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## Review

# Effectiveness and moderators of cancer patient-caregiver dyad interventions in improving psychological distress: A systematic review and meta-analysis



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#### ABSTRACT

Objective: As patients and family caregivers are increasingly viewed as a dyadic whole, growing studies have emerged that identify ways to improve the two parties' emotional distress. However, the specific effectiveness, quality, and optimal intervention details of these studies are unclear. Our objective is to synthesize the effectiveness of existing dyadic interventions for improving the psychological distress of cancer patient-caregiver dyads and identify potential moderators that influence intervention effectiveness.

*Methods:* PubMed, Cochrane Library, Web of Science, CINHAL, Embase, and Clinical Trials were searched to identify all randomized controlled trials from inception until June 2021. Two reviewers performed the process independently. The Cochrane Risk of Bias tool was used for quality assessment. We calculated effect sizes (Hedges' adjusted g) by standard mean difference. Potential moderators influencing the intervention effects were explored.

Results: We included 28 articles, of which 12 were available for meta-analysis. In total, 4784 participants were included, who were primarily middle-aged (M=58 years old), with the highest proportion reporting a diagnosis of "mixed cancer" (30%). Patients' anxiety (g=-0.31; 95% CI:-0.51 to -0.12; P=0.001;  $I^2=17\%$ ) and cancerrelated distress (g=-0.32; 95% CI:-0.46 to -0.18; P<0.0001;  $I^2=0\%$ ) were statistically significantly improved from baseline to post-intervention. Interventionist, delivery type, duration, and frequency were potential moderators for psychosocial interventions on negative emotions.

*Conclusions*: Face-to-face, relatively shorter interventions led by psychologists in moderator analysis seem to have better performance. Cancer dyad-based interventions were efficacious in improving the emotional distress of both parties in the dyad, but the effect was more apparent in patients than in family caregivers. However, the long-term effects were modest for both groups.

# Introduction

The International Agency for Research on Cancer<sup>1</sup> estimated that 19.3 million new cancer cases were diagnosed globally in 2020. The cancer trajectory often presents a tiresome and difficult challenge, not only for patients but also for family caregivers. Family caregivers, defined as family members or significant others who provide emotional and physical support for patients, often do so without expecting anything in return.<sup>2,3</sup> Physical discomfort, fatigue, sleep problems, overload, and mental distress are the main problems reported by patients with cancer and their family caregivers.<sup>4,5</sup> In addition, primary caregivers are frustrated by the high caregiving burden, lack of independence and freedom, and the need, at times, to hide their depression symptoms.<sup>6</sup> Negative emotions are infectious to make cancer dyads suffer more. Multiple

studies have produced statistics which indicate that varying degrees of emotional problems exist among patients with cancer and family caregivers. A cross-sectional study found one-third of cancer survivors and family caregivers experienced anxiety and depression. The consecutive challenges of "dealing with the emotions of the initial diagnosis or recurrence, uncertainty about the future, managing cancer pain, caring for the patient and managing emotions" can be difficult for both cancer survivors and informal caregivers. Many psychosocial interventions have been developed to address the overwhelming distress in recent years. Non-pharmacological methods have been utilized to change an individual's behavior, including psychological, educational, and behavioral components, 9,10 such as informational sessions, mindfulness meditation, teaching cognitive and behavioral coping strategies, and peer support. Therefore, a critical analysis is necessary to determine the most

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effective interventions to manage the symptoms of emotional distress in patients and their family caregivers.

With the introduction of various dyadic theories, 11-13 the concept of the patient-caregiver dyad was proposed and is, indeed, worthy of attention. Patient-caregiver dyad states are an interdependent whole and not just a "receiver" or "giver"; it requires work together to cope with the illness. Considering the patient and the family caregiver as a unit and promoting joint physical and psychological outcomes for each other was a new perspective proposed to address their psychosocial problems. In recent years, several meta-analyses have been conducted to better understand the impact of psychosocial interventions on cancer dyads. The majority of studies have focused on the domains of physical symptoms, psychological, social functioning, and overall quality of life (QoL). In addition, the few published systematic reviews or meta-analyses that have assessed the impact of psychosocial interventions on the mental health of cancer dyads have limitations. For instance, Badr<sup>14</sup> and Wang et al<sup>15</sup> did carry out a meta-analysis, but they are mainly focused on couple-based interventions while not analyzing other caregiver roles related to the effect of dyadic emotional outcomes. Gabriel<sup>16</sup> and Regan et al<sup>17</sup> conducted systematic reviews for cancer dyads without performing meta-analyses. Hence, it is indisputable that treating patients and their family caregivers as a dyadic unit can provide new directions and perspectives for improving emotional outcomes and overall QoL for both populations. 18,19

Numerous researchers highlight physical and mental health problems among cancer dyads. Although these non-pharmacological interventions have shown some degree of effectiveness,  $^{20,21}$  what remains unknown is whether the interventions will affect this group differently and whether interventions delivered in varied forms, durations, and frequency will impact emotional distress differently. Only limited conclusions can be drawn from the available reviews regarding the effectiveness of psychosocial interventions in improving emotional distress in cancer dyads. This systematic review aims to find and synthesize available evidence to bridge the gap, providing insight and direction for clinical staff to address these emotional problems.

The objectives of this systematic review are as follows: (1) explore the effects of current interventions on patients with cancer and their family caregivers' emotional outcomes (symptoms of depression, anxiety, cancer-related distress); (2) conduct further analyses targeting variables of interest that may influence the effect of the intervention to clarify potential moderating effects.

## Methods

Review and synthesis were performed following the PRISMA 2020 statement. <sup>22</sup> This study was registered on Open Science Framework (https://doi.org/10.17605/OSF.IO/WXTUV).

# Inclusion and exclusion criteria

- (1) Population: patients diagnosed with cancer and their family caregiver (The caregiver is the family member who undertakes the primary care, including the spouse, children, parents, siblings, etc.); any patients/caregivers aged ≤ 18 years old and receiving palliative care at the end of life were excluded.
- (2) Intervention: dyad intervention or treatment that consider the patient and family caregiver as a holistic unit.
- (3) Comparison: control group was not restricted; usual routine care, waitlist control, or other types of interventions were eligible.
- (4) Outcome: any emotional outcomes, such as anxiety, depression, despair, and distress, were measured, while studies that only reported patient or partner outcomes but not both were ineligible. It is worth noting that the emotions mentioned above should be a symptom rather than a disorder.

(5) Study type: randomized control trial design study.

#### Literature search

We searched for journal articles published from inception until June 2021 in the electronic databases PubMed, Cochrane Library, Web of Science, CINHAL, Embase, Clinical Trials, and reviewed the reference lists of selected publications. Medical Subject Headings (MeSH) and free text terms were combined to form the search strategy. The search terms reflected combinations of the following keywords: (neoplasm\* OR tumor\* OR cancer\*) AND ((patient\* OR client\*) AND (caregiver\* OR carer)) AND (dyad\* intervention OR dyad\* pattern) AND (emotion OR mood). The detailed search strategies are presented in the Supplementary Table.

