who is not depressed (13-17). This is in line with studies demonstrating a bidirectional relationship between care recipients' and caregivers' depression; those caring for someone who is depressed are more likely to be depressed themselves, and vice versa (18, 19). Therefore, interventions are not only needed to help caregivers manage their own depression, but also to support them in managing the care recipient's depressive symptoms. The aim of this

systematic review was to examine the effect of non-pharmacological interventions for caregivers that a) target improving caregivers' depressive symptoms, b) help caregivers manage the depressive symptoms of the person for whom they provide care, or c) both a) and b).

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) was followed (20) and the review was prospectively registered (PROSPERO registration number: CRD42018100397).

Criteria for considering studies

Types of studies

Eligible studies were published (or in-press) randomized controlled trials (RCTs) or quasi-experimental trials published between January 1st 1985 and May 30th 2019 where a group of adult caregivers received an intervention designed to help them manage their own depressive symptoms and/or the depressive symptoms of the adult for whom they provide care. Eligible studies had to report comparative data to evaluate the difference(s) between the control and intervention groups; however, all types of control groups were eligible, including usual care. *Types of participants*

Caregivers were defined as a family member, spouse, adult child, friend, or any other significant person involved in providing unpaid assistance to an individual requiring care. Care recipients were anyone needing assistance from a caregiver due to aging or a chronic, physical condition or neurocognitive disorder and reporting co-morbid mild depressive symptoms. Care recipients with a mental illness (e.g., schizophrenia) or advanced or palliative disease were excluded as the needs of these groups differ and in the case of advanced disease grief and bereavement play a role (21-23).

To be included the caregiver and/or the care recipient had to report at least mild depressive symptoms at baseline according to the following instruments (sample mean rounded to the nearest integer):

- Beck Depression Inventory (scores ≥ 10) (24)
- Beck Depression Inventory-II (scores \geq 13) (25)
- Centre for Epidemiological Studies Depression 20 items (scores \geq 16) (26, 27)
- Centre for Epidemiological Studies Depression 10 items (scores \geq 10) (28)
- Hamilton Depression Rating Scale Depression subscale (scores ≥ 8) (29)
- Hospital Anxiety and Depression Scale Depression (scores ≥ 8) (30)
- Patient Health Questionnaire (scores \geq 5) (31)
- Geriatric Depression Scale (scores ≥ 11) (32)

If an instrument measuring a similar concept, such as burden or distress, was used for screening potential participants, the study was included if the sample mean baseline depressive symptoms was measured and met the threshold for mild depressive symptomatology.

Types of interventions

Non-pharmacological interventions that employed cognitive, physical, emotional, and/or social strategies to reduce depressive symptoms were eligible. The intervention could be administered to the caregiver alone or to the care recipient-caregiver dyad, as long as the focus remained on the caregiver. Interventions including a pharmacological component were excluded; however, if the participants received medication as part of usual care (either intervention or control group) the study was not excluded.

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Types of outcomes

The primary outcome was caregivers' depressive symptoms. Secondary outcomes were not determined a priori and all outcomes reported in at least three studies were considered.

Search methods

The development of the search strategies was in consultation with an academic librarian. Eligible studies were first identified through a comprehensive electronic search of MEDLINE, EMBASE, PsycINFO, the Cumulative Index to Nursing & Allied Health Literature (CINAHL), and the Cochrane Library. Only French or English studies published since 1985 were selected. The search strategy used a combination of keywords and medical subject heading terms targeting: a) *caregiver* (e.g., caregiver(s), carer, caretaker(s), friend(s); b) *depression* (e.g., depression, depressive disorder); c) *interventions* (e.g., exercise, exercise therapy, self-help, counseling, psychological); and d) *study design* (e.g., control groups, experimental design). The complete search for one database is included in Appendix A. Retrieved studies were downloaded to EndNote. Secondary search strategies included: a) verifying the reference lists of relevant reviews and manuscripts retrieved; b) contacting researchers who conduct work in this area; c) using the *'find similar'* function in PubMed; and d) manually searching relevant journals.

Data collection

Selection of studies

The original search was run in February 2017, and two trained research assistants (RAs) and selected authors assessed the eligibility of retrieved titles and abstracts. Full-texts of eligible citations were then obtained, and their reference lists were examined to identify additional

studies. The inclusion/exclusion of full-texts was confirmed by two authors, and discrepancies were discussed at regular team meetings to reach a consensus. The search was updated in May 2019 (see Figure 1), where one RA screened titles and abstracts and an additional RA confirmed the eligibility of the full-texts identified.

Data extraction

Data were extracted using a standardized Excel form based on the Cochrane Handbook for Systematic Reviews of Interventions (33), previously used by the team (34-36), and piloted on the first three studies. For the remaining studies, data were extracted by one trained RA and verified by at least one other author. If some of the data were unclear, the authors of the original studies were contacted. Discrepancies were discussed and resolved at team meetings.

Data items and coding

The data extraction form documented: a) reviewers' names; b) authors and year; c) country; d) study design; e) type of control group; f) aim(s); g) theoretical framework; h) population (age, sex, depression level, relationship, sample size); i) confirmation of eligibility; j) unit of allocation (caregiver versus care recipient-caregiver dyad); k) setting, l) sample size; m) summary of the intervention and control groups; n) intervention content; o) delivery format (e.g., face-to-face, self-directed); p) mode of delivery (e.g., face-to-face, self-directed); q) provider, r) intensity of the intervention a (37); s) fidelity; t) uptake rate, u) primary and secondary outcomes; v) timing of measurement; and w) effect. If authors used more than one instrument to measure the same outcome, extracted data reported the outcome most often used across studies. If studies had more than one experimental arm, only those arms that met the inclusion criteria were included. The outcome data were categorized into three timeframes: T1 – baseline to \leq 3 months post-baseline, T2 – > 3 post-baseline to \leq 12 months, and T3 – \geq 12 months post-baseline. If two data outcome points within the same timeframe were reported, the data closest to the mid-point of the timeframe was used.

In addition, 13 depression self-management skills were extracted from the included interventions: a) decision-making, b) problem-solving, c) resource utilization, d) partnership with healthcare professional, e) taking action, f) behavioural activation, g) cognitive restructuring, h) self-monitoring, i) health habits, j) communicating about depression, k) social support, l) relaxation activity, and m) self-tailoring (see supplementary materials Appendix B) (38-44). Interventions are often not labelled as self-management but included many of the key self-management skills shown to be effective in reducing depressive symptoms. Self-management is a recommended treatment for adults with mild to moderate depressive symptoms and as an adjunct to more intensive treatments for adults experiencing severe depressive symptoms (45). *Quality assessment*

The methodological quality of studies was assessed by two trained RAs using a combination of criteria from the Cochrane Collaboration's Risk of Bias tool (33) and CONSORT statement (46), and included: a) trial design, b) inclusion criteria specified, c) pre-specified primary and secondary outcomes, d) psychometric properties of instruments provided, e) power calculation explicit, f) target sample size reached, g) randomization method specified and truly random, h) randomization allocation concealed, i) outcome assessors blind to treatment allocation, j) participants blind to treatment allocation, k) interventionists blind to treatment allocation, l) participant flow described, m) intention-to-treat analysis used, n) > 80% of sample in final analysis, and o) reasons for withdrawal and/or attrition stated. Each item was scored as either positive (1) or negative (0). A total out of 15 was calculated for each study. Studies were considered to be of high methodological quality if at least 12 of criteria were met, moderate

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quality if 7-11 of the criteria were met, and low if less than 7 criteria were met (47). If information was not reported or was ambiguous, attempts were made to the contact the authors for clarification.

Data Analysis

A meta-analysis was performed by calculating a pooled Cohen's d as well as a Cohen's d for the outcomes at each time point. Cohen's d is defined as the mean difference between the intervention and the control group divided by the pooled standard deviation (Cohen, 1988). If a study utilized both intention-to-treat and per protocol analyses, the data from the per protocol analysis was included in the meta-analysis. If a manuscript did not include all the data needed for the meta-analysis, attempts were made to contact the authors.

