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Review article

Anxiety Among Adolescent Survivors of Pediatric Cancer



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ABSTRACT

Purpose: The purpose of this review was to synthesize current knowledge about anxiety among adolescent survivors of pediatric cancer and highlights areas for future research.

Methods: Systematic literature searches were conducted in five databases for articles published anytime before December 28, 2015. Manuscripts were reviewed by a team of six coders. Included manuscripts reported outcomes relevant to anxiety, worry, and post-traumatic stress in survivors of pediatric cancer (age at the time of study: 10–22 years) who were off treatment.

Results: Twenty-four articles met inclusion criteria. Included results were categorized into the following domains: post-traumatic stress, anxiety, cancer-related worry, and interventions. With the exception of post-traumatic stress, there was little research about anxiety in this population; however, studies generally indicated that adolescent survivors of pediatric cancer are at elevated risk for anxiety, post-traumatic stress symptoms, and cancer-related worry.

Conclusions: This review provides preliminary evidence that anxiety is a relevant, but understudied, psychosocial outcome for adolescent survivors of pediatric cancer. More research is needed to better understand the presentation of anxiety in this population, its effect on survivors' quality of life, and possible areas for intervention.

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IMPLICATIONS AND CONTRIBUTION

This overview will establish a foundation for the implementation of anxiety screening and the development of evidence-based interventions to target anxiety and related symptoms in this population. Targeting these symptoms could prove to be useful in supporting psychosocial adjustment during adolescence and as these patients transition into adulthood.

Approximately, 10,380 children under the age of 15 years were diagnosed with cancer in 2016 [1], and around 5,000 adolescents aged 15–19 years are diagnosed with cancer

annually [2]. Approximately, 85% of children and adolescents with cancer survive at least 5 years after diagnosis [3]. With growing numbers of pediatric and adolescent cancer survivors [3,4], it is crucial to investigate the long-term effects the cancer experience may have on psychosocial adjustment. It is particularly important to investigate psychosocial outcomes for adolescents who have survived cancer, as adolescence is a unique and important phase in psychological development [5,6] that represents a period of increased risk for adverse psychosocial

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outcomes [7]. Despite a growing interest in the psychosocial outcomes of adolescent survivors of pediatric cancer, anxiety is understudied in this population, with few studies examining anxiety as a main outcome variable [8]. It is necessary to address this gap in the literature, as there is meta-analytic evidence from adult samples that anxiety is an important and prevalent psychosocial outcome among cancer survivors [9].

Previous research examining anxiety in adolescent survivors (e.g., [10–12]) has focused primarily on post-traumatic stress disorder (PTSD) and post-traumatic stress symptoms (PTSS). These studies have indicated that survivors report significant PTSS, meeting diagnostic criteria for PTSD at similar rates as adolescents who have experienced other traumas. A large portion of survivors report PTSS, such as re-experiencing and arousal, and survivors' PTSS are significantly related to parental PTSS [10]. Given the documented prevalence of PTSS and the evidence that anxiety, in general, may be an important psychosocial outcome for adolescent cancer survivors, it is critical to examine the literature about anxiety in this population.

This article will review literature regarding psychosocial functioning among adolescent survivors of pediatric cancer and psychosocial interventions targeting this population with the aim of synthesizing current knowledge about anxiety and highlighting areas for future research. This review aims to identify research relating to anxiety both at clinical (as defined by any edition of the DSM to accommodate the recent reclassification of disorders in the DSM-5 [13]) and subclinical levels.

Methods

Search strategy

Systematic searches were conducted in five databases for articles published before December 28, 2015. Authors hypothesized that research in this area would be limited [8] and, therefore, chose not to set any limitations on the research publication date. The search was limited to human only, English language, and adolescents (depending on database, this term included ages 13–18 years or 13–19 years). The databases were MEDLINE (via PubMed), Embase, The Cochrane Library, Web of Science, and PsycINFO (via OVID). For PubMed, Embase, The Cochrane Library, and PsycINFO, controlled vocabulary and text words were used in the development of search strategies. The Web of Science database does not employ controlled terminology, so was searched using only text words. All results were combined in a bibliographic management tool (EndNote). Duplicates were eliminated.

For MeSH and keyword terms, see PubMed search strategy in Appendix A. Generally, the search strategy had three components and all concepts were linked together with the AND operator: (1) adolescent cancer survivor terms including neoplasms, cancers, adolescents, juveniles, children, survivors, and survivorship; (2) psychosocial intervention terms including psychotherapy, behavior, cognitive behavioral therapy, talk therapy, psycho-pharmacology, mindfulness, and social adjustment; and (3) anxiety terms including panic disorders, social phobias, PTSD, OCD, depressive disorders, fear, worry, and nervousness. Controlled vocabularies were searched for and included in the search strategy for the searches in PubMed, Embase, Cochrane, and PsycINFO. The Web of Science search combined the keywords of all three concepts only.

Alternate sources were searched for gray literature items to reduce publication bias: the Society for Research on Adolescence (<http://www.s-r-a.org/>), Society for Adolescent Health and Medicine (<http://www.adolescenthealth.org/Home.aspx>), and the International Society of Paediatric Oncology (<http://www.siop-online.org/>).

Eligibility criteria

Eligibility was based on the following predefined inclusion criteria:

Sample: The sample included adolescents, aged 10–22 years at the time of assessment, who had completed any treatment regimen before study recruitment for any cancer diagnosis at any age. We intended to include only studies with samples aged 13–19 years. However, many published studies include these participants in a subject pool with broader age categories. Therefore, an age range of 10–22 years was chosen as the inclusion criterion to avoid eliminating samples that consisted primarily of survivors falling in our target age range. This inclusion criterion is similar to that used in a systematic review of psychosocial interventions for adolescents with cancer [14]. International samples were included if the article was published in English.

Study Design: Quantitative, qualitative, mixed methods, descriptive studies, intervention studies, pilot studies, case studies, peer-reviewed journal articles, white papers, and epub ahead of print articles were included.

Outcome: Anxiety, common proxies for anxiety (e.g., worry and fear), and post-traumatic stress.

Exclusion: Articles not available in English, conference abstracts, review papers, commentaries, books, and unpublished dissertations.

Study selection

Titles and abstracts were independently reviewed by two members of the review team. Discrepancies ($n = 281$ of 3,009 titles and 178 of 789 abstracts) were discussed with the entire review team of six coders if resolution was not achieved within a review pair. Potentially relevant articles were reviewed in full by one member of the review team; articles determined to meet inclusion criteria were further reviewed by two authors (G.A.M. and C.G.S.). Three additional eligible studies were identified through reference review of the included studies.

Synthesis of findings

Anxiety-related information from included articles was organized into the following categories: post-traumatic stress, anxiety, cancer-specific worries, and interventions. When possible, effect sizes were calculated for significant results for ease of between-study comparisons.

Study quality was assessed using a modified version of the Downs and Black Quality Study checklist [15]. This modified version of the checklist has been used in a previously published systematic review [16]. See Appendix B for a list of quality indicators.