#### Data extraction

We entered all records into EndnoteX9, and two reviewers (PXN and JYF) sifted the articles independently. All search results were screened twice. Any disagreements were addressed through discussion and consensus by the third member (WHH). Two reviewers separately extracted data using Microsoft Excel software. Double-checks were conducted after entering all data. The synthesis table included the primary author, published year, setting, cancer type, intervention (therapy, delivery/dosage, refusal rate, follow-up, retention rate), psychological measurement tool, and main findings.

## Quality appraisal

We used the Cochrane risk of bias tool of the Review Manager 5.4.1 software to evaluate quality assessment. The RoB 2.0 tool provides a framework for assessing the risk of bias in a single RCT result,<sup>23</sup> which contains six items in five domains. All studies included were evaluated independently by two reviewers, who classified the risk of bias for each study as "low risk," "unclear," or "high risk." The third reviewer resolved discrepancies.

## Data synthesis

Since standard mean deviation could pool the different units of various rating instruments in the meta-analysis, we used standard mean deviation and 95% confidence interval (CI) to calculate the effect size of the continuous variables. We used Hedges' adjusted g as effect size to provide a better estimate when the sample size was small.  $^{24}$   $I^2 \geq 50\%$  suggested significant heterogeneity, and further sensitivity analyses reduce it. A random-effects model was used since the interventions included in the analysis varied by method, population, measurement tools, and follow-up time. In most cases, the baseline influence two group effects when performing pre-post design studies. When only including post-test results tend to exaggerate in statistics, thus the true effect values are underestimated. We, therefore, weighted the differences between pre- and post-means, as recommended by Morris  $^{25}$  because effect sizes were defined using pretest and post-test information.

The moderator analysis explores the direction and strength of the relationship between dyadic negative emotions (independent variables) and the intervention effects (dependent variables). Based on previous studies, we identified several factors that may influence the effect of dyadic interventions. The moderator analysis in this paper was limited to groups with at least three studies. Usually, the number of studies is represented by k in a meta-analysis, while n is the number of participants in each study.

We used Duval and Tweedie's trim-and-fill method $^{26}$  through the computer program CMA 3.0 to generate funnel plots containing observed studies and imputed studies. Egger's regression test $^{27}$  was also used to clarify publication bias.

#### Results

#### Search outcomes

In total, 28 full-text articles were extracted and tabulated, 12 of which were synthesized as part of a meta-analysis. As illustrated in the PRISMA flow chart (Fig. 1), a total of 4135 study records were identified. After reading 3413 titles/abstracts, we reviewed 130 full texts. Ninety-one studies were excluded after a full-text screening, and the main reasons for exclusion were shown in Fig. 1. In addition, we identified eight cited references and finally included four studies. Ultimately, 28 eligible studies were identified for this systematic review.

#### Study characteristics

Most of the studies were conducted in the United States (k = 19); the rest were performed in China (k = 3), Australia (k = 2), the United Kingdom (k = 2), Denmark (k = 1), and Belgium (k = 1). The characteristics of the 28 studies included in the systematic review are summarized in Table 1 and are described in detail in Table 2.

#### **Participants**

The patients/family caregivers recruited at baseline totaled 4784 participants from 28 studies, ranging from 30<sup>28</sup> to 968, <sup>29</sup> with eight studies involving a sample size of fewer than 50. The average age ranged from 43.70 to 67.50 for patients and 48.27 to 63.56 for family caregivers. The roles played by the family caregivers varied: the spouse was the family member involved most often, followed by adult children, parents, siblings, friends, or significant other. Mixed cancer (30%) was the most common cancer type, followed closely by prostate (21%) and breast (14%). The mean refusal rate varied from 5.2%<sup>30</sup> to 82.2%. <sup>31</sup> The mean retention rate at final follow-up ranged from 16.67%<sup>28</sup> to 95.9%. <sup>32</sup> Distress screenings, which assess participants with high distress levels, were conducted at the beginning of four studies. <sup>29,33–35</sup> Some studies paid more attention to patients <sup>36</sup> than to family caregiver involvement or the dyad intervention, while Badr et al <sup>37</sup> and Clark et al <sup>38</sup> assigned

patients and family caregivers to different sessions.

#### Interventions

The frequency of the intervention ranged from 4 times  $^{32,34,39-43}$  to daily,  $^{44}$  and the total duration varied from 78 min  $^{34}$  to 24 h.  $^{30}$  Nearly half of the interventionists were nurses  $^{28,29,32,36,48,54,56}$  or psychologists,  $^{37,40,42,43,53}$  even for both.  $^{33,41}$  Interventions included supportive communication, coping skill development, family-oriented supportive education, health management, mindfulness, yoga, and music therapy.

Couple-based interventions were more common (k=13) compared to treatments that mixed various family caregiver roles. They often focused on dyad coping<sup>34,37,45,46</sup> and communication.<sup>31,39,40,42</sup> Half of the studies examined face-to-face interventions (k=14); five programs involved technology-based interventions,<sup>31,35,37,43,47</sup> while others involved telephone (k=3).

#### Comparison group

Six studies compared the experiential group with groups who had undergone other interventions.  $^{29,31-33,42,48,49}$  Chambers  $et\ al,\ ^{33}$  respectively, compared nurse-led and psychologist-led interventions. Two studies considered multiple comparison groups: two versions of one program were implemented: brief or extensive  $^{48}$  and Milbury et al  $^{42}$  compared the effects of couple-based meditation, supportive-expressive, and TAU (Treatment as usual).

## Outcome measures and timing

Anxiety, depression, distress, and hopelessness were included when measuring mood states. Many studies have involved specific anxiety or depression scales to measure this outcome, while some studies also used QoL emotional subscales. Most studies measured negative emotions, only three 41,48,50 investigated positive ones, such as well-being, satisfaction, hopefulness, and calmness. An appropriate cortisol level, a hormone produced by the adrenal glands, can help the body cope with stress, 51 and the hormone is a closely relevant emotional state. However, only one study 48 employed this objective laboratory indicator to indirectly reflect

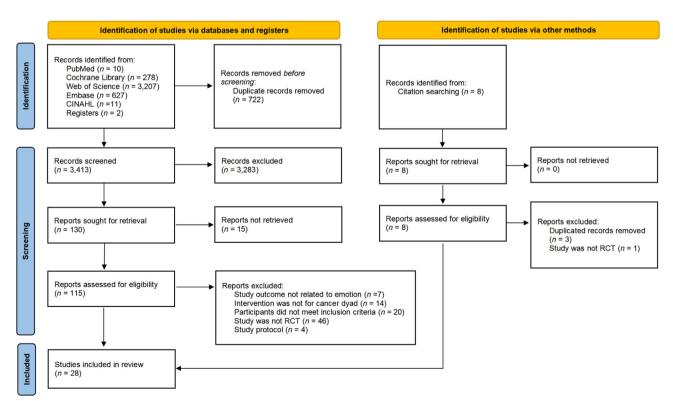


Fig. 1. Flow diagram depicting the literature search in accordance with PRISMA 2020 guidelines.