Heterogeneity was assessed using the Higgin's I^2 statistic, a measure of inconsistency that describes the percentage of variation between studies above that expected by chance alone (48). An I^2 of 0% reflects that all variability is consistent with sampling error rather than being due to true differences between studies. I^2 values of 25% are categorized as low, 50% as moderate, and 75% as high heterogeneity (48). Fixed-effect models were conducted for I^2 values lower than 25% and random-effect models were conducted for I^2 values higher than 25% (33).

The significance level for all statistical tests was set at p < 0.05 and all tests were twosided. STATA (version 15.1) was used to perform the analyses. Effect sizes (ESs) for the outcomes are reported in forest plots for each time point (T1 –T3). If insufficient data were reported for inclusion in the meta-analysis, the manuscript was considered for descriptive review only. Egger's test and funnel plots were computed for the primary outcome based on the first (T1) and second time (T2) point to examine potential publication bias.

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The extent to which the pooled ESs for the primary outcome varied according to the following participant (moderators) and intervention characteristics (mediators) were examined using meta-regression (49): condition for which the care recipient required support, caregiver or dyad participated in the intervention, mode of delivery, intervention provider, individual or group intervention, total duration of the intervention, whether the intervention was tailored, and type and number self-management skills included. To be included in the meta-regressions characteristics needed to be included in at least 4 studies for each level of the variable (50). A *p* value < 0.05 was established to identify significant mediators.

Results

Study selection

See Figure 1 for details of the search strategy and reasons for exclusion. A total of 16 full-texts were included in this review, 15 had sufficient data to be included in the meta-analysis and the remaining one is reported descriptively only (51).

Description of studies

The 16 studies are described in Table 1. Most studies were conducted in the United States (n = 9) with remaining studies from Europe (n = 4), China (n = 2) or Hong Kong (n=1). Most (n = 14) studies were two-group RCTs.

Author, Year, Country, QSA (/15)	Aim(s)	Caregiver Demographics	Care Recipient Demographics	Intervention conditions and assessments	Outcome(s) [Primary (P), Secondary (S), Unspecified (O)]
			Caregiver Depresse	ed	
		Info provided separated by race or	Alzheimer's or related		
		ethnicity	disorder		
		Hispanic or Latino (n=168)			
		Treatment group (n=82)	Hispanic or Latino		
		Mean age: 59.7 (SD=14.3)	<u>(n=168)</u>		
		% women: 80.5	Treatment group		
		% spouse: 43.9	(n=82)		
		Depression (CESD-10): 10.9	Mean age: 77.9		
		(SD=7.2)	(SD=9.3)		
		Control group (n=86)	% women: 65.9		
		Mean age: 59 (SD=13.6)	Control group (n=86)	1: Intervention tailored to caregiver risk profiles. 12	
		% women: 83.7	Mean age: 77.6	individual sessions [9 in nome (1.5nrs each) + 5 phone $(20 - 1)$] + 5	
D-114 -1		% spouse: 39.5	(SD=9.9)	sessions (30 min each)] + 5 group telephone support sessions	
Belle et al., 2006	To evaluate effect	Mean baseline depression score	% women: 64	(median 3.5 nrs each). Strategies included providing into,	P: T2=C for
2006	of a multicomponent	(CESD-10): 10.4 (SD=7.3)		didactic instruction, role playing, problem solving, skills	
			White or Caucasian	training, and stress management.	
USA	intervention for	White or Caucasian (n=182)	<u>(n=182)</u>	C: Caregivers matted education materials $+$ two <15 min	depression
	caregivers to	Treatment group (n=96)	Treatment group	prone carls at 5- and 5- months.	-
RCT(2)	reduce depression	Mean age: 63.5 (SD=11.7)	(n=96)	Format: Individual and group. Face-to-face and telephone	
groups)	and increase	% women: 80.2	Mean age: 77.5	contact.	
054.11	quality of life.	% spouse: 59.4	(SD=8.8)	Accuracy description of the second se	
QSA :11		Depression (CESD-10): 9.5 (SD=5.5)	% women: 45.8	acgree.	
		Control group (n=86)	Control group (n=86)	Intervention dynation: 6 months	
		Mean age: 63.2 (SD=12.8)	Mean age: 78.6	Timing of manufactures, 6 months next heading	
		% women: 81.4	(SD=9.3)	i ming of measures: o-months post-baseline.	
		% spouse: 54.7	% women: 54.7		
		Mean baseline depression score			
		(CESD-10): 10.6 (SD=6.6)	Black or African		
			American (n=168)		
		Black or African American (n=168)	Treatment group		
		Treatment group (n=83)	(n=83)		
		Mean age: 60.9 (SD=12.9)	Mean age: 80.8		
		% women: 84.3	(SD=8.6)		
		% spouse: 31.3	% women: 68.7		

Table 1. Descriptive summary of included studies (N=16) (N=16)

		Mean baseline depression score (CESD-10): 9.3 (SD=6.2) Control group (n=85) Mean age: 57.1 (SD=12.8) % women: 88.2 % spouse: 28.2 Mean baseline depression score (CESD-10): 8.9 (SD=6.0)	Control group (n=85) Mean age: 80 (SD=8.5) % women: 61.2		
Blom et al., 2015 The Netherland s RCT (2 groups) QSA:12	To evaluate the effect of an Internet self-help course "Mastery over Dementia" (MoD) designed to reduce caregiver depression and anxiety.	N=251 (T=151, C=100) Mean age: T = 61.54 (SD = 11.93), C = 60.77 (SD = 13.07) % women: T = 69.8, C = 68.8 % spouse: T = 59.7, C = 56.3 Mean baseline depression score (CES-D 20 item): T=17.89 (SD=9.14), C= 16.61 (SD=9.68)	Dementia N = 245 (T = 149, C = 96) Mean age: T = 76.36 (SD = 9.45), C = 75.2 (SD = 9.32) % women: T = 61.1, C = 59.4	T: Internet course with 8 lessons, 1 booster session and coach guidance and monitoring. Covered coping with behavioural problems, relaxation, arranging help, cognitive restructuring and assertiveness training. C: E-bulletins with practical information for dementia caregivers. Format: Individual. Provider: Guidance from coach (psychologist with training in CBT and experience in field of dementia) through electronic feedback. Total length of intervention: n/a Intervention duration: 5 to 6-months. Timing of measures: Brief assessment after 4 th MoD lesson or e-bulletin (data not available) and 5-6 months post- baseline.	P : T2=C for depression S : T2=C for anxiety
Gallagher- Thompson et al., 2015 USA RCT (2 groups) QSA :7	To evaluate the effect of a Fotonovela which illustrates strategies to cope with stress and caregiving.	N = 110 (T = 55, C = 55) Mean age: T = 53.6 (SD = 10.76), C = 56.18 (SD = 11.18) % women: T = 85.5, C = 78.2 % spouse: T = 10.9, C = 10.9 Mean baseline depression scores (CES-D 20-item) : T=19.66 (SD=11.85), C=16.81 (SD=13.74)	Dementia or serious memory problems N = 110 (T = 55, C = 55) Mean age : T = 80.93 (SD = 9.16), C = 82.91 (SD = 8.15)	 T: 16-page Fotonovela picture book illustrating ways to cope with difficult behaviour, manage stress and ask for help from family members. Access to one group meeting in which caregiver problems were discussed and information provided (offered to T and C group participants). C: Usual information. Participants provided publicly available pamphlet about managing CG stress called: "Take Care of Yourself: 10 ways to be a healthier caregiver." Optional group meeting (same as T group). Format: Individual and self-directed (with one optional group meeting). Provider: Primarily self-directed with optional group meeting lead by research assistants. Total length of intervention: n/a Intervention duration: n/a Timing of measures: 4- and 6-months post-baseline. 	O : T2=C for depression

