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PSYCHOSOCIAL INTERVENTIONS FOR DEPRESSION, ANXIETY, AND QUALITY OF LIFE IN CANCER SURVIVORS: META-ANALYSES*

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ABSTRACT

Objective: The purpose of this meta-analysis was to investigate the effects of cognitive behavioral therapy (CBT) and patient education (PE) on commonly reported problems (depression, anxiety, pain, physical functioning, and quality of life (QOL)) in adult cancer survivors. *Methods:* Meta analyses of randomized controlled trials of CBT and PE were conducted. MEDLINE, PSYCHINFO and the Cochrane Database were searched from 1993-2004. The effects of individual versus group interventions and short (<8 months) versus long (>8 months) term follow up are also reported. *Results:* Fifteen studies met quality criteria. The sample size was 1,492 adult cancer survivors with an age range of 18-84. 790 were randomly assigned to intervention groups and 702 to control groups. CBT varied in duration from 4 weekly one-hour sessions to 55 weekly two-hour sessions. PE ranged from a single 20-minute session to 6 weekly one-hour sessions. Follow up ranged from 1 week to 14 months. CBT was effective for depression (ES = 1.2; 95% CI = 0.22-2.19), anxiety (ES = 1.99; 95% CI = 0.69-3.31), and QOL

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(ES = 0.91; 95% CI = 0.38-1.44). QOL was improved at both short and (ES = 1.45, 95% CI = .43-2.47) and long term (ES = .26; 95% CI = .06-.46) follow up. PE was not related to improved outcomes. *Conclusions:* CBT is related to short-term effects on depression and anxiety and both short and long term effects on QOL. Individual interventions were more effective than group. Various CBT approaches provided in an individual format can assist cancer survivors in reducing emotional distress and improving quality of life.

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Key Words: meta-analysis, cancer survivors, cognitive-behavioral interventions, depression, anxiety, pain, physical functioning, quality of life

INTRODUCTION

For all cancers combined, the number of people living at least five years post diagnosis has increased from 50% in 1976 to over 64% in 2001 [1]. There are an estimated 9.8 million cancer survivors in the United States, and this number is expected to continue to rise as the population ages and cancer detection and treatment improve [2]. Despite increased longevity, the effectiveness of various approaches to improving the quality of life in survivors is not well understood [3]. Quality of life (QOL), including a patient's sense of well-being and function [4] can be affected by depression, anxiety, and pain [5, 6].

Approximately 16-25% of newly diagnosed cancer patients experience depression or an adjustment disorder with depressed mood [7]. Depression has also been associated with functional limitations in cancer survivors [8] and both anxiety and depression can independently contribute to functional and overall health [9, 10]. Effective long-term management of these problems remains a challenge [11].

Cognitive Behavior therapy (CBT) with cancer survivors typically includes stress management and problem solving [12] although other approaches are considered CBT interventions as long as they are based on the assumptions that cognitions can be monitored and altered, and in turn may facilitate behavior change [13]. In contrast, patient education (PE) typically includes information regarding the illness or symptom(s), symptom management, and/or discussion of treatment options [14] and may include the use of booklets, videos or other educational materials [15]. While both approaches are used with cancer survivors [12], the effects on specific outcomes is not well understood and clinical decisions regarding their differential use in practice remains unclear.

Previous meta-analyses on the effects of early attempts to use such interventions in cancer survivors have reported modest results, which may be a function of the outcomes investigated. Chow et al. [16] reported no effects on mortality, which may be an inappropriate outcome to attribute to these types of interventions.

Fawzy et al. [12] reported a small effect (ES = 0.24) on emotional adjustment. Meyer and Mark [17] noted small effect sizes for emotional adjustment (ES = 0.24), functional adjustment (ES = 0.19), treatment and disease related symptoms (ES = 0.26), and a global measure combining the previous outcomes (ES = 0.28), with no differences by type of treatment (behavioral, non-behavioral, educational, or social support). Rehse and Pukrop [18] concluded a modest effect (ES = 0.31) on QOL, with longer interventions (>12 weeks) being more effective than shorter term interventions. While these various approaches result in modest improvements in global measures of adjustment, the effects of interventions on specific clinical problems such as depression, anxiety, fatigue, pain, and QOL may provide more precise information [19]. Devine [20] observed a modest effect of psychoeducational interventions on pain (ES = 0.36) while Sheard and Maguire [21] concluded that psychological interventions (e.g., individual therapy and relaxation) for anxiety was associated with an effect size of 0.42 and had no impact on depression. These investigators reported larger effect sizes when limiting results to only the highest quality studies (e.g., randomized studies generated a larger effect size than non-randomized; 0.5 vs. 0.19). Further, studies meeting their quality criteria (randomized, >75% quality score, and >40 sample size) generated a much larger effect than those using lower quality designs; 0.63 vs. 0.24 [21].

The purpose of the present meta analysis was to quantify the specific effects of CBT and PE for treatment of depression, anxiety, pain, physical functioning, and QOL reported in randomized controlled trials in adult cancer survivors. CBT was operationalized as including any specific psychological or psychosocial intervention that was relatively brief, goal oriented, based on learning principles of behavior change, and was directed at effecting change in a specific clinical outcome [13]. To address the question of duration of the effects of the various interventions, only studies reporting outcomes at a follow-up time point were selected. The present review defined survivorship as onset at time of diagnosis [22, 23].

METHODS

Study Selection

The MEDLINE database of the National Library of Medicine, PSYCHINFO database provided by Ovid, and the Cochrane Database for Systematic Reviews were searched from 1993 - November 2004. This time frame was selected because it covered the duration following the Meyer and Mark review [17] (the review most similar to the present one) until the present and would allow for an updated examination of the literature. The search used the key words (limited to humans and English language): cancer, anxiety, depression, quality of life, fatigue, stress, pain, physical function, social, self-management, evidenced-based, interventions, and random/randomized. References of reviewed articles were also

searched. Initial studies were screened for inclusion based on abstracts. Inclusion criteria were: adult cancer patient (all types of cancer and all stages of disease), control group, randomization, measurable outcomes of interest (anxiety, depression, fatigue, QOL, physical function, and pain), and at least one follow-up assessment beyond post-treatment, which allowed for examination of duration of effects.