**Table 1** Study characteristics of the systematic review (k = 28).

Item	k (%)	Mean
Cancer type		
Breast	4 (14)	
Lung	4 (14)	
Prostate	6 (21)	
Myeloma other	2 (7)	
Gastrointestinal	2 (7)	
Head and neck	2 (7)	
Mixed	8 (30)	
Role of caregiver		
Spouse only	13 (46)	
Family member or other	15 (54)	
Age(year)		
Patient		58.26
Caregiver		55.35
Sample size		171
Refusal rate		41.18%
Retention rate		68.77%
Interventionist		
Psychologist	5 (18)	
Nurse	7 (25)	
Psychologist and nurse	2 (7)	
Therapist	8 (29)	
Online resources	2 (7)	
Other	4 (14)	
Type of control group		
Usual care	18 (64)	
Wait-list control	3 (11)	
Other intervention	7 (25)	
Follow-up		
0	13 (46)	
1	4 (14)	
2	5 (18)	
3	3 (11)	
4	3 (11)	
Distress screening	4 (14)	
Cost-benefit analysis	2 (7)	
Intention-to-treat	11 (39)	
Per-protocol	1 (4)	

k, number of studies.

anxiety or depression levels. No follow-up was done for 13 studies; 4 recorded one follow-up. Outcomes were measured at two time-points in five studies and at three time-points in three studies. Follow-up ranged from 1 to 14 months.

## Results of the meta-analysis

Although numerous rating tools were used to measure emotional outcomes, variables that could be pooled and meta-analyzed were symptoms of depression, anxiety, and cancer-related distress (Fig. 2, Table 3). Inevitably, varying degrees of heterogeneity were introduced due to differences in interventions, study subjects, measurement tools, and so on. The following will be described in different dimensions.

# Depressive symptom

The eight studies on patients  $^{34,36,37,40,44,48,52,53}$  were combined into subgroups from baseline to immediately post-intervention; pooled results were not statistically significant (g=0.04; 95% CI:-0.41 to 0.48; P=0.86;  $I^2=88\%$ ). When the study  $^{48}$  with an intervention comparison was excluded, they showed small but statistically significant results (g=-0.19; 95% CI:-0.36 to -0.01; P=0.04;  $I^2=16\%$ ). However, as seen in the subgroup containing three studies  $^{40,48,53}$  from the post-intervention follow-up at 5 weeks to 14 months, the reduction in patient depression had a long-term effect at follow-up and had a medium clinical effect compared to the immediately post-intervention subgroup (g=-0.68; 95% CI:-1.77 to 0.41; P=0.22;  $I^2=93\%$ ).

In terms of family caregivers, greater heterogeneity was demonstrated in seven  $studies^{34,37,40,44,48,52,53}$  from baseline to post-intervention (g = -0.44; 95% CI: -1.03 to 0.15; P = 0.15;  $I^2 =$ 91%), even two studies<sup>34,53</sup> showed better results for reducing depression in the control group. We found some interesting results when we explored the reasons for the high heterogeneity in caregiver depression. Lambert et al<sup>34</sup> provided a health education booklet and a short follow-up to the control group contributed better results for them. Mosher et al<sup>53</sup> speculated peer help plus coping skills would have less impact than only coping skills for patients with advanced cancer, but draw a contrastive conclusion. Participants in this study had high coping self-efficacy levels at baseline, so there was little potential to produce positive change in them through such interventions. From the same three follow-up studies on patients, the long-term depression status of the caregivers did not change noticeably (g = -0.56; 95% CI: -1.82 to 0.69; P = 0.38;  $I^2 = 95\%$ ). Notably, Hsiao et al<sup>48</sup> found a greater effect in the couples' support group among caregivers when comparing couples' and individuals' support groups.

#### Anxiety

Seven studies measuring patient anxiety<sup>34,36,40,44,48,52,53</sup> showed a statistically significant difference and small clinical effect from baseline to post-intervention (g=-0.31;95% CI:-0.51 to  $-0.12;P=0.001;I^2=17\%$ ). Similarly, after excluding the Hsiao et al<sup>48</sup> study, only a small clinical significance was observed from post-intervention to follow-up phase (g=-0.32;95% CI:-0.65 to  $0.02;P=0.06;I^2=0\%$ ). However, family caregiver outcomes in the category of anxiety were not statistically significant either at post-intervention (g=0.12;95% CI:-0.16 to  $0.44;P=0.37;I^2=63\%$ ) or during follow-up (g=-0.08;95% CI:-0.34 to  $0.19;P=0.57;I^2=0\%$ ). This demonstrates that these interventions reviewed in this study were highly effective in reducing patients' anxiety compared to care as usual but had no significant effect on family caregivers other than those reported by Hsiao et al. 48

### Cancer-related distress

Cancer-related distress was conceptualized in this meta-analysis as other negative emotions triggered by cancer, such as despair, sadness, stress, apprehension, symptom distress, and so on. Seven studies  $^{31,32,37,44,52-54}$  measured this outcome. Although different assessment tools were used, the final pooled results showed that patients' cancer-related distress was statistically significant and without heterogeneity at post-intervention (g=-0.32; 95% CI:-0.46 to -0.18; P<0.0001;  $I^2=0\%$ ). The impact of family caregivers on improving a negative mood was not obvious (g=0.02; 95% CI:-0.23 to 0.26; P=0.89;  $I^2=52\%$ ).

## Moderator analysis

To further explore the intervention effects, we conducted a moderator analysis (Table 4). Four variables were included as moderators: intervention delivery type (face-to-face, online, telephone), interventionist role (nurse, psychologist, therapist), frequency of intervention (time), and duration of sessions (hour). An individual with a psychologist's background provided a significant intervention effect compared to what an experienced therapist or nurse provided, related to either anxiety (k = 5, g = -0.36, P = 0.001) or distress (k = 3, g = -0.31, P = 0.01). The face-to-face approach produced more significant effects in reducing distress (k = 3, g = -0.42, P = 0.04). The effect was better if the frequency was lower (fewer than 6–7 times) and the duration shorter (fewer than 6–7 h).

## Quality assessment

Three studies<sup>31,33,34</sup> were ranked as high-quality, meaning each bias rating was "low risk." The lack of allocation concealment and

 Table 2

 Systematic review of randomized interventions involving psychological distress among cancer dyads (k = 28).