Hou et al., 2014 Hong Kong RCT (2 groups) QSA :12	To evaluate the feasibility and effect of a mindfulness- based stress reduction (MBSR) program to improve mental health among caregivers.	N = 141 (T = 70, C = 71) Mean age: T = 57.9 (SD = 8.49), C = 57.08 (SD = 9.21) % women: T = 86.7, C = 80.6 % spouse: T = 37.1, C = 43.7 Mean baseline depression scores (Chinese Center for Epidemiologic Studies Depression Scale -CES-D 20- item): T = 16.91 (SD=8.97), C= 17.55 (SD=8.92).	Chronic illness or chronic condition	 T: 8 weekly 2-hour session led by instructors and CD-guided daily home practice (instructed to do 30-45 min/day). Covered body scan, meditation, yoga, and mindfulness. C: Self-help book with supportive information and health education. Format: Group class and individual home practice. Provider: Instructors had completed professional training in MBSR and had 3-years teaching experience in MBSR. Total length of intervention: 3,060 minutes Intervention duration: 2-months. Timing of measures: 2- and 5-months post-baseline. 	P: T1>C for depression ($d=-$ 0.41) T2>C for depression ($d=-$ 0.36) S: T1>C for anxiety ($d=-$ 0.36) T2=C for anxiety
King et al., 2007 USA Single- group with historical matched control group. QSA:5	To examine the effect and durability of a caregiver problem-solving intervention on caregiver and stroke survivor outcomes.	N= (completers)=30 (T= 15, Historically matched control=15) Mean age: T = 62.3 (SD = 9.9), C = 62.7 (SD = 12.2) % women: T = 66.7, C = 60.0 % spouse: T = 93.3, C = 93.3 Mean baseline depression scores (CES-D 20-item): T= 19.3 (SD=8.2), C= 19.6 (SD=7.3)	Stroke N = 30 (T = 15, C = 15) Mean age: T = 66.2 (SD = 10.8), C = 64.3 (SD = 10.1) % women: T = 42.6, C = 38.7	 T = 10 guided sessions with manual (45-60 min each). Covered problem-solving skills, CBT-based strategies (e.g., relaxation and reframing negative thoughts), stress management, self-care, and behaviour management. C: 15 matched controls who participated in a descriptive study of stroke CGs and survivors. Matched on CES-D scores, gender, age, race, and caregiving relationship. Received usual care. Format: Individual. Introduction and first 2-3 sessions conducted face-to-face. Remaining 7-8 sessions conducted by telephone. Provider: Nurses. Total length of intervention: 525 minutes Intervention duration: 2- to 2.5-months. Timing of measures: 2- to 2.5-months and 4- to 4.5 months post-baseline. 	O : T1>C for depression (<i>d</i> =- 0.80)
King et al., 2012 USA RCT (2 groups) QSA :8	To evaluate a caregiver problem- solving intervention designed to reduce and prevent negative outcomes during the first caregiving year.	N = 255 (T = 136, C = 119) Mean age: T = 54.5 (SD = 15.1), C = 54.6 (SD = 13.3) % women: T = 76.5, C = 80.7 % spouse: T = 61.8, C = 63.9 Mean baseline depression scores (CES-D 20-item): T=23.4 (SD=9.43), C=22.64 (SD=9.68)	Stroke N = 248 (T = 136, C = 112) Mean age: T = 61.2 (SD = 14.6), C = 61.5 (SD = 14.7) % women: T = 42.6, C = 38.7	 T: Manual with 10 guided sessions (mean session duration 37 min). Covered stress management, problem-solving skills and coping with emotional responses. Participants identified caregiving problems and developed problem-solving strategies. C: Waitlist control with 2 well-being check-ins (2nd and 5th month). After 6-months, option to have five 30-min telephone sessions with supportive listening with no problem solving or information giving. Format: Individual. When possible first two session done face-to-face, others via telephone. 	O: T2=C for depression and anxiety T3=C for depression and anxiety

				 Provider: Nurse practitioner or advanced clinical psychology doctoral student. Total length of intervention: 370 minutes Intervention duration: 3- to 4-months. Timing of measures: 3- to 4- months, 6-months, and 12-months post-baseline. 	
Lavretsky et al., 2012 USA Pilot RCT (2 groups) QSA :11	To evaluate the effect of Kundalini yoga and Kirtan Kriya meditation compared to passive relaxation with instrumental music to improve mental health and depression scores	N = 39 (T = 23, C = 16) Mean age: T = 60.5 (SD = 28.2), C = 60.6 (SD = 12.5) % women: T = 100, C = 87 Mean baseline depression scores (HAM-D): T = 11.4 (SD=4.0), C = 11.9 (SD=4.1)	Dementia	 T: Daily yogic practice with ancient chanting meditation (Kirtan Kriya) for 8 weeks (12 min/day). Both T and C groups received psychoeducation about dementia and caregiver health. C: Daily relaxation with instrumental music for 8 weeks (12 min/day). Psychoeducation (see above). Format: Individual. One face-to-face baseline visit. Intervention self-directed. Provider: Self-directed. Total length of intervention: n/a Intervention duration: 2-months. Timing of measures: 2-months post-baseline or at early termination. 	P : T1=C
López et al., 2007 Spain RCT (3 groups) QSA :9	To compare the effect of two interventions [traditional weekly sessions (TT) and minimal therapist contact sessions (MTC)] to a waitlist control group in improving the emotional well- being of family caregivers.	Note: Demographic data only presented for full sample. N = 91 (T-MTC = 28, T-TT=24, C = 39) Mean age: 53.9 (SD=11.6) % women: 86.8 % spouse: 33.0 Mean baseline depression scores (BDI): T-MTC= 12.68 (SD=7.31), T- TT= 17.29 (SD=8.19), C= 14.23 (SD=8.76)	Physically impaired older adults Mean age: 77.3 (SD=8.4) % dementia: 80.2 % women: 69.2	 T-TT: Eight 60-min weekly counselling sessions focused on learning cognitive behavioural skills, diaphragmatic breathing, increasing pleasant activities, cognitive restructuring, problem-solving, and improving self-esteem. Included written material and homework. T-MTC: Three 90-minute sessions. Between sessions reading materials provided and three phone contacts. Same CBT skills and similar schedule as the TT with less therapist contact. C: Waitlist control. No information or therapist contact provided. Format: Individual face-to-face and reading materials. Provider: Therapist. Total length of intervention: 480 minutes (TT), 300 minutes (MCT) Intervention duration: 2-months Timing of measures: 2-months post-baseline. 	O: TT-T1>C for depression (<i>d</i> =- 1.13) and anxiety (<i>d</i> =-1.21) MTC-T1=C for depression• MTC-T1>C for anxiety•
Losada et al., 2012 Spain	To evaluate Cognitive- Behavioural Therapy (CBT) or Acceptance and	N = 135 (T-CBT = 42, T-ACT = 45, C = 48) Mean age: T-CBT = 61.48 (SD = 12.4), T-ACT = 61.69 (15.31), C =	Dementia	 T-CBT: 8 weekly sessions (about 90 minutes each). Cognitive restructuring, assertive skills/asking for help, relaxation and increasing pleasant activities. T-ACT: 8 weekly sessions (about 90 minutes each). Acceptance of aversive events and their causes, selecting 	P : CBT T1>C for depression (<i>d</i> =-0.96)