Results

Twenty-four articles met inclusion criteria. Please see PRISMA diagram for a summary of articles excluded at each phase of

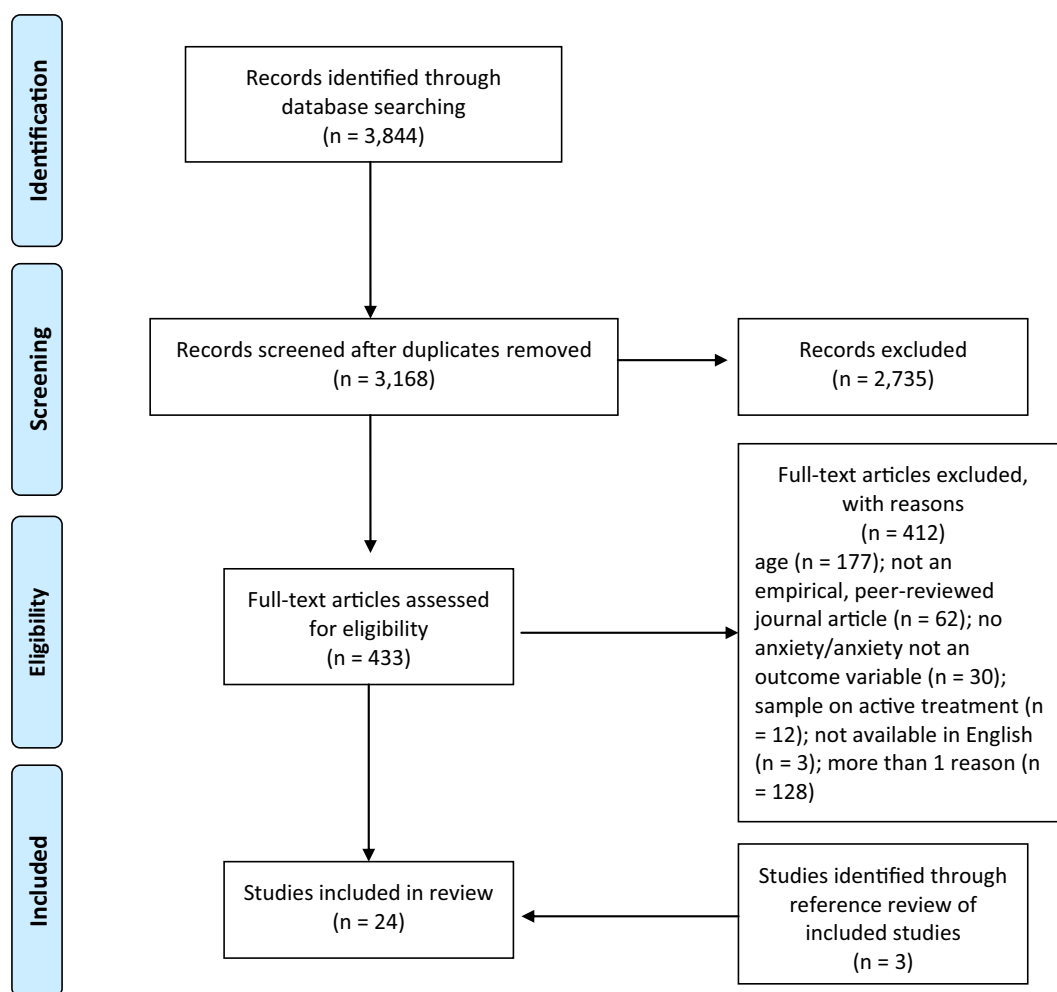


Figure 1. PRISMA flow diagram.

coding (Figure 1). Twenty (83%) articles were quantitative studies [11,12,17–34], one (4%) was qualitative [35], and three (13%) utilized a mixed-methods approach [10,36,37]. The three mixed-methods studies, the qualitative study, and 17 of the quantitative studies [10,17–21,23–37] were cross-sectional, descriptive studies, and three of the quantitative studies were longitudinal intervention studies [11,12,22]. Of the quantitative studies, three of the cross-sectional studies [10,17,19] utilized samples from one of the included intervention studies [11], one intervention study [22] utilized a sample from a broader intervention study [38], and two cross-sectional studies [29,30] utilized the same sample. All other quantitative studies utilized separate samples. Table 1 provides information regarding the aims, study designs, samples, and anxiety-related findings of the included studies.

Twelve (50%) studies examined anxiety, PTSD/PTSS, or worry as part of a larger study with multiple outcomes [12,20–23,25,27,29,31–34,36]. Five (21%) studies examined PTSD or PTSS as a main outcome variable [10,11,17,24,30]. Four (17%) studies assessed anxiety, PTSD/PTSS, or worry as a potential correlate of their outcomes of interest [18,19,28,35]. Two (8%) studies examined worry as a primary outcome variable [26,37].

Sample sizes ranged from 18 for a pilot study [12] to 407 for a national follow-up study [25]. Studies generally included

survivors with a range of diagnoses, with leukemia being the most prevalent. It was not possible to determine the range of time since treatment completion because not all studies reported this information and the studies that did report it varied in the level of description provided. Most samples included survivors that had been off treatment for at least 1 year.

Twenty-two measures were used to assess anxiety and related constructs. Table 2 provides a list of measures. Eleven studies utilized self-report questionnaires or diagnostic interviews to assess PTSD/PTSS [10–12,17–19,23,24,28–30], nine studies included self-report questionnaires to assess symptoms of anxiety [11,12,20,25,29,30,32–34], and one study utilized a semistructured interview to assess anxiety [35]. One study utilized a multi-informant measure of child/adolescent behavior and self-perceptions that included adolescent, parent, and teacher reports [21]. Four studies included multiple measures of PTSD/PTSS [10,12,23,24], and two studies assessed both PTSD/PTSS and anxiety [11,12]. One study administered a self-report scale of cancer-related worry [31], and one study utilized a measure of perceptions of infertility risks including worry about infertility [26]. Two studies utilized worry questionnaires designed by study investigators [22,37], and one study developed a questionnaire to assess the fear of relapse [27].

The 23 quantitative and mixed-method studies were assessed using the modified Downs and Black study quality checklist, which includes nine quality indicators [15]. Of these, seven (29%) satisfied all nine indicators [11,17,18,25,29–31]. Eight (33%) were only missing one of the nine quality indicators [10,19,21,26–28,33,34], with the majority of these studies not specifying whether the participants were representative of the population from which they were recruited. Four studies (17%) were missing two of the nine quality indicators [5,22,24,32]. Four studies that did not meet criteria were to be considered a high-quality study: two studies (9%) missing three quality indicators [12,20] and two studies (9%) missing four quality indicators [36,37]. Studies not meeting the quality criteria were included in the review to provide ideas for future directions, given the dearth of literature in this area.

Study findings

Post-traumatic stress. Forty-two percent of included studies assessed PTSD and/or PTSS. Rates of clinical PTSD in these studies ranged from 3.0% to 13.8% [10,17,23,24], with most studies finding rates higher than previously reported rates for adolescents in the general population (3.7% for males and 6.3% for females) [39]. Arpawong et al. [18] found that in a sample of survivors who had completed treatment within the previous 6 months, the mean PTSD score fell below the clinical cutoff.

Gerhardt et al. [24], however, found that a smaller percentage of survivors met criteria for PTSD than healthy controls who had experienced other traumatic events (3% and 6%, respectively; $d = -.40$). In this study, 31% of traumatic events reported by survivors were cancer related, and no survivors who reported a cancer-related trauma met criteria for PTSD, compared with 22% of those reporting other traumas. Cancer-related traumas reported by survivors included painful procedures, stem cell transplant, knowing children who died, and the overall cancer experience.

PTSD was more common in survivors whose families indicated poor functioning ($d = .40$), particularly in regard to problem solving, affective responsiveness, and affective involvement (d 's = .60–.85) [17]. In an investigation of repressive coping style (i.e., a strategy of self-protection that involves dismissing or ignoring strong emotions), Erickson et al. [23] found that 100% of survivors who met criteria for PTSD displayed coping styles that were not repressive, and those who did not cope repressively reported more distress than repressive peers.

Studies also reported on PTSS not meeting criteria for a clinical diagnosis of PTSD. Gerhardt et al. [24] found that 7% of survivors reported at least one current PTSS (compared with 8% of healthy peers; $d = -.08$), and 20% of survivors reported a lifetime history of PTSS (compared with 13% of healthy peers; $d = .28$). Of survivors who reported cancer-related trauma, 60% reported at least one PTSS, compared with 73% of survivors who reported other types of trauma. Those who reported other types of trauma endorsed a higher number of PTSS than survivors who reported on cancer-related trauma. Survivors in this study reported fewer dissociative symptoms than comparison peers ($d = -.36$).