Author Sample demographics and (Year), follow-up Country		Therapy type, intervention delivery/dosage	Intervention and control group	Assessment tool	Main findings		
Gremore et al (2021), USA	21), couples skills, CBT  Refusal rate: NS  Retention rate: 85% to-face supportive communication  FP: post-intervention, 3 sessions delivered by licensed		I: couple-based supportive communication (CSC) C: TAU	CES-D, PROMIS-anxiety	Patients' and partners' anxiety and depression effect sizes ranged from small to large, but partners' results changed less.		
Steel et al (2021), USA	months N: diagnosed cancer patients and their family caregivers Refusal rate: 22% Retention rate: 27.7% FP: post-intervention, 6 months	clinical psychologist Therapy: CBT Delivery/dosage: eight to twelve 60-min weekly video contact sessions and 24-hr available website delivered by master's level therapists	I: web-based stepped collaborative care intervention C: screening and referral	CES-D, FACT-G, FACT-Fatigue	Experimental group demonstrated clinical improvement in survival rate, but not to a statistically significant degree.		
Tiete <i>et al</i> (2021), Belgium	N: diagnosed cancer patients and their family caregivers. Refusal rate: 64% Retention rate: 94% FP: post-intervention	Therapy: self-disclosure listening, support seeking negotiation Delivery/dosage: four weekly 60- min sessions delivered by licensed psychologist over 1 month	I: cancer-related patient- caregiver communication intervention C: wait-list control	HADS	Intervention had no significant effect on emotional distress.		
Wolff et al (2021), USA	N: breast cancer patients and their family caregivers. Refusal rate: 27.1% Retention rate: 81.8% FP: post-intervention, 3-, 9-, 12-month interviews	Therapy: establish shared visit agenda, facilitate MyChart patient portal access Delivery/dosage: 24-hr available MyChart usage over six weeks	I: patient–family agenda setting intervention C: TAU	PHQ-2, GAD-2, FACT-B	Anxiety was more severe between baseline and nine months among control caregivers (18.2% vs. 12.7%).  There are no differences between groups in patients' or caregivers' anxiety, understanding of the disease, or satisfaction with cancer care after nine months.		
Milbury et al (2020), USA	N: lung cancer couples Refusal rate: 37% Retention rate: 65% FP: post-intervention, 4, 12 weeks	Therapy: CBM: interconnection, mindfulness, compassion and meditations, emotional sharing SE: dyadic-based cancer-related concerns coping Delivery/dosage: four 60-min weekly educational videoconferences delivered by	I1: couple-based meditation intervention (CBM) I2: supportive-expressive intervention (SE) C: TAU	CES-D, IES, FACT-Spiritual Well- Being Scale	CBM couples experienced significant reduction in depressive symptoms compared to TAU, and it had a moderate effect size on depressive symptoms compared to SE. Patients with CBM benefited more than those in the SE group.		
Lau <i>et al</i> (2020), China	N: lung cancer and their family caregivers Refusal rate: 5.2% Retention rate: 40.1% FP: post-intervention, 16, 24 weeks	licensed psychologist Therapy: 1-BMS: psychoeducational (acupressure and Qigong), mindfulness-based relaxation CBT: relaxation, dysfunctional coping patterns, mood diary, reappraisal, cognitive continuum, cost-benefit analysis, positive self- statements Delivery/dosage: eight weekly 3-hr	I: integrative body-mind- spirit intervention (I-BMS) C: cognitive behavioral therapy (CBT)	Emotional subscale of FACT-G, emotional vulnerability subscale of HWS, DAS, HADS	IBMS showed a statistically significant reduction in HADS-depression compared to CBT. The effect sizes of the comparison between the two groups were expected to be small.		
Li <i>et al</i> (2019), China	N: patients with lung cancer and treated with icotinib and their family caregivers Refusal rate: 12% Retention rate: 87%	sessions facilitated by trained facilitators over 8 weeks Therapy: physical therapy, coping and communication strategies, mental health, knowledge education Delivery/dosage: six 45-min sessions of multidisciplinary components delivered by physicians	I: wellness-education intervention C: TAU	HADS-anxiety, HADS-depression	Intervention group exhibited better changes in patient and caregiver quality of life, HADS, and intimacy subscales.		
Kubo <i>et al</i> (2019), USA	FP: post-intervention N: patients diagnosed with cancer and their family caregivers Refusal rate: 45% Retention rate: 74% FP: post-intervention	and nurses Therapy: mindfulness meditation instructions Delivery/dosage: mindfulness program used daily via phone application over 8 weeks	I: mobile/online-based (mHealth) mindfulness intervention C: wait-list control	HADS-anxiety, HADS-depression, DT	No statistically significant differences in change in anxiety, depression, sleep, and fatigue were observed between study arms.		
Mosher <i>et al</i> (2018), USA	N: patients with gastrointestinal cancer and their family caregivers Refusal rate: 21% Retention rate: 78% FP: post-intervention	Therapy: manage physical symptoms and stress, maintain relationship Delivery/dosage: five 50- to 60-min telephone-based coping skills sessions delivered by trained psychologist	I: peer helping + coping skills group C: coping skills group	PROMIS-anxiety, PROMIS-depression, DT	The intervention had no effect on patient pain, caregiver burden, patient and caregiver fatigue, mental health outcomes, or social outcomes. These results also did not change over time.		
Paterson et al (2018), UK	N: patients with metastatic prostate cancer and their family caregivers Refusal rate: 34.2%	Therapy: informational materials, holistic needs assessment, group- based seminar, individualized self- management care plans	I: multimodality supportive care (Thriver Care) intervention C: TAU	HADS	No statistically significant changes in anxiety, depression, and health- related QoL scores over time between or within groups. (continued on next page)		

