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REVIEW ARTICLE

Association between dyadic interventions and outcomes in cancer patients: a meta-analysis

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Abstract

Purpose Patient–caregiver dyadic interventions are when "interventions are offered to cancer patients and their family caregivers together as the unit of care." The purpose of the present study was to determine the association of dyadic intervention for cancer patients and their family caregivers with quality of life (QOL), and other outcomes for people with cancer.

Methods Literature searches were conducted using the electronic databases to identify all randomized clinical trials on cancer patient–caregiver dyads. Meta-analysis was used to analyze data.

Results Twenty-three RCTs provided data on 2317 patient–caregiver dyads. In the meta-analysis, at the 0- to 3-month follow-up, dyadic intervention was associated with statistically and clinically significant improvements in patient total QOL (standardized mean difference [SMD], 0.25; 95% confidence interval [CI], 0.01–0.50); the total spiritual aspect of QOL (SMD, 0.28; 95% CI, 0.06–0.50); the emotional (SMD, 0.16; 95% CI, 0.02–0.29), social (SMD, 0.21; 95% CI, 0.07–0.36), and mental (SMD, 0.26; 95% CI, 0.07–0.46) aspects of QOL; depression (SMD, − 0.35; 95% CI, − 0.65 to − 0.05); anxiety (SMD, − 0.42; 95% CI, − 0.70 to − 0.13); relatedness (SMD, 0.18; 95% CI, 0.04–0.32); and marital functioning (SMD, 1.01; 95% CI, 0.05–1.97). At the 3.1- to 6-month follow-up, dyadic intervention was associated with significant improvements in patient social aspect (SMD, 0.19; 95% CI, 0.03–0.35) and depression (SMD, − 0.29; 95% CI, − 0.56 to − 0.03). There was no association between dyadic interventions and the patient functional and physical aspects of QOL. Dyadic intervention was associated consistently with no improvements in hopelessness, pain, fatigue, and survival.

Conclusions In this review, dyadic interventions for caregivers and cancer patients were associated with improvements in multiple psychosocial aspects of patient outcomes.

Keywords Cancer patient · Caregiver · Dyads · Meta-analysis

Background

Helping patients with serious illnesses such as cancer achieve the best possible quality of life (QOL) is a shared goal among medical and care communities [1]. Family members are playing an increasingly important role in caring for cancer patients, especially given the trends in demographic changes worldwide (the continually aging population, the increasingly large number of cancer survivors with advances in cancer treatment, prolonged courses of treatment, and extended long-term survival) and a shortage of health care providers which are contributing to a shift from hospital- to community- and home-based care [2–4]. Prior research showed that both cancer patients and their family caregivers often experience physical and psychological symptoms and face social and spiritual problems because of the stress of caregiving caused by potentially increased burdens and strains [5–7]. In recent years, researchers have developed various family member-involved models that target both patients and their caregivers, with respect to providing physical, social, psychological, and spiritual support [2, 6, 8–12]. The current research data support the

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beneficial effects of these models on caregiver outcomes [2, 4]; however, their effects on patient outcomes have yet to be determined. Regan et al. [13] reviewed the literature published between 1990 and 2011 on couple-based interventions for cancer patients and their partners and reported that these interventions enhanced patient psychological and social adjustment such as communication and relationship functioning with small-to-medium effect sizes ($d \sim 0.35$–0.45). In contrast, a subsequent 2014 systematic review by Griffin et al. [14] found that family-involved interventions were not superior to usual care or active controls at improving cancer patient outcomes, which diverges from the common assumption that the patient will benefit from improving family member preparation and reducing their distress.

Among the many interventions utilized with patients and/or their caregivers, we noted the growing emphasis on trials conducted with the patient–caregiver dyad. Patient–caregiver dyadic interventions are when "interventions are offered to cancer patients and their family caregivers together as the unit of care" [10]. In other words, this type of intervention means that when researchers recruit patients for experimental projects, they must also recruit their family caregivers to participate in the study and receive targeted interventions. Psychoeducational interventions [4, 9] (e.g., information and skills related to caregiving tasks were combined with information and skills related to coping and relationships, health and emotional care, social support) were the predominant approaches to patient–caregiver dyad intervention research. Most research targeted dyadic communication and relationships and dyadic coping and adjustment strategies.

Although substantial progress has been made in this area in recent years, few studies have identified these trials and determined their effects on patient outcomes. Through the presented meta-analysis, we provide a summary of patient–caregiver dyadic interventions tested in published randomized clinical trials (RCTs) and estimate the associations of these interventions with cancer patients' outcomes. These outcomes were assessed using measures grounded in psychosocial theory and family theory, which can be summarized across several general areas (QOL, emotions, family relationships, marital functioning, etc.). In the present study, because the QOL concept is often applied to oncology patients, and the topic of improving the QOL of cancer patients has gained prominent attention by patients themselves, clinicians, family members, and most palliative care or oncology organizations, patient QOL and its main dimensions (physical, mental, functioning, social, and spiritual aspects) were used as the primary outcomes in the present study. Other important psychosocial indicators, such as relationship with caregivers, marital functioning (if it was evaluated), anxiety, depression, hopelessness, etc., were used as secondary outcomes. In addition, pain and fatigue were selected for meta-analysis because they are thought to be the most common symptoms in cancer patients and can greatly affect their QOL. Furthermore, survival was mentioned as it was an indicator of concern for many clinicians. We also identified some limitations in existing studies and discuss some clinical implications and directions for future research that could improve care strategies for patient–caregiver units in practice settings.

Methods

Literature search

The methods applied for reviewing the literature and reporting the meta-analysis results followed the preferred reporting items in systematic review and meta-analyses (PRISMA) guidelines [15]. We searched the following electronic databases for studies published through May 2018: PubMed, EMBASE, CINAHL, Cochrane CENTRAL, Chinese Biomedical Literature Database, PsycINFO, Web of Science, Chinese National Knowledge Infrastructure (CNKI), and Wanfang Data. The search strategies were tailored to each database. For PubMed, search strategies utilized a combination of keywords and medical subject headings to represent the definitions of cancer, caregiver, dyad, and RCTs. Similar strategies were used to search the other databases. The original search terms used were "caregiver," "family," "carer," "cancer patient," "spouse," "partner," "couple," and "randomized controlled trial." Additional terms included "neoplasms," "oncology," and "oncologic," along with more terms to search for interventions ("therapy," "treatment," "caregiving," "care").

Study eligibility

Two investigators independently evaluated all records for eligibility. Interventions were included if (1) the RCT investigated caregiver–patient dyad (such as caregivers include spouses and family members) care interventions targeting adult cancer patients (≥ 18 years) and reported on at least 1 of 15 patient-level outcomes: QOL (total score and physical, emotional, functional, social, mental, and spiritual aspects), depression, anxiety, hopelessness, relatedness, marital functioning, fatigue, survival, and pain; and (2) the intervention was psychosocially, cognitively, or behaviorally oriented; interventions were excluded if (1) they were conducted in a pediatric setting or (2) study interventions targeted the caregiver only or patient only.

Quality assessment

The quality of included studies was evaluated using the approach recommended by the Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green,

2011). The recommended six domains include seven items (random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective reporting, and other bias) via six criteria: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias [16]. All included studies were assessed independently, and the risk of bias of each item was categorized as "low," "unclear," or "high." Disagreements between two reviewers were resolved by the third reviewer. The risk of bias was independently rated by two investigators.

Synthesis

To account for variability in the timing of study end points, clinically relevant follow-up periods of 0–3, 3.1–6, and ≥ 6.1 months were used. For studies that reported outcomes at more than one time point within the same 1–3- or 3.1–6-month windows, data for both time points, signified by the symbols − 1 and − 2 (e.g., Northouse, 2007–1), were analyzed. Intervention protocols that included more than one experimental arm were classified into two different studies (signified by symbols as -a and -b as well as whether the same author published two or more papers in the same year).

Statistical methods

Due to the variety of instruments used to evaluate QOL and other outcomes, pooled effects were summarized as standardized mean differences (SMDs) with 95% CIs in all analyses (the SMD was interpreted per Cohen's definitions: 0.2 to 0.5 was defined as a small effect size, 0.5 to 0.8 represented a moderate effect size, and > 0.8 represented a large effect size). Given the heterogeneity across trials, Der Simonian–Laird random effects models were constructed using Revman version 5.3. All significance tests were two-tailed, with $P < 0.05$ considered statistically significant. The proportion of variability in point estimates, attributable to between-study heterogeneity, was quantified by the I^2 statistic and interpreted qualitatively as low (25%–50%), moderate (50%–75%), or high (75%–100%). All studies included in the meta-analysis had comparable baseline characteristics between intervention and control groups.

