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TITLE PAGE

Interventions for the Treatment of Cancer-Related Traumatic Stress Symptoms: A Systematic Review of the Literature

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ABSTRACT

Objective

Cancer has been reported to trigger symptoms of post-traumatic stress disorder (PTSD) in a substantial proportion of individuals. Despite the significant burden associated with these symptoms, there are as yet no therapeutic guidelines. This systematic review aims to evaluate the effectiveness of interventions for cancer-related post-traumatic stress in order to provide an evidence base for developing appropriate clinical practice.

Methods

Databases searched until April 2018 included, Psych INFO, EMBASE, Medline and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). No restrictions to study design were applied. Participants aged 18 years or older who received their cancer diagnosis in adulthood and had symptoms of cancer-related PTSD were included. Due to significant clinical heterogeneity, a meta-analysis was not performed.

Results

Of 508 unique titles, eight studies met study inclusion criteria: five RCTs, one before-and-after study, one case series and one case study. Interventions were predominately psychological and were administered to patients with a range of cancer types. Eye Movement Desensitisation and Reprocessing and cognitive behavioural therapy-based interventions were associated with reduced symptomatology, however, overall the methodological quality of studies had limitations.

Conclusions

At present there is only weak evidence available for the effectiveness of psychological interventions in reducing symptoms of cancer-related PTSD. The majority of interventions were administered to all cancer patients regardless of whether they showed pretreatment levels of post-traumatic stress. Future studies would be better targeted towards patients with a

diagnosis of cancer and who have significant levels of cancer-related post-traumatic symptoms. Higher quality trials are also needed before treatment recommendations can be made.

Keywords: cancer, oncology, PTSD, traumatic stress, systematic review, psychological interventions

BACKGROUND

The diagnosis and treatment of cancer is acknowledged as a potential stressor that can lead to significant psychological distress including symptoms of depression and anxiety, as well as symptoms of post-traumatic stress. Experiencing distress in response to cancer is common and can occur at critical times throughout the course of the disease. Patients' emotional reactions may range from normal feelings of fear and vulnerability to more rare but disabling psychopathologies. Studies have repeatedly demonstrated that a proportion of cancer patients exhibit symptoms of cancer-related post-traumatic stress[1].

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V), post-traumatic stress disorder (PTSD) is a psychiatric condition that can occur following exposure to one or more traumatic events that involve the threat of serious injury or death to oneself or others (Criterion A) [2]. Four core symptom clusters comprise PTSD in accordance with DSM-V: involuntary re-experiencing of stressful events (Criterion B), avoidant behaviour (Criterion C), negative thoughts and cognitive appraisals (Criterion D), and hyper-arousal or reactivity (Criterion E). In order for the diagnosis of PTSD to be met, these symptoms need to be present for more than a month (Criterion F) and to cause significant impairment in functioning (Criterion G). Prevalence estimates of cancer-related PTSD range between 7-14% [3], with an additional 10-20% of patients experiencing sub-syndromal post-traumatic stress symptoms (i.e. PTSS) [4 5]. Both PTSD and PTSS have been associated with increased

distress and impaired quality of life [6], and have been reported in newly-diagnosed patients as well as in long-term survivors [7]. Furthermore, PTSD as a comorbidity has been shown to have a negative impact on health-related outcomes such as drug adherence and morbidity and mortality rates [8 9].

As Cordova et al explained in their recent qualitative review of the cancer-related PTSD literature, the applicability of a PTSD diagnosis to distress arising from cancer has not been without controversy[10]. In contrast to DSM-IV, the revised PTSD diagnostic criteria in DSM-V suggest that a life-threatening medical condition, such as cancer, does not necessarily constitute a traumatic event if no sudden, catastrophic events have occurred. The revised PTSD criteria draw attention to the importance of carefully considering differential diagnoses such as that of an adjustment disorder. The use of the latter diagnosis might be more appropriate for patients presenting with sub-syndromal cancer-related PTSD symptoms, as well as for those whose experience of cancer does not qualify as traumatic based on the current diagnostic criteria [3,10,11]. Arguably, this is a complex diagnostic issue, which, of course, has implications for how cancer-related PTSD is treated.