Kazak [10] found that 18% of adolescent survivors reported moderate to severe PTSS, as indicated by scoring ≥ 25 on the Post-Traumatic Stress Disorder Reaction Index. Survivors had significantly lower PTSS scores than their mothers ($d = .51$) and had lower rates of PTSD, both at the time of the study ($d = .46$)

and since diagnosis ($d = .80$). PTSS were positively correlated with generalized anxiety [11], and survivors' PTSS were related to parents' PTSS [10,11]. Seventy-three percent of survivors met criteria for re-experiencing symptoms, 13% for avoidance symptoms, and 41% for arousal symptoms. There was little concordance between diagnostic PTSD in parents and adolescents (0%–5%), although there was a high level of concordance for re-experiencing symptoms (62% for fathers and 72% for mothers) [10].

Ozono et al. [30] found that 11% of survivors reported severe PTSS, compared with 21% of mothers ($d = -.42$) and 22% of fathers ($d = -.47$). Specifically, parents reported higher rates of intrusion and avoidance symptoms than survivors (d 's = .57–.69). Survivors' PTSS were significantly correlated with mothers' PTSS ($d = .82$), but not with fathers'. This study found a nonsignificant trend for an inverse relationship between PTSS and family functioning, particularly relating to family roles ($d = .51$).

Several variables were related to PTSS. Two studies found a positive link between PTSS and late effects of treatment ($d = .84$ – 1.13) [24,30], and survivors who had experienced relapse reported higher PTSS than those in continuous remission ($d = .68$) [29]. One study [19] found that PTSS were positively related to age at diagnosis, such that survivors who were aged 5 years or older at diagnosis reported higher levels of PTSS ($d = .47$). PTSS were also positively correlated to perceived life threat ($d = .63$) and treatment intensity ($d = .70$) [19], and PTSS were positively related to trait anxiety ($d = 1.3$) [30]. Two studies assessing the relationship between PTSS and the time since diagnosis found insignificant results [24,30].

Erickson et al. [23] found that most survivors had mean PTSS scores in the mild range on the Child Posttraumatic Stress Reaction Index, Revision 2, compared with the normative sample utilized by the measure's developers. This study found no statistically significant differences in PTSS for survivors displaying a repressive coping style and survivors who displayed other coping styles. However, authors reported moderate to large effect sizes, indicating that repressors reported fewer trauma symptoms than those who did not cope repressively ($d = .79$) and that repressors' PTSS were less severe than those reported by survivors with other coping styles ($d = .54$). Specifically, those with repressive coping reported fewer dissociative symptoms than survivors with other coping styles ($d = .36$) and the normative sample.

Conflicting results were found among studies that assessed the relationship between PTSS and post-traumatic growth (PTG). Barakat et al. [19] found a positive relationship between PTSS and PTG ($d = .74$), which was significant over and above age at diagnosis and illness-specific appraisals. However, Michel et al. [28] did not find a significant relationship between PTSS and an element of PTG. In a sample of adolescents who had completed treatment within the past 6 months, Arpawong et al. [18] found a negative relationship between PTSS and PTG in univariate analyses ($d = -.45$), but a positive relationship in multivariate analyses including race/ethnicity, cancer diagnosis, depressive symptoms, and quality of life.

Anxiety. The review yielded varied findings about anxiety. Gianinazzi et al. [25] found that adolescent survivors reported more anxiety than the comparison sample on the Brief Symptom Inventory (BSI; $d = .23$), but self-reported anxiety was

Table 1
Included studies

Reference	Quality rating	Scientific aims	Study design	Sample size	Age at the time of study	Time since treatment completion	Cancer diagnosis	Summary of anxiety-related findings
Post-traumatic stress Alderfer et al., 2009 [17]	9 ^a	To examine the functioning of families with an adolescent survivor and the relationship between family functioning and adolescent PTSD	Cross-sectional; descriptive; quantitative	144 survivors (150 families)	M = 14.6 (2.4); 11–19 years	M = 5.3 (2.9); 1–12 years	Leukemia (31%); solid tumors (22%); lymphoma (22%); bone tumors (8%); other (17%)	<ul style="list-style-type: none"> • 8% of survivors met criteria for PTSD at some point since their diagnosis. • Survivor PTSD was significantly related to poor family functioning, particularly in the areas of problem solving, affective responsiveness, and affective involvement.
Arpawong et al., 2013 [18]	9 ^a	To examine PTG and its correlates among an ethnically diverse sample of AYA survivors recently off treatment	Cross-sectional; descriptive; quantitative	94	M = 12.3 (3.1); 11–21 years	≤6 months	Leukemia (38%); lymphoma (24%); soft tissue tumors (20%); CNS tumors (10%); other (8%)	<ul style="list-style-type: none"> • Survivors' mean PTSD score fell below the clinical cutoff. • Univariate analyses yielded a negative relationship between PTG and PTSS; multivariable analyses yielded a positive relationship.
Barakat et al., 2006 [19]	8 ^a	To describe PTG following pediatric cancer survival	Cross-sectional; descriptive; quantitative	150	M = 14.7 (2.4); 11.1–19.3 years	M = 5.3 (2.9); ≥1 year	Solid tumors (35%); leukemia (31%); lymphoma (21%); other (13%)	<ul style="list-style-type: none"> • PTSS were moderately positively correlated with PTG, perceived life threat, and treatment intensity. • PTSS were significantly associated with PTG over and above the age at diagnosis and illness-specific appraisals. • Those diagnosed after the age of 5 reported more PTSS than those diagnosed at age 5 years or younger, and PTG and PTSS remained significantly correlated for both subsamples.
Erickson et al., 2008 [23] ^f	7 ^a	To investigate how repressive style influences psychological distress in adolescent cancer survivors	Cross-sectional; descriptive; quantitative	29	M = 15.3 (1.8); 12–18 years	≥1 year	Leukemia (31%); solid tumors (24%); lymphoma (21%); sarcomas (14%); other (10%)	<ul style="list-style-type: none"> • 14% of survivors met criteria for PTSD. • 100% of those with PTSD exhibited a coping style that was not repressive. • There was a nonsignificant trend for repressors to report fewer and less severe trauma symptoms than those with other coping styles, particularly with regard to dissociative symptoms. • Compared with the norm sample of the CPTS-RI, survivors' mean PTSS scores

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Table 1
Continued

Reference	Quality rating	Scientific aims	Study design	Sample size	Age at the time of study	Time since treatment completion	Cancer diagnosis	Summary of anxiety-related findings
Gerhardt et al., 2007 [24]	7 ^a	To examine PTSS and PTSD among emerging adult survivors of pediatric cancer in comparison with healthy peers	Cross-sectional; descriptive; quantitative	56 survivors; 60 healthy peers	M = 18.6 (.8) years	Not reported	Lymphoma (39%); leukemia (37%); solid tumors (24%)	<p>were in the mild range, with repressors reporting slightly less symptoms than those with other coping styles.</p> <ul style="list-style-type: none"> • A smaller proportion of survivors met criteria for PTSD or reported current/past PTSS than comparison peers, particularly with regard to dissociative symptoms. • Survivors reported more PTSS about noncancer traumas than about the cancer experience. • Late effects were positively correlated with PTSS.
Kazak et al., 2004a [10]	8 ^a	To examine how PTSD and PTSS cluster within families of adolescent survivors of pediatric cancer	Cross-sectional; descriptive; mixed-methods	150 survivors; 146 mothers; 106 fathers	14.7 (2.4); 11.1–19.3 years	5.3 (2.9) years	Leukemia (31%); solid tumors (35%); lymphomas (21%); other (13%)	<ul style="list-style-type: none"> • 18% of survivors reported moderate to severe PTSS. • 5% of survivors met criteria for current PTSD; 8% met criteria for PTSD at some point since diagnosis. • 73% of survivors met criteria for re-experiencing symptoms; 13% met criteria for avoidance symptoms; 41% met criteria for arousal symptoms. • Survivors had lower PTSS scores than their parents, and mothers' rates of PTSD were higher than survivors'. • Concordance rates were low between survivors and parents for current/past diagnosis of PTSD (0%–5%). • There was high concordance among survivors and their parents for re-experiencing symptoms (62%–72%)
Kazak, 2004b [11] ^c	9 ^a	To assess an intervention to reduce cancer-related PTSS symptoms in adolescent survivors of pediatric cancers and their families	Longitudinal; intervention; quantitative	150 survivors; 146 mothers; 106 fathers	M = 14.6 (2.4); 10.8–19.3 years	1–10 years	Leukemia (31%); solid tumors (23%); lymphoma (23%); bone tumors (8%); other (16%)	<ul style="list-style-type: none"> • Intrusion, avoidance, and arousal scores on the IES-R and total PTSD-RI score were each significantly correlated with more general anxiety symptoms. • PTSS and anxiety scores for mothers, fathers, and survivors were inter-related.