Quality was assessed by a modified version of the Jadad six-item checklist (randomization, double blinding, descriptions of withdrawals and dropouts, statistical analyses, inclusion and exclusion criteria, and adverse effects) [24]. Each trial was scored between 0–5. The checklist was modified to better reflect methodological quality. Scores on the original checklist may reflect the amount of information provided in the report rather than the quality of the methodology. The checklist was modified such that studies that did not specify the exact method of randomization were retained. Studies were excluded if they were not randomized or controlled, received a score of less than four on the Jadad checklist [16], did not report follow-up data, or did not report data on the targeted outcomes. Study quality was assessed independently by two authors and disagreements were resolved by consensus by all three authors. Dissertations were excluded because full texts were not consistently available.

Data Extraction and Analysis

Age, gender, cancer type and location, time since diagnosis, intervention characteristics (e.g., group CBT, individual CBT, PE), and longest follow-up data on outcomes (including anxiety, depression, physical function, pain, QOL) were extracted from eligible studies. Table 1 provides the information from all studies that met inclusion criteria (see Table 1). Data from treatment and comparison groups for each outcome were collected for all studies. All data were analyzed using Comprehensive Meta Analysis [18], and effect sizes for each outcome are reported using Cohen's d [25]. This effect size represents the standardized mean difference between the experimental group and comparison group. Thus, a d of 1 indicates a change in magnitude equivalent to one standard deviation. Three ranges of effect sizes are commonly reported: small (d = 0.2-0.5), medium (d = 0.5-0.7), and large (d = 0.8-2.0) [25]. When different outcomes were assessed within a study, the study was reported multiple times. Assessment for heterogeneity was determined using the Q statistic [26]. Analyses with statistically significant Q values were adjusted using Hedges' g to compute effect size [27].

Sensitivity analyses were performed to determine whether intervention features (i.e., group vs. individual; or CBT vs. PE) and length of follow-up (short term, less than 8 months vs long term, greater than 8 months) differentially impacted results. On outcomes that revealed statistically significant results, publication bias was assessed using the Egger's test [28].

RESULTS

Studies Included in Meta Analysis

There were 207 articles identified from the MEDLINE database, 382 from PSYCHINFO, and three from the Cochrane Database for Systematic Reviews. Of these, 189 abstracts met inclusion criteria. Exclusions were based on the following: 105 did not implement an appropriate intervention, 10 were not fully randomized, 11 did not measure the outcomes of interest, eight did not use cancer survivors, eight were dissertations, five were duplicate studies retrieved from different databases, four examined a pediatric population, two were planned study descriptions, and one was not peer-reviewed. Overall, 35 articles were reviewed for quality. From these, two presented duplicate data reported in different journals, 12 did not meet quality assessment criteria (score of <4 on the checklist), and six did not include follow-up data. The total number of studies included in each meta analysis varied based on the specific outcome studied. The characteristics of each of the studies used to compute effect sizes are presented in Tables 1 and 2.

Cancer Survivors

There were 1,492 survivors included in the analyses: 790 were randomly assigned to interventions and 702 were controls. A typical control group included "usual care," (i.e., medical management only). The participants ranged in age from 18 to 84. All types of cancers were included. The breakdown of cancer type can be seen in Tables 1 and 2. The average length of follow up (weighted for number of subjects in each study) was 7.9 months.

Outcomes: Depression, Anxiety, Pain, Physical Function, and QOL

The Profile of Mood States (POMS) [29] was commonly used to measure depression and the State-Trait Anxiety Inventory (STAI) [30] was common for anxiety (state form). Pain was typically assessed using a single-item visual analogue scale ranging from 0-10, with 0 being "no pain" and 10 being the "worst pain imaginable" [31]. Physical functioning was assessed using the Functional Living Index for Cancer (FLIC) [32], and QOL using the Functional Assessment of Cancer Treatment [33]. Table 3 displays a summary of the effect sizes and significance levels for each outcome by intervention delivery type (individual or group) and the combined effects for both types (see Table 3).

Depression

Five studies measured the effect of CBT on depression at follow up. Four contained one treatment group whereas the Nezu and colleagues [34] study contained

Table 1. Cognitive Behavior Therapy Studies

Authors	Group (*n*)	Number of sessions	Cancer survivors	Mean age (*SD*)	Cancer type	Outcomes measured	Length of follow-up
Edmonds et al. [50]	Cognitive Behavioral Tx (CBT) (30) Control (36)	35 wkly group + 20 wkly ind 2 hr sessions	66 women	50.61 (9.0)	Breast	Depression, Anxiety, QOL	14 mo
Larson et al. [51]	CBT (23) Control (18)	2 sessions 90 min	41 women	56 (13)	Breast	Depression	1 wk
Baider et al. [52]	Progressive Muscle Relaxation (PMR) (63) Control (27)	6 wkly 1 hr group sessions	49 men 69 women	53.3 (15.5)	Various types	QOL	6 mo
Lev et al. [53]	CBT (25) Control (28)	5 monthly indiv sessions + 8 hr workshop	53 women	18-70	Breast	Anxiety, QOL	8 mo
Allen et al. [37]	Problem Solving (87) Control (77)	2 indiv 2 hr sessions + 4 phone sessions	164 women	42.3 (5.3)	Breast	Physical function, QOL	8 mo