Advances in treatments and increased public awareness mean that more people than ever live with and beyond cancer. At the same time, the number of new cases worldwide is expected to rise by over 70% in 2030 [12]. Therefore, as the number of people diagnosed with cancer increases and cancer survivorship improves, cancer-related PTSD becomes a more prominent issue and thus providing for cancer patients' physical and psychological needs becomes increasingly important. In contrast to the considerable body of literature investigating the prevalence and detection of cancer-related PTSD symptoms, work focusing on interventions targeting clinical and/or subclinical cancer-related PTSD is sparse. Due to the aforementioned significant impairments associated with cancer-related post-traumatic stress , it is important to assess the effectiveness of psychological treatments in this group of patients, as well as to

take into account how therapies may have a different effect on syndromal and sub-syndromal cancer-related PTSD symptoms. Evidence-based treatments such as Eye Movement Desensitization and Reprocessing (EMDR) therapy and cognitive-behavioural therapy (CBT) are available for PTSD and, indeed, there have been promising reports of their effectiveness in cancer patients [13 14,15].

To the best of our knowledge, only one review to date has examined the evidence base for psychological interventions targeting symptoms of cancer-related post-traumatic stress. Nenova et al examined the efficacy of CBT-based interventions however they did not explicitly include studies where patients were screened for baseline PTSD symptoms[13]. In this instance, interventions were delivered to patients united by a diagnosis of cancer and not to those patients presenting with symptoms of cancer-related PTSD. Interestingly, the authors did acknowledge that that the effectiveness of interventions may have been dependent on participants' baseline levels of distress[13]. Furthermore, Nenova's work is limited to literature published between 1994 and 2010 and, therefore, we believe that our review provides a timely summary of the most recent literature in the field.

The aim of the present study was to review systematically the evidence on the effectiveness of interventions for reducing symptoms of cancer-related post-traumatic stress. The current study extends previous work by focusing exclusively on cancer patients suffering from cancer-related post-traumatic stress and by summarising the evidence for several types of interventions [13].

MATERIAL AND METHODS

Search strategy and selection criteria

A qualitative systematic review examining existing primary studies of interventions for cancer-related post-traumatic stress was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review was registered on the Prospero database with the registration number CRD42017069394.

Inclusion criteria were organised based on the PICO (i.e. Patient, Intervention, Comparison, Outcome) reporting structure. The population of interest was cancer patients with cancer-related PTSD/PTSS, who were aged 18 years or more, and who had received their cancer diagnosis as adults. Studies with a subgroup analysis of cancer patients scoring highly on PTSD measures were included in this review. As there are low numbers of interventional studies, no restrictions were made to specific cancer types. No restrictions were applied to study design due to the paucity of studies in this field. Similarly, no limits were applied to intervention type, with both psychological and pharmacological interventions included. Eligibility criteria extended to individual, couple or group settings and all modes of delivery (in person, virtual or over the phone). The primary outcome was cancer-related post-traumatic stress determined by either structured interview using the Structure Clinical Interview for DSM IV/V (SCID) [2] or the Clinician-Administered PTSD Scale (CAPS) [16], or by validated PTSD self-report scales which included the Impact of Events Scale (IES) [17], revised Impact of Events Scale (IES-R) [18], the Posttraumatic diagnostic stress scale (PDS) [19], PTSD Symptom Scale (PSS) [20], Short Post-Traumatic Stress Disorder Rating Interview (SPRINT) [21], or the PTSD Checklist (PCL-C) [22]. Studies were excluded if assessment of cancer-related PTSD symptoms was based on non-validated instruments, or on a PTSD

measure combined with non-PTSD measures (such as depression or anxiety scales) with no outcome data presented for those scoring highly specifically on PTSD measures. No publication date or status restrictions were applied. Studies were limited to English language publications only.

Studies were identified using the online electronic databases Medline, EMBASE, PSYCHInfo, and CINAHL. The search was done by LD and EM on the 10th of April 2018. The search strategy used variations for the terms "PTSD", "cancer" and "intervention". The full list of search terms is provided in Appendix 1. Reference lists of papers looking at cancer-related post-traumatic stress were manually scanned. Two authors (LD, EM) independently screened all titles and abstracts of the identified articles and when eligibility was established, the full text was read. Any discrepancies regarding inclusion were resolved by discussion with a third author (AK).