Results

Study characteristics

From the selection process illustrated in Fig. 1, 23 RCTs [10, 17–38] were chosen for analysis. The contents of the intervention protocols were primarily comprehensive, including family involvement, optimistic attitude, coping effectiveness, and symptom management ($n = 8$; 35%) [10, 18–20, 22, 30, 35, 37], followed by psychological education ($n = 7$; 30%) [17, 21, 27, 29, 31, 34, 36], physical training ($n = 2$; 9%) [25, 32], palliative care ($n = 2$; 9%) [23, 39], symptom management ($n = 1$; 4%) [38], and relationship enhancement therapy ($n = 1$; 4%) [28]. One intervention that included encouraging early discussion of life expectancy and end-of-life care was excluded from this meta-analysis because some caregivers did not participate in trials [40]. The formats for delivering the interventions were face-to-face visits ($n = 8$; 35%), telephone contact ($n = 7$; 30%), and a combination of both ($n = 8$; 35%). The majority of interventions included print materials, such as an instructional manual or booklet, and three of the interventions involved video/audio materials for home use or Web-based education and support. Interventions were mainly delivered by nurses, psychologists, or professionals. Of 23 unique trials, 18 compared a family intervention to usual care or wait list, and five compared one family intervention to another family intervention (active control). The characteristics of the included literature are shown in Supplemental Table 1.

Study quality

The calculated risks of bias for the included studies are shown in Supplemental Table 2, Supplemental Fig. 1, and Supplemental Fig. 2. All of the included studies reportedly randomized participants to either a treatment group or a control group, but some studies did not state the details of their randomization procedures. Interventions were mainly carried out by trained psychologists or nurses; therefore, the interventions could not be blind to participants or physicians. Allocation concealments were not adequately described. The risk of other bias was categorized as high in two studies [17, 18] because of the unclear design of research protocols (although they were reported to be randomized controlled studies, no detailed randomized method was described) with results that were very different from other similar studies (the standard deviation of the effect sizes and the heterogeneity of the study were large).

Effect sizes

Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, and 15 present an overview of the study findings for the multiple outcomes assessed.

Total QOL

QOL was assessed in 18 studies (78.3%). However, only nine studies [17, 18, 20, 21, 23, 24, 26, 29, 42] reported total scores for QOL. Compared to that in the control group, a statistically significant improvement in the total QOL score after

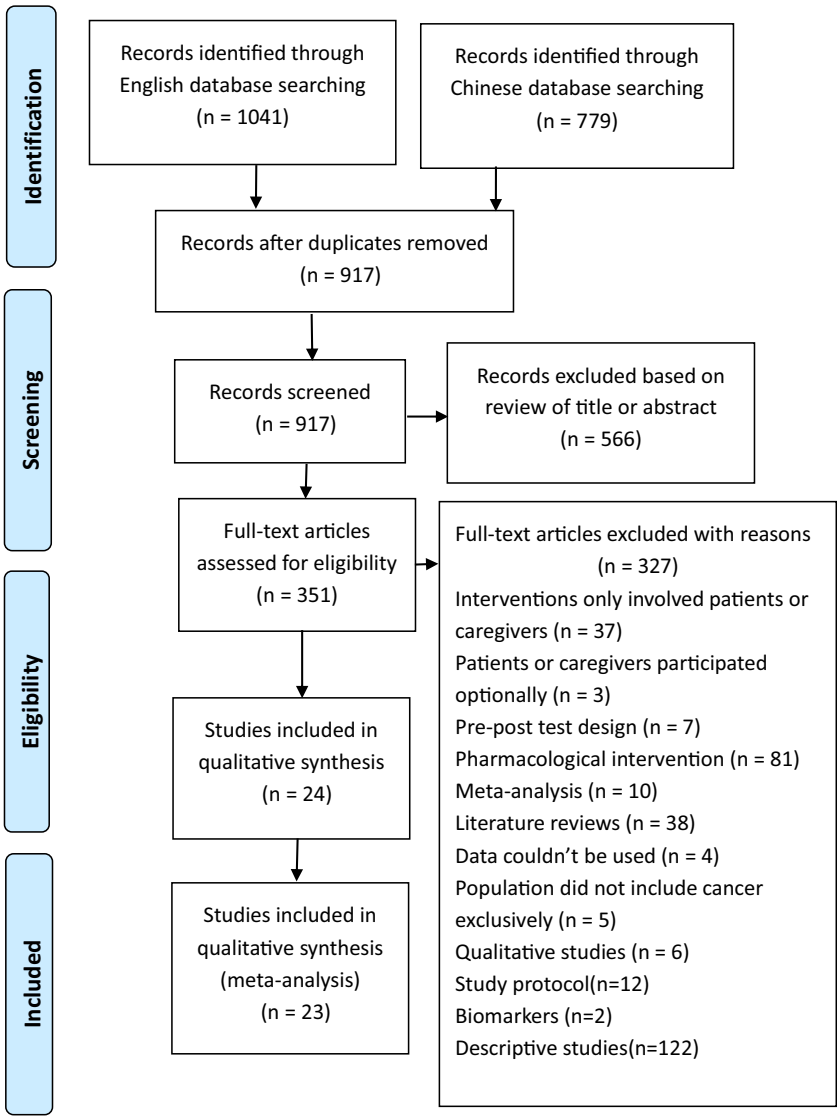

Fig. 1 Flow diagram of studies included and excluded at each stage of review

intervention was observed (standardized mean difference [SMD], 0.35; 95% confidence interval [CI], 0.07–0.63; I^2 = 88%). However, the effect size was no longer significant (SMD, 0.15, 95% CI, − 0.01 to 0.30, I^2 = 55%) once studies with a high risk of bias [17, 18] were excluded (see Fig. 2).

Subscales of QOL

To assess how intervention impacted QOL, we assessed the subscales of QOL separately, according to six aspects: social, emotional, functional, physical, mental, and spiritual well-being.

Physical aspect Analysis of the data from nine studies [10, 18, 19, 21, 22, 27, 36–38] that assessed patients' physical well-being or physical health showed that the overall effect size was small and not significant (SMD, 0.03; 95% CI, − 0.10 to 0.16; I^2 = 59%) (see Fig. 3).

Emotional aspect On analysis of data from the seven studies [10, 18, 19, 21, 22, 25, 26] that assessed patients' emotional well-being during the first 3 months following the intervention, the effect size was small but significant (SMD, 0.16; 95% CI, 0.02–0.29; I^2 = 0%). However, the interventions were not superior to usual care for improving patients' emotional well-being at the 3- to 6-month follow-up (SMD, 0.08; 95% CI, − 0.08 to 0.25, I^2 = 0%), nor at the 6-month or later follow-up (SMD, 0.26; 95% CI, − 0.44 to 0.96, I^2 = 84%) (see Fig. 4).

Social aspect Patients' social well-being was conceptualized as the ability to carry out domestic and family roles and increased interactions with family members, friends, and peers. Seven studies [10, 18, 21, 27, 30, 31, 42] reported detailed data on the social dimension after intervention. Compared to the control group, statistically significant improvements in social health after intervention were observed at the 0- to 3-month follow-up (SMD, 0.21; 95% CI, 0.07–0.36; I^2 = 0%)

Table 1 Random-effects meta-analysis of randomized clinical trials on the association between patient-caregiver dyad care and patient total quality of life

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Bénédicte Belgacem et al. 2013 [21]	46.4	18.9	33	36	20	34	1–3 m	Face to face	Unclear	SF36
Yael Schenker 2016 [7]	65.1	14.8	20	63.8	8.1	10	3 m	Face to face	Unclear	QUAL-E
Areej El-Jawahri 2016 [23]	94.33	20.60	80	86.60	20.59	77	2 weeks	Face to face	Unclear	FACT-BMT
Areej El-Jawahri 2016 [23]	112.00	16.46	75	106.66	16.46	74	3 m	Face to face	Unclear	FACT-BMT
Li Jia 2012 [17]	80.6	4.9	62	69.6	4.7	58	2 m	Face to face	High	TDL
Emily Arden-Close 2013 [29]	56.00	15.53	53	60.26	11.77	49	3 m	Mail + telephone	Low	FACT-G
Matthew M. Clark 2013 [22]	74.2	12.6	54	68.7	13.1	63	1 m	Telephone + face to face	Unclear	FACT-G
Jennifer L Steel 2016 [24]	82.4	15.2	15	63.2	21.5	12	6 m	Web + telephone + face to face	Low	FACT-G
Emily Arden-Close 2013 [29]	56.3	14.96	53	60.26	12.58	49	6 m	Mail + telephone	Low	FACT-G
Laurel L. Northouse 2007 [20]	87.2	10.6	112	85.5	10.3	123	4 m	Telephone + face to face	Low	FACT-G
Jingmei Chen 2012 [18]	60.84	5.15	45	57.79	4.68	45	12 m	Telephone + face to face	High	QLICP-BR
Laurel L. Northouse 2007 [20]	87	10.8	107	86.9	10.6	121	8 m	Telephone + face to face	Low	FACT-G
Laurel L. Northouse 2007 [20]	86.1	10.9	104	85.8	10.7	114	12 m	Telephone + face to face	Low	FACT-G
Matthew M. Clark 2013 [22]	77.6	12.1	51	77.7	11.8	59	27 weeks	Telephone + face to face	Unclear	FACT-G