Trask et al. [35]	CBT (18) Control (16)	4 wkly indiv sessions	25 men 42 women	22-71	Various types	Anxiety, QOL, Depression, Pain, Physical function	6 mo
Cheung et al. [38]	PMR (29) Control (30)	2 indiv 20 min training sessions	40 men 19 women	56.4 (13.5)	Colorectal	Anxiety, QOL	10 wk
Kissane et al. [54]	CBT (154) Control (149)	20 wkly 90 min group sessions	303 women	20-65	Breast	Anxiety, Depression	12 mo
Nezu et al. [34]	Problem Solving (45) Control (44)	10 wkly indiv 1.5 hour sessions	30 men 59 women	49.2 (NR)	Various types	Depression, QOL	6 mo
Taylor et al. [39]	Support (40) Control (33)	8 wkly 2 hr group sessions	73 women	55.9 (11.3)	Breast	QOL	12 mo
Zakowski et al. [55]	Expressive Writing (62) Control (42)	20 min per day 3 days	56 men 48 women	25-84	Prostate or gynecological	QOL	6 mo

NR = Not reported

Table 2. Patient Education Studies

Authors	Group (*n*)	Number of sessions	Cancer survivors	Age (*SD*)	Cancer type	Outcome	Length of follow-up
Oliver et al. [31]	Patient Education (34) Control (33)	1 session 20 min	25 men 42 women	55.8 (NR)	Various types	Pain	2 wk
Lepore et al. [56]	Patient Education (86) Control (80)	6 wkly 1 hr group lectures + 45 min discussion group	126 men	65.1 (6.6)	Prostate	Depression, Physical function	12 mo
Wells et al. [36]	Patient Education (24) Control (19)	20 min lecture + 4 wkly phone calls	28 men 15 women	53 (14.5)	Various types	Pain	6 mo
Yates et al. [14]	Patient Education (70) Control (70)	2 wkly indiv sessions	NR	56 (11.93)	Various types	Anxiety, Depression, Pain, QOL	2 mo

NR = Not reported

Table 3. Effects of CBT Interventions in Cancer Survivors

	CBT Intervention						Education Intervention			
	Individual		Group		Combined		Individual		Combined	
Outcome variables	Effect size	(No. studies)	Effect size	(No. studies)	Effect size	(No. studies)	Effect size	(No. studies)	Effect size	(No. studies)
Anxiety	2.41***	(3)	.027	(1)	1.99**	(4)	−.023	(1)		
Depression	1.44**	(4)	.096	(1)	1.21**	(5)			−.06	(2)
Pain	.019	(1)					.243	(3)		
Physical functioning	−.653	(2)					.144	(1)		
Quality of life	.952***	(7)	.367	(2)	.91 ***	(8)	−.042	(1)		

Note: Combined = Individual and group intervention studies combined to determine an overall effect. No group studies for education.
*$p < .05$. **$p < .01$. ***$p < .001$.

two treatment groups, one in which patients attended meetings alone, and a second where meetings were attended with a "significant other." The "significant other" group showed larger effects on depression. There was a large effect size for the five studies (g = 1.21, $p < 0.05$; 95% CI 0.22-2.19). Figure 1 displays the Forest plots that represent the effect sizes for CBT on depression.

In contrast, the two PE studies did not result in significant effects on depression at follow up (d = –0.06, $p = 0.55$; 95% CI –0.24-0.13).

A sensitivity analysis revealed that the four studies that used an individual approach resulted in a large clinical effect (g = 1.44, $p < 0.05$; 95% CI 0.29-2.59). The single study that employed a group format had no effect (d = 0.09, $p = 0.41$; 95% CI –0.13-0.32).

Anxiety

Four studies used CBT for anxiety and a large effect was observed (g = 1.99, $p < 0.01$; 95% CI 0.69-3.31). Figure 2 displays the Forest plots representing the effect sizes of CBT on anxiety. Trask et al. [35] reported multiple outcome measures of anxiety (see Figure 2).

As with depression, the single trial using PE resulted in no effect on anxiety at follow-up (d = –0.02, $p = 0.89$; 95% CI –0.36-0.31).

A sensitivity analysis revealed a large effect size for individual treatment (g = 2.41, $p < 0.01$; 95% CI 1.26-3.55) and no effect for group interventions (d = 0.03, $p = 0.82$; 95% CI –0.20-0.25). Figure 3 displays the results from the individual CBT.