RCT (3 group) QSA:10	Commitment Therapy (ACT) to improve symptoms of depression and anxiety in dementia caregivers.	62.28 (SD = 12.92) % women: T-CBT = 90.5, T-ACT = 82.2, C = 81.02 % spouse: T-CBT = 31, T-ACT = 48.9, C = 41.7 Mean baseline depression scores (CES-D 20-item): T- CBT = 27.88 (SD=1.49), T- ACT=28.18 (SD=1.44) C= 28.10 (SD=1.39)		 courses of action consistent with personal values and acting upon those decisions. C: Minimal support 2-hour workshop with booklet and education about dementia. Format: Individual face-to-face. Provider: Clinical psychologists with master's or doctoral preparation also trained in CBT and ACT principles and techniques. Total length of intervention: 720 minutes (CBT), 720 minutes (ACT) Intervention duration: 2-months. Timing of measures: 2- and 8-months post-baseline. 	CBT T1=C for anxiety CBT T2>C for depression (<i>d</i> =- 0.77) CBT T2=C for anxiety ACT T1>C for depression and anxiety• ACT T2=C for depression and anxiety•
Nunez- Naveira et al., 2016 Denmark, Poland, and Spain Pilot RCT (2 groups) QSA:6	To evaluate the impact of the understAID intervention on the psychological well-being of caregivers, to assess caregiver satisfaction with the intervention, and to test the technical and pedagogical specifications of the intervention.	N = 77 (T=41, C=36) Mean age: Not specified. % women: T = 58.1, C = 70 % spouse: Not specified. Mean baseline depression scores (CES-D 20-item): T=19.4, SD=9.03, C= (21.42, SD=8.64)	Dementia	T: Internet application with 5 modules covering information about cognitive declines, daily tasks, behavioural changes, social activities and coping with stress. Daily task section to create a calendar schedule and a social network section allowing caregivers to interact with each other. C: Usual care. No access to the internet application. Format: Individual. Online. Provider: Self-directed. Social network section of intervention moderated by researchers. Total length of intervention: n/a Intervention duration: 3-months of self-directed use. Frequency and duration of use not specified. Timing of measures: 3-months post-baseline.	O : T1=C for depression
Pan & Chen, 2019 China	To explore the effect of a cognitive behavioral intervention on the depressive	N = 112 (T=56, C=56) Mean age: T= 63.3 (SD=11.2), C=62.1 (SD=10.6) % women: T=55.4, C= 69.6 % spouse: T=50.0, C=46.4	Alzheimer's disease, vascular dementia, or MMSE< 17) N = 112 (T=56, C=56)	T: Five month (60-minute) in-home cognitive behavioural sessions and telephone consultations (20 to 30-min) aimed at receiving participant feedback and reinforcing content after each session. Intervention included five modules all based on CBT principles.	O : T2>C for depression (<i>d</i> =- 0.48)

RCT (2	symptoms and	Mean baseline depression scores	Mean age: T=79.0	C: Five monthly (5- to 10-min) casual conversations about	
groups)	coping strategies	(CES-D 10-item): T= 13.9 (SD=3.5),	(SD=9.4), C= 80.0 (9.8)	daily life and health with nurses at home, in hospital, or by	
	of family	C=13.2 (SD=3.1)	% women : T=71.4,	telephone.	
QSA:11	caregivers of		C=55.4	Format: Individual, face-to-face, telephone.	
	people with			Provider: Nurses.	
	dementia.			Total length of intervention: 425 minutes	
				Intervention duration: 5-months.	
				The Delaying of measures: 5- and 7-months post-baseline.	
				1: Benavioural coaching with workbook with strategies to	
	To evaluate a			and behavioural activation. Included 10 videos (30 min	
Steffen et	telehealth	N = 74 (T = 33 C = 41)		each) 10 weekly phone calls (30-50 min each) and 2	
a1 2016	intervention for	Mean age: $All = 60.3$ (SD = 10.8)	Dementia or	maintenance calls from a coach	
di., 2010	emotionally	% women: $All = 100$	neurocognitive	C: Received a basic care guide on dementia and care	
USA	distressed women	% snouses: 52.2	disorder	challenges Caregivers received 7 bi-weekly phone calls (20	$\mathbf{P} \cdot \mathbf{T} = \mathbf{C}$ for
0.511	caregivers of	Mean baseline depressive	N = 74	min each) to check on safety, provided suggestions based on	depression and
RCT (2	people with	symptoms (BDI-II): T=13.1	Mean age: $All = 77.4$	guide, and answer questions.	anxiety
Groups)	progressive	(SD=8.0), C=17.0 (SD=8.8)	(SD = 9.4)	Format: Individual. Video, booklet, telephone.	2
1 /	neurocognitive		· · · ·	Provider: Doctoral level clinical psychologist and trained	
QSA:8	disorders.			master's level clinicians.	
-				Intervention duration: 3.5-months (14-weeks).	
				Timing of measures: 3.5-months (14-weeks) and 9.5-	
				months post-baseline.	
				T: 16 telephone calls (initial phone call ~60 min and follow-	
				up calls15- to 30 min) that covered dementia education,	
				emotional support, coping strategies, health habits,	
Tremont et	To evaluate the	N = 250 (T = 133, C = 117)	Dementia	psychoeducation to assist with problem solving. Termination	
al., 2015	effect of a	Mean age: $T = 63.32$ (SD = 12.3), C	N = 250 (T = 133, C =	letter and package of education materials provided.	
	telephone	= 62.03 (SD $= 13.75$)	117)	C: 16 telephone support calls with non-directive support	
USA	intervention to	% women: T = 80, C = 76	Mean age: T = 79.22	(mean duration 30.1 min). Package of educational materials	\mathbf{P} : T2=C for
$\mathbf{PCT}(2)$	depression and	% spouse: T = 51, C =51	(SD = 9.11), C = 76.74	provided.	depression
roups	burden in	Mean baseline depressive	(SD = 10.93)	via telephone with some written materials	
groups)	dementia	symptoms (CES-D 20-item):	% women: T = 55, C =	Provider . Master's level therapists with experience working	
OSA ·13	caregivers	T=17.04 (SD=11.7), C=17.7	57	with neonle with dementia and/or caregivers	
2011.12	cui ogi (ci b.	(SD=11.7)		Total length of intervention: 397.5 minutes	
				Intervention duration: 6-months.	
				Timing of measures: 6-months post-baseline.	

Yoo et al., 2019 South Korea RCT (2 groups) QSA :8	To evaluate the effect of a multicomponent therapeutic intervention program (I- CARE) on reducing burden in caregivers of people with dementia.	N = 38 (T=19, C=19) Mean age: T=65.9 (SD=13.4), C=63.3 (SD=13.3) % women: T=73.7, C=84.2 % spouse: T=78.9, C=57.9 Mean baseline depressive symptoms (GDS): T=13.8 (SD=6.0), C=13.4 (SD=8.7)	Dementia	 T: Four sessions (~60 min each). One group session on dementia education. Three individual sessions of individual counselling focused on CBT, stress, and coping. One session on daily activities. C: Waitlist control. Format: Group and individual face-to-face sessions. Provider: Physician & psychologist Total length of intervention: 240 minutes Intervention duration:.8- to 10-weeks (2- to 2.5-months) Timing of measures: 2- to 2.5-months post-baseline. 	P: T1=C for depression
			Care Recipient Depre	ssed	
Horton- Deutsch et al., 2002 USA Pilot quasi- experiment al (2 groups non- randomize d) QSA:5	To evaluate the feasibility of implementing a multicomponent intervention to support family caregivers of elderly persons with depression.	N = 25 (T = 12, C = 13) Mean age: T = 67.6 (SD = 9.28), C = 67.1 (SD = 14) % women: T = 83.3, C = 61.5 % spouse: T = 58, C = 62 Mean baseline depression scores (CES-D 20-item): Not specified.	Older adults with depression N = 25 (T = 12, C = 13) Mean age: $T = 80.9$ (SD = 7.79), C = 76.9 (SD = 6.5) % women: $T = 33.3$, C = 53.8 Mean baseline depression scores (GDS): Not specified.	 T: Expanded home care services. Average of 9 home visits (1h15 on average). In addition to standard home care, clinical profile and initial assessment, stressors and resources of the family were identified, and the Interpersonal Psychotherapy for Depression framework was used to work through problems. Caregiver and care recipient participate in the intervention. C: Individual standard home care (hours not specified). Format: Face-to-face. Provider: Nurse. Total length of intervention: 675 minutes Intervention duration: 2-months. Timing of measures: 2-months baseline. 	O : T1=C for depression °
		Cal	regiver or Care Recipient	Depressed	
Smith et al., 2012 USA RCT (2 groups) QSA:10	To evaluate the effect of a web- based psychoeducationa l intervention to support caregivers of stroke survivors with depression or reduce caregivers' depression.	N = 32 (T = 15, C =17) Mean age: T = 55.3 (SD = 6.9), C = 54.9 (SD = 12.9) % women: T = 100, C = 100 % spouse: T = 100, C = 100 Mean baseline depressive symptoms (CES-D 20-item): T=21.7 (SD=13.2), C=17.7 (SD=11.7)	Stroke N = 32 (T = 15, C = 17) Mean age: $T = 59.9$ (SD = 8.2), C = 59.1 (SD = 13.6) All male spouses Mean baseline depressive symptoms (CES-D 20-item): T=	 T: Internet course that covered topics regarding feelings, understanding what it is like to be a care recipient, listening, coping with stress, non-verbal behaviour. Care recipient involved in some homework assignments. C: Access to resource room only and weekly caregiver tip. No guide beyond initial explanation of resource room. Both T and C groups provided toll-free phone number in case technological problems were encountered or for medical emergency. Halfway through both conditions received a call from an RA to see if they had technical difficulties. 	P : T1>C for depression (<i>d</i> =- 0.82) T2=C for depression