Table 1
Continued

Reference	Quality rating	Scientific aims	Study design	Sample size	Age at the time of study	Time since treatment completion	Cancer diagnosis	Summary of anxiety-related findings
Michel et al., 2009 [28]	8 ^a	To describe factors associated with benefit finding among survivors of pediatric cancer and to determine the association between survivors' benefit finding and parents' PTG	Cross-sectional; descriptive; quantitative	41 survivors (48 families)	M = 13.7 (1.1); 12.0–15.9 years	M = 6.6 (2.9); 2.9–13.9 years	Leukemia (50%); CNS tumors (17%); solid tumors (33%)	<ul style="list-style-type: none"> • There was no relationship between PTSS and benefit finding.
Ozono et al., 2007 [30]	9 ^a	To investigate factors related to severe PTSS in adolescent survivors of pediatric cancer and their parents	Cross-sectional; descriptive; quantitative	88 survivors; 87 mothers; 72 fathers	M = 16.2 (2.3); 12–20 years	≥1 year	ALL (52%); other leukemia (16%); malignant lymphoma (10%); infant neuroblastoma (12%); other solid tumors (10%)	<ul style="list-style-type: none"> • 11% of survivors reported severe PTSS, a lower rate than was present in parents. • Parents reported higher rates of intrusion and avoidance than survivors. • There were significant intercorrelations between adolescents' PTSS scores and those of their mothers, but no significant correlation between adolescents' and fathers' scores. • Medical sequelae and higher trait anxiety were related to severe PTSS.
Ozono et al., 2010 [29]	9 ^a	To identify distinct clusters of families that include a pediatric cancer survivor, and identify differences between the clusters as related to anxiety, depression, and PTSS	Cross-sectional; descriptive; quantitative	88 survivors; 87 mothers; 72 fathers	M = 16.2 (2.2); 12–20 years	≥1 year	All (52%); other leukemia (16%); malignant lymphoma (10%); infant neuroblastoma (12%); other solid tumors (10%)	<ul style="list-style-type: none"> • Survivors who had experienced relapse reported greater PTSS than those in continuous remission.
Anxiety Bauld et al., 1998 [20]	6	To examine the psychosocial status of adolescent survivors in comparison with healthy peers	Cross-sectional; descriptive; quantitative	32 survivors; 34 healthy peers	M = 14.9 (1.6); 12–17 years	M = 8 years; 0–2 years (25.0%); 2–5 years (15.6%); >5 years (59.4%)	Primarily ALL (percentage not reported)	<ul style="list-style-type: none"> • Survivors reported higher state anxiety than healthy peers.
Carpentieri et al., 2003 [21]	8 ^a	To describe the psychosocial and behavioral functioning of adolescents previously treated for brain tumors	Cross-sectional; descriptive; quantitative	32	M = 14.5; 12–18 years	M = 4.1; 1.5–12 years	Low-grade astrocytoma (44%); craniopharyngioma (16%); medulloblastoma (13%); optic glioma (6%); other (22%)	<ul style="list-style-type: none"> • Adolescent self-report did not indicate elevations on any anxiety-related measures compared with measure norms.

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Table 1
Continued

Reference	Quality rating	Scientific aims	Study design	Sample size	Age at the time of study	Time since treatment completion	Cancer diagnosis	Summary of anxiety-related findings
Erickson et al., 2008 [23] ^c	7 ^a	To investigate how repressive style influences psychological distress in adolescent cancer survivors	Cross-sectional; descriptive; quantitative	29	M = 15.3 (1.8); 12–18 years	≥1 year	Leukemia (31%); solid tumors (24%); lymphoma (21%); sarcomas (14%); other (10%)	<ul style="list-style-type: none"> Survivors who exhibited repressive coping style reported less anxiety than survivors with other coping styles and than comparison peers
Gianinazzi et al., 2013 [25]	9 ^a	To evaluate psychological distress in adolescent survivors of pediatric cancer in comparison with siblings, psychotherapy patients, and a healthy sample; to determine risk factors for psychological distress in this population	Cross-sectional; descriptive; quantitative	407 survivors; 102 siblings; 56 psychotherapy patients; 93 healthy peers	M = 17.9 (1.5); 16–19 years	Not reported; off-treatment status confirmed by author	Leukemia (33%); CNS tumors (17%); lymphoma (13%); renal tumors (10%); other (27%)	<ul style="list-style-type: none"> Survivors scored higher on anxiety than on any other BSI-18 subscale. Survivors reported greater anxiety than the healthy sample. Survivors' anxiety scores did not differ from their siblings. Survivors who scored above the distress threshold reported more anxiety than psychotherapy patients.
McLoone et al., 2011 [35]	n/a ^b	To examine key factors related to adolescent cancer survivors' transition back to school	Cross-sectional; descriptive; qualitative	19 survivors (22 families)	M = 16.7 (2.2); 12–20 years	M = 35.0 (20.1); 5.4–66.9 months	Leukemia (32%); lymphoma (21%); sarcoma (32%); other (21%)	<ul style="list-style-type: none"> 64% of survivors experienced anxiety that was a barrier to school re-entry. Survivors experienced anxiety regarding exams and catching up on missed academic material, as well as social anxiety and lowered personal confidence.
Pendley et al., 1997 [32]	7 ^a	To examine body image and social adjustment in adolescents who completed cancer treatment in comparison with healthy peers	Cross-sectional; descriptive; quantitative	21 survivors; 21 healthy peers	11–21 years	M = 17 (8.7); 6–30 months	Lymphoma (43%); leukemia (38%); other solid tumors (19%)	<ul style="list-style-type: none"> Survivors did not differ significantly from healthy peers on social anxiety. Generalized social anxiety and distress, distress due to new situations and fear of negative evaluation from peers were positively related to illness impact and negatively related to perceived body image. Survivors who had been off treatment ≥ 1 year reported greater distress due to new situations and fear of negative evaluation from peers than those who had been off treatment < 1 year.