Pain

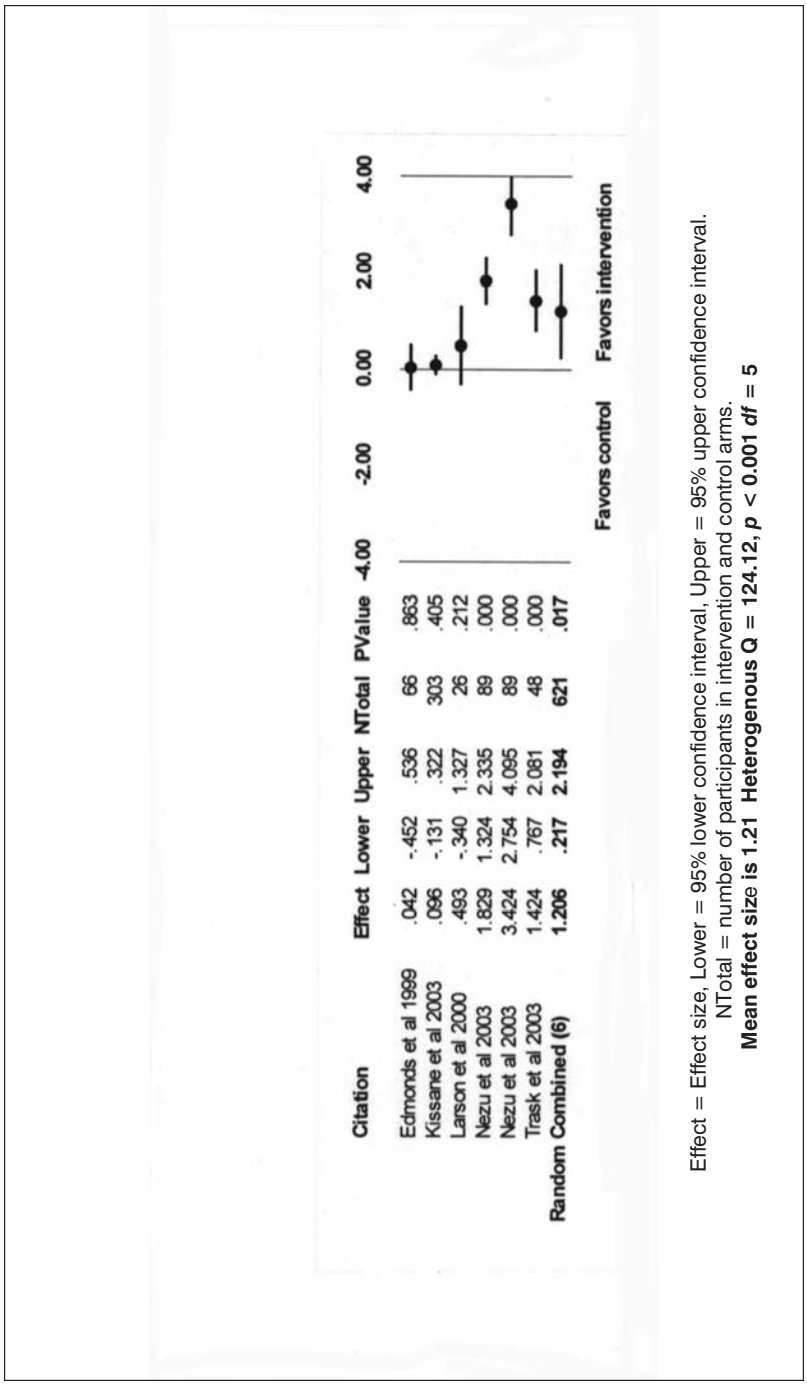
While CBT was used for management of depression and anxiety, PE was more common for pain. The single CBT study revealed no effect on pain (d = 0.02, $p = 0.95$; 95% CI –0.56-0.60). There was also no effect for the three PE studies (d = 0.24, $p = 0.06$; 95% CI –0.01-0.49). Figure 4 illustrates the Forest plots of effect sizes for PE on pain including both the outcome measures (average and worst pain levels) reported in the Wells et al. study.

Physical Functioning

Three studies evaluated physical functioning. The two CBT studies revealed no effect (g = –0.65, $p = 0.52$; 95% CI –2.65-1.35). Similarly, no effect on physical functioning was found for the study using group PE (g = 0.14, $p = 0.19$; 95% CI –0.07-0.36).

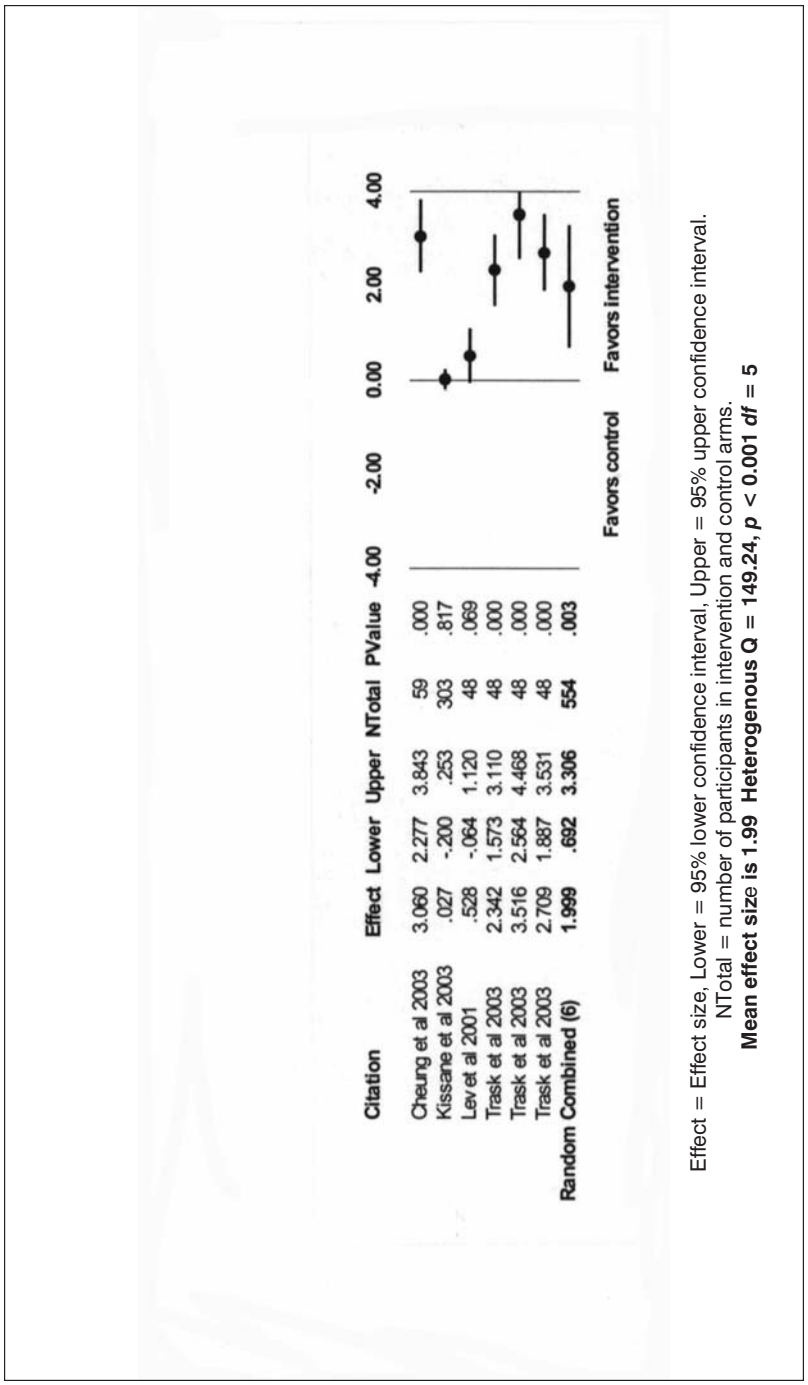
Quality of Life

There were eight studies that used CBT and measured QOL at follow-up. The multiple QOL measures reported in the Allen et al. [37], Cheung et al. [38], and