TDL:Tang DanLin quality of life scale, *FACT-G* The Functional Assessment of Cancer Therapy-General (FACT-G Version4), *FACT-BMT* The 47-item Functional Assessment of Cancer Therapy–Bone Marrow Transplant, *SF Physical* physical subscale from the Medical Outcomes Study 12-item short form (MOS SF-12), *SF Mental* mental subscale from the MOS SF-12, *FACT-G* Functional Assessment of Cancer Treatment-General

Table 2 Random-effects meta-analysis of randomized clinical trials on the association between patient-caregiver dyad and patient physical domain of quality of life

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Laurel L. Northouse 2013-E [10]	20.56	5.30	99	21.58	5.69	104	3 m	Face to face + telephone	Low	FACT-G
Laurel Northouse 2005 [19]	50.80	9.3	69	49.90	9.8	65	3 m	Face to face + telephone	Low	BHS
Bénédicte Belgacem 2013 [21]	44.0	35.8	33	36.3	30.0	34	1–3 m	Face to face	Unclear	SF36
Kerri M. Winters-Stone 2015 [25]	47.7	9.9	30	47.4	8.6	26	3 m	Face to face	Low	SF36
Laurel L. Northouse 2013-B [10]	19.72	5.39	99	21.58	5.69	104	3 m	Face to face + telephone	Low	FACT-G
Janette Perz 2015 [36]	50.4	7.2	26	44.0	10.1	33	1.5 m	Telephone	Unclear	SF-12
Janette Perz 2015 [36]	47.7	9.9	26	43.0	13.5	33	3 m	Telephone	Unclear	SF-12
Sylvie D. Lambert 2016 [37]	0.81	0.13	19	0.84	0.14	13	2 m	Telephone + booklets +multimedia	Low	AQoL
Matthew M. Clark 2013 [22]	67.7	20.7	54	57.7	21.7	63	1 m	Telephone + face to face	Unclear	FACT-G
Terry A. Badger 2011 [27]	60.45	20.60	34	63.15	19.40	36	2 m	Telephone	Low	UCLA-PSI
Terry A. Badger 2011 [27]	61.64	18.7	34	58.86	21.3	36	4 m	Telephone	Low	UCLA-PSI
Laurel L. Northouse 2013-E [10]	20.03	5.77	99	21.49	5.76	104	6 m	Face to face + telephone	Low	FACT-G
Laurel L. Northouse 2013-B [10]	18.88	6.59	99	21.49	5.76	104	6 m	Face to face + telephone	Low	FACT-G
Laurel Northouse 2005 [19]	49.72	9.2	69	49.80	9.7	65	6 m	Face to face + telephone	Low	FACT
Kerri M. Winters-Stone 2015 [25]	49.3	9.2	30	48.1	8.1	24	6 m	Face to face	Low	SF36
Laurel L. Northouse 2007 [20]	48.6	6.7	112	48.7	6.5	123	4 m	Telephone + face to face	Low	MOS SF-12
Jingmei Chen 2012 [18]	56.04	6.48	45	52.12	5.15	45	12 m	Telephone + face to face	High	QLICP-BR
Laurel L. Northouse 2007 [20]	42.7	6.5	104	42.5	6.4	114	12 m	Telephone + face to face	Unclear	MOS SF-12
Laurel L. Northouse 2007 [20]	43.3	6.6	107	43.6	6.5	121	8 m	Telephone + face to face	Unclear	MOS SF-12
Matthew M. Clark 2013 [22]	76.4	17.8	51	76.7	16.6	59	27 weeks	Telephone + face to face	Unclear	FACT-G

FACT-G the general Functional Assessment of Cancer Therapy (version 4); *UCLA prostate index* fatigue and the urinary, bowel, and sexual functioning subscales from the UCLA Prostate Cancer Index; *SF-12* The Medical Outcomes Study Health Survey Short Form; *AQoL* the Assessment of Quality of Life-8 Dimensions (AQoL-8D)

Table 3 Random-effects meta-analysis of randomized clinical trials on the association between patient-caregiver dyad care and patient emotional domain of quality of life

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Laurel L. Northouse 2013-E [10]	18.39	4.69	99	17.31	5.06	104	3 m	Face to face + telephone	Low	FACT-G
Laurel Northouse 2005 [19]	51.34	9.5	69	49.13	9.9	65	3 m	Face to face + telephone	Low	FACT
Bénédicte Belgacem 2013 [21]	33.3	43.5	33	16	31.2	34	1-3 m	Face to face	Unclear	SF36
Kerri M. Winters-Stone 2015 [25]	54.6	6.4	30	54.8	7.8	26	3 m	Face to face	Low	SF36
Laurel L. Northouse 2013-B [10]	17.84	5.04	99	17.31	5.06	104	3 m	Face to face + telephone	Low	FACT-G
Matthew M. Clark 2013 [22]	79.8	15.5	54	78.4	17.5	63	1 m	Telephone + face to face	Unclear	FACT-G
Yael Schenker 2016 [7]	17.6	2.4	20	18.4	1.8	10	3 m	Face to face	Unclear	PEACE
Laurel L. Northouse 2013-E [10]	17.71	5.05	99	16.95	5.92	104	6 m	Face to face + telephone	Low	FACT-G
Laurel L. Northouse 2013-B [10]	17.09	5.01	99	16.95	5.92	104	6 m	Face to face + telephone	Low	FACT-G
Laurel Northouse 2005 [19]	51.12	10.8	69	48.81	10.7	65	6 m	Face to face + telephone	Low	FACT
Kerri M. Winters-Stone 2015 [25]	52.7	9.0	30	54.6	7.8	24	6 m	Face to face	Low	SF36
Jingmei Chen 2012 [18]	58.65	5.64	45	55.26	5.11	45	12 m	Face to face + telephone	High	QLICP-BR
Matthew M. Clark 2013 [22]	80.0	12.6	51	81.2	14.1	59	27 weeks	Telephone + face to face	Unclear	FACT-G

QLICP-BR, Quality of life scale for breast cancer developed by zheng Yang et al

and the 3- to 6-month follow-up (SMD, 0.19; 95% CI, 0.03–0.35; $I^2 = 0\%$), but not at the 6-month or later follow-up (SMD, 0.14; 95% CI, − 0.23 to 0.52) (see Fig. 5).

Functional aspect Five studies [10, 23, 25, 27, 42] provided data for the functional aspect of QOL 0 at a 3-month follow-up; two [10, 25] provided these data at 3- to 6-month follow-ups and one [22] provided these data at a 6-month follow-up. Improvement in the functional aspect of QOL was not observed at the 0- to 3-month follow-up (SMD, 0.16; 95% CI, − 0.02 to 0.34; $I^2 = 46\%$), the 3- to 6-month follow-up (SMD, − 0.04; 95% CI, − 0.22 to 0.14; $I^2 = 0\%$), or the 6-month or later follow-up (SMD, − 0.08; 95% CI, − 0.46 to 0.29) (see Supplemental Fig. 3).

Mental aspect Five studies [19, 21, 35–37] reported detailed data on mental health at 0 to 3 months after intervention. Compared to the control group, a statistically significant improvement in mental health after intervention was observed (SMD, 0.26; 95% CI, 0.07–0.46; $I^2 = 0\%$). However, intervention for caregiver–patient dyads was not associated with a change in mental health at the

Table 4 Random-effects meta-analysis of randomized clinical trials on the association between patient-caregiver dyad care and patient functional domain of quality of life

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Laurel L. Northouse 2013-E [10]	19.42	5.53	99	19.78	6.11	104	3 m	Face to face + telephone	Low	FACT-G
Kerri M. Winters-Stone 2015 [25]	49.3	8.9	30	49.1	7.3	26	3 m	Face to face	Low	SF36
Laurel L. Northouse 2013-B [10]	19.01	5.67	99	19.78	6.11	104	3 m	Face to face + telephone	Low	FACT-G
Terry A. Badger 2011 [27]	46.45	11.9	34	42.76	14	36	2 m	Telephone	Low	UCLA-PSI
Areej El-Jawahr 2016 [23]	94.33	20.60	80	86.60	20.60	77	2 weeks	Face to face	Unclear	FACT-BMT
Areej El-Jawahr 2016 [23]	112.00	16.34	75	106.66	16.34	74	3 m	Face to face	Unclear	FACT-BMT
Kerri M. Winters-Stone 2015 [25]	49.3	8.9	30	49.1	7.3	26	3 m	Face to face	Low	SF36
Matthew M. Clark 2013 [22]	64.5	17.8	54	57.1	21.3	63	1 m	Telephone + face to face	Unclear	FACT-G
Laurel L. Northouse 2013-E [10]	19.06	5.71	99	18.89	6.46	104	6 m	Face to face + telephone	Low	FACT-G
Laurel L. Northouse 2013-B [10]	18.01	6.44	99	18.89	6.46	104	6 m	Face to face + telephone	Low	FACT-G
Kerri M. Winters-Stone 2015 [25]	50.1	8.1	30	49.5	7.0	25	6 m	Face to face	Low	SF36
Matthew M. Clark 2013 [22]	69.9	19.4	51	71.4	17.5	59	27 weeks	Telephone + face to face	Unclear	FACT-G