Table 1
Continued

Reference	Quality rating	Scientific aims	Study design	Sample size	Age at the time of study	Time since treatment completion	Cancer diagnosis	Summary of anxiety-related findings
Servtziglou et al., 2008 [33]	8 ^a	To assess the psychosocial well-being of AYA survivors of pediatric cancer compared with healthy peers	Cross-sectional; descriptive; quantitative	45 survivors; 57 healthy peers	M = 19.8; 15–29 years (reported for total AYA sample, although results split into adolescents and YA groups)	≥2 years	Leukemia (50%); sarcoma (18%); non-Hodgkin's lymphoma (12.6%); Hodgkin's lymphoma (9%); other (12%)	<ul style="list-style-type: none"> • There was a nonsignificant trend for both male and female adolescent survivors to report higher state and trait anxiety than the comparative sample.
Yallop et al., 2013 [34]	8 ^a	To describe self-reported psychosocial well-being of adolescent pediatric cancer survivors compared with healthy peers	Cross-sectional; descriptive; quantitative	170 survivors; 9,107 healthy peers	M = 15.3; 12–18 years	≥2 years	Leukemia (38%); CNS tumors (13%); lymphoma (11%); renal tumors (11%); other (28%)	<ul style="list-style-type: none"> • 7% of the sample reported elevated anxiety. • Anxiety was not found to be related to any demographic or cancer characteristics. • Survivors did not differ significantly from healthy peers on anxiety measures.
Cancer-specific worries Fritz and Williams, 1988 [36]	5	To describe variables relevant to adjustment in adolescent survivors of pediatric cancer	Cross-sectional; descriptive; mixed methods	41	M = 17.3 (3.1) years	2–8 years	Leukemia (34%); Hodgkins disease (21%); non-Hodgkins lymphoma (22%); bone sarcoma (10%); other (13%)	<ul style="list-style-type: none"> • 26% of participants were "extremely preoccupied with their physical health in a hypochondriacal manner," as evidenced by hypervigilance regarding their bodies and bodily functions. • Very few adolescents felt comfortable discussing their illness because they felt unsure about others' reactions and were concerned that disclosing might reduce their attractiveness to potential romantic partners. • Participants expressed concerns about fertility.
Gilleland Marchak et al., 2015 [26]	8 ^a	To assess awareness of risk and worry about infertility among female adolescent survivors of pediatric cancer and their parents	Cross-sectional; descriptive; quantitative	48 survivors; 41 parents	M = 15.0 (3.3); 10–21 years	7.4 years (3.6)	Leukemia (42%); lymphoma (13%); sarcoma (21%); non-CNS solid tumors (25%)	<ul style="list-style-type: none"> • 71% of participants reported worry about infertility. • Survivors worried less frequently about infertility than parents. • Worry about infertility was positively predicted by awareness of infertility risk, survivor age, and bone marrow transplantation.
Hill et al., 1998 [27]	8 ^a	To examine the long-term psychosocial functioning of childhood ALL survivors who received either CRT with IT-MTX or IV-MTX with IT-MTX	Cross-sectional; descriptive; quantitative	32 (19 CRT with IT-MTX; 13 IV-MTX with IT-MTX)	CRT with IT-MTX: M = 16.7; IV-MTX with IT-MTX 16.6; 14–18 years	≥1 year	ALL (100%)	<ul style="list-style-type: none"> • Adolescents had a mean fear of relapse score of 9.3 (.6) on a 5- to 25-point scale. This score did not differ significantly between treatment groups or from young adults in the sample.

(continued on next page)

Table 1
Continued

Reference	Quality rating	Scientific aims	Study design	Sample size	Age at the time of study	Time since treatment completion	Cancer diagnosis	Summary of anxiety-related findings
Paxton et al., 2010 [31]	9 ^a	To explore the relationship between physical activity and HRQOL in survivors of pediatric cancer	Cross-sectional; descriptive; quantitative	94	M = 14.3 (1.8); 11.0–17.9 years	≥1 year	CNS tumors (43%); lymphoma (43%); leukemia (15%)	<ul style="list-style-type: none"> Overall, AYAs who perceived their illness to be caused by chance reported less fear of relapse. When accounting for family adjustment, AYAs who lived with family members reported greater fear of relapse if they did not perceive their illness to be caused by chance. Adolescents reported less cancer-related worry than young adults.
Weigers et al., 1999 [37]	5	To examine self-reported worries of long-term survivors of pediatric cancer recruited from the CCCF relative to worries of adolescent healthy peers. To assess the generalizability of the CCCF findings, worries of CCCF participants were compared with pediatric cancer survivors recruited from a children's hospital	Cross-sectional; descriptive; mixed methods	228 CCCF survivors; 93 children's hospital survivors; 257 healthy peers	CCCF sample: M = 17.6; 14–21 years; children's hospital sample: M = 18.3; 15–22 years	Not reported	CCCF sample: Leukemia (36%); lymphoma (24%); bone tumors (18%); CNS tumors (6%); other (17%). children's hospital sample: leukemia (33%); bone tumors (24%); lymphoma (21%); Wilms' tumor (5%); other (18%)	<ul style="list-style-type: none"> The CCCF sample worried less about having headaches, dying, how their body looked, getting tired, and getting a cold or the flu than healthy peers. The CCCF sample reported more worry than healthy peers about fertility and the risk of cancer for their children. The CCCF sample was generally comparable to the children's hospital sample of adolescent survivors. Worry about relapse was predicted by age; a diagnosis of CNS tumor or lymphoma; and worry about relapse when ending treatment. Worry about fertility was predicted by: age; gender; a diagnosis of Wilms' tumor or "other malignancies"; and worry about fertility when treatment ended.
Interventions Cox et al., 2008 [22]	7 ^a	To identify targets for interventions to promote BSE among female survivors of pediatric cancer and to describe the effects of a risk-counseling	Longitudinal; intervention; quantitative	149	Median = 15.0 (mean not reported); 12.0–19.1 years	≥2 years	Leukemia/Lymphoma (59%); Solid Tumors (41%)	<ul style="list-style-type: none"> Survivors reported a decrease in general fears about cancer at postintervention. Less worry about appearance at baseline was associated with increased BSE postintervention.

Table 1
Continued

Reference	Quality rating	Scientific aims	Study design	Sample size	Age at the time of study	Time since treatment completion	Cancer diagnosis	Summary of anxiety-related findings
Kazak et al., 1999 [12]	6	To describe the results of a pilot study of Surviving Cancer Competently Intervention Program (SCCIP), a family intervention designed to reduce distress in adolescent survivors of pediatric cancer and their families	Longitudinal; intervention; quantitative	18	M = 13.3 (2.2); 10–17 years	≥1 year	Not reported	<ul style="list-style-type: none"> Higher grade in school was associated with increased BSE postintervention and interacted with two fear items; not fearing the return of cancer and not having general fears about cancer. At postintervention, survivors' mean overall PTSS scores decreased, as did avoidance scores. Mean anxiety scores decreased, particularly physiological anxiety/worry and oversensitivity.
Kazak et al., 2004b [11] ^c	9 ^a	To assess an intervention to reduce cancer-related PTSS symptoms in adolescent survivors of pediatric cancers and their families	Longitudinal; intervention; quantitative	150 survivors; 146 mothers; 106 fathers	M = 14.6 (2.4); 10.8–19.3 years	1–10 years	Leukemia (31%); Solid Tumors (23%); Lymphoma (23%); Bone Tumors (8%); Other (16%)	<ul style="list-style-type: none"> At follow-up, survivors in the treatment group showed a significantly greater decrease in arousal symptoms than the control group. There was a higher dropout rate for the intervention group among survivors who indicated greater PTSS symptoms at baseline.

ALL = acute lymphoblastic leukemia; AYA = adolescent and young adult; BSE = breast self-examination; BSI = Brief Symptom Inventory; CCCF = Candlelighters Childhood Cancer Foundation; CNS = central nervous system; CRT with IT-MTX = centigray of cranial radiation with intrathecal methotrexate; CPTS-RI = Child Posttraumatic Stress Reaction Index, Revision 2; HRQOL = health-related quality of life; IES-R = Impact of Events Scale-Revised; IV-MTX with IT-MTX = intermediate dose systemic methotrexate with intrathecal methotrexate; PTG = post-traumatic growth; PTSD-RI = Post-Traumatic Stress Disorder Reaction Index; YA = young adult.

^a Indicates a “high-quality” study; studies were considered “high quality” if they satisfied ≥7 of 9 quality indicators.

^b Not included in quality assessment due to qualitative nature of the study.

^c Additional results from study are described in another part of the table.