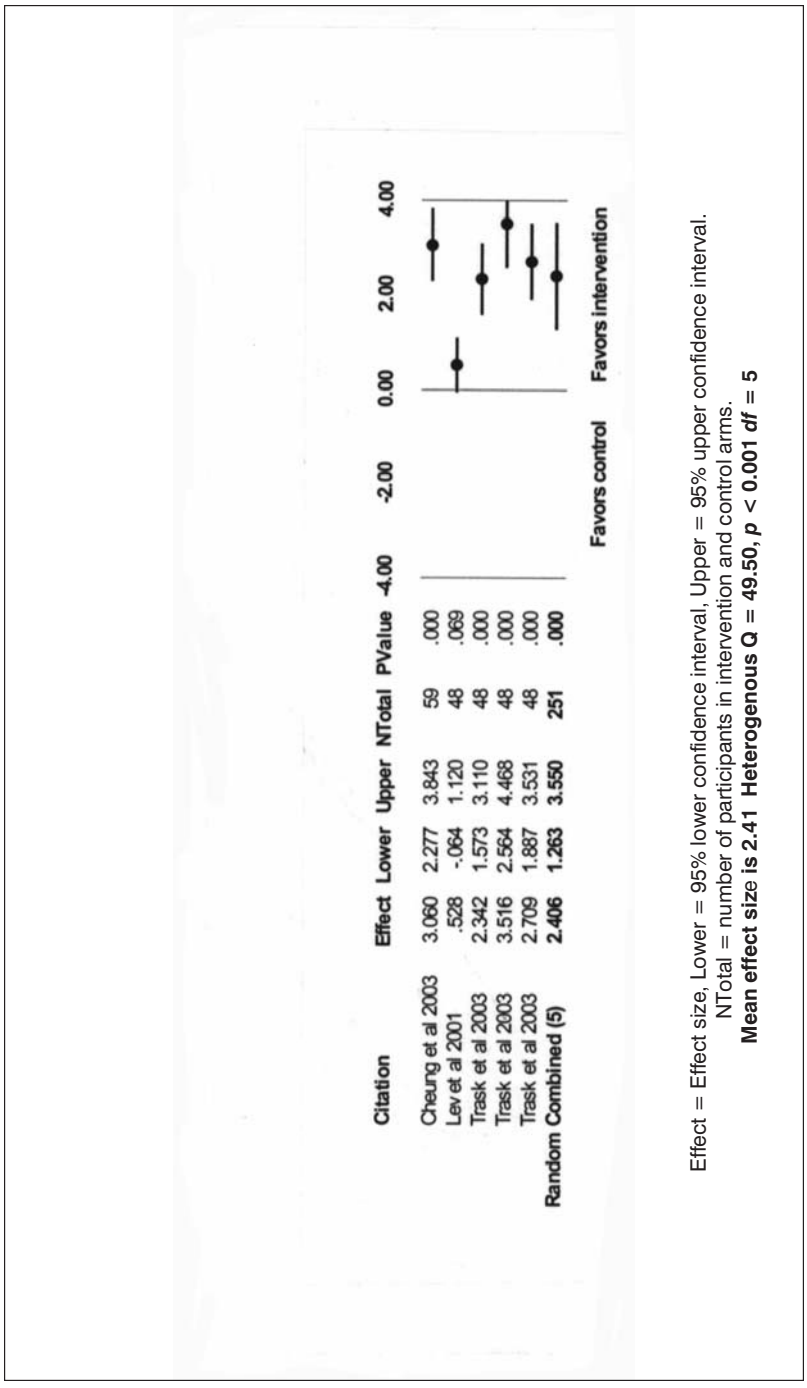
Effect = Effect size, Lower = 95% lower confidence interval, Upper = 95% upper confidence interval.
NTotal = number of participants in intervention and control arms.
Mean effect size is 1.21 Heterogenous Q = 124.12, $p < 0.001$ $df = 5$

Figure 1. CBT intervention for depression.