	21.3 (SD=12.9), C=	Format: Online with emails and chat messages from
	19.3 (SD=13.4)	professional coach. Primarily individual with access to
		message boards and online chat.
		Provider: PhD student in Nursing.
		Total length of intervention: n/a
		Intervention duration: 2.75 months (11-weeks).
		Timing of measures: 2.75- and 3.75-months post-baseline
		(11- and 15-weeks respectively)

Notes: Only depression and anxiety reported. T1 – baseline to ≤ 3 months post-baseline, T2 - > 3 post-baseline to < 12 months, and $T3 - \geq 12$ months postbaseline. T > C = treatment statistically significantly superior to control; T < C = control statistically significantly superior to treatment; T = C = no statistically significant differences between treatment and control. Effect size was calculated as the mean difference of the two study groups divided by the pooled standard deviation of the difference (Cohen, 1988). *Length of the intervention was based on the mean or median number of minutes reported by authors. If only mean or median duration of individual sessions reported, this was multiplied by the number of intervention sessions. If the range of individual sessions was provided (e.g., 15 to 30 minutes per session), the midpoint (e.g., 22.5) was multiplied by the number of sessions. CES-D = Centre for Epidemiological Studies depression; GDS= Geriatric Depression Scale; HAM-D= Hamilton Depression Rating Scale; BDI= Beck Depression Inventory; BDI-II: Beck Depression Inventory-II; MMSE= Mini Mental Status Examination; QSA = quality score appraisal (scores out of 15). °Data not available for meta-analysis. Results as reported by authors. • In studies with 3 groups (2 treatment and 1 control) only one treatment group was included in the meta-analysis to ensure the independence of the control data (i.e., both treatment data are compared with the same control data). The outcome data from the intervention arm that most resembled the other included interventions was included in the meta-analysis. Findings from the second intervention arm are included as reported by the authors.

Participants

Overall, the studies included a total of 2178 participants (mean=94, SD=129.18, range=25-518), this included 2123 caregivers (51-66) and 57 care recipients (51,65). Fourteen studies solely targeted the caregivers (52-65) and two studies targeted the care recipient-caregiver dyad (51, 66). Samples often contained more women than men. The mean reported age of caregivers ranged from 54 to 68 years, and that for the care recipients from 60 to 83 years. The most common condition (n = 10/16, see Table 1) of the care recipient was dementia. *Type of interventions*

A total of 18 interventions were included (two studies evaluated more than one intervention) (59, 60). Interventions are summarized in Table 1. Most interventions (n = 16) were delivered solely to the caregiver to help them manage their own depression (52-65). One intervention was delivered to the care recipient-caregiver dyad and aimed to support the caregivers in caring for older adults with depression (51). The remaining intervention was also delivered to the dyad and was the only one with the dual focus on assisting caregivers manage their own depression as well as supporting them in managing the care recipients' depression (66).

Interventions lasted between 2 and 6 months (n = 15, mean = 3.02 months) (51-53, 55-66). The total number of minutes of the interventions range from 240 to 2170 minutes (n = 13, mean = 717.04 minutes) (51, 52, 55-60, 62-66) and the number of sessions ranged from 1 to 56 (n = 15, mean = 13.26 sessions) (51-65).

In terms of delivery format, 14 interventions used an individual format (51, 53, 56-64, 66). The remaining four interventions combined individual and group formats (52, 54, 55, 65). For the mode of delivery, three interventions were purely self-directed (54, 58, 61). The

remaining 15 interventions were provider led and most commonly by a nurse (51, 56, 57, 62) or psychologists (53, 60, 65). Two interventions were web-based (53, 66), five were delivered face-to-face (51, 55, 58, 60, 65), two via telephone (63, 64), and four used combined face-to-face and telephone contacts (52, 56, 57, 62). Two were face-to-face and gave caregivers complementary written materials (64, 67).

Most interventions (51-54, 56, 57, 59, 61-66) focused on a combination of: a) stress management, b) disease or symptom management, c) management of behaviours of care recipients with neurological or cognitive disorders, and/or d) emotional and affective management. Two interventions delivered conventional Cognitive-Behavioural Therapy (CBT) (60, 65) and one intervention Acceptance and Commitment Therapy (ACT) (60). Two interventions focused solely on the use of relaxation techniques (e.g., yoga, mindfulness) (55, 58).

Self-management skills were retrieved from 17 interventions (one did not have enough information (61)), with a mean of 4.29 self-management skills per intervention (SD =4.18, range=1-13). A summary of the self-management skills coded for each intervention is provided in Appendix B. The most frequently reported skills were relaxation (52, 53, 55-60, 62, 63, 66), cognitive restructuring (52-54, 56, 57, 59, 60, 62-65), behavioural activation (52, 56, 57, 59, 60, 62-66), developing social support (51-54, 56, 57, 59, 62, 64, 66) and resource utilization (51, 52, 54, 56, 57, 59, 63-66).

Quality assessment

The quality assessment summary score is included in Table 1 and detailed in Appendix C. The average quality assessment score was in the moderate range 8.76/15 (*SD*=2.59, range = 5 – 13). Three studies (53, 55, 64) were of high methodological quality.

Outcomes: Descriptive and meta-analysis

Primary outcome: Caregivers' depression

An Egger's test and funnel plots were computed and did not reveal publication bias at T1 (p=0.323) nor T2 (p=0.116) (Appendix D). At T1, eight studies were included in the metaanalysis (see Figure 2) and the pooled ES of -0.62 (95% CI -0.81, -0.44) was statistically significant. There was no significant heterogeneity (p=0.337). The largest ES at T1 was for a CBT intervention with minimal therapist contact (59) at -1.13 (95% CI -1.67, -0.58). At T2, the pooled ES for the 10 studies in the meta-analysis (see Figure 2) was also statistically significant (-0.19, 95% CI -0.29, -0.09) with no heterogeneity (p=0.513). The largest ES at T2 was for a conventional CBT intervention (60). At T3, there was only one study (57) and the ES was not significant = 0.13 (95% CI -0.20, 0.45).

The only study not included in the meta-analysis (51) was a pilot reporting no significant overall differences between the intervention and control groups.

Secondary outcome

Over 30 secondary outcomes were extracted; however, based on our a priori criteria outlined in the methods, the only secondary outcome that qualified was anxiety. At T1, a significant pooled ES of -0.65 (95% CI -1.14, -0.15) favoring the interventions was obtained (see Figure 3). However, there was significant heterogeneity ($I^2 = 71.3\%$; p=0.031). At T2, the

pooled ES was also statistically significant (-0.17, 95% CI -0.32, -0.01) with no heterogeneity (p=0.458) (see Figure 3). At T3, there was only the study (57) and the ES was not significant at -0.023 (95% CI -0.348, 0.303).