Table 2
Anxiety measures utilized

Construct ^a	Measure	Type	Utilized by
PTSD	Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA; Newman et al., 2004)	Diagnostic interview	Erickson et al., 2008 [23]
	Kiddie-Schedule for Affective Disorders and Schizophrenia-Epidemiologic Version-5 (K-SADS-E-5; Orvaschel, 1995)	Diagnostic interview	Gerhardt et al., 2007 [24]
	Structured Clinical Interview for DSM-IV, PTSD Section (SCID-NP; First et al., 1995)	Diagnostic interview	Alderfer et al., 2009 [17]; Kazak, 2004a [10]
PTSS	Adolescent Dissociative Experiences Scale-II (A-DES; Armstrong et al., 1997)	Self-report questionnaire	Gerhardt et al., 2007 [24]
	Child Posttraumatic Stress Reaction Index Revision 2 (CPTS-RI Revision 2; Rodriguez et al., 2001)	Self-report questionnaire	Erickson et al., 2008 [23]
	Impact of Events Scale (IES; Horowitz et al., 1979)	Self-report questionnaire	Kazak et al., 1999 [12]
	Impact of Events Scale-Revised (IES-R; Weiss & Marmar, 1997)	Self-report questionnaire	Barakat et al., 2006 [19]; Kazak, 2004a [10]; Kazak et al., 2004b [11]; Ozono et al., 2007 [30], 2010 [29]
	Post-Traumatic Stress Disorder Reaction Index (PTSD-RI; Pynoos et al., 1987)	Self-report questionnaire	Kazak et al., 1999 [12], 2004a [10], 2004b [11]
	Trauma Symptom Checklist for Children-Alternate version (TSCC-A; Briere, 1996)	Self-report questionnaire	Erickson et al., 2008 [23]
	University of California at Los Angeles Post-Traumatic Stress Disorder Reaction Index for DSM IV–Revision 1 (UCLA PTSD Reaction Index; Pynoos et al., 1998)	Self-report questionnaire	Michel et al., 2009 [28]
	University of California at Los Angeles Post-Traumatic Stress Disorder Reaction Index for DSM-IV, Adolescent Version (Steinberg et al., 2004)	Self-report questionnaire	Arpawong et al., 2013 [18]
Anxiety	Brief Symptom Inventory-18 (BSI-18; Derogatis, 2000)	Self-report questionnaire	Gianinazzi et al., 2013 [25]
	State-Trait Anxiety Inventory (STAI; Spielberger, 1983)	Self-report questionnaire	Bauld et al., 1998 [20]; Kazak et al., 1999 [12], 2004b [11]; Ozono et al., 2007 [30], 2010 [29]; Servitzoglou et al., 2008 [33]
	Behavioral Assessment System for Children (BASC; Reynolds and Kamphaus, 1992)	Self-, parent-, and teacher-report questionnaires	Carpentieri et al., 2003 [21]
	Multidimensional Anxiety Scale for Children-short form (MASC-10; March et al., 1997)	Self-report questionnaire	Yallop et al., 2013 [34]
	Revised Children's Manifest Anxiety Scale (RCMAS; Reynolds and Richmond, 1985)	Self-report questionnaire	Kazak et al., 1999 [12], 2004b [11]
Cancer-related worry	Semistructured interview about challenges to school re-entry	Semistructured interview	McLoone et al., 2011 [35]
	Social Anxiety Scale for Children-Revised (SASC-R; La Greca, 1992)	Self-report questionnaire	Pendley et al., 1997 [32]
	Cancer module of the Pediatric Quality of Life (PedsQL; Ewing et al., 2009)	Self-report questionnaire	Paxton et al., 2010 [31]
	Study-designed questionnaire to assess worry	Self-report questionnaire	Weigers et al., 1999 [37]
	Study-designed questionnaire to assess worry and sense of susceptibility	Self-report questionnaire	Cox et al., 2008 [22]
Cancer-related worry	Study-designed questionnaire to assess fear of relapse	Self-report questionnaire	Hill et al., 1998 [27]
	Perception of infertility risks	Self-report questionnaire	Gilleland Marchak et al., 2015 [26]

PTSD = post-traumatic stress disorder; PTSS = post-traumatic stress symptom.

^a Some studies utilized specific sections of more general measures to assess anxiety and related constructs.

comparable to that of their siblings. Survivors who scored above the distress threshold on the BSI reported more anxiety than psychotherapy patients ($d = .46$). Survivors scored higher on anxiety than any other BSI subscale. Bauld et al. [20] found that adolescent survivors reported higher state anxiety than healthy peers ($d = .61$). However, Servitzoglou et al. [33] did not find significant differences between survivors and healthy peers on state or trait anxiety. Adolescent survivors of brain tumors did not experience more anxiety than the sample on which the Behavioral Assessment System for Children was normed, as per self-report, parent, and teacher reports [21]. Pendley et al. [32] found that adolescent survivors with varying diagnoses reported similar levels of social anxiety to healthy peers. However, 7% of adolescents with a range of cancer diagnoses who had been off treatment for at least 2 years reported elevated anxiety on the Multidimensional Anxiety Scale for Children—short form [34]. Sixty-four percent of survivors experienced anxiety that served as a barrier to school re-entry according to parent report and self-report [35]. Survivors reportedly experienced anxiety about exams, missed academic material, social anxiety, and low self-confidence.

Yallop et al. [34] found no relation between anxiety and any demographic or illness characteristics. Survivors with a repressive coping style reported less anxiety than both the comparison sample and survivors with other coping styles ($d = .13$) [23]. In terms of social anxiety, Pendley et al. [32] found that generalized social anxiety and distress, distress due to new situations, and fear of negative evaluation were positively related to perceived illness impact (d 's = 1.15–1.62) and negatively related to perceived body image (d 's = .70–1.96). Survivors off treatment for at least 1 year reported greater distress due to new situations ($d = 1.17$) and fear of negative evaluation from peers ($d = 1.19$) than survivors who had been off treatment less than 1 year.

Cancer-specific worries. Weigers et al. [37] found that survivors worried less than healthy controls about headaches, dying, body image, being tired, and catching the cold or flu (d 's = .21–.45) but worried more about cancer risk for their children ($d = .56$). Adolescents expressed concerns about disclosing their illness to others because they were unsure how others would respond. They were particularly concerned about disclosing their illness to potential romantic partners because they worried that their cancer history would make them less attractive [36]. Although adolescent survivors report cancer-specific worries, Paxton et al. [31] found that adolescent survivors reported less cancer-related worry than young adult (YA) survivors ($d = -.24$).

Adolescent and YA survivors of acute lymphoblastic leukemia scored, on average, between 9 and 10 (depending on treatment regimen) on a 25-point fear of relapse scale [27]. For the overall sample, survivors who perceived their illness to be due to chance reported lower fear of relapse. In this study, adolescent survivors did not differ significantly from YAs with regard to fear of relapse. Weigers et al. [37] found that fear of relapse was predicted by age, such that fears began to increase around the age of 16 years and continued to rise until the age of 22 years (the upper age limit for the sample), and was positively predicted by worry about relapse upon treatment completion and a diagnosis of a central nervous system tumor, bone tumor, or lymphoma. In a mixed-methods study of developmental issues experienced by adolescent cancer survivors, Fritz and Williams ([36], p. 713) found that 26% of their sample were “extremely preoccupied with their health in a hypochondriacal manner,” justifying scrutiny of their bodies and

bodily functions as “preventative surveillance.” Survivors were particularly concerned with symptoms that were similar to those that preceded their cancer diagnoses.

Several studies assessed worry about fertility. Fritz and Williams [36] reported that although survivors responded affirmatively to questions about fertility concerns during interviews, they did not generate these concerns spontaneously. Over two third of the participants had not discussed fertility with their oncologists, with some indicating that they were delaying confirmation of possible infertility and others indicating that they “were meaning to ask, but always forgot (p. 714).” Weigers et al. [37] found that survivors were more worried about fertility than comparison peers ($d = .31$), and worry about fertility was positively related to age, gender, worrying about fertility upon treatment completion, and a diagnosis of lymphoma, Wilms’ tumor, or a broad category of “other” malignancies. Coding for the gender variable was not specified; therefore, it is unknown whether worry about fertility was higher for boys or girls. With respect to age, worry about fertility began to rise around the age of 16 years and continued to rise until the age of 22 years (the upper age limit for the sample).