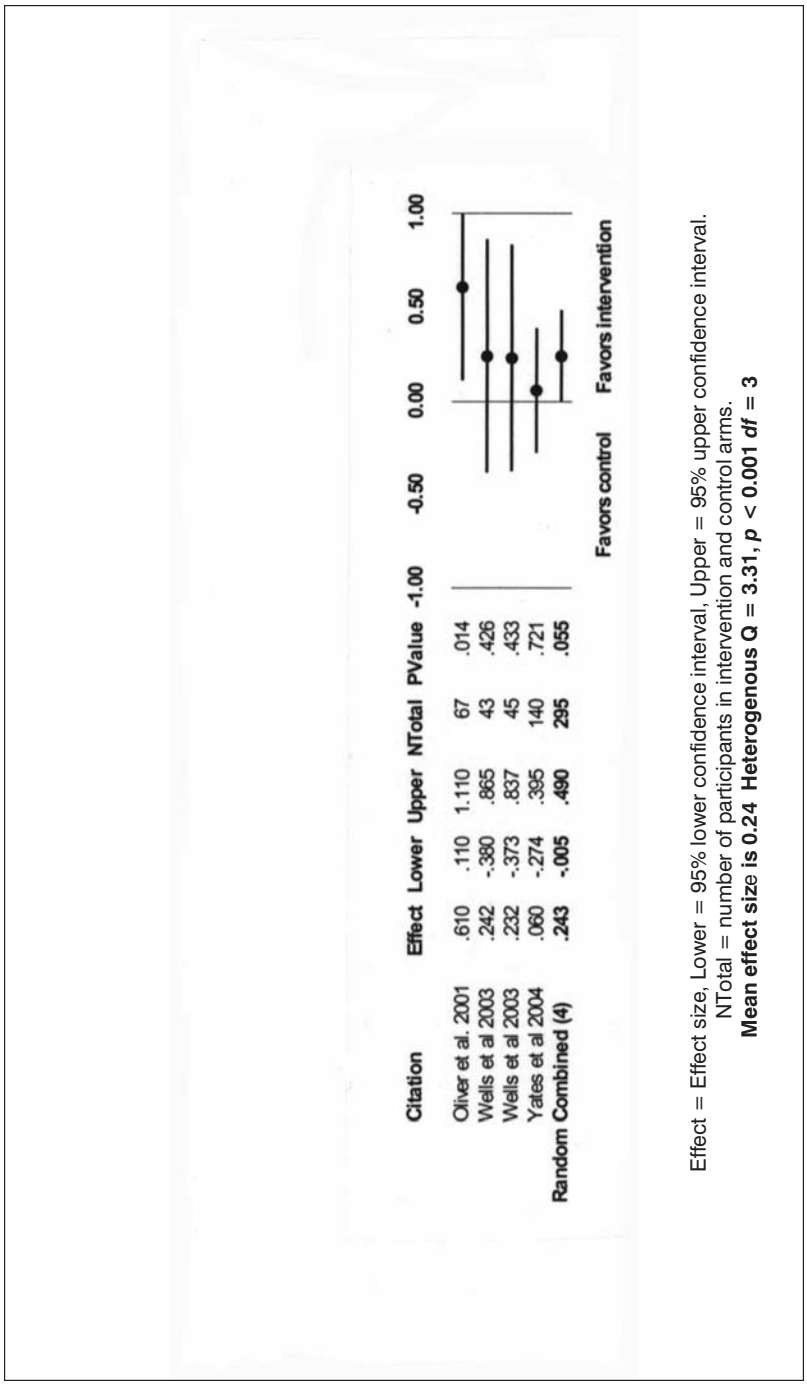
Effect = Effect size, Lower = 95% lower confidence interval, Upper = 95% upper confidence interval.
NTotal = number of participants in intervention and control arms.
Mean effect size is 1.99 Heterogenous Q = 149.24, $p < 0.001$ $df = 5$

Figure 2. CBT intervention for anxiety.



Effect = Effect size, Lower = 95% lower confidence interval, Upper = 95% upper confidence interval.
NTotal = number of participants in intervention and control arms.
Mean effect size is 2.41 Heterogenous Q = 49.50, $p < 0.001$ $df = 5$

Figure 3. Individual CBT intervention for anxiety.



Effect = Effect size, Lower = 95% lower confidence interval, Upper = 95% upper confidence interval.
NTotal = number of participants in intervention and control arms.
Mean effect size is 0.24 Heterogenous Q = 3.31, $p < 0.001$ $df = 3$

Figure 4. Patient Education intervention for pain.

Nezu et al. [34] were included in the analysis. A large effect was found in these studies (g = 0.91, $p < 0.01$; 95% CI –0.38-1.44) (see Figure 5).

The single study using PE did not result in a significant effect on QOL (d = –0.04, $p = 0.80$; 95% CI –0.38-0.29).

A sensitivity analysis revealed that the seven studies using an individual approach resulted in a large effect (g = 0.95, $p < 0.01$; 95% CI –0.37-1.54 (see Figure 6), whereas the one study that used a group format (Taylor et al. [39]) resulted in no effect (d = 0.37, $p = 0.06$; 95% CI –0.02-0.75).