Data analysis

Two authors (LD and EM) independently performed the data extraction for eligible papers using a data extraction form and any disparities were settled by consensus. The following variables were extracted:

- General: author, year, title, journal, country, total number of participants, study design
- Participants: gender, age range, ethnicity, cancer type, socioeconomic status, PTSD diagnostic criteria
- Intervention: setting, category of intervention (psychological, pharmacological), specific name of intervention, delivery of intervention, duration of intervention, frequency of intervention, point of intervention onset (at diagnosis, during treatment, at treatment completion, at survivorship stage), follow-up, randomisation, blinding

- Results: Main outcome measures, secondary outcome measures, narrative findings, adherence levels, patient satisfaction, effect sizes

Risk of bias was assessed for each study using study design specific validated tools. The Cochrane risk of bias tool was used for RCTs, the NIH Quality Assessment Tool for Case Series Studies, and the NIH Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group. As the included RCTs involved behavioural interventions, the domain of participant and personnel blinding of the Cochrane Risk of Bias Tool was assessed using proposed criteria established for such study types [23]. No formal assessment of quality tool was identified for case studies.

Due to significant clinical (i.e. variability in participant characteristics, intervention components and outcome measures) and methodological (i.e. variability in study designs) heterogeneity across studies a meta-analysis could not be performed. Since our primary interest is to inform clinical practice, we report the main findings stratified by intervention category: EMDR, CBT-based and other.

RESULTS

Our electronic search yielded 508 unique papers. From this, 74 were included after the title search. Following abstract screening this number was reduced to 22 eligible papers for full text review. A further 16 papers were identified by reference chaining (Figure 1). Eight published papers entered this review. Papers were excluded either because no subgroup analysis was performed for participants scoring highly on PTSD measures, or due to using a combination of PTSD and non-PTSD tools without reporting specifically on patients scoring highly on the PTSD measures, or because non-validated PTSD tools were used (Appendix 2).

The types of interventions, settings, patient characteristics, measures of post-traumatic stress, and the key narrative findings are reported in Table 1. Of the eight eligible papers, there were five RCTs [14 24 25,26 27], one case series [28], one case study [29], and one before-and-after study [15].

The interventions broadly fell into three main groups. Two studies investigated the effects of EMDR [14 15], four looked at CBT-based treatments [24 26 28 24] and two were interventions not belonging to either of these categories [26,27]. There were considerable differences in participant characteristics, intervention delivery, follow-up protocols and outcome assessment across the studies. The total duration of intervention varied considerably with the shortest duration of treatment lasting three days through to the longest lasting 12 months.

Most studies contained a mixture of active cancer treatment and follow-up patients [24,28 27], two studies involved participants who had completed their cancer treatment [26 29], a single study looked only at newly diagnosed patients [25] and two studies investigated the effects of cancer status on the efficacy of the cancer-related PTSD intervention [14,15 28]. Three studies focused on breast cancer patients [26,27 28], two covered mixed tumour groups [14 15], two focused on haematological malignancies [29 24], and one on head and neck cancer [25].

The included studies were generally of low methodological quality (Table 2). Within the RCTs, there was frequent failure to disclose randomisation methods and allocation concealment. Blinding of participants and personnel was either not specified or participants were informed of whether they had been allocated to the intervention or control group. Another common methodological flaw was failure to account for cases lost to follow-up. No studies reported reliable change indices and only 2 studies included effect sizes. Publication bias could not be assessed due to the small number of studies included in this review (i.e. <10).

EMDR

Capezzani's small RCT (*n* = 31) compared the effects of EMDR against CBT in a group predominately composed of women with a range of cancer types [14]. Patients in the follow-up phase of their cancer management were randomised to receive either EMDR or CBT, whereas those in active treatment were automatically assigned to EMDR with no control group. EMDR was superior to CBT in reducing PTSD scores in follow-up patients. Secondary analysis showed that EMDR was equally effective in reducing PTSD symptomatology both for patients undergoing treatment as well as for those in follow up. Jarero et al evaluated the effects of a group-variant of EMDR in a population of women with mixed cancer types living in sheltered housing in Mexico [15]. The intervention was delivered over the shortest time period of all studies in this review with a total treatment duration of just three days. In keeping with Capezzani's findings, the authors concluded that EMDR was effective in reducing PTSD symptoms for both active and follow-up cancer patients and this effect was maintained at 90 days.

CBT

In their RCT of head-and-neck cancer patients, Kangas et al found that CBT, when compared with supportive counselling, was associated with a clinically significant improvement in PTSD scores in the subgroup of patients with clinical or subclinical baseline levels of PTSD [25]. In the largest study included in this review, DuHamel et al found that participants undergoing a ten session, telephone-delivered CBT (T-CBT) were less likely to meet diagnostic criteria for PTSD at both six and 12 months follow up assessments [24]. Although T-CBT reduced total PTSD symptom scores, it was effective for intrusive thoughts and avoidance but not for numbing and hyperarousal. It should be noted that the control group was an assessment-only condition.