Gilleland Marchak et al. [26] found that 71% of female survivors worried about infertility, although they worried less frequently than their parents ($d = .52$). In this sample, older survivors who were more aware of their risk of infertility reported more worries about infertility than younger survivors and survivors who were less aware of the risk for infertility. In a multivariate regression analysis, awareness of infertility risk, current age, and history of bone marrow transplant were significantly related to worry about infertility, but the history of uterine/ovarian problems was not.

Interventions. Three studies examined the effects of two interventions on anxiety and related constructs. Cox et al. [22] conducted secondary analyses examining the effect of a health promotion intervention [38] on breast self-examination in a sample of female adolescent survivors. Although this intervention did not specifically target worry or anxiety, participants in the intervention group reported a decrease in general fears about cancer at postintervention, despite an increase in perceptions of the seriousness of their vulnerability to late effects.

Kazak et al. [11,12] developed the Surviving Cancer Competently Intervention Program, a 1-day intervention program for adolescent survivors of pediatric cancer and their families to reduce distress and improve family functioning. The group-based intervention draws upon cognitive behavioral therapy and family therapy approaches. In the pilot study [12], survivors’ mean PTSS and anxiety scores, particularly physiological anxiety/worry and oversensitivity, decreased from preintervention to post-intervention evaluations. In a larger study [11], survivors who participated in the Surviving Cancer Competently Intervention Program showed significant reductions in arousal symptoms ($d = .51$). No other symptom reductions reached statistical significance. The authors noted that there was a higher intervention dropout rate among survivors who indicated higher PTSS at baseline.

Discussion

This review summarized anxiety-related findings across 24 published studies about psychosocial outcomes for adolescent survivors of pediatric cancer. Overall, PTSD and PTSS were the most commonly assessed forms of anxiety or related constructs.

PTSS were common among adolescent survivors, although diagnosable PTSD was less common [10,17,18,23,24,30]. Rates of PTSD were generally higher than those found among adolescents in the general population, but lower than those reported by adolescents who experienced other traumas [24,39]. Preliminary evidence found that PTSS were positively related to poor family functioning [17], parents' PTSS [10,11,30], late effects of treatment [24,30], disease recurrence [29], trait and generalized anxiety [11,30], coping style [23], perceived life threat [19], and treatment intensity [19]. Survivors who were older at diagnosis reported higher PTSS than peers diagnosed at a younger age [19], but time since diagnosis was not a significant predictor of PTSS [24,30].

Studies examining more generalized anxiety found mixed results, with some samples reporting higher levels of anxiety than comparison peers [20,25,34], and others reporting comparable levels of anxiety [21,32,33]. The reason for this discrepancy is unclear; however, it may be due to the various anxiety measures utilized or that none of the questionnaires were designed for specific use with adolescent cancer survivors. Survivors described anxiety that interfered with school re-entry [35]. Survivors who exhibited repressive coping style reported less anxiety than both survivors with other coping styles and healthy peers [23]. There was preliminary evidence that social anxiety was related to perceived illness impact and low body image and that survivors who had been off treatment for longer were at higher risk for social anxiety [32]. In addition, it appeared that anxiety may be more relevant for adolescent survivors than other forms of distress, such as depression [25].

Survivors reported less worry than healthy peers about headaches, dying, body image, being tired, and minor illnesses [37]. However, they had unique concerns, such as fear of relapse [27,37], worries about fertility [26,36,37], concerns about cancer risk for their children [37], and disclosing their illness to peers and potential romantic partners [36]. These illness-specific worries may not be detected by existing anxiety measures. Worries appeared to be related to several factors, including age [26,31,37], diagnosis [26,37], gender [37], risk awareness [26], and perceiving their illness as not being caused by chance [27].

Overall, research supports that adolescent survivors are at risk for anxiety-related distress. It is important to address adolescent survivors' anxiety, health worries, and PTSS/PTSD, not only for the purpose of improving mental health outcomes and quality of life but also because there is evidence that worry is positively related to maladaptive health behaviors (e.g., alcohol consumption and smoking) [40] and negatively related to adaptive health behaviors (e.g., exercise) [31].

Existing interventions have shown preliminary effectiveness in treating anxiety and related symptoms [11,12,22]. However, additional research is needed to thoroughly assess the full range of anxiety-related symptoms experienced by this population and develop treatments to effectively target these symptoms. These results are consistent with the findings of a recent systematic review by our group assessing psychosocial outcomes for cancer survivors diagnosed specifically during adolescence or young adulthood. The prior review found evidence that survivors may be at risk for anxiety, PTSD/PTSS, and worry, and called for targeted additional research [16].

Limitations

These findings present several limitations. First, with the exception of PTSD/PTSS, anxiety-related research with this

population has been limited. There is some evidence to suggest that adolescent survivors experience anxiety and worry that does not fall into the category of post-traumatic stress and that worry and anxiety may influence health behaviors. However, there is little research about these outcomes, and few studies have examined anxiety, PTSD/PTSS, or worry as a main outcome variable.

Only one study used a valid and reliable measure designed for use with children and adolescents with cancer [31], and that measure only assessed worry about treatment demands. It is unclear if generic psychosocial assessments are adequate to detect the specific concerns of this population, and the broad range of measures makes cross-sample comparisons difficult. In addition, research about anxiety in this population has been primarily cross-sectional and has generally included samples with broad ranges of time since treatment completion. Therefore, there is little information about how anxiety and its relationship with other psychosocial variables may change over time. The presented studies also do not typically account for other factors that could affect anxiety in this population, such as demographic variables and participants' baseline psychological functioning before their diagnosis.

Finally, four studies did not provide sufficient information to be considered high-quality studies [12,20,36,37]. However, there were no notable differences between these studies and those that were considered high quality.

Future directions

To address the range and severity of anxiety-related symptoms adolescent survivors experience, several future directions are recommended. In particular, it would be useful to develop and validate a developmentally appropriate cancer-specific anxiety measure for this population to determine if traditional anxiety measures are adequate to detect the specific concerns of this population. Cancer- and age-specific validated measures could provide more robust data on the prevalence and nature of these symptoms, allow assessment of the degree to which these symptoms interfere in functioning, and facilitate comparison across samples. Future research should investigate the effects of anxiety, cancer-related worry, and PTSS that do not meet criteria for diagnosis of an anxiety- or trauma-related disorder. Longitudinal assessments would facilitate better understanding of the natural trajectory of anxiety-related symptoms over time.

With regard to clinical implications, regular screening for anxiety and related symptoms should be implemented in survivorship clinics in accordance with the standards of psychosocial care for children with cancer and their families [41,42]. Screening is particularly important in this population, as one study [36] found that adolescents did not volunteer information regarding concerns about sensitive topics, such as fertility, unless directly asked. In addition, interventions should be developed to address areas that have the greatest need based upon descriptive studies, and it will be important to investigate the role of incorporating survivors' family members into the interventions. With respect to fertility concerns, the American Society of Clinical Oncology's recommendations for fertility preservation, which indicate that potential loss of fertility and available interventions be discussed with patients of reproductive age as soon as possible [43], could be adapted to incorporate discussions with pediatric survivors when they reach reproductive age.

There is growing evidence that adolescent survivors of pediatric cancer may be at risk for anxiety, cancer-specific worry, and PTSS/PTSD. However, there are still gaps in our understanding of these symptoms and related processes. Additional research is needed to better understand the unique needs of this population and develop appropriate interventions.