Follow-Up

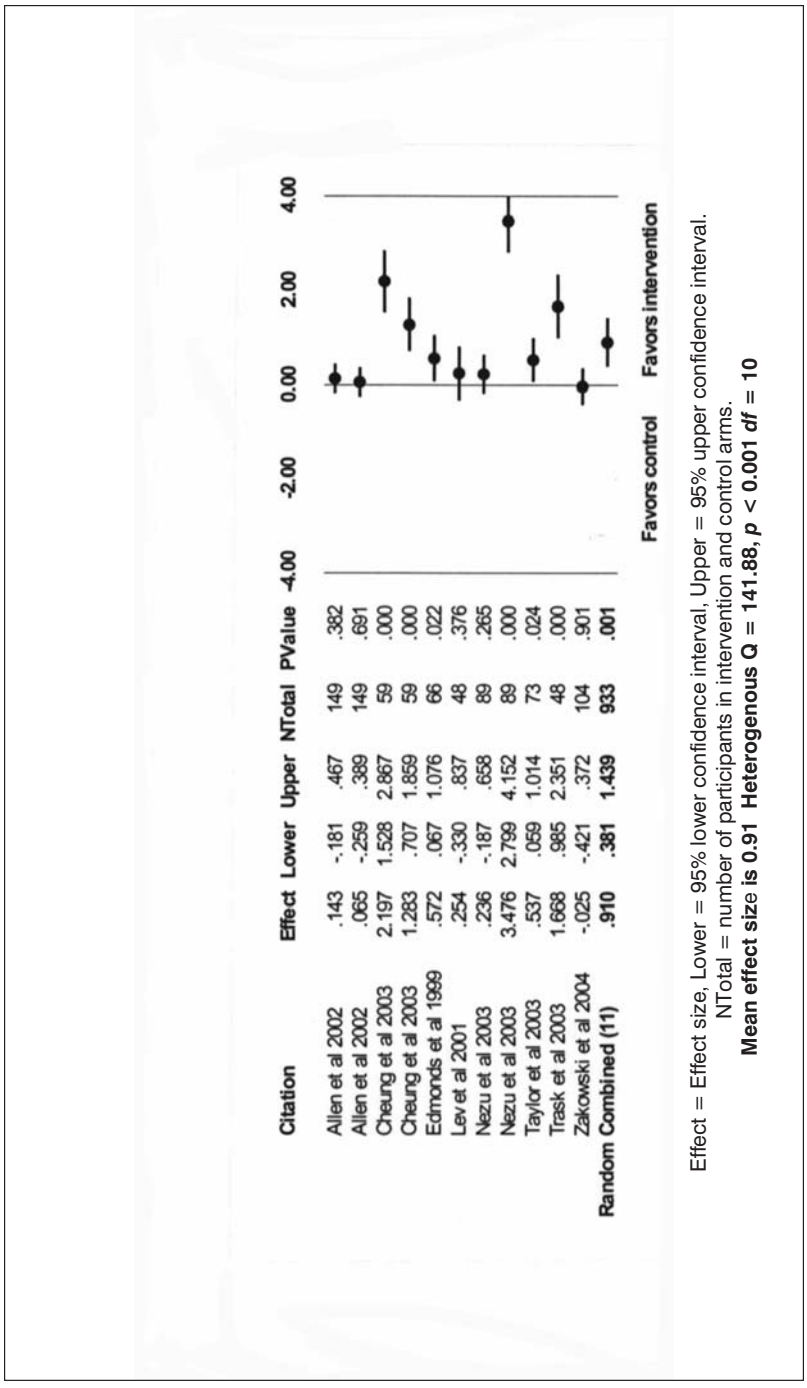
Sensitivity analyses were preformed on each outcome by length of follow-up (short-term vs. long-term). The median follow-up length was calculated and a median split was performed. Based on the median split, short-term follow-up was less than eight months and long-term was greater than eight months. Neither CBT nor PE produced significant long-term effects on depression. However, CBT had a strong effect in the short-term (g = 1.81, $p < 0.01$; 95% CI 0.72-2.89), whereas PE did not. Similarly, there were no long-term effects of CBT on anxiety despite a strong short-term effect (d = 2.87, $p < 0.01$; 95% CI 2.38-3.34). PE showed no short-term effects on anxiety. No PE study included a long-term follow-up on anxiety, and therefore this outcome could not be determined. For pain, there was also an absence of long-term follow-up. In the short-term, neither CBT nor PE had an effect on pain.

Analyses indicated significant short and long term effects of CBT on QOL (g = 1.45, $p < 0.01$; 95% CI 0.43-2.47), (d = 0.26, $p < 0.05$; 95% CI 0.06-0.46), respectively. There were no short-term effects of PE on QOL.

Egger's test was conducted to assess the probability of publication bias for the studies included in the depression, anxiety, and QOL analyses. There was no evidence of such bias for the depression ($p < .37$) and anxiety ($p < .17$) outcomes, however the test revealed a possible publication bias for the QOL studies ($p < .03$). This may be accounted for by the quality criteria for study inclusion, as several studies did not meet these criteria in the present analyses. Many of these studies had inconsistent findings. Further, the heterogeneity of QOL measures used in various studies may contribute to a false-positive finding in the Egger's test [28].