In a case series of five women, Beatty and Koczwara concluded that CBT delivered as a stress management group programme was effective at reducing PTSD symptoms; at one month follow-up, two patients had achieved recovery, one patient had improved and the other two patients had deteriorated to baseline levels [28]. Finally, DuHamel reported that a trauma-focused intervention (a variant of CBT that has been found to be effective in reducing PTSD symptoms after trauma resulted in recovery from clinically significant post-traumatic stress, however this was based on the findings from a single patient[29].

Other

Marcus et al assessed the efficacy of telephone-counselling combined with a resource booklet compared to a resource booklet alone in 304 women with breast cancer[26]. Based on a subgroup of patients who exceeded the normative threshold for intrusive symptoms, the combined intervention yielded a 50% reduction in cancer-related distress whereas patients in the control group did not improve [26]. It is not clear why the authors do not use the IES total score in their analysis but only report on the intrusion subscale scores.

Levine's study assessed the effectiveness of a complementary/ alternative oriented intervention (CAM) involving a combination of yoga, meditation, imagery & expressive arts. In a subgroup of patients with PTSD at baseline (n = 28), they found that CAM was less effective at improving re-experiencing and avoidance PTSD symptoms when compared to a standard support group [27]. However, both the CAM and the support group were effective in reducing symptoms of arousal.

DISCUSSION

Only eight studies met the criteria for inclusion in this review. This small number suggests that the literature on the treatment of post-traumatic stress occurring as a result of cancer is

scarce, despite the substantial burden on those living with and beyond cancer. The majority of the studies focused on CBT-based interventions with a couple of studies examining the effects of EMDR and the rest evaluating the effectiveness of counselling and complementary therapy.

EMDR was found to be effective in both active and follow-up cancer patients, and more effective than CBT in follow-up patients, however the small sample sizes (n = 55) in the 2 included studies should temper such conclusions. To the best of our knowledge, no other studies have investigated EMDR in cancer patients despite increasing evidence that EMDR is an effective therapeutic strategy for clinical PTSD in other patient groups such as those suffering from chronic pain and cardiac events [30 31].

CBT delivered in person, in a group or individually, or over the telephone, was associated with reductions in PTSD symptoms in all four studies in line with the findings of Nenova's review [13]. The positive effects were maintained in the follow up assessments with the exception of a single study which found that two of the five participants who received group stress management CBT deteriorated at 1 month follow-up in comparison to post-treatment levels [28]. This should be interpreted with caution given the limitations of a case series design.

Complementary/alternative oriented intervention was effective in reducing levels of cancer-related traumatic stress but not as effective as the control support group [27]. The only study assessing a telephone counselling intervention reported significant improvements at 18 months after study enrolment for patients with symptoms of intrusion suggestive of the need for clinical referral [26].

Interventions did not always act uniformly on key features of cancer-related PTSD. Telephone CBT was more effective in reducing intrusive thoughts and avoidance than symptoms of hyper-arousal and numbing [24]. Similarly, standard support group care improved

re-experiencing and avoidant symptoms whereas complementary treatment did not change these parameters [27]. Both treatments were effective for arousal and overall PCL-C scores. This may be the case with respect to the effects of group stress management CBT as well; beneficial effects of CBSM have been previously found specifically for intrusive symptoms [2]. Evidence from studies assessing the efficacy of PTSD treatments in non-cancer trauma populations suggests that interventions may act differentially resulting in improvements for specific symptom domains rather than for total PTSD symptoms [33]. This is perhaps not unexpected in cancer-related PTSD symptoms, given that the definition is rather heterogeneous (e.g. presence of several different symptom clusters, degrees of symptom severity and chronicity and overlap between symptoms of PTSD and those of other mood and anxiety disorders)[34]. This makes the evaluation of treatment outcomes challenging. Furthermore, given that the clinical picture in cancer-related PTSD is often complex, correct clinical formulation can be challenging. This is important, as effective treatment is contingent upon correct application of trauma-focused techniques emerging from the clinical formulation. A more precise description of the nature and course of cancer-related PTSD will enable a better understanding of this condition which in turn may promote more effective treatment planning and delivery.