## Table 2 (continued)

Author (Year), Country	Sample demographics and follow-up	Therapy type, intervention delivery/dosage	Intervention and control group	Assessment tool	Main findings	
	Retention rate: 95.9% FP: post-intervention	<b>Delivery/dosage:</b> four face-to-face sessions delivered by nurse over 3 months				
McCaughan et al (2018), JK	N: prostate cancer couples Refusal rate: 74% Retention rate: 79% FP: post-intervention, 1 month	Therapy: symptom and uncertainty management, positive thinking, couple communication Delivery/dosage: nine weekly programs (three 2-hr small group and two telephone sessions) delivered by trained facilitators	I: psychosocial intervention (CONNECT) C: TAU	ssosQ	The men in the intervention group were better at communication and support outcomes than the men in the control group. Partners in the study may have benefited the mos because they may need intervention more than men.	
Milbury <i>et al</i> (2018), ISA	N: patients with glioma undergoing radiotherapy and their caregivers Refusal rate: 30% Retention rate: 95% FP: post-intervention	Therapy: mindfulness meditation, postures, breathing exercises  Delivery/dosage: twelve 45-min yoga sessions delivered by certified therapist	I: dyadic yoga (DY) intervention C: wait-list control arm	MDASI-BT affective factor, CES-D	DY patients showed clinically significant improvements in overa cancer symptom severity, depression, and psychological QoI DY caregivers showed clinically significant improvements in depressive symptoms, fatigue, and mental QoL.	
Badr <i>et al</i> (2018), USA	N: couples with head and neck cancer Refusal rate: 29.2% Retention rate: 93.3% FP: post-intervention	Therapy: self-management, communication, coping skills Delivery/dosage: six 60-min telephone-based interventions delivered by trained psychologist	I: spouses coping with the head and neck radiation experience (SHARE) by phone C: usual medical care (UMC)	PROMIS-anxiety, PROMIS-depression, IES	Patients and spouses in the experimental group demonstrated moderate to large effects relative to depression and cancer-specific distress.	
Porter <i>et al</i> (2017), JSA	N: couples with gastrointestinal cancer Refusal rate: 82.2% Retention rate: 90.6% FP: post-intervention	Therapy: self-disclosure, communication skills Delivery/dosage: six 60-min sessions delivered by trained therapists	I: couples communication skills training C: healthy lifestyle information	IES	No significant differences between CCST and HLI were noted in cancer related distress for patients.	
Mazanec <i>et al</i> (2017), JSA	N: patients with multiple myeloma cancer and their family caregivers Refusal rate: 48% Retention rate: 16.67% FP: 6, 12 weeks	Therapy: home-based, low-impact walking activity Delivery/dosage: one in-person psychoeducational session delivered by nurse; self-monitoring walking activity (30 min/day, 5 times/week)	I: family-centered psychoeducational intervention C: attention-control group	PROMIS-anxiety, PROMIS-depression, DT	At least 40% of patients in the intervention group showed improvement in depression, anxiety, and emotional distress. Caregivers showed little improvement in outcome variables	
Lambert <i>et al</i> (2016), australia	N: couples with prostate cancer Refusal rate: 39.9% Retention rate: 76.2% FP: 1 follow-up call, twice a week, last 2 months	Therapy: 4 booklets about coping skills Delivery/dosage: 4 self-directed follow-up calls delivered by research assistant	I: coping together C: minimal ethical care (MEC)	HADS-anxiety, HADS-depression, IES-R	Both groups reported a decrease in distress, but the experimental grou showed a smaller decrease than th control group.	
Hsiao <i>et al</i> (2016), China	N: couples with breast cancer Refusal rate: 69.1% Retention rate: 92.5% FP: 2nd, 5th, 8th, 14th months post-intervention	Therapy: CSG: family resilience, mindfulness-based therapy; ISP: body-mind-spirit holistic psychotherapy Delivery/dosage: CSG: eight 120- min weekly small group sessions; ISP: five 30- to 60-min telephone calls Trained principal investigator	I: couples support group (CSG) C: individual support program (ISP)	BDI, STAI, MLQ	For patients, CSG reduces intimacy anxiety more than ISP. CSG appear to be more effective for partners as it reduces partner anxiety and depression and improves positive mood.	
Ovorak <i>et al</i> (2015), ISA	N: patients diagnosed with cancer and their family caregivers Refusal rate: NS Retention rate: NS FP: post-intervention	(nurse) delivered both over 2 months Therapy: stress management, emotional expression, wellness, connection, creativity Delivery/dosage: six 60-min twice weekly sessions delivered by therapists over 3 weeks	I: music therapy support groups (MTSG) C: TAU	POMS, STAI-S, FACT-G	The experimental group showed statistically significant improvements in mood and anxiety	
Chambers et al (2014), australia	N: patients and caregivers who called cancer information and support cancer helplines Refusal rate: 70.5% Retention rate: 73% FP: post-intervention, 3, 6, 12 months	Therapy: Nurse-led: self-management resource kit, brief psychoeducation Psychologist-led: the psychological impact of cancer, coping, stress management skills, problem-solving, cognitive therapy, enhancing support networks Delivery/dosage: one nurse-led session or five psychologist-led sessions delivered by telephone	I1: nurse-led self- management intervention I2: psychologist-led cognitive behavioral intervention	BSI-18, IES, DT, PTGI	For all participants, overall psychological and cancer-specific distress decreased over time, positive adjustment increased, and cancer-specific distress had a moderate to large effect. Only the psychologist-led intervention produced a significant decline in distress for less-educated participants.	
Northouse et al (2013), JSA	N: patients diagnosed with advanced breast, lung, colorectal, or prostate cancer and their caregivers Refusal rate: 45.9%	Therapy: family involvement, optimistic attitude, coping effectiveness, uncertainty reduction, symptom management Delivery/dosage: Brief: two 90-min home visits and one 30-min phone	I1: Brief FOCUS program I2: Extensive FOCUS program C: TAU	BHS, Emotional subscale of FACT-G, MUIS	A significant increase in emotional QoL was reported for control, Extensive, and Brief patients at the 3-month follow-up. However, no significant change was observed fo	

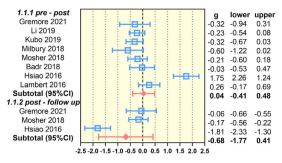
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Table 2 (continued)

Author Sample demographics and (Year), follow-up Country		Therapy type, intervention delivery/dosage	Intervention and control group	Assessment tool	Main findings		
_	Retention rate: 62.4% FP: post-intervention, 16, 24 weeks	session; Extensive: takes twice as long as Brief version; both delivered by master's-prepared nurses			caregivers' emotional QoL at the 3- month and 6-month follow-ups.		
Clark <i>et al</i> (2013), USA	N: radiation therapy for patients with advanced cancer and their caregivers Refusal rate: 25% Retention rate: 79.7% FP: post-intervention, 4, 8, 18, 27 weeks (final intervention)	Therapy: education, cognitive behavioral strategies, open discussion, support Delivery/dosage: six 90-min sessions delivered by trained therapists over 6 weeks	I: structured multidisciplinary intervention C: TAU	FACT-G, CQOLC	There was no difference in mood states between the two groups.		
Ledderer <i>et al</i> (2013), Denmark	N: lung or gynecological cancer patients and their family caregivers Refusal rate: 80.7% Retention rate: 47.6% FP: 2, 12 months	Therapy: supportive talks, residential rehabilitation course Delivery/dosage: 3 nurse-led, 1-h supportive talks over 2 months; one 5-day residential rehabilitation course delivered by nurses and psychologists	I: new multimodal psychosocial rehabilitation intervention C: TAU	WHO-5	The QoL and well-being of patients and their caregivers were improved in the intervention group and the control group, but no significant difference was found between the two groups.		
Manne <i>et al</i> (2011), USA	N: couples with prostate cancer Refusal rate: 79% Retention rate: 81.7% FP: post-intervention	Therapy: didactic content, in-session skill practice, home practice assignments, CBT Delivery/dosage: five 90-min couples' sessions delivered by therapists	I: intimacy-enhancing psychological intervention C: TAU	MHI-38, IES	After IET treatment, survivors showed a significant reduction in high-level cancer concerns, while for partners, the IET group improved cancer-specific distress.		
Kayser et al (2010), USA	N: couples with breast cancer Refusal rate: 61.3% Retention rate: 74.6% FP: post-intervention, 6 months	Therapy: individual coping, communication skills Delivery/dosage: nine 1-hr biweekly sessions delivered by trained master's level social workers	I: Partners in Coping Program (PICP) C: hospital standard social work services (SSWS)	Emotional well-being of FACT-B, QL-SP	The mean score of patients' QoL in the PICP arm was higher, but no statistically significant difference. Partners in the PICP consistently scored higher on emotional well- being than those in the SSWS.		
Campbell et al (2007), USA	N: couples with prostate cancer Refusal rate: 71.3% Retention rate: 75% FP: post-intervention	Therapy: cognitive and behavioral techniques, symptom management Delivery/dosage: six 1-hr weekly telephone sessions delivered by trained therapists	I: telephone-based coping skills training intervention (CST) C: TAU	SF-36 [MCS], SESCI, CSI, POMS-SF	CST partners reported less caregiver strain, depression, fatigue and more vigor; observed effect sizes were close to the level of statistical significance.		
Giesler <i>et al</i> (2005), USA	N: couples with prostate cancer Refusal rate: 67.6% Retention rate: 85.9% FP: post-intervention, 4, 7, 12 months	Therapy: symptom management, tailored psychoeducational strategies  Delivery/dosage: 6 monthly nurse-led sessions (twice in person and 4 times by telephone)	I: interactive computer program intervention C: TAU	CES-D, SF-36	The intervention group showed long-term improvements in cancer concerns.		
Northouse et al (2005), USA	N: breast cancer patients and their family caregivers. Refusal rate: 20% Retention rate: 74% FP: 3 months (post initial intervention), 6 months (post booster phase)	Therapy: family involvement, optimistic attitude, coping effectiveness, uncertainty reduction, symptom management Delivery/dosage: three 90-min home visits and two 30-min follow-up phone calls delivered by master's-prepared nurse	I: family-based intervention (FOCUS program) C: TAU	BHS, MUIS, FACT, SF-36	Patients with recurrent breast cancer who participated in FOCUS reported significantly lower feelings of hopelessness at the 3-month follow-up than patients in TAU.		
Christensen et al (1983), USA	N: postmastectomy patients and their husbands Refusal rate: NS Retention rate: NS FP: post-intervention	Therapy: communication, problem- solving techniques Delivery/dosage: 4 weekly therapist-led tailored sessions	I: structured couples treatment program C: TAU	PSI, BDI, STAI	The anxiety levels of the couples were similar pre- and post-intervention.		