Table 5 Random-effects meta-analysis of randomized clinical trials on the association between caregiver-patient dyad care and patient social domain of quality of life

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Laurel L. Northouse 2013-E [10]	22.56	3.88	99	21.84	5.71	104	3 m	Face to face + telephone	Low	FACT-G
Bénédicte Belgacem 2013 [21]	55.7	24.3	33	50.0	24.3	34	1-3 m	Face to face	SF36	
Laurel L. Northouse 2013-B [10]	23.10	4.00	99	21.84	5.71	104	3 m	Face to face + telephone	Low	FACT-G
Terry A. Badger 2013 [31]	55.28	11.33	36	53.06	15.13	34	2 m	Telephone	Unclear	QOL-BC
Terry A. Badger 2011 [27]	70.26	11.00	34	64.06	16.9	36	2 m	Telephone	Low	PSS-FA
Matthew M. Clark 2013 [22]	85.6	12.4	54	83.7	13.3	63	1 m	Telephone + face to face	Unclear	FACT-G
Terry Badger 2013–1 [30]	65.7	3.3	18	58.1	4.6	9	4 m	Telephone	Unclear	QOL-BC
Terry A. Badger 2013 [31]	59.42	11.99	36	56.38	14.38	34	4 m	Telephone	Unclear	QOL-BC
Terry Badger 2013–2 [30]	65.0	4.0	13	58.1	4.6	9	4 m	Telephone	Unclear	QOL-BC
Laurel L. Northouse 2013-E [10]	22.15	4.09	99	21.9	5.49	104	6 m	Face to face + telephone	Low	FACT-G
Laurel L. Northouse 2013-B [10]	22.67	4.23	99	21.9	5.49	104	6 m	Face to face + telephone	Low	FACT-G
Terry A. Badger 2011 [27]	72.89	10.00	34	66.72	16.5	36	4 m	Telephone	Low	SWB
Jingmei Chen 2012 [18]	57.68	6.12	45	53.72	5.44	45	12 m	Telephone + face to face	High	QLICP-BR
Matthew M. Clark 2013 [22]	84.6	14.4	59	82.5	15.0	51	27 weeks	Telephone + face to face	Unclear	FACT-G

PSS-FA Perceived Social Support-Family scale, *SWB* The 8-item social well-being scale

3- to 6-month follow-up (SMD, 0.13; 95% CI, − 0.08 to 0.33; $I^2 = 0\%$) or at the 6-month or later follow-up (SMD, 0.05; 95% CI, − 0.26 to 0.36; $I^2 = 69\%$) (see Supplemental Fig. 4).

Spiritual aspect From analysis of the data from two studies [27, 30] that evaluated changes in spiritual functioning in the first 3 months post-intervention, the overall effect size was not significant (SMD, 0.26; 95% CI, − 0.07 to 0.60; $I^2 = 0\%$). At the 3- to 6-month follow-up, although the overall effect was positive, it was not significant (SMD, 0.29; 95% CI, 0.00–0.58; $I^2 = 0\%$). Analysis of the data from the six studies that evaluated the spiritual aspect of QOL at the 0- to 6-month follow-up showed an overall effect that was significant (SMD, 0.28; 95% CI, 0.06–0.50; $I^2 = 0\%$) (see Supplemental Fig. 5).

Table 6 Random-effects meta-analysis of randomized clinical trials on the association between caregiver-patient dyad care and patient mental domain of quality of life

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Laurel Northouse 2005 [19]	51.34	9.5	69	49.13	9.9	65	3 m	Face to face + telephone	Low	BHS
Bénédicte Belgacem 2013 [21]	58.5	23.6	33	52.4	16.8	34	1–3 m	Face to face	Unclear	SF36
Janette Perz 2015 [36]	49.3	9.8	26	45.2	12.0	33	1.5 m	Telephone	Unclear	SF-12
Janette Perz 2015 [36]	50.0	11.4	26	45.8	13.0	33	3 m	Telephone	Unclear	SF-12
Sylvie D. Lambert 2016 [37]	0.60	0.18	19	0.60	0.22	13	2 m	Telephone + booklets + CD and DVD	Low	AQoL
Jeremy Couper 2015 [35]	4.79	0.54	29	4.64	0.57	32	2.5 m	Face to face	Low	MHI
Laurel L. Northouse 2007 [20]	52.4	6.5	112	51.9	6.6	123	4 m	Telephone + face to face	Low	MOS SF-12
Laurel Northouse 2005 [19]	51.12	10.8	69	48.81	10.7	65	6 m	Face to face + telephone	Low	BHS
Jeremy Couper 2015 [35]	4.44	0.54	29	4.58	0.57	32	9 m	Face to face	Low	MHI
Laurel L. Northouse 2007 [20]	53.1	7.1	104	53.6	7.1	114	12 m	Telephone + face to face	Low	MOS SF-12
Laurel L. Northouse 2007 [20]	53.4	7.1	107	53.8	7.1	121	8 m	Telephone + face to face	Low	MOS SF-12
Jingmei Chen 2012 [18]	58.65	5.64	45	55.26	5.11	45	12 m	Telephone + face to face	High	QLICP-BR

MHI 38-item Mental Health Inventory

Table 7 Random-effects meta-analysis of randomized clinical trials on the association between caregiver-patient dyad care and patient spiritual domain of quality of life

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Terry A. Badger 2013 [31]	45.58	3.83	36	43.71	7.31	34	2 m	Telephone	Unclear	QOL-BC
Terry A. Badger 2011 [27]	40.97	7.60	34	39.15	9.4	36	2 m	Telephone	Low	QOL-BC
Terry A. Badger 2011 [27]	41.29	9.90	34	38.88	9.20	36	4 m	Telephone	Low	QOL-BC
Terry Badger 2013–1 [30]	54.1	3.0	18	50.9	4.2	9	4 m	Telephone	Unclear	QOL-BC
Terry A. Badger 2013 [31]	46.11	3.61	36	44.50	6.55	34	4 m	Telephone	Unclear	QOL-BC
Terry Badger 2013–2 [30]	56.9	3.6	13	50.9	4.2	9	4 m	Telephone	Unclear	QOL-BC

QOL-BC Quality of Life-Breast Cancer version questionnaire

QOL-BC 8-item spiritual well-being subscale of the Quality of Life Breast Cancer instrument

Fatigue

Six trials [23, 24, 27, 31, 32, 38] reported changes in the symptom of fatigue, and analysis of the data demonstrated that a care program targeting caregiver–patient dyads was not associated with changes in fatigue symptoms at the 0- to 3-month follow-up (SMD, 0.04; 95% CI, − 0.15 to 0.24; I^2 = 42%) or at the 3- to 6-month follow-up (SMD, − 0.20; 95% CI, − 0.51 to 0.10; I^2 = 0%) (see Supplemental Fig. 6).

Pain

Only four trials [21, 24, 32, 38] reported changes in pain level post-intervention, and analysis showed that caregiver–patient dyad care was not associated with a change in pain at the 0- to 3-month follow-up (SMD, − 0.07; 95% CI, − 0.36 to 0.22; I^2 = 51%) or at the 3- to 6-month follow-up (SMD, − 0.66; 95% CI, − 1.44 to 0.12) (see Supplemental Fig. 7).

Anxiety

Nine studies [17, 19, 23, 27, 32, 34, 36–38] evaluated changes in anxiety during the first 3 months post-intervention, and the overall effect size was moderate and significant (SMD, − 0.42; 95% CI, − 0.70 to − 0.13; I^2 = 81%). Thus, the interventions were superior to usual care for reducing patients' anxiety, and the effect appeared to last for at least 3 months. However, no trials tested the long-term effectiveness of the interventions on anxiety. When the study [17] with a high risk of bias was excluded, the overall effect was attenuated but still significant (SMD, − 0.30; 95% CI, − 0.48 to − 0.12; I^2 = 46%) (see Supplement Fig. 8 and Fig. 9).