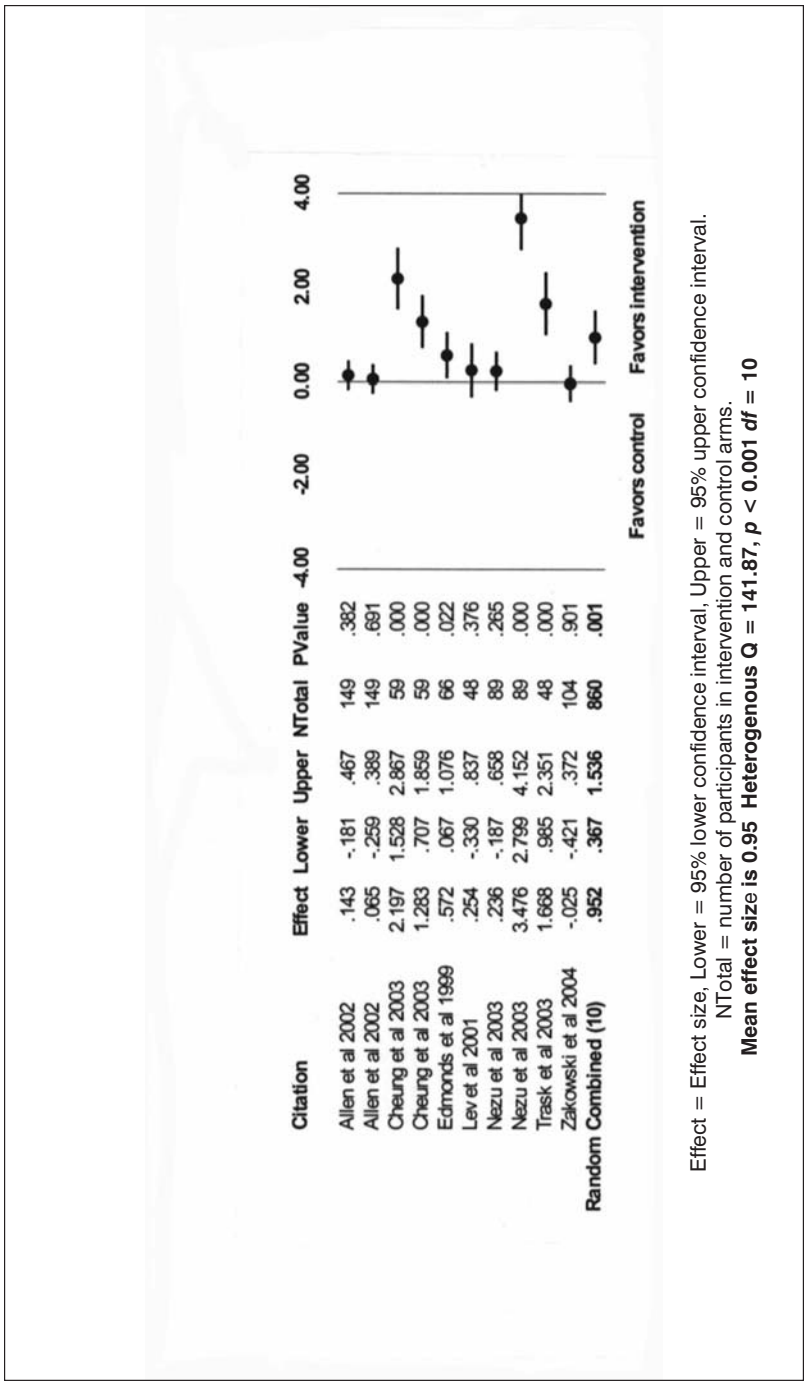
DISCUSSION

The present meta analyses indicates that CBT is effective for the short-term management (<8 months) of depression, anxiety, and QOL in cancer survivors. CBT also has long-term effects (>8 months) on QOL. Individually based interventions were more effective than those delivered in a group format. Pain was not effectively managed by the CBT but PE was effective up to eight months. CBT



Effect = Effect size, Lower = 95% lower confidence interval, Upper = 95% upper confidence interval.
NTotal = number of participants in intervention and control arms.
Mean effect size is 0.91 Heterogenous Q = 141.88, $p < 0.001$ $df = 10$

Figure 5. CBT intervention for quality of life.



Effect = Effect size, Lower = 95% lower confidence interval, Upper = 95% upper confidence interval.
NTotal = number of participants in intervention and control arms.
Mean effect size is 0.95 Heterogenous Q = 141.87, $p < 0.001$ $df = 10$

Figure 6. Individual CBT intervention for quality of life.

was not useful for improving physical functioning in cancer survivors, despite its use for this purpose in other chronic illnesses [40].

Individual CBT, such as problem solving, appears to be useful for cancer survivors for depression and anxiety. These approaches typically employ weekly, goal oriented visits. The magnitude of these effects was larger than prior meta analyses. Perhaps when interventions are targeted at specific clinical problems and only high quality studies are considered, the outcome is more focused and larger effect sizes are observed [21]. This explanation is further supported by the Nezu et al. [34] study where a global problem solving intervention resulted in a larger effect size for a global measure of QOL than for the specific problem of depression. The larger effect sizes also may reflect recent refinements in the delivery of such interventions subsequent to the completion of previous meta analyses.

The current analyses were completed on studies conducted after earlier meta-analyses were reported. It was the intent of this review to consider more recent studies, as interventions for cancer survivors are continuously being refined [41]. Since past analyses have indicated positive, yet smaller, effects, including these studies would have attenuated the observed effects, but not eliminated them.

While antidepressive and anxiolytic medications are commonly prescribed for cancer survivors [4], adherence can be a problem. In those cases, non pharmacological management using CBT represent a viable alternative or adjunct [42]. Effective management of depression and anxiety in these cases may impact other outcomes [6], such as global health, cognitive functioning, and fatigue [43]. While complementary and alternative medicine and exercise-based interventions represent potential options [44], this review only focused on CBT and PE interventions. Increased physical functioning is also a goal for many cancer survivors [45] yet the approaches studied in the present analyses did not improve physical functioning.

Pain is a prevalent symptom in many cancer survivors [4] and insufficient pain control remains a concern in many survivors [46]. While PE is often used, its effect on pain revealed only a trend of a small effect. There is a need to develop complimentary approaches for pain management in cancer survivors.

Little is known about QOL in cancer survivors, despite its importance in long-term health [3]. The findings in this study demonstrated a large effect of individual CBT on overall QOL. PE did not affect QOL. While this conclusion is based on only one study, it was sufficiently powered. Because QOL is comprised of many different aspects (i.e., social, physical, psychological, and spiritual functioning) [6], it is possible that variability in QOL measures and variation in the types of educational interventions used (e.g., booklet, telephone calls, face-to-face contact) limited their impact on QOL. Future research should refine the clinical measurement of QOL.

The investigation of short- and longer-term follow-up indicated that individual CBT has short-term effects on both depression and anxiety. Long-term effects were not observed. Andersen [47] recently noted that treatment effects in past studies have tended to be transitory. Although long-term cancer survivors do

report high levels of QOL, there are studies that indicate the presence of depressive symptoms that are not detected [46]. At this point in the development of interventions for cancer survivors, periodic follow-up, self-monitoring, and the use of short acting interventions for depression and anxiety may be useful because interventions directed at specific behavior change does improve targeted outcomes. Continued research on patient education interventions is warranted given their widespread use.

There are limitations in the present meta analyses. The studies included a heterogeneous sample of cancer patients, both in terms of diagnosis and stage of disease. Sixty percent of patients receiving CBT were breast cancer survivors, compared to only 17% receiving PE. While the limited number of studies in this area necessitated this approach, it is possible that an interaction exists between mode of intervention and cancer type, disease severity, and stage of cancer survivorship. Also, the analysis did not consider patient adherence, which is known to be modest in medical patients [48]. Cost benefit implications of the interventions also needs to be addressed [49].

The present review provides information on the effectiveness of CBT on some common problems reported by cancer survivors. It is noteworthy that quality RCTs that would meet inclusion criteria for fatigue, long-term cognitive limitations, activity levels and work related problems were not available and therefore could not be included. There is a need for well-controlled clinical trials that are based on the natural history and patterns of prevalent problems in cancer survivors. While options are currently available to manage emotional distress and QOL, a more complete understanding of clinical problems within cancer survivors represent important next steps [41]. The present study suggests that while the long-term effects of these approaches need to be improved, viable clinical options exist.

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