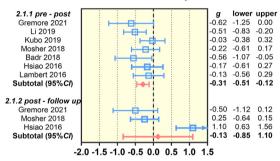
BDI, Beck Depression Inventory; BHS, Beck Hopelessness Scale; BSI, Brief Symptom Inventory; CBM, couple-based meditation intervention; CBT, cognitive behavioral therapy; CES-D, Center for Epidemiological Studies-Depression Measure; CSC, couple-based supportive communication; CSG, couples support group; CQOLC, Caregiver Quality of Life Index—Cancer Scale; CSI, Caregiver Strain Index; DAS, Death Anxiety Scale; FACT-B, Functional Assessment of Cancer Therapy—Breast; FACT-G, Functional Assessment of Cancer Therapy—General; FP, Follow-up; GAD-2, Generalized Anxiety Disorder-2 Scale; HADS, Hospital Anxiety and Depression Scale; HWS, Holistic Well-Being Scale; IES, Impact of Events Scale; MDASI-BT, MD Anderson Symptom Inventory Brain Tumor Module; MHI, Mental Health Inventory; MLQ, Meaning of Life Questionnaire; MUIS, Mishel Uncertainty in Illness Scale; NCCN DT, NCCN Distress Thermometer; NS, not specified; PHQ-2, Two-Question Patient Health Questionnaires; POMS, Profile of Mood States; POMS-SF, Profile of Mood States-Short Form; PROMIS, Patient-Reported Outcomes Measurement Information System; PSI, Psychological Screening Inventory; PTGI, Posttraumatic Growth Inventory; QL-SP, Quality of Life Questionnaire for Spouses; SESCI, Self-Efficacy for Symptom Control Inventory; SF-36 [MCS], Medical Outcomes Study 36-Item Short-Form Survey, Mental Component Summary; SE, supportive-expressive intervention; SSOSQ, 16-Item Symptom Scale of the Omega Screening Questionnaire; STAI-S, State Trait Anxiety Inventory-State Anxiety; TAU, treatment as usual; WHO-5, WHO-Five Well-Being Index.

#### 1.1 Patients' Depression



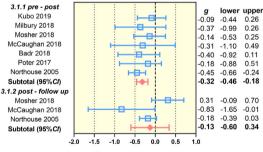
- subgroup of pre and post intervention: Heterogeneity: Tau² = 0.354; df = 7 (P = 0.00); l² = 88% Test for overall effect: Z = 0.171 (P = 0.864)
- subgroup of post and follow up:
   Heterogeneity: Tau² = 0.867; df = 2 (P = 0.00); l² = 93%
   Test for overall effect: Z = -1.219 (P = 0.223)

#### 2.1 Patients' Anxiety



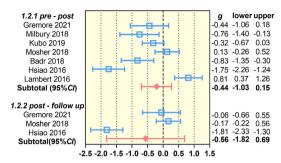
- subgroup of pre and post intervention:
   Heterogeneity: Tau² = 0.009; df = 6 (P = 0.30); P = 17%
   Test for overall effect: Z = -3.33 (P = 0.001)
- subgroup of post and follow up:
   Heterogeneity: Tau² = 0.68; df = 2 (P = 0.00); P = 92%
   Test for overall effect: Z = 0.25 (P = 0.802)

## 3.1 Patient cancer-related distress



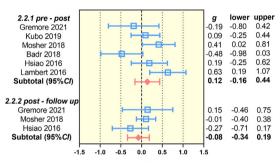
- subgroup of pre and post intervention:
   Heterogeneity: Tau² = 0.00; df = 6 (P = 0.641); P = 0%
   Test for overall effect: Z = -4.363 (P < 0.000)</li>
- subgroup of post and follow up:
   Heterogeneity: Tau² = 0.219; df = 2 (P = 0.002); P = 84%
   Test for overall effect: Z = -0.67 (P = 0.503)

## 1.2 Caregivers' Depression



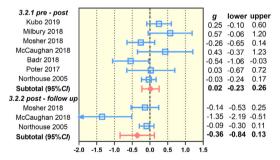
- subgroup of pre and post intervention:
  Heterogeneity: Tau² = 0.575; df = 6 (P < 0.000); P = 91%
  Test for overall effect: Z = -1.452 (P = 0.147)
- subgroup of post and follow up: Heterogeneity:  $Tau^2 = 1.163$ ; df = 2 (P < 0.000); P = 95%Test for overall effect: Z = -0.88 (P = 0.379)

#### 2.2 Caregivers' Anxiety



- subgroup of pre and post intervention:
   Heterogeneity: Tau² = 0.086; df = 5(P = 0.018); P = 63%
   Test for overall effect: Z = 0.90 (P = 0.368)
- subgroup of ppst and follow up:
   Heterogeneity: Tau² = 0.00; df = 2 (P = 0.503); P = 0%
   Test for overall effect: Z = -0.572 (P = 0.567)

## 3.2 Caregiver cancer-related distress



- subgroup of pre and post intervention:
   Heterogeneity: Tau<sup>2</sup> = 0.05; df = 6 (P = 0.05); P = 52%
   Test for overall effect: Z = 0.138 (P = 0.890)
- subgroup of post and follow up: Heterogeneity: Tau² = 0.128; df = 2 (P = 0.017); P = 76% Test for overall effect: Z = -1.446 (P = 0.148)

Fig. 2. Forest plots of patient and partner effect sizes and 95% confidence intervals.

blinding were major causes for the poor quality of these studies. Seven studies  $^{28,37,39,45,50,54,55}$  declared randomized allocation but did not describe the process. About three-fifths of the studies (k=15) described the allocation concealment, and 14 were blinded (5 single-blind and 2 double-blind). Blinding was not conducted largely because the nature of psychosocial intervention makes it difficult to blind, but some studies  $^{50}$  minimized the adverse effects of non-blinding by informing participants that they had been randomly assigned to one of two different interventions. Although the baseline of some studies  $^{32,34,37,40,43,53,55,56}$  was unbalanced, we

retained them because baselines were analyzed to reflect intra-individual changes. Nearly all the studies demonstrated no other biases; only one<sup>50</sup> was rated "high risk" due to unequal allocation to groups (Fig. 3).