Depression

Twelve studies [23, 24, 26, 27, 30–34, 36–38] evaluated changes in patients' depression during the first 3 months

Table 8 Random-effects meta-analysis of randomized clinical trials on the association between caregiver-patient dyad care and patient fatigue

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Areej El-Jawahri 2016 [23]	27.59	11.68	79	23.71	11.64	77	0.5 m	Face to face	Unclear	FACT Fatigue
Areej El-Jawahri 2016 [23]	37.60	9.52	73	35.60	9.52	74	3 m	Face to face	Unclear	FACT Fatigue
Terry A. Badger 2013 [31]	23.78	17.58	36	29.21	20.27	34	2 m	Telephone	Unclear	MFI
Terry A. Badger 2011 [27]	24.48	19.2	34	27.06	17.5	36	2 m	Telephone	Low	MFI
William Collinge 2013 [32]	3.70	2.15	45	4.37	2.26	50	1 m	Multimedia	Low	FACT Fatigue
Areej El-Jawahr 2016 [23]	37.60	9.42	73	35.60	9.42	74	3 m	Face to face	Unclear	FACT Fatigue
Catherine E. Mosher 2016 [38]	3.84	2.03	51	3.81	2.31	55	0.5 m	Telephone	Low	FSI
Catherine E. Mosher 2016 [38]	4.28	2.47	51	3.63	2.86	55	1.5 m	Telephone	Low	FSI
Terry A. Badger 2011 [27]	21.69	17.5	34	26.81	17.5	36	4 m	Telephone	Low	MFI
Jennifer L Steel 2016 [24]	28.3	9.4	15	31.1	11.4	12	6 m	Web + telephone + face to face	Low	FACT-Fatigue
Terry A. Badger 2013 [31]	20.22	20.09	36	22.09	19.10	34	4 m	Telephone	Unclear	MFI

FSI the Fatigue Symptom Inventory, *MFI* 20-item Multidimensional Fatigue Inventory, *PSS-10* the Perceived Stress Scale

Table 9 Random-effects meta-analysis of randomized clinical trials on the association between caregiver-patient dyad care and patient depression

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Linda M. McLean 2013 [33]	15.89	11.7	18	14.33	10.9	18	3 m	Face to face	Low	BDI-II
Yael Schenker 2016 [7]	5.1	4.3	20	5.9	3.6	10	3 m	Face to face	Unclear	HADS
Areej El-Jawahri 2016 [23]	6.74	4.04	80	8.49	4.03	77	2 weeks	Face to face	Unclear	HADS
Areej El-Jawahri 2016 [23]	3.49	3.29	74	5.19	3.29	74	3 m	Face to face	Unclear	HADS
Li Jia 2012 [17]	40.6	4.3	62	53.6	5.7	58	2 m	Face to face	High	SDS
Terry A. Badger 2013 [31]	6.75	7.98	36	10.56	10.03	34	2 m	Telephone	Unclear	CES-D
Terry A. Badger 2011 [27]	9.06	9.7	34	11.33	9.2	36	2 m	Telephone	Low	CES-D
Terry Badger 2013–1 [30]	13.6	2.5	18	10.6	3.5	9	2 m	Telephone	Unclear	CES-D
Terry Badger 2013–2 [30]	9.4	3.1	13	10.6	3.5	9	2 m	Telephone	Unclear	CES-D
Janette Perz 2015 [36]	8.6	1.5	26	8.9	1.7	33	1.5 m	Telephone	Unclear	HADS
Janette Perz 2015 [36]	8.7	1.7	26	8.7	1.6	33	3 m	Telephone	Unclear	HADS
Sylvie D. Lambert 2016 [37]	2.3	3.2	19	2.6	3.5	13	2 m	Telephone + booklets + CD and DVD	Low	HADS
William Collinge 2013 [32]	2.17	1.62	45	2.52	1.85	50	1 m	Multimedia	Low	FACT-G
Hoda Badr 2013 [41]	11.65	3.77	20	16.00	5.69	19	2 m	Telephone	Unclear	PROMIS
Catherine E. Mosher 2016 [38]	6.36	3.75	51	8.36	5.67	55	2 weeks	Telephone	Low	GAD-7
Catherine E. Mosher 2016 [38]	6.71	4.77	51	7.18	5.25	55	6 weeks	Telephone	Low	GAD-7
Linda M. McLean 2013 [33]	15.00	6.4	22	12.94	7.6	18	Post INT	Face to face	Low	BDI-II
Terry A. Badger 2013 [31]	5.44	8.62	36	9.94	11.47	34	4 m	Telephone	Unclear	CES-D
Jennifer L Steel 2016 [24]	15.3	10.5	15	24.7	15.07	12	6 m	Web + telephone + face to face	Low	CES-D
Terry Badger 2013–1 [30]	8.2	2.2	18	8.2	2.2	18	4 m	Telephone	Unclear	CES-D
Terry A. Badger 2011 [27]	8.86	10.00	34	11.18	13.4	36	4 m	Telephone	Low	CES-D
Terry Badger 2013–2 [30]	6.2	2.7	13	7.7	3.2	9	4 m	Telephone	Unclear	CES-D

PROMIS Patient Reported Outcomes Measurement Information System, The Patient Health Questionnaire-8 and Generalized Anxiety Disorder seven-item scale (GAD-7), *CES-D* 20-item Center for Epidemiological Studies-Depression Scale, *HADS* the Hospital Anxiety and Depression Scale, *BDI-II* Beck Depression Inventory-II

Table 10 Random-effects meta-analysis of randomized clinical trials on the association between caregiver-patient dyad care and patient anxiety

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Hoda Badr 2015 [34]	12.35	4.46	20	14.84	4.96	19	2 m	Telephone	Unclear	PROMIS
Yael Schenker 2016 [7]	4.6	2.3	20	6.3	2.9	10	3 m	Face to face	Unclear	HADS
Areej El-Jawahr 2016 [23]	4.08	3.05	74	4.84	3.03	74	3 m	Face to face	Unclear	HADS
Areej El-Jawahri 2016 [23]	4.08	3.08	80	6.33	3.09	77	2 weeks	Face to face	Unclear	HADS
Li Jia 2012 [17]	37.6	6.8	62	48.9	5.7	58	2 m	Face to face	High	SAS
Catherine E. Mosher 2016 [38]	3.72	3.45	51	6.68	6.48	55	2 weeks	Telephone	Low	GAD-7
Catherine E. Mosher 2016 [38]	4.06	3.82	51	5.45	5.93	55	6 weeks	Telephone	Low	GAD-7
Terry A. Badger 2011 [27]	30.72	8.37	34	31.53	9.18	36	2 m	Telephone	Low	CES-D
Terry A. Badger 2011 [27]	28.61	8.56	34	31.41	10.44	36	4 m	Telephone	Low	CES-D
Janette Perz 2015 [36]	11.0	1.4	26	10.4	1.8	33	1.5 m	Telephone	Unclear	HADS
Janette Perz 2015 [36]	11.2	1.6	26	10.9	1.8	33	3 m	Telephone	Unclear	HADS
Sylvie D. Lambert 2016 [37]	3.2	3.4	19	4.4	4.1	13	2 m	Telephone + booklets + CD and DVD	Low	HADS
William Collinge 2013 [32]	2.72	1.59	45	3.43	2.21	50	1 m	Multimedia	Low	FACT-G

Table 11 Random-effects meta-analysis of randomized clinical trials on the association between caregiver-patient dyad care and patient relatedness

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Hoda Badr 2015 [34]	12.60	1.39	20	11.00	2.08	19	2 m	Telephone	Unclear	PROMIS
Linda M. McLean 2013 [33]	33.73	5.4	22	30.94	9.6	18	Post INT	Face to face	Low	RFCS
Linda M. McLean 2013 [33]	32.67	10.0	22	29.00	10.1	18	3 m	Face to face	Low	RFCS
N. Heinrichs 2012 [28]	138.5	22.5	34	128.1	25.7	28	Post	Face to face	Low	DCI
Laurel L. Northouse 2013-E [10]	4.39	0.56	99	4.26	0.79	104	3 m	Face to face + telephone	Low	SSS
Laurel L. Northouse 2013-B [10]	4.31	0.59	99	4.26	0.79	104	3 m	Face to face + telephone	Low	SSS
Jeremy Couper 2015 [35]	7.76	2.75	29	8.22	2.77	32	2.5 m	Face to face	Low	FRI
Terry A. Badger 2011 [27]	18.32	1.90	34	17.45	2.60	36	2 m	Telephone	Low	PSS-FA
Janette Perz 2015 [36]	33.1	6.6	26	32.5	6.8	33	1.5 m	Telephone	Unclear	DAS
Janette Perz 2015 [36]	33.2	4.0	26	33.1	7.4	33	3 m	Telephone	Unclear	DAS
Sylvie D. Lambert 2016 [37]	17.1	1.7	19	17.4	1.3	13	2 m	Telephone + booklets + multimedia	Low	DAS
Laurel L. Northouse 2013-E [10]	4.27	0.64	99	4.21	0.69	104	6 m	Face to face + telephone	Low	SSS
Laurel L. Northouse 2013-B [10]	4.26	0.59	99	4.21	0.69	104	6 m	Face to face + telephone	Low	SSS
N. Heinrichs 2012 [28]	139.9	25.5	33	128.1	27.1	25	6 m	Face to face	Low	DCI
Terry A. Badger 2011 [27]	18.55	1.70	34	17.53	3.40	36	4 m	Telephone	Low	PSS-FA
Jeremy Couper 2015 [35]	10.10	2.64	29	9.13	2.04	32	9 m	Face to face	Low	FRI
N. Heinrichs 2012 [28]	134.5	26.4	30	141.2	24.0	18	12 m	Face to face	Low	DCI

RFCS Relationship-Focused Coping Scale, *SSS* modified version of the family support subscale of the Social Support Questionnaire, Relatedness scores can range from 4 to 16; higher scores indicate greater relationship quality, *PSS-FA* Perceived Social Support-Family scale, *DAS* the Brief Dyadic Adjustment Scale, *R-DAS* The Revised-Dyadic Adjustment Scale, *FRI* the validated 12-item Family Relationship Index, *DCI* Dyadic Coping Inventory (range, 35–175 for total score, with < 111 low dyadic coping, 111–145 moderate dyadic coping, and > 145 high dyadic coping)

following intervention. Meta-analysis showed that the interventions were successful at reducing patients' depression. Even when data from a study with a high risk of bias [17] were excluded from the analysis, the overall effect size remained significant (SMD, − 0.27; 95% CI, − 0.39 to − 0.15; I^2 = 8%). Four studies [27, 30, 31, 42] valuated changes in patients' depression between 3 and 6 months post-intervention, and the overall effect was again significant (SMD, − 0.29; 95% CI, − 0.56 to − 0.03; I^2 = 0%) (see Supplement Fig. 10 and Fig. 11).