Moderator and mediator analyses for intervention characteristics

A summary of the moderator and mediator analyses is presented in Table 2. At T1, there were enough data to analyse two mediators (control group and mode of delivery), neither were significant. At T2, there were enough data to conduct a meta-regression on 17 mediators (see Table 2), and results were significant for three self-management skills: a) taking action (yes/no) (p=0.038); b) problem solving (yes/no) (p=0.022); and c) decision making (yes/no) (p=0.035).

Mediator variables		T1: post-in	tervention to \leq 3-months	T2: >3-months to <12-months				
	(N	= 8, unless	not enough data for analys	sis)	(N = 10)	, unless n	ot enough data for anal	ysis)
	# of	Pooled	P-value [95%CI]	I ²	# of	Pooled	P-value [95%CI]	I ²
	studies	ES			studies	ES		
Control group								
Active/therapeutic elements	4	-0.57	<0.001 [-0.82; -0.33]	15%	5	-0.32	0.003 [-0.52; -0.11]	0%
Non-active/therapeutic	4	-0.70	<0.001 [-1.00; -0.41]	24%	5	-0.16	0.007 [-0.27; -0.04]	0%
Disease type								
Dementia	5	-0.62	<0.001 [-0.88; -0.35]	0%	8	-0.17	0.001 [-0.28; -0.07]	0%
Other	3	-0.74	0.002 [-1.21; -0.26]	60%	2	-0.37	0.018 [-0.67; -0.06]	0%
Mode of delivery								
Included face-to-face contact	4	-0.66	<0.001 [-1.02; -0.30]	44%	4	-0.19	0.004 [-0.33; -0.06]	18%
Other (e.g., telephone, online)	4	-0.66	<0.001 [-0.95; -0.36]	0%	6	-0.20	0.012 [-0.35; -0.04]	0%
Provider								
Professional	6	-0.72	<0.001 [-0.98; -0.45]	27%	8	-0.21	0.001 [-0.34; -0.08]	11%
Self-directed	2	-0.44	0.031 [-0.84; -0.04]	0%				
Length of intervention (min)*								
240-525	3	-0.81	<0.001 [-1.24; -0.39]	25%	3	-0.17	0.075 [-0.35; 0.02]	20%
720-3060	3	-0.66	0.001[-1.03; -0.28]	39%	4	-0.25	0.039 [-0.49; -0.01]	41%
Number of sessions								
< 10	4	-0.71	<0.001 [-1.08; -0.34]	55%	4	-0.29	0.003 [-0.47; -0.10]	17%
≥ 10	3	-0.65	<0.001 [-1.06; -0.23]	0%	5	-0.15	0.020 [-0.27; -0.02]	0%
Tailored intervention								
No	3	-0.47	0.001 [-0.74; -0.19]	0%	4	-0.21	0.018 [-0.38; -0.04]	0%
Yes	5	-0.76	<0.001 [-1.02; -0.51]	14%	6	-0.19	0.003 [-0.31; -0.06]	21%
		D	epression self-managemen	t skills			·	
Decision-making								
No	5	-0.55	<0.001 [-0.78, -0.32]	0%	6	-0.30	<0.001 [-0.46; -0.15]	0%
Yes	2	-1.01	<0.001 [-1.45; -0.57]	0%	4	-0.12	0.070 [-0.25; 0.01]	0%
Problem-solving								
No	5	-0.55	<0.001 [-0.78; -0.32]	0%	4	-0.37	0.001 [-0.6; -0.15]	0%
Yes	2	-1.01	<0.001 [-1.45; -0.57]	0%	6	-0.15	0.010 [-0.26; -0.04]	0%
Resource utilization								
No	3	-0.57	0.001 [-0.92; -0.23]	36%	4	-0.34	0.003 [-0.56; -0.12]	28%
Yes	4	-0.82	<0.001 [-1.15; -0.50]	0%	6	-0.14	0.023 [-0.26; -0.02]	0%
Forming partnerships with HCPs								
No	6	-0.67	<0.001 [-0.94; -0.40]	32%	7	-0.24	<0.001 [-0.37; -0.11]	5%
Yes	1				3	-0.14	0.077 [-0.29; 0.02]	0%

Table 2. Results by Mediator for Primary Outcome of Depression

Mediator variables		T1: post-in	tervention to \leq 3-months	T2: >3-months to <12-months				
	(N	= 8, unless	not enough data for analys	is)	(N = 10)	, unless n	ot enough data for anal	ysis)
	# of	Pooled	P-value [95%CI]	I ²	# of	Pooled	P-value [95%CI]	I ²
	studies	ES			studies	ES		
Taking action								
No	5	-0.55	<0.001 [-0.78; -0.32]	0%	6	-0.30	<0.001 [-0.46; -0.15]	0%
Yes	2	-1.01	<0.001 [-1.45; -0.57]	0%	4	-0.12	0.070 [-0.25; 0.01]	0%
Behavioural activation								
No	2	-0.41	0.006 [-0.71; -0.12]	0%	3	-0.23	0.011 [-0.41; -0.05]	0%
Yes	5	-0.86	<0.001 [-1.14; -0.58]	0%	7	-0.18	0.004 [-0.30; -0.06]	14%
Cognitive restructuring								
No	3	-0.47	0.001 [-0.74; -0.19]	0%	2	-0.37	0.018 [-0.67; -0.06]	0%
Yes	4	-0.87	<0.001 [-1.17; -0.57]	0%	8	-0.17	0.001 [-0.28; -0.07]	0%
Self-monitoring								
No	4	-0.59	0.001 [-0.93; -0.24]	43%	4	-0.27	0.002 [-0.43; -0.10]	0%
Yes	3	-0.88	<0.001 [-1.26; -0.51]	0%	6	-0.15	0.017 [-0.29; -0.04]	1%
Health habits								
No	6	-0.67	<0.001 [-0.94; -0.4]	32%	5	-0.24	0.004 [-0.41; -0.08]	15%
Yes	1				5	-0.17	0.010 [-0.29; -0.04]	0%
Communicating about depression								
No	5	-0.67	<0.001 [-0.97; -0.35]	44%	7	-0.24	<0.001 [-0.37; -0.11]	5%
Yes	2	-0.81	0.003 [-1.34; -0.27]	0%	3	-0.14	0.077 [-0.29; 0.02]	0%
Social support								
No	4	-0.53	<0.001 [-0.77; -0.29]	7%	3	-0.34	0.085 [-0.73; 0.05]	46%
Yes	3	-0.96	<0.001 [-1.35; -0.58]	0%	7	-0.17	0.002 [-0.28; -0.06]	0%
Relaxation activities								
No	2	-0.42	0.006 [-0.75;-0.08]	0%	2	-0.18	0.105 [-0.40; 0.04]	0%
Yes	5	-0.86	<0.001 [-1.14; -0.58]	0%	8	-0.21	0.001[-0.33; -0.08]	13%
Self-tailoring								
No	2	-0.41	0.006 [-0.17;-0.12]	0%	5	-0.24	0.003 [-0.40; -0.08]	0%
Yes	5	-0.86	< 0.001 [-1.14; -0.58]	0%	5	-0.16	0.012 [-0.29; -0.04]	11%
Number of skills								
1-3	2	-0.41	0.006 [-0.71; -0.12]	0%	2	-0.31	0.015 [-0.56; -0.06]	0%
4-6	2	-0.73	0.006 [-1.25; -0.21]	37%	3	-0.38	0.032 [-0.73; -0.03]	50%
7-13	3	-0.96	<0.001 [-1.35; -0.58]	0%	5	-0.13	0.049 [-0.26; 0.00]	0%

Notes: Shaded cells indicate significant results at p < 0.05. If $l^2 > 25\%$ then random effect model is used to compute the pooled effect size. ES=effect size (Cohens'd). l^2 =Higgin's statistic measure of heterogeneity. l^2 values of 25% are categorized as low, 50% as moderate, and 75% as high heterogeneity. *Length of the intervention was based on the mean or median number of minutes reported by authors. If only mean or median duration of individual sessions reported, this was multiplied by the number of intervention sessions. If the range of individual sessions was provided (e.g., 15 to 30 minutes per session), the midpoint (e.g., 22.5) was multiplied by the number of sessions.