## Publication bias

Visual inspection of the filled funnel plot after using the trim-and-fill method<sup>26</sup> and the Egger test<sup>27</sup> (P = 0.96, P = 0.33, P = 0.45, P = 0.23, P = 0.74) identified no publication bias (Fig. 4).

**Table 3**Pooled effect size of outcomes for cancer patients and their family caregivers.

Aspects/	k	n	Pooled effect size SMD	I <sup>2</sup> for
outcomes			(95%CI)	heterogeneity
Patients' depression	on syn	nptom		
Pre to post	8	691	0.04 ( - 0.41, 0.48)	88%
Post to follow-	3	220	-0.68 ( - 1.77, -0.41)	93%
up				
Patients' anxiety s	ympt	om		
Pre to post	7	651	-0.31 ( - 0.51, $-0.12$ )	17%
Post to follow-	3	220	0.13 (-0.85, 1.10)	92%
up				
Patients' cancer-re	lated	distres	s	
Pre to post	7	758	-0.32 ( - 0.46, $-0.18$ )	0%
Post to follow-	3	498	-0.13 (-0.60, 0.34)	84%
up				
Caregivers' depres	sion s	ymptoi	n	
Pre to post	7	532	-0.44 ( - 1.03, 0.15)	91%
Post to follow-	3	220	-0.56 (-1.82, 0.69)	95%
up				
Caregivers' anxiety	y sym	ptom		
Pre to post	6	492	0.12 ( - 0.16, 0.44)	63%
Post to follow-	3	220	-0.08 ( - 0.34, 0.19)	0%
up				
Caregivers' cancer	-relat	ed disti	ress	
Pre to post	7	758	0.02 ( - 0.23, 0.26)	52%
Post to follow-	3	498	-0.36 ( - 0.84, 0.13)	76%
up				

k, number of studies; n, number of patient-caregiver dyads.

## Discussion

This systematic review places cancer family caregivers and patients in equally important positions, and it demonstrates a better change effect of intervention when adding baseline into the meta-analysis. Moderator analysis and publication bias checks ensured that our results were more rigorous and objective. The results showed that dyadic intervention had a short-term improvement with a statistical effect on patient anxiety and cancer-related distress. For family caregivers, the effect sizes of cancer-related distress and depressive symptoms were only small to medium at follow-up without statistical significance. Regarding the type of

intervention, face-to-face (compared with telephone and online) and shorter interventions (compared with session duration longer than  $6-7\,h$ ) led by psychologists with professional backgrounds (compared with nurses and therapists) seem to have a better performance.

Of the studies we included, although the emotional distress of most patients or family caregivers improved to some extent, two-thirds of the studies did not show a statistically significant change. Among these psychosocial interventions that promote communication, disclosure, mutual support, and ultimately deepen intimacy, such as active meditation, skill training, and relaxation training, seem to be more effective. In addition, our study showed a statistically significant improvement in anxiety and cancer-related distress in patients with cancer from baseline to immediate intervention completion, but not statistically significant improvements over the follow-up period, which was consistent with the findings of Hu<sup>57</sup> and Wang et al. 15 Notably, neither anxiety nor cancer-related distress among family caregivers showed significant improvement from baseline to follow-up. Thus, cancer involves a long-term struggle between dyads and disease, and various factors, such as disease progression, treatment options, and family social support, may affect dyads differently. It is undeniable that family caregivers and cancer patients have an interdependent relationship<sup>58</sup> therefore, dyadic interventions are still necessary for this population. While incorporating family caregiver involvement in the treatment, many interventions ultimately put more emphasis on improving physical and psychological patient outcomes.<sup>36</sup> Future studies need to design better interventions that enhance the dyadic mental health of all involved.

Although this article does not emphasize the moderator analysis results, we found some thought-provoking conclusions. First, the face-to-face intervention delivery format produced the most significant results. This finding is similar to those of a recent systematic review for patients with colorectal cancer. The face-to-face sessions can increase participant adherence, making for a deeper, more trusted relationship between interventionist and participant. As technology continues to emerge, more and more researchers are using new techniques to practice intervention effects. Some studies suggested that social media may be a useful tool to communicate health-related information and support cancer dyads. However, fewer online interventions (k = 7) were included in this review compared to face-to-face modalities (k = 14), which could may have led to the conclusion be one of the reasons why we conclude that face-to-face

**Table 4**Moderator analyses for patient emotional outcomes.

Outcomes and moderators	Level	k	Hedges' g	SE	Lower limit	Upper limit	Z-value	P-value
Depression								
Delivery type	Face-to-face	6	-0.21	0.46	-1.11	0.69	-0.45	0.65
	Telephone	3	-0.05	0.15	-0.34	0.23	-0.35	0.73
Interventionist	Psychologist	5	-0.16	0.11	-0.37	0.05	-1.48	0.14
	Therapist	5	-0.14	0.53	-1.19	0.90	-0.27	0.79
Frequency intervention (time)	< 6	4	-0.04	0.13	-0.29	0.21	-0.32	0.75
	≥ 6	7	-0.21	0.33	-0.86	0.45	-0.62	0.54
Anxiety								
Delivery type	Face-to-face	5	-0.13	0.32	-0.76	0.49	-0.42	0.68
	Telephone	3	-0.20	0.12	-0.43	0.03	-1.72	0.09
Interventionist	Psychologist	5	-0.36	0.11	-0.58	-0.15	-3.37	0.00*
	Therapist	4	0.18	0.28	-0.36	0.73	0.66	0.51
Frequency intervention (time)	< 6	5	-0.28	0.10	-0.49	-0.08	-2.68	0.00*
	≥ 6	5	-0.04	0.27	-0.58	0.50	-0.15	0.88
Session duration (hr)	< 6	7	-0.29	0.08	-0.45	-0.13	-3.52	0.00**
	≥ 6	3	0.17	0.49	-0.84	1.09	0.26	0.08
Cancer-related distress								
Delivery type	Face-to-face	3	-0.42	0.21	-0.84	-0.01	-2.02	0.04*
	Online	3	-0.19	0.13	-0.45	0.07	-1.41	0.16
	Telephone	4	-0.18	0.21	-0.58	0.22	-0.89	0.38
Interventionist	Psychologist	3	-0.31	0.12	-0.55	-0.07	-2.51	0.01*
	Therapist	5	-0.22	0.13	-0.47	0.02	-1.77	0.08
Frequency intervention (time)	< 7	6	-0.15	0.06	-0.27	-0.03	-2.39	0.02*
	≥ 7	4	-0.23	0.14	-0.49	0.04	-1.69	0.09
Session duration (hr)	< 7	5	-0.23	0.10	-0.43	-0.04	-2.40	0.01*
	≥ 7	5	-0.13	0.07	-0.27	0.01	-1.82	0.07

SE, standard error; \*P < 0.05; \*\*P < 0.001.