Hopelessness

Four trials [10, 19, 20, 23] reported changes in feelings of hopelessness post-intervention. Meta-analysis showed that interventions were not effective at reducing patient hopelessness by the 1- to 3-month follow-up (SMD, − 0.23; 95% CI, − 0.91 to 0.44; I^2 = 0%) or at the 3- to 6-month follow-up (SMD, − 0.81; 95% CI, − 0.44 to 0.22; I^2 = 0%). Moreover, the overall effect size was not significant (SMD, − 0.16; 95% CI, − 0.49 to 0.17; I^2 = 0%) (see Supplement Fig. 12).

Table 12 Random-effects meta-analysis of randomized clinical trials on the association between caregiver-patient dyad care and caregiver marital functioning

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Linda M. McLean 2013 [33]	56.27	4.6	22	43.44	10.3	18	Post INT	Face to face	Low	RDAS
Linda M. McLean 2013 [33]	55.39	6.3	22	44.17	10.2	18	3 m	Face to face	Low	RDAS
N. Heinrichs 2012 [28]	38.6	8.4	34	37.2	10.1	28	Post	Face to face	Low	QMI
N. Heinrichs 2012 [28]	36.5	9.9	33	33.8	10.8	25	6 m	Face to face	Low	QMI
N. Heinrichs 2012 [28]	36.9	11.1	30	38.2	8.3	18	12 m	Face to face	Low	QMI

RDAS The Revised Dyadic Adjustment Scale, *QMI* Quality of Marriage Index (range, 6–45)

Table 13 Random-effects meta-analysis of randomized clinical trials on the association between caregiver-patient dyad care and caregiver hopelessness

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Linda M. McLean 2013 [33]	7.78	3.9	22	5.62	5.4	18	Post INT	Face to face	Low	BHS
Linda M. McLean 2013 [33]	6.95	5.8	22	5.78	6.0	18	3 m	Face to face	Low	BHS
Laurel L. Northouse 2013-E [10]	3.89	3.63	99	4.42	4.56	104	3 m	Face to face + telephone	Low	BHS
Laurel L. Northouse 2013-B [10]	4.10	4.04	99	4.42	4.56	104	3 m	Face to face + telephone	Low	BHS
Laurel Northouse 2005 [19]	3.56	4.3	69	3.96	4.1	65	3 m	Face to face + telephone	Low	BHS
Laurel L. Northouse 2013-E [10]	4.44	4.14	99	4.91	5.47	104	6 m	Face to face + telephone	Low	BHS
Laurel L. Northouse 2013-B [10]	4.46	4.10	99	4.91	5.47	104	6 m	Face to face + telephone	Low	BHS
Laurel L. Northouse 2007 [20]	2.23	2.4	112	2.69	3.1	123	4 m	Telephone + face to face	Low	BHS
Laurel Northouse 2005 [19]	4.20	4.9	69	3.46	4.0	65	6 m	Face to face + telephone	Low	BHS
Laurel L. Northouse 2007 [20]	2.62	2.7	107	2.67	3.1	121	8 m	Telephone + face to face	Unclear	BHS
Laurel L. Northouse 2007 [20]	2.72	2.7	104	2.57	3.1	114	12 m	Telephone + face to face	Unclear	BHS

BHS Beck Hopelessness Scale

Relatedness

Upon analysis of data from eight studies [10, 27, 28, 33–37] that assessed patients' relatedness with their important persons during the first 3 months following the intervention, the effect size was small but significant (SMD, 0.16; 95% CI, 0.03–0.29; $I^2 = \%$). However, the effect size was not significant at the 3- to 6-month follow-up (SMD, 0.14; 95% CI, −0.03, 0.31; $I^2 = 0\%$), nor at the 6-month or later follow-up (SMD, 0.16; 95% CI, −0.36 to 0.68; $I^2 = 65\%$) (see Supplement Fig. 13).

Marital functioning

Marital functioning was conceptualized as marital or sexual satisfaction, family support, and couple communication. Two studies [28, 33] evaluated changes in marital relationships during the first 3 months following intervention, and the overall effect size was significant (SMD, 1.01; 95% CI, 0.05–1.97; $I^2 = 85\%$). One study evaluated changes in marital–family relationships at 3–6 months post-intervention, but the effect was no longer significant at this follow-up (SMD, 0.09; 95% CI, −0.30 to 0.48). Thus, our analysis showed that dyadic interventions were superior to usual care for improving patient marital functioning, but this positive effect was not long lasting (see Supplement Fig. 14).

Survival

Only one trial [43] tested survival after dyadic intervention and specified survival as a secondary end point. Contrary to the researchers' hypothesis, patients with a caregiver participant who received the intervention had lower survival (Wald = 4.31; HR = 1.52; CI, 1.02–2.25, $P = 0.04$) compared to those without.

Table 14 Random-effects meta-analysis of randomized clinical trials on the association between caregiver-patient dyad care and caregiver pain

Source	Intervention			Control			Follow-up	The format of intervention	Risk of bias	Instrument
	M	SD	N1	M	SD	N2				
Jennifer L Steel 2016 [24]	4.7	1.5	15	6.1	2.6	12	6 m	Web + telephone + face to face	Low	BPI
Bénédicte Belgacem 2013 [21]	60.7	28.4	33	49.3	27.4	34	1–3 m	Face to face	Unclear	SF36
Catherine E. Mosher 2016 [38]	2.24	2.16	51	2.62	2.34	55	2 weeks	Telephone	Low	BPI
Catherine E. Mosher 2016 [38]	2.64	2.49	51	2.77	2.48	55	6 weeks	Telephone	Low	BPI
William Collinge 2013 [32]	2.62	1.92	45	3.46	2.46	50	1 m	Multimedia	Low	FACT-G

BPI, The Brief Pain Inventory Short Form, The Fatigue Symptom Inventory

FACT-G, The Brief Pain Inventory Short Form

Table 15 Pooled effect sizes of outcomes for cancer patients

Aspects/outcomes	Number of trials	Number of patient–caregiver dyads	Pooled effect size SMD (95% CI)	I^2 for heterogeneity
Total quality of life				
0–3 months	6	622	0.25 (0.01, 0.50)*	54%
3.1–6 months	3	364	0.19 (− 0.34, 0.71)	77%
> 6 months	3	556	0.01 (− 0.15, 0.18)	0%
Physical aspect of QOL				
0–3 months	9	1000	0.09 (− 0.13, 0.30)	63%
3.1–6 months	6	899	− 0.12 (− 0.30, 0.06)	40%
> 6 months	3	646	0.12 (− 0.15, 0.40)	65%
Emotional aspect of QOL				
0–3 months	7	810	0.16 (0.02, 0.29)*	0%
3.1–6 months	4	594	0.08 (− 0.08, 0.25)	0%
> 6 months	2	200	0.26 (− 0.44, 0.96)	84%
Social aspect of QOL				
0–3 months	6	730	0.21 (0.07, 0.36)**	0%
3.1–6 months	5	595	0.19 (0.03, 0.35)*	0%
> 6 months	2	200	0.40 (− 0.12, 0.93)	71%
Functional aspect of QOL				
0–3 months	6	955	0.16 (− 0.02, 0.34)	46%
3.1–6 months	3	461	− 0.04 (− 0.22, 0.14)	0%
> 6 months	1	110	− 0.08 (− 0.05, 0.21)	NA
Mental aspect of QOL				
0–3 months	5	412	0.26 (0.07, 0.46)**	0%
3.1–6 months	2	369	0.13 (− 0.08, 0.33)	0%
> 6 months	3	597	0.05 (− 0.26, 0.36)	69%
Spiritual aspect of QOL				
0–3 months	2	140	0.26 (− 0.07, 0.60)	0%
3.1–6 months	3	189	0.29 (0.00, 0.58)	0%
Fatigue				
0–3 months	5	750	0.40 (− 0.15, 0.24)	42%
3.1–6 months	3	167	− 0.20 (− 0.51, 0.10)	0%
Pain				
0–3 months	3	374	− 0.07 (− 0.36, 0.22)	51%
3.1–6 months	1	27	− 0.66 (− 0.14, 0.12)	NA
Anxiety				
0–3 months	8	971	− 0.30 (− 0.48, − 0.12)**	46%
Depression				
0–3 months	11	1096	− 0.26 (− 0.39, − 0.13)**	8%
3.1–6 months	4	225	− 0.29 (− 0.56, − 0.03)*	0%
Hopelessness				
0–3 months	4	620	− 0.23 (− 0.91, 0.44)	0%
3.1–6 months	4	775	− 0.31 (− 0.84, 0.22)	0%
> 6 months	1	446	0.05 (− 0.49, 0.59)	NA
Relatedness				
0–3 months	9	868	0.18 (0.04, 0.32)*	6%
3.1–6 months	4	534	0.16 (− 0.01, 0.33)	0%
> 6 months	2	109	0.09 (− 0.56, 0.74)	65%
Marital functioning				
0–3 months	2	143	1.01 (0.05, 1.97)*	85%
> 6 months	2	106	0.09 (− 0.30, 0.48)	0%

NP not applicable

*$p < 0.05$; **$p < 0.001$

Discussion

In this meta-analysis, caregiver–patient dyadic interventions were associated with significant improvements in the emotional, social, spiritual, and mental aspects of patient QOL, and also in their relationships with caregivers, marital functioning, depression, and anxiety. The effect sizes for most of these indicators were only small to medium, but the associations remained statistically significant, even when sensitivity analyses were restricted to trials with a low or fair risk of bias. However, some effects were observed only at the 0- to 3-month follow-up and not sustained to the 3- to 6-month follow-up or beyond.