Many studies did not meet our inclusion criteria after full-text screening as a result of failure to identify participants who suffered from symptoms of post-traumatic stress. This is representative of much of the work into treatments for cancer-related post-traumatic stress, where patient inclusion criteria includes a diagnosis of cancer rather than the existence of cancer-related post-traumatic stress symptoms. The importance of baseline screening was highlighted in Nenova et al's systematic review of CBT-based interventions [13]. They found that 68% of included studies did not show an effect on cancer-related PTSD symptoms. However, when they examined the subset of studies that specifically screened for highly

distressed patients, the interventions were found to be effective. In fact, in the study of phone counselling included here, no significant effect of telephone counselling on PTSD symptoms was identified until patients were dichotomised into high and low levels of baseline PTSD [26]. This yielded dramatically different results with significant improvement in PTSD symptoms for those scoring highly for intrusion at baseline, compared to no improvement in those with low baseline scores. We were unable to make a distinction between PTSD and PTSS in this review due to the small number of studies available, however, it would be of interest to explore whether interventions vary in efficacy depending on levels of PTSD symptomatology. This becomes increasingly important given that, depending on symptom severity and chronicity, cancer-related PTSD/PTSS can be complex to differentiate from other common emotional responses to cancer such as fear of recurrence and adjustment disorder.

Another methodological limitation that we encountered was the use of diverse measures to screen for symptoms of PTSD. Studies often used non-validated measures or combined validated PTSD measures with scales assessing other outcomes such as depression or overall psychological distress. Assessing the efficacy of an intervention when it is delivered to patients without the condition it is intending to treat, may underestimate its beneficial effects. Consequently, delivering treatments for cancer-related PTSD when they have been validated only in cohorts including individuals not suffering from the specific symptoms may be inappropriate.

Finally, only one study used a manualised intervention format[24], however, the authors did not report whether the therapists delivering the intervention were evaluated for adherence to this manual. Manualisation provides a standard for delivery of an intervention enabling uniformity of treatment delivery.

Study limitations

This systematic review has some limitations. Studies were limited to English language only. Due to the paucity of interventional studies targeting cancer-related post-traumatic stress, we kept our inclusion criteria broad in terms of the study design and cancer types. As a result, the variation between studies makes it difficult to compare treatments and, therefore, to draw any firm conclusions. It is for this reason that we could not perform a meta-analysis. Furthermore, the studies that were included had considerable methodological weaknesses as discussed already. Similarly, in keeping with our broad inclusion criteria, we considered secondary findings from subgroups of patients with significant post-traumatic stress symptoms even though these were not the study's primary endpoints.

The aforementioned methodological issues and limitations in the existing literature give rise to recommendations for future research directions. Given the prevalence of PTSS/PTSD in cancer patients and the associated burden, it is unclear why there are not more interventional studies specifically targeting these symptoms. Well-designed trials are required in order to evaluate better the efficacy of well-established treatments such as CBT and EMDR both for syndromal and subsyndromal cancer-related PTSD. Therefore, future studies should pre-screen for symptoms of cancer-related PTSD using validated tools and follow a consistent reporting standard. Finally, a manualised approach to intervention delivery with assessment of therapist adherence is recommended in order to promote treatment integrity.

In order to develop research in this area further, it would be useful to examine the comparative efficacy of interventions in patients with different cancer types and with varying degrees of cancer-related PTSD symptomatology. Given that in the UK there is a national mandate for cancer patients in need of psychological support to be referred to primary care mental health services, it may be that routine data from those services could be used in order

to monitor the effectiveness of NICE-recommended psychological therapies such as CBT and EMDR. For example, the Improving Access to Psychological Therapies (IAPT) service, which has been tasked with providing support to patients with cancer, has adopted a clinical outcomes monitoring system and data sets are made publicly available[35].

Clinical Implications

Both CBT and EMDR are recommended by NICE for the treatment and prevention of PTSD in adults however there is no specific recommendation for their use in cancer-related PTSD[36]. This article provides evidence to support their effective use in treating cancer-related PTSD. Nevertheless, further work needs to be done before a firm recommendation can be made. Although PTSD-specific interventions such as CBT and EMDR have shown promising results, study numbers were small and there was wide variation in methodology, quality and participant characteristics thus limiting the strength of conclusions that can be drawn. Furthermore, conceptual issues specific to cancer-related PTSD such as the difficulty in pinpointing a specific traumatic event, the unfolding nature of possible stressors and the overlap between symptoms of PTSD and other anxiety and mood disorders common amongst cancer patients need to be better addressed in future studies assessing the effectiveness of treatments for cancer-related PTSD.