Discussion

This is the first systematic review to critically appraise the effect of interventions either aimed at reducing caregivers' depression or helping the caregiver manage the care recipient's depression. Sixteen studies were reviewed. Meta-analysis techniques were conducted for the primary outcome (depression) and a secondary outcome (anxiety). An examination of a moderator and several mediators on the effects of non-pharmacological interventions was also conducted. The key findings are: a) interventions were successful in reducing caregivers' depression and anxiety, b) however, the effect reduced over time, and c) the significant mediators were self-management skills taking action, problem solving, and decision making.

The non-pharmacological interventions reviewed were successful in reducing caregivers' depression. This is consistent with previous meta-analyses on the effects of "generic" caregiver interventions in lowering depression and anxiety (as the main psychological symptoms among caregivers) (37, 68). However, the ESs for both depression and anxiety in the present meta-analysis were in the small to moderate range in comparison to mostly small ESs in previous meta-analyses (37, 68). Typically, generic caregiver interventions provide a range of information and coping skills training to help caregivers feel better equipped to manage the challenges of their role, which in turn might result in lowering depression and anxiety (37, 68). Generic interventions are often offered regardless of caregivers' baseline emotional well-being. However, the present meta-analysis suggests that targeted caregiver interventions might be more efficacious than generic ones. A conclusion further supported by Sheard and Maguire (69) reporting ESs of 0.85 and 0.94 for anxiety and depression, respectively, when interventions included patients who screened positive for these symptoms, which is in comparison to ESs of 0.33 for anxiety and 0.16 for depression among non-screened patients.

Although in the present meta-analysis ESs were significant post-intervention, the longerterm effects were less pronounced. Thus, to increase the durability of intervention effects, booster or maintenance sessions might be needed. Intervention boosters are typically contacts that are beyond the main intervention, are shorter in duration than the initial intervention, and are designed to reinforce key content from the initial intervention (70). Only one RCT in the present meta-analysis included a booster session (53); however, the final outcome measurement was performed prior to the booster, precluding any conclusions about its impact. Tolan et al. (71) found that families who received a booster intervention following a family-focused prevention program reported sustained benefits. Evidence in the physical activity literature also supports the use of boosters to achieve sustained behavior outcomes (70).

In terms of active components of the interventions, three self-management skills (taking action, problem solving, and decision making) were identified as significant mediators for the primary outcome of depression. These findings align with previous studies (40) emphasizing that learning self-management skills enhance self-efficacy, ultimately resulting in changes in health behaviors and health status. However, there is increasing evidence that not all self-management skills are equally efficacious. For instance, a systematic review by Schaffler et al. (72) suggested that self-management interventions were more efficacious when these included problem-solving, taking action, and resource utilization. Our analyses further provide support for including problem-solving and taking action in future interventions.

Unfortunately, the sample size was too small to examine a number of mediators and much remains unknown about the optimal components of this kind of intervention. Many studies included caregivers of care recipients with dementia, and future studies need to examine the impact of these interventions among other caregiver sub-groups. Most interventions were

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delivered to the caregiver alone and it is not known whether there is an advantage to including the care recipient-caregiver as a dyad. A previous systematic review (73) by our team showed that dyadic caregiver interventions are more efficacious than caregiver-only intervention. Also, none of the studies reviewed included physical activity, despite the extensive literature on the efficacy of physical activity for depression (74) and one review finding that physical activity interventions can significantly decrease caregivers's distress and increase their well-being, quality of life, and sleep quality (75).

Limitations of this review include missing details on the study design. We often did not receive responses from authors asking for more information. For all studies, no in-depth information was provided on medication type (e.g., anti-depressor, anxiolytic, etc.) and dosage for intervention and control groups. Also, this review focused on interventions that included a component relevant to mood/depression and it is recognized that interventions focused on broader issues of caregiver well-being (e.g., burden, communications skills) were most likely excluded from this review. Also, there was significant heterogeneity for the pooled ES of anxiety post-intervention, and no further investigation of the specific source was conducted due to the small number of studies. However, all studies were associated with a significant improvement of anxiety baseline post-intervention and were based on similar interventions. As 10/16 studies were focused on caregivers of patients with dementia, the generalizability of the findings might be limited to this caregiver sub-group.

Conclusion

Non-pharmacological interventions are associated with improvement of depression and anxiety in caregivers, particularly in the short-term. The main recommendation for future

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interventions is to include the three key self-management skills of problem-solving, taking action, and decision-making. Extending the effects of these interventions will need to be the focus of future studies, particularly examining the impact of booster sessions. Other aspects of these interventions still need evidence, including whether a dyadic focus has advantages. Also, examining the effect of these interventions among caregivers other than those with dementia should be the focus of future studies.

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Conflict of Interest

We have no conflict of interest to declare.

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Supplementary Material

Appendix A. Sample Search Strategy Database(s): PsycINFO 1987 to February Week 3 2017

#	Searches	Results
1	caregivers/	23191
2	(caregiv* or carer\$1 or caretak*).ti,ab,kw.	50794
3	exp spouses/ or exp couples/ or exp significant others/	22378
4	(wife or wives or husband or husbands or couple or couples or partner or partners or spouse or family member*).ti.	25248
5	"support person".ti,ab.	178
6	"close relative\$1".ti,ab.	924
7	"next of kin".ti,ab.	342
8	"significant other\$1".ti,ab.	4724
9	or/1-8	93324
10	exp Major Depression/	108334
11	"Depression (emotion)"/	11956
12	(depression or depressive or depressed or dysthymia or dysthymic or mood*).ti,ab,kw.	251132
13	or/10-12	255858
14	self care skills/ or exp self help techniques/ or self efficacy/	28975
15	(self care* or self manage* or self regulat* or self help* or self efficacy or self direct* or self maintenance or self maintain* or self monitor*).ti,ab,kw.	69486
16	exp exercise/ or respite care/ or exp behavior therapy/ or exp psychotherapy/ or exp psychoeducation/ or exp counseling/ or exp health education/ or social support/ or family therapy/ or education/	271135
17	(education* or psychoeducat* or psycho educat* or counselling or counselling or psychosocial or psycho social or exercis* or behavior therap* or behaviour therap* or teaching).ti,ab,kw.	499271
18	or/14-17	713297
19	experimental controls/ or evidence based practice/ or exp experimental design/ or treatment effectiveness evaluation/	72722
20	(random* or RCT or RCTs or quasi experimental or quasiexperimental or assign* or placebo* or blind* or conceal* or mask* or allocat* or control group\$1 or pragmatic or crossover or cross over).ab.	294065
21	19 or 20	348232
22	19 or 20 or 21	348232
23	9 and 13 and 18 and 22	705
24	limit 23 to ((english or french) and yr="1996 -Current")	614

-			110	benana D		i unu Svi		inis addi e	Joed by	III COI VO	nuon						
Definitions ³ of self-management skills	Belle (2006)	Blom (2015)	Gallagher- Thompson (2015)	Horton- Deutsch (2002)	Hou (2014)	King (2007)	King (2012)	Lavretzky (2012)	López (2007)	Losada (2015)	Nunez- Naveira (2016) ²	Pan (2019)	Smith (2012)	Steffen (2016)	Tremont (2015)	Yoo (2019)	Total
Decision-making Having needed information to adjust to issues related to chronic illness (part of problem-solving)	1	0	0	0	0	1	1	0	1	0	n/a	0	0	1	1	0	6
Problem Solving A systematic approach to addressing challenges; includes learning skills such as defining a problem, identifying solutions, and evaluating outcomes	1	1	0	0	0	1	1	0	1	0	n/a	1	0	1	1	0	8
Resource utilization Learning how to find needed resources	1	0	1	1	0	1	1	0	1	0	n/a	0	1	1	1	1	10
Partnership with HCP Learning to make informed decisions related to treatment with HCPs. Often includes strategies for providing updates, feedback and concerns as well as asking questions and keeping track of information	1	0	0	0	0	0	1	0	0	0	n/a	0	1	0	0	0	3
Taking action Related to changing behaviour, carrying out a plan to achieve a goal	1	0	0	0	0	1	1	0	1	0	n/a	0	0	1	1	0	6
Behavioural activation Setting goals to incrementally increase positive activities	1	0	0	0	0	1	1	0	1	1	n/a	1	1	1	1	1	10