The results of this study differed from the conclusion of a prior review by Griffin and colleagues [14] that family caregiver-involved interventions were not superior to active controls or usual care. More specifically, for patient QOL, only one study of five studies in their review reported an improvement in global QOL for patients immediately following the

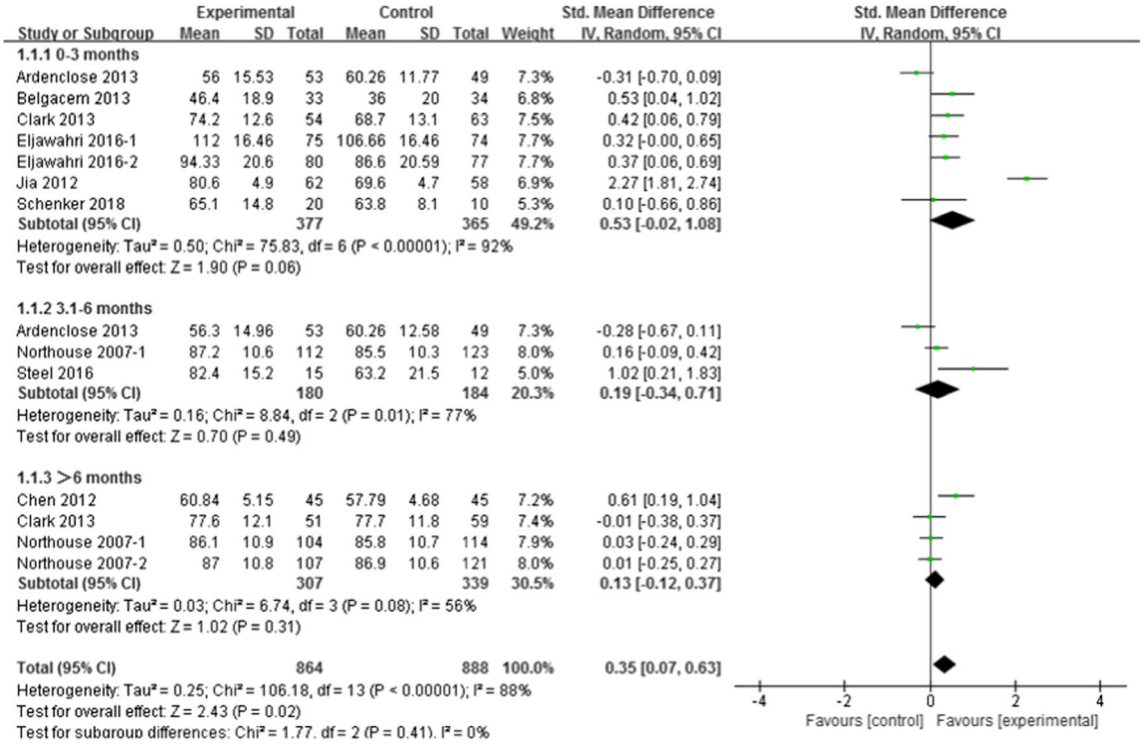

Fig. 2 Effect sizes for total quality of life. Note: The text at the bottom of Figs. 2, 3, 4, and 5 and supplementary Figs. 3 to 14 reads "Test for subgroup differences"