In particular, accuracy in diagnosing cancer-related PTSD relative to other trauma and stress-related disorders has important treatment implications. For example, a therapy that is appropriate for the treatment of cancer-related PTSD (e.g. EMDR) may appear ineffective when it is mistakenly administered to patients suffering from adjustment disorder rather than cancer-related PTSD.[11] Further research is needed in order to understand better the extent to which the experience of cancer is traumatogenic and to address diagnostic problems pertaining to cancer-related PTSD, taking into account the possibly moderating role of factors

such as individual vulnerability to trauma and the availability of supportive resources when dealing with cancer [10, 37]. Given the beneficial role of social support in aiding adjustment to life with and beyond cancer, future studies aiming to understand better the aetiology and epidemiology of cancer-related PTSD could also examine the relationship between levels and types of cancer-related post-traumatic stress symptoms and the presence of social support.[37]

Overall, our findings suggest that existing, empirically validated PTSD treatments such as CBT-based therapies and EMDR can be adapted to address cancer-related PTSD with comparably promising results. However, methodological limitations of the existing research, as well as diagnostic and conceptual difficulties surrounding cancer-related PTSD preclude firm recommendations. Further research to address these is likely to have important implications for clinical practice by enabling the fine-tuning of existing interventions in order to maximise their effective use in oncology settings.

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CONFLICT OF INTEREST STATEMENT

No conflicts of interest to disclose.

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Table 1: Studies of cancer-related PTSD interventions-summary of findings

Author	Study location	Study characteristics	Diagnoses of PTSD	Intervention & setting	Control	PTSD measure	Narrative findings
EMDR							
Capezzani et al (2013)[12]	Italy	RCT *n* = 31 29/31 women Mean age range: 50.82 – 53.40 Cancer: breast, colon, uterus, thyroid, melanoma, lung, stomach	CAPS	EMDR Once weekly sessions over 8 weeks Individual & face-to-face	CBT	CAPS IES-R	EMDR significantly more effective than CBT in particular for reducing intrusive symptoms in follow-up cancer patients. EMDR also effective in active cancer patients. Nil dropouts
Jarero et al (2015)[13]	Mexico	Before-and-After design *n*= 24 All women Mean age: 54.16 Cancer: cervical, breast, colon, bladder, skin	SPRINT PTSD= > 14	EMDR-IGTP 6 sessions over 3 days Group & face-to-face	NA	SPRINT	Intensive EMDR-IGTP effective for both active & follow-up cancer groups with cancer-related PTSD Nil dropouts
CBT-based							
DuHamel et al (2010)[23]	USA	RCT *n* = 89 41/89 women Mean age range: 49.38-52.19	CAPS PCL-C PTSD = 3 or 4 symptom cluster criteria on PCL-C, or ≥ 1 SD above mean PCL-C, or scores > cut-off for 1 symptom cluster on	T-CBT & workbook 10 sessions over 10-16 weeks Individual & not-face-to-face	Assessment only	PCL-C CAPS	T-CBT participants are less likely to meet diagnostic criteria for PTSD at 12 months than those is assessment-only group (OR 0.07, 95% CI 0.006 – 0.88). Although T-CBT reduced total PTSD symptom scores, it was effective for

		Cancer: blood-bourne malignancy	PCL-C and 2 clinical subscales of either BSI or BSI Global Severity Index				intrusive thoughts and avoidance but not for numbing and hyperarousal. Dropouts 10%.
Kangas et al (2013)[24]	Australia	RCT *n* = 35 but 26 with PTSD or subthreshold PTSD 7/35 women Mean age: 58.6 Cancer: Head and neck	CAPS PTSD = 3/3 or 2/3 criteria of scale.	CBT with HNC-specific behavioural activation. Once weekly sessions over 6 weeks with booster session at 10 weeks	Supportive counselling Once weekly sessions over 6 weeks with booster session at 10 weeks	CAPS	Overall, of those with PTSD or sub-threshold PTSD at baseline, a greater proportion of patients in the CBT condition had clinically significant improvement at 12 months compared with the SC group (67% versus 20%, F = 2.97, p <0.036). Dropouts: CBT arm 48%, SC arm 43%.
Beatty and Koczwara (2010)[27]	Australia	Case series *n* = 5 All women Mean age 50.2 Cancer: Breast	Posttraumatic Stress Scale-Self Report PSS-SR PTSD = ≥ 1 re-experiencing item + ≥ 2 arousal items, ≥ 3 avoidance items	CBSM 10 sessions over 10 weeks Group & face-to-face	NA	PSS-SR	CBSM partially effective for reducing PTSD in breast cancer but did not lead to enduring gains. CBSM also negatively affects social support and cognitive avoidance. No dropouts.
DuHamel et al (2000)[28]	USA	Case study *n* = 1 Male Age: 40 Cancer: Leukaemia	DSM-IV SCID	trauma-focused intervention Individual & face-to-face	NA	PCL-C IES SCID	Patient no longer met SCID criteria for PTSD following assessment. PCL-C and IES significantly lower at 1 and 6 months post-treatment (p < 0.025). No dropout.
Other							