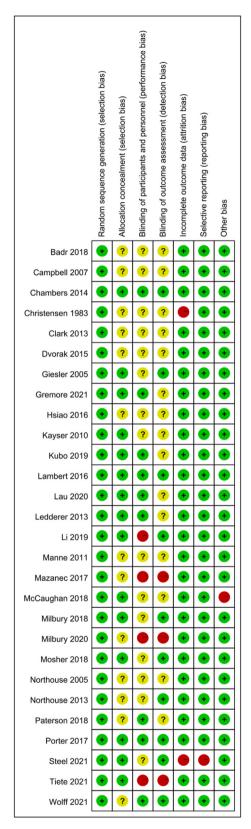


Fig. 3. Risk of bias summary.

interventions are better. Compen et al<sup>61</sup> conducted a cost-utility analysis for in-person and online formats. Both groups can reduce costs while improving poor cancer patients' QoL. It should be clear that online interventions are not only beneficial but also not inferior to face-to-face ones.<sup>62,63</sup> As interventions via the Internet or videoconferences are

more creative and shorter, more large-sample and high-quality studies are needed in the future to compare these two forms of interventions.

Our conclusion related to intervention duration and frequency contrasts with those from other research. In our review, shorter interventions seem to have better performance, while some studies suggested longer intervention duration might produce more lasting effects. <sup>59,64</sup> Northouse et al<sup>29</sup> designed the FOCUS program to include two experiment groups of different lengths but did not find a difference between the two groups. However, both the Brief version and the Extensive version improved emotional QoL. This may provide us with a new idea about the duration and frequency of the study. A well-designed, shorter intervention may generate more desirable effects. Moreover, this approach brings other benefits, such as saving resources and increasing participant involvement rates.

In comparing the types of interventionists, psychologists had the best intervention effects compared to nurses and therapists, consistent with Bard's moderator analysis findings. <sup>65</sup> It might be attributed to a lack of training, experience, or professional dialog among nurses when providing psychosocial care. <sup>66</sup> However, regardless of who leads the intervention, participant perspectives need to be considered. Appropriate tailored therapies for participants are much better than intensive psychosocial interventions implemented by medical professionals. <sup>67</sup>

Finally, we need to point out that the evidence available in this systematic review is limited. Our review's quality was uneven, with many studies not addressing specific allocation concealment strategies and blinding details. In addition, we found that most studies have focused on developed countries and middle-aged and elderly populations. A lack of reflection in some low- and middle-income areas, young cancer dyads, and other races limits the generalizability of our results. Therefore, higher-quality and broader randomized controlled trials of the patient-caregiver dyad are needed.

#### Limitations

There are several limitations in our meta-analysis. (1) When searching the database, we only reviewed literature published in English. This may have led us to omit other results that were reported in articles published in minor languages. (2) Publication bias is inevitable for all systematic reviews. However, we tried to reduce this bias by refining the search strategy, finding alternative citation sources, and using specific statistical methods whenever possible. (3) To control the quality of the studies included, we included only RCTs; other quasi-experiments or pretest-post-test designs that met the inclusion criteria were excluded. (4) Patients with terminal cancer often face more intense stressful emotions, and their family caregivers may also experience grief. Cancer does not simply bring on these emotions but another fear of imminent death. Articles introducing palliative interventions may have biased results. So we excluded some studies designed for advanced cancer dyads with only a few months left in the life cycle. But this may have missed some meaningful results.

## Clinical implications

This review clarifies the current state of the literature on dyadic interventions for patients with cancer and their family caregivers and provides some credible data. Much remains to be done in this area, however. First, the control group in most studies was not rational. Only one study<sup>48</sup> compared couple intervention with patient individual intervention. Many studies used the dyadic intervention as the experimental group and usual care as the control group. At this point, we cannot clarify whether the effect was produced by the group therapy or by the dyadic intervention. Therefore, in the study design phase, we can set up multiple control groups, such as individual interventions for patients and routine care as a control group at the same time. If only one control group can be used, considering the resource issues, perhaps some form of blank group intervention can be added to the usual care group as

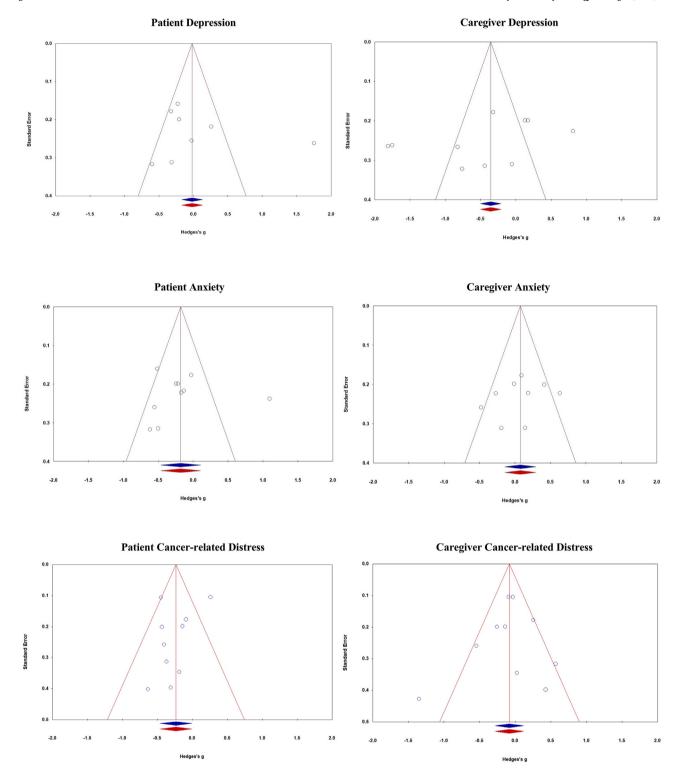


Fig. 4. Filled funnel plot of depression, anxiety, and cancer-related distress after using trim-and-fill method.

well. Second, with the advent of new technology such as the Internet, some studies examined various electronically implemented interventions. <sup>68,69</sup> However, the patients with cancer we included were generally older, and these middle-aged and older groups may be less adaptable to new technology. <sup>70</sup> Future studies should consider the acceptability of this population at the study design stage. Third, with

cancer rejuvenation, more interventions designed for younger dyadic units need to be considered because they may face different challenges than the old—balancing cancer with work, family, and child-rearing issues. <sup>71</sup> Finally, despite the scope of the review being large, studies on low- and middle-income country regions remain missing. <sup>72</sup> Cancer is a global problem, and populations in low-income areas may face more

emotional distress. At the same time, in low- and lower-middle-income countries, advanced cancer stage, and low education levels also affect anxiety and depression levels. $^{73}$ 

#### **Conclusions**

We reviewed the various types of dyad cancer interventions. Face-to-face, relatively shorter interventions led by psychologists seem to have a moderating effect. In conclusion, the results of this systematic review suggest that cancer dyad-based interventions can improve emotional distress. However, patients showed a greater improvement in their negative emotions than family caregivers. How to better address caregivers' psychological distress and how to maintain the long-term effects of the intervention need to be explored by further high-quality investigations in the future.

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Nil.

## **Authors' contributions**

Xuenan Pang: literature search, software, data curation, writing original draft preparation. Yanfei Jin: conceptualization, methodology, literature search, data curation. Honghong Wang: visualization, writing/reviewing, editing.

## Declaration of competing interest

None declared.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.apjon.2022.100104.

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