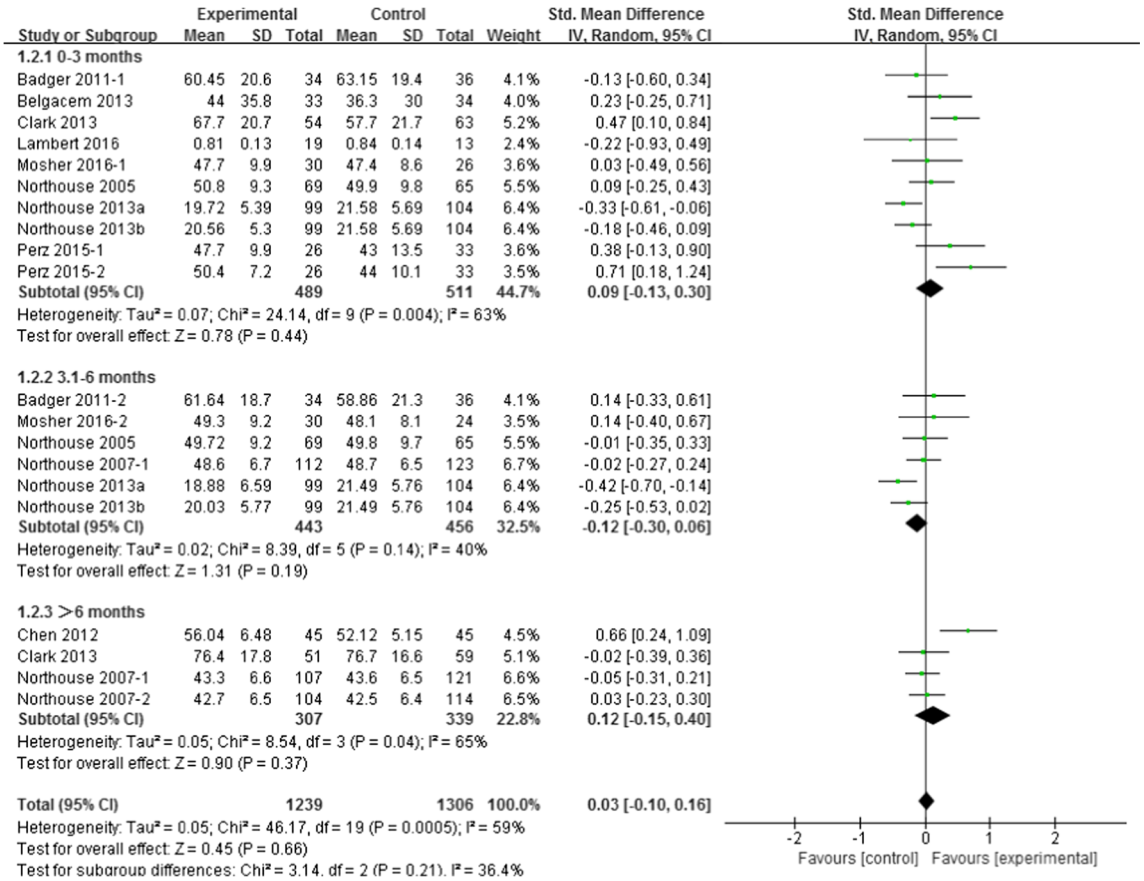

Fig. 3 Effect sizes for physical aspect

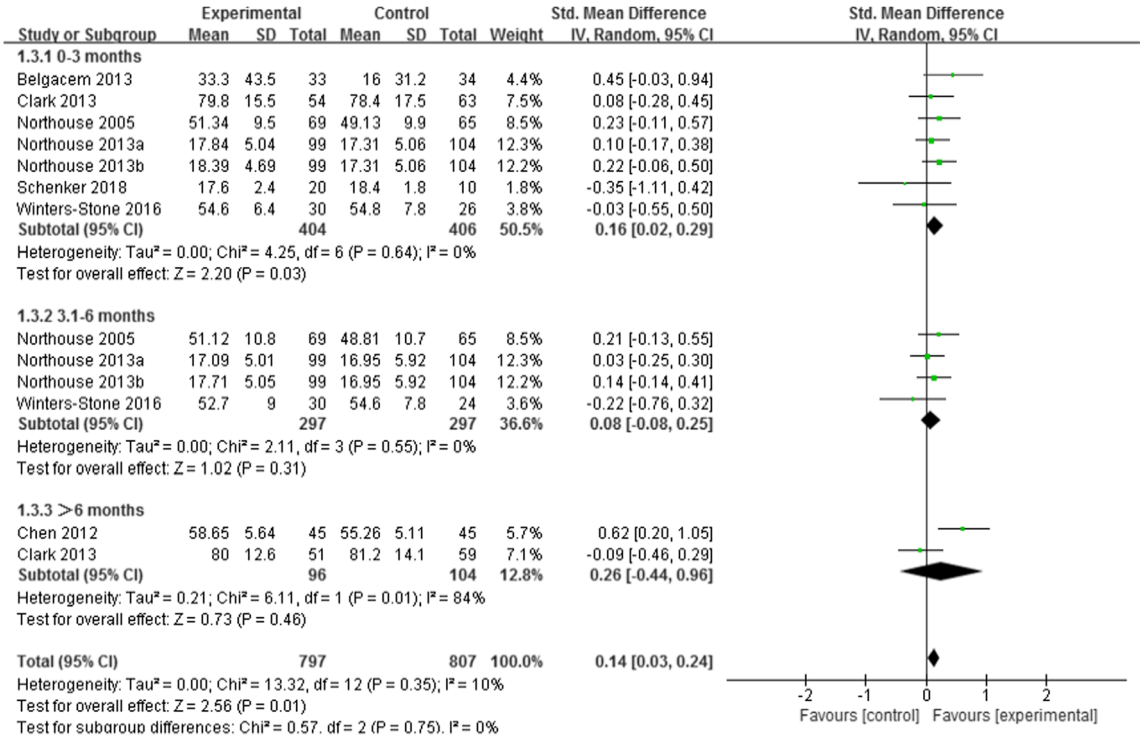

Fig. 4 Effect sizes for emotional aspect

intervention, whereas the other four studies reported no significant change. Also, in their review, only three among ten trials assessing patients' general psychological functioning reported significant findings. Finally, their analysis identified a moderate risk of bias, imprecise effect size, poor methodological quality, and small sample sizes among the included studies. They indicated that the overall strength of evidence for the superiority of family-involved interventions was low. One explanation for the discrepancy between their findings and ours might be differences in the inclusion criteria used. The present study evaluated

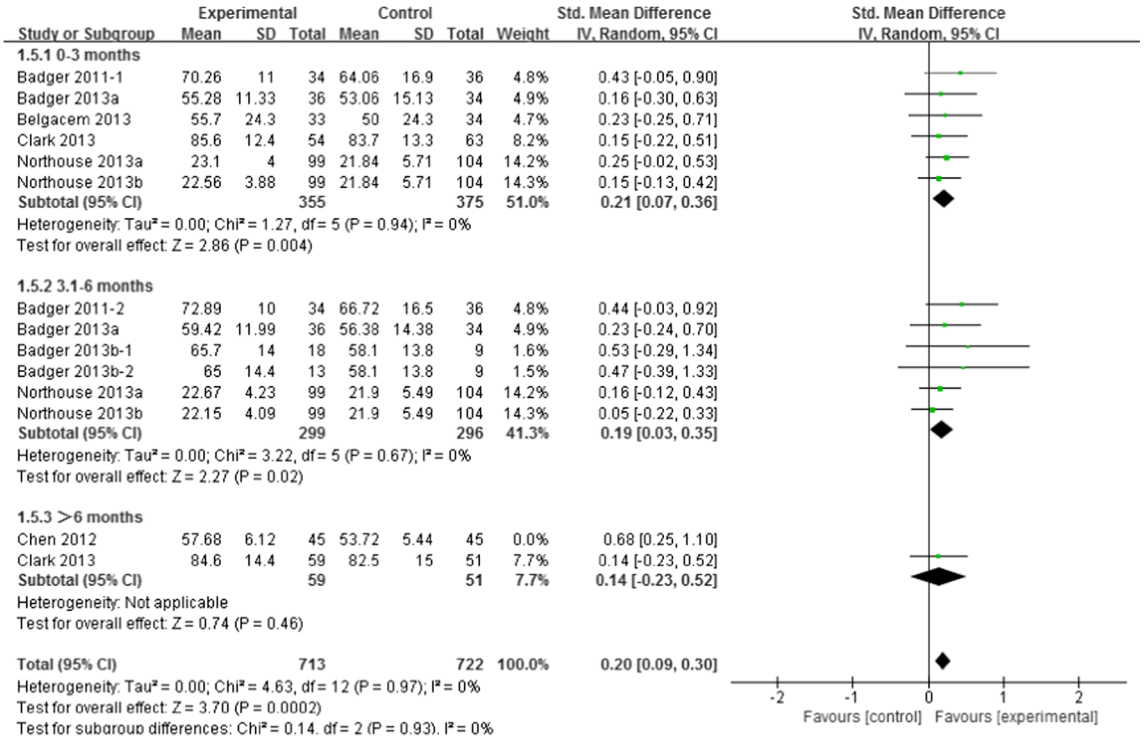

Fig. 5 Effect sizes for social aspect when the high risk of bias studies are excluded

the efficacy of interventions specifically targeting patient–caregiver dyads, whereas the systematic review by Griffin et al. mainly identified trials including family members. In their review, several studies were even designed to primarily improve family member outcomes, which could have affected the findings regarding the significant effects of interventions. This may also indicate that improvements in family member outcomes are insufficiently effective at benefiting patients.

According to the present meta-analysis, patient–caregiver dyadic interventions were not effective at reducing patients' pain and fatigue compared with observations after usual care or in active controls. In particular, physical and functional well-being showed no significant changes following intervention. This is consistent with the conclusion of Regan et al. [13] but inconsistent with the results of a review published in 2013 by Hoda Badr and Paul Krebs [41], in which the largest effect size of couple-based interventions for cancer patients was for physical outcomes ($g = 0.31$). One reason for this finding is that many of the tested interventions were conducted in seriously ill populations, but Hoda Badr and Paul Krebs focused on early-stage cancer patients (most studies were conducted in breast and prostate cancer populations). The physiological functions of these patients with advanced cancer could not be enhanced greatly because of their health deterioration. Therefore, for late-stage patients, it may be unrealistic to expect rapid improvement in their overall QOL; rather, it might be more realistic to attempt to maintain their physical well-being and promote their comfort.

Survival was reported as an outcome in one trial in this review. Nicholas et al. [43] studied whether patients with advanced cancers had a higher survival when receiving care from a family caregiver. Contrary to the researchers' hypothesis, patients with a family caregiver showed lower survival than those without. This may due to patients' self-perceived burden on their family caregivers [44, 45]. Suffering from cancer limits individuals' ability to care for themselves independently, and these patients may see themselves as a burden on their loved family members. Research has provided evidence that this reluctance to burden others may result in emotional problems [46] and impact patients' behaviors. Notably, no trial has yet shown a decrease in survival after administration of intervention programs for patient–caregiver dyads.

Clinical implications

There are several clinical implications from the present review. First, health professionals working with cancer patients should consider the needs of the patient–caregiver dyad when formulating care program protocols. Even though a large body of evidence shows that interventions provided to caregivers can have positive effects on caregivers' outcomes, this does not mean that cancer patients will definitely obtain great care from the better-prepared caregivers. The ultimate patient outcomes depend on the response of the patient–caregiver unit. Thus, in order to provide optimal holistic cancer care, the care should focus on the needs of the patient–caregiver dyad. Second, this review provides clear evidence that interventions provided to patient–caregiver units can have many positive effects on important patient outcomes. The tested interventions significantly reduced patients' depression and anxiety and improved their social well-being, emotional functioning, and marital and family relationships. Another key implication is the need for health workers to include a more precise patient assessment upon new patient admission. As above mentioned, some patients may see themselves as a burden on their caregivers, because of their lost ability to care for themselves. This may lead to negative emotions or behaviors in these patients and, in turn, diminish the effects of clinical intervention. More research is needed to identify patients who are at higher risk for pre-existing emotional or behavioral problems, so that appropriate interventions can be targeted to them. All patients should be provided with a basic psychological assessment as the first step of a comprehensive cancer care planning program. This will help to identify patients who are at greater risk of experiencing a negative emotional burden and more likely to benefit from additional interventions.

Study limitations

First, because of the diversity among the tested interventions, this review could not discern the associations between specific dyadic interventions with a particular content or format and patient outcomes. Future research should aim to identify and establish optimal models and efficacious components of dyadic intervention programs that help patient–caregiver dyads. Second, we did not include studies published in languages other than English and Chinese, unpublished studies, dissertations, or abstracts from conference proceedings, which is likely to introduce an upward bias into the size of the effects. Third, several identified trials could not be included in this meta-analysis, because caregiver participation was optional [40] or data remained translated [47]. We also excluded quasi-experimental studies [46, 48–50], pre–post comparing programs [51–56], and a study in which the control group did not meet the inclusion criteria [57]. However, these studies did demonstrate benefits of interventions to patients. Given these limitations, the results of this meta-analysis should be interpreted cautiously.

Conclusions

In this meta-analysis, interventions for caregiver–patient dyads were associated with improvements in multiple psychosocial dimensions of patient QOL, relatedness, marital functioning, depression, and anxiety. However, many of these effects were no longer significant at later follow-ups, and there

was no significant association between the dyadic interventions and patient physiological aspects such as physical and functional well-being, pain, fatigue, and survival.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Data disclosure Both the corresponding author and the first author have full control of all primary data and agree to allow the journal to review their data if requested.

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