Marcus et al (2010)[25]	USA	Case series *n* = 304 but do not specify number with significant PTSD All women Half sample < 50 years Cancer: breast	IES (intrusion subscale only) High risk of PTSD = score > 20	telephone counselling programme + resource booklet 16 sessions over 12 months Individual & not face-to-face	resource booklet only	IES - only intrusion subscale	Significant reduction in cancer-related distress in participants scoring high levels of distress at baseline in the telephone counselling group compared to no change in those given only the resource book (Effect size 0.5). Dropouts at 6 months 12%, 12 months 14%.
Levine et al (2005)[26]	USA	RCT *n* =181 but 26 with significant PTSD All women Mean age: 45 (of all participants) Cancer: breast	PCL-C PTSD = combined cut-off of > 44 and cluster method	CAM – involved yoga, meditation, imagery & expressive arts Twice weekly sessions over 12 weeks Group & face-to-face	Standard support group – unstructured psychoeducational support group Once weekly sessions over 12 weeks. Group & face-to-face	PCL-C	PTSD more improved in standard support group versus CAM group however QOL more improved in CAM group. No dropouts for subgroup with significant PTSD symptoms.

CAPS = Clinician-Administered PTSD Scale, PTSD = post-traumatic stress disorder, RCT = randomised controlled trial, EMDR = Eye-movement desensitisation and reprocessing therapy, CBT = Cognitive behavioural therapy, IES-R = revised Impact of Events Scale, SPRINT = short PTSD rating interview, IGTP = integrative group treatment protocol, HNC = head and neck cancer, PCL-C = PTSD Checklist, T-CBT = telephone CBT, PSS-SR = Posttraumatic Stress Scale-Self Report, CBSM = Cognitive Behaviour Stress Management, DSM-IV SCID = Structured Clinical Interview for he Diagnostic and Statistical Manual of Mental Disorders, CAM = Complementary/ alternative intervention programme, QOL = quality of life

Table 2: **Quality assessment**

Study	Quality Tool	Quality Rating
Capezzani et al (2013)[11]	Cochrane	Unclear risk of bias
Jarero et al (2015)[12]	NIH Quality Assessment Tool	Poor
DuHamel et al (2010)[23]	Cochrane	Unclear risk of bias
Kangas et al (2013)[24]	Cochrane	High risk of bias
Marcus et al (2010)[25]	Cochrane	High risk of bias
Levine et al (2005)[26]	Cochrane	High risk of bias
Beatty and Koczwara (2010)[27]	NIH Quality Assessment Tool	Fair
DuHamel et al (2000)[28]	NA	NA

NIH = National Institutes of Health.

ADDITIONAL INFORMATION

- Ethics approval and consent to participate

Not applicable. No ethics approval and consent was required.

- Consent for publication

This manuscript does not contain any individual person's data in any form

- Availability of data and material:

All data is presented in the main manuscript or additional supporting files

- Conflict of interest

The authors declare no conflict of interest

- Funding

No funding was used.

- Authors' contributions

AK was the principal investigator for the review. Input on design was provided by all authors (LD, EM, AK) throughout the project. LD and EM ran the searches, performed data extraction and conducted the AMSTAR ratings under supervision by AK. All authors edited and reviewed consecutive drafts of the paper for content, the presentation, and discussion about the findings and interpretation at each stage of the review process, as well as the structure of the paper. All authors (LD, EM, AK) commented on and approved the final version. LD and EM contributed equally to this paper.

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