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Supplementary Data

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References

- [1] Key statistics for childhood cancer. Available at: <http://www.cancer.org/cancer/cancerinchildren/detailedguide/cancer-in-children-key-statistics>. Accessed September 22, 2016.
- [2] Key statistics for cancers in adolescents. Available at: <http://www.cancer.org/cancer/cancerinadolescents/detailedguide/cancer-in-adolescents-key-statistics>. Accessed September 22, 2016.
- [3] Howlander N, Noone AM, Krapcho M, et al. SEER cancer Statistics review, 1975–2013. Bethesda, MD: National Cancer Institute; 2016.
- [4] Cancer incidence and survival among children and adolescents: United States SEER Program 1975–1995. Bethesda, MD: National Cancer Institute, SEER Program; 1999.
- [5] Erikson EH. Identity and the life Cycle. New York, NY: International Universities Press; 1959.
- [6] Steinberg L, Morris AS. Adolescent development. *Annu Rev Psychol* 2001; 52:83–110.
- [7] Steinberg L. Cognitive and affective development in adolescence. *Trends Cogn Sci* 2005;9:69–74.
- [8] McDonnell G, Baily C, Schuler T, et al. Anxiety among adolescent survivors of pediatric cancer: A missing link in the survivorship literature. *Palliat Support Care* 2015;13:345–9.
- [9] Mitchell AJ, Ferguson DW, Gill J, et al. Depression and anxiety in long-term cancer survivors compared with spouses and healthy controls: A systematic review and meta-analysis. *Lancet Oncol* 2013;14:721–32.
- [10] Kazak AE. Posttraumatic stress disorder (PTSD) and posttraumatic stress symptoms (PTSS) in families of adolescent childhood cancer survivors. *J Pediatr Psychol* 2004;29:211–9.
- [11] Kazak AE, Alderfer MA, Streisand R, et al. Treatment of posttraumatic stress symptoms in adolescent survivors of childhood cancer and their families: A randomized clinical trial. *J Fam Psychol* 2004;18:493–504.
- [12] Kazak AE, Simms S, Barakat L, et al. Surviving cancer Competently intervention Program (SCCIP): A cognitive-behavioral and family therapy intervention for adolescent survivors of childhood cancer and their families. *Fam Process* 1999;38:176–91.
- [13] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th edition. Washington, DC: American Psychiatric Association; 2013.
- [14] Seitz DC, Besier T, Goldbeck L. Psychosocial interventions for adolescent cancer patients: A systematic review of the literature. *Psycho-oncology* 2009;18:683–90.
- [15] Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1998;52:377–84.
- [16] Barnett M, McDonnell G, DeRosa A, et al. Psychosocial outcomes and interventions among cancer survivors diagnosed during adolescence and young adulthood (AYA): A systematic review. *J Cancer Survivorship* 2016; 10:814–31.
- [17] Alderfer MA, Navsaria N, Kazak AE. Family functioning and posttraumatic stress disorder in adolescent survivors of childhood cancer. *J Fam Psychol* 2009;23:717–25.
- [18] Arpawong TE, Oland A, Milam JE, et al. Post-traumatic growth among an ethnically diverse sample of adolescent and young adult cancer survivors. *Psycho-oncology* 2013;22:2235–44.
- [19] Barakat LP, Alderfer MA, Kazak AE. Posttraumatic growth in adolescent survivors of cancer and their mothers and fathers. *J Pediatr Psychol* 2006; 31:413–9.
- [20] Bauld C, Anderson V, Arnold J. Psychosocial aspects of adolescent cancer survival. *J Paediatr Child Health* 1998;34:120–6.
- [21] Carpentieri SC, Meyer EA, Delaney BL, et al. Psychosocial and behavioral functioning among pediatric brain tumor survivors. *J Neuro-Oncology* 2003;63:279–87.
- [22] Cox CL, Montgomery M, Rai SN, et al. Supporting breast self-examination in female childhood cancer survivors: A secondary analysis of a behavioral intervention. *Oncol Nurs Forum* 2008;35:423–30.
- [23] Erickson SJ, Gerstle M, Montague EQ. Repressive adaptive style and self-reported psychological functioning in adolescent cancer survivors. *Child Psychiatry Hum Dev* 2008;39:247–60.
- [24] Gerhardt CA, Yopp JM, Leininger L, et al. Brief report: Post-traumatic stress during emerging adulthood in survivors of pediatric cancer. *J Pediatr Psychol* 2007;32:1018–23.
- [25] Gianinazzi ME, Rueegg CS, Wengenroth L, et al. Adolescent survivors of childhood cancer: Are they vulnerable for psychological distress? *Psycho-oncology* 2013;22:2051–8.
- [26] Gilleland Marchak J, Elchuri SV, Vangile K, et al. Perceptions of infertility risks among female pediatric cancer survivors following gonadotoxic therapy. *J Pediatr Hematol Oncol* 2015;37:368–72.
- [27] Hill JM, Kornblith AB, Jones D, et al. A comparative study of the long term psychosocial functioning of childhood acute lymphoblastic leukemia survivors treated by intrathecal methotrexate with or without cranial radiation. *Cancer* 1998;82:208–18.
- [28] Michel G, Taylor N, Absolom K, et al. Benefit finding in survivors of childhood cancer and their parents: Further empirical support for the Benefit Finding Scale for Children. *Child Care Health Dev* 2009;36:123–9.
- [29] Ozono S, Saeki T, Mantani T, et al. Psychological distress related to patterns of family functioning among Japanese childhood cancer survivors and their parents. *Psycho-oncology* 2010;19:545–52.
- [30] Ozono S, Saeki T, Mantani T, et al. Factors related to posttraumatic stress in adolescent survivors of childhood cancer and their parents. *Support Care Cancer* 2007;15:309–17.
- [31] Paxton RJ, Jones LW, Rosoff PM, et al. Associations between leisure-time physical activity and health-related quality of life among adolescent and adult survivors of childhood cancers. *Psycho-oncology* 2010;19:997–1003.
- [32] Pendley JS, Dahlquist LM, Dreyer Z. Body image and psychosocial adjustment in adolescent cancer survivors. *J Pediatr Psychol* 1997;22:29–43.
- [33] Servitzoglou M, Papadatou D, Tsiantis I, et al. Psychosocial functioning of young adolescent and adult survivors of childhood cancer. *Support Care Cancer* 2008;16:29–36.
- [34] Yallop K, McDowell H, Koziol-McLain J, et al. Self-reported psychosocial wellbeing of adolescent cancer survivors. *Eur J Oncol Nurs* 2013;17: 711–9.
- [35] McLoone JK, Wakefield CE, Butow P, et al. Returning to school after adolescent cancer: A qualitative examination of Australian survivors' and their families' perspectives. *J Adolesc Young Adult Oncol* 2011;1:87–94.
- [36] Fritz GK, Williams JR. Issues of adolescent development for survivors of childhood cancer. *J Am Acad Child Adolesc Psychiatry* 1988;27:712–5.
- [37] Weigers ME, Chester MA, Zebrack BJ, et al. Self-reported worries among long-term survivors of childhood cancer and their peers. *J Psychosocial Oncol* 1999;16:1–23.
- [38] Hudson MM, Tyc VL, Srivastava DK, et al. Multi-component behavioral intervention to promote health protective behaviors in childhood cancer survivors: The protect study. *Pediatr Blood Cancer* 2002;39:2–11.
- [39] Kilpatrick DG, Ruggiero KJ, Acierno R, et al. Violence and risk of PTSD, major depression, substance abuse/dependence, and comorbidity: Results from the National Survey of Adolescents. *J Consult Clin Psychol* 2003;71:692–700.
- [40] Cox CL, McLaughlin RA, Steen BD, et al. Predicting and modifying substance use in childhood cancer survivors: Application of a conceptual model. *Oncol Nurs Forum* 2006;33:51–60.
- [41] Lown EA, Phillips F, Schwartz LA, et al. Psychosocial follow-up in survivorship as a standard of care in pediatric oncology. *Pediatr Blood Cancer* 2015;62(Suppl 5):S514–84.
- [42] Wiener L, Kazak AE, Noll RB, et al. Standards for the psychosocial care of children with cancer and their families: An introduction to the special issue. *Pediatr Blood Cancer* 2015;62(Suppl 5):S419–24.
- [43] Lee SJ, Schover LR, Partridge AH, et al. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. *J Clin Oncol* 2006;24:2917–31.