Appendix B. Self-Management skills addressed by intervention¹

Definitions ³ of	Belle	Blom	Gallagher-	Horton-	Hou	King	King	Lavretzky	López	Losada	Nunez-	Pan	Smith	Steffen	Tremont	Yoo	Total
self-management	(2006)	(2015)	Thompson	Deutsch	(2014)	(2007)	(2012)	(2012)	(2007)	(2015)	Naveira	(2019)	(2012)	(2016)	(2015)	(2019)	
skills			(2015)	(2002)				-			$(2016)^2$						
Cognitive	1	1	1	0	0	1	1	0	1	1	n/a	1	0	1	1	1	11
<i>restructuring</i>																	
and deconstruct																	
negative thinking																	
patterns and																	
more balanced way																	
Self-monitoring	1	0	0	0	0	1	1	0	0	1	n/a	0	1	1	1	0	8
Monitoring symptoms																	
and the impact of treatment strategies																	
Health habits	1	0	0	0	0	0	1	0	0	0	n/a	1	1	0	1	0	5
Learning the	1	0	°	Ũ	Ŭ	Ŭ	-	0	0	0	11 u	1	1	Ū	-	Ū	5
relationship between																	
nealth habits and mental health and																	
how to carry out																	
these habits																	
Communicating	1	0	0	0	0	1	1	0	0	0	n/a	0	1	0	0	0	4
about depression																	
the experience of																	
depression and																	
related needs		-			0	1	-	-	-	0	1			0	1	0	10
Social Support	I	1	I	1	0	l	I	0	I	0	n/a	1	1	0	1	0	10
support																	
Relaxation	1	1	0	0	1	1	1	1	1	1	n/a	1	1	1	0	0	11
activity																	
Learning and																	
unaertaking relaxing activities																	
Self-tailoring	1	0	0	0	0	1	1	0	1	1	n/a	0	1	0	1	1	8
Evaluating one's		-	-	-	-			-				-		-			-
needs and learning																	
when to apply the other skills																	
Total	13	4	3	2	1	11	13	1	9	5	n/a	6	9	8	10	4	

Notes: ¹These interventions were highly tailored based on the participant needs of preferences. As such, not all participants addressed all of the skills outlined here. ²Nunez-Naveira (2016): not enough information reported to code selfmanagement skills. ³References: (BC Partners for Mental Health and Addictions Information, 2003; Bilsker, Goldner, & Anderson, 2012; Bilsker, 2005; Houle, Gascon-Depatie, Bélanger-Dumontier, & Cardinal, 2013; Lorig & Holman, 2003; Michie et al., 2008; van Grieken et al., 2015; van Grieken, Kirkenier, Koeter, & Schene, 2014b). Abbreviations: HCP, healthcare professional; n/a, none-applicable.

Article	Trial design (design and allocation ratio)	Inclusion criteria specified	Pre-specified primary and secondary outcomes	Psychometric properties provided	Explicit power calculation	Target sample size reached*	Randomization method specified	Randomization - Allocation concealed	Outcome assessors blind	Participants blind to treatment allocation	Intervention ists blind	Participant flow described	Intention- to-treat data analysis	>80% of sample in final analysis	Reason for attrition stated	Total score
Belle et al, 2006	1	1	1	0	1	0	1	1	1	0	0	1	1	1	1	11
Blom et al, 2015	1	1	1	0	1	1	1	1	1†	1	0	1	1	0	1	12
Gallagher- Thompson et al, 2015	1	1	1	1	0	0	0	0	0	0	1‡	1	0	0	1	7
Horton- Deutsch et al, 2002	1	1	0	1	0	0*	0	0	0	0	0	0	0	1	1	5
Hou et al, 2014	1	1	1	0	1	1	1	1	1	0	0	1	1	1	1	12
King et al., 2007	1	1	0	1	0	0*	0	0	0	0	0	1	0	0	1	5
King et al, 2012	1	1	0	1	0	0	1	0	1	0	0	1	1	0	1	8
Lavretsky et al, 2012	1	1	1	0	0	0*	1	1	1	1	1‡	1	0	1	1	11
López et al., 2007	1	1	1	1	0	0	1	0	0	1	0	1	1	1	0	9
Losada et al, 2012	1	1	1	1	0	0	1	1	1	1	0	1	0	0	1	10
Nunez- Naveira et al, 2016	1	1	0	0	0	0*	1	0	0	0	1‡	1	0	0	1	6
Pan & Chen, 2019	1	1	0	1	1	1	1	1	1	1	0	1	0	0	1	11
Smith et al, 2012	1	1	1	1	0	0	1	0	1	1	0	1	0	1	1	10
Steffen et al, 2016	1	1	1	0	0	0	1	1	1	0	0	1	0	0	1	8
Tremont et al, 2015	1	1	1	1	1	1	1	0	1	1	0	1	1	1	1	13
Yoo et al., 2019	1	1	1	0	0	0	1	1	1	0	0	1	0	0	1	8
Total	16	16	11	9	4	4	13	8	11	7	3	15	6	7	16	-

Appendix C. Quality Assessment

Notes: If a criterion was met, a score of 1 was attributed. If a criterion was not met, a score of 0 was attributed. The criterion of pre-specified primary and secondary outcomes was met if the authors identified a primary outcome or stated a primary hypothesis (H1) and subsequent hypothesis (H2, H3, etc.). The randomization – allocation concealed criterion was met if the individual who conducted the randomization was independent from the research team and research process (e.g., development of the research project, data collection, data analysis). Participants blind to treatment allocation criterion was met if the participants were blinded to group assignment (e.g., experimental, control); participants being blind to the study hypotheses was not considered sufficient to meet this criterion. Rate of attrition (\geq 80% of sample in final analysis) was based on last follow-up measure reported. *Pilot studies. For pilots, if a rationale for the needed sample size was provided and achieved, this was considered sufficient for meeting the target sample size. †Self-reported outcomes. ‡Purely self-directed interventions. Studies were considered to be high methodological quality if 75% of criteria were met (minimum score of 12 out of 15).



Appendix D. Funnel plots

Egger test \rightarrow Test of H0: no small-study effects P = 0.323 (NO BIAS) Begg test \rightarrow p-value=0.386



Egger test \rightarrow Test of H0: no small-study effects P = 0.116 (NO BIAS) Begg test \rightarrow p-value=0.152

Section/topic	#	Checklist item	Page #							
TITLE										
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1							
ABSTRACT										
Structured	2	Provide a structured summary including, as applicable: background; objectives; data sources; study	4							
summary		eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results;								
		limitations; conclusions and implications of key findings; systematic review registration number.								
INTRODUCTION										
Rationale	3	Describe the rationale for the review in the context of what is already known.	5							
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants,	6							
		interventions, comparisons, outcomes, and study design (PICOS).								
METHODS										
Protocol and	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if	6							
registration		available, provide registration information including registration number.								
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g.,	6							
		years considered, language, publication status) used as criteria for eligibility, giving rationale.								
Information	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors	7							
sources		to identify additional studies) in the search and date last searched.								
Search	8	Present full electronic search strategy for at least one database	7							
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review,	7							
		and, if applicable, included in the meta-analysis).								
Data collection	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate)	8							
		and any processes for obtaining and confirming data from investigators.								
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any	8							
		assumptions and simplifications made.								
Risk of bias in	12	Describe methods used for assessing risk of bias of individual studies, and how this information is	9							
studies		to be used in any data synthesis								
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9							
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including	9							
		measures of consistency (e.g., I ²) for each meta-analysis.								

Appendix E. PRISMA 2009 Checklist