


A review of psychosocial interventions targeting families of children with cancer

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Review Article

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Abstract

Objective. Psychosocial interventions in families of children with cancer are considered an effective way of empowering family members to tackle the complex hurdles they face. The ability of parents to develop adaptive coping strategies during the child’s treatment is not only important to their own mental and physical health, but also to their child’s well-being and long-term adjustment with the disease.

Methods. The aim of this review was to evaluate the existing literature for the period from 2009 to 2017 on psychosocial interventions targeting families of children with cancer. We searched the PubMed database using the following combination of keywords: “cancer AND children AND (intervention OR training) AND (mothers OR primary caregivers OR parents OR fathers OR siblings).”

Results. After careful evaluation of 995 papers, 17 full-text papers were found to match our criteria (12 randomized controlled trials and 5 quasi-experimental studies). The quality of the studies was assessed using the Delphi score questionnaire, and the score of the reviewed studies ranged from 3 to 5. The findings suggest that most interventions reduced distress and improved coping strategies among participants. Interventions, mainly cognitive behavioral therapy and problem-solving skills training targeting maternal distress, were associated with improved adjustment outcomes in mothers of children with cancer.

Significance of results. Psychosocial interventions are helpful, and efforts should be made to promote them in a larger scale. Protocols should be implemented to ensure that all parents benefit. Computer-assisted methods may provide additional benefit by improving cancer-related knowledge and cancer-related communication.

Introduction

Regardless of significant therapeutic advances, cancer remains a major cause of death among children, while its global age-standardized incidence rates are on the increase (Steliarova-Foucher et al., 2017). The 10-year overall survival rate has improved to 83%, but almost all survivors suffer from a chronic health condition that may be severe, disabling, life-threatening, or fatal by age 50 years (Bhakta et al., 2017).

Undoubtedly, one of the most life-changing and stressful experiences a parent may face is having their child diagnosed with cancer, a potentially lethal disease. The parent’s life becomes impacted by fear of death, treatment demands, side-effects, financial burden, and a negative effect on family’s relations (Klassen et al., 2007). Apart from the post-diagnosis acute stress, parents must quickly become acquainted to a significant amount of information related to cancer, while simultaneously they are required to modify their roles and routines to cater to the child’s imminent needs. This demanding situation could, in theory, have negative consequences on the parents’ relationship, but there are limitations in understanding the data. A population-based study from the USA reported no impact on divorce rates (Syse et al., 2010). However, a recent study also from the USA indicated a 10% divorce rate of parents post-diagnosis, but previous marriage quality was not assessed (Lau et al., 2014).

The study by Lau et al. also pointed out that during children’s active treatment, parents’ professional lives were seriously compromised, as 46% were at risk of loss of employment, 51% had decreased opportunities to work, and 68% had to reduce their work hours (Lau et al., 2014). Another study from Sweden indicated a statistically significant 21% reduction in mothers’ earnings and a statistically significant 10% reduction in fathers’ earnings for the year of diagnosis when compared with a control group of mothers and fathers, respectively (Lindahl Norberg et al., 2017).

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The literature on psychological health among parents reports worse physical and psychosocial quality of life (QoL), including elevated levels of psychological distress such as anxiety, depression, sleep disturbances, somatic symptoms, fear of disease recurrence, extensive worry and fatigue, and post-traumatic stress (PTS) symptoms compared with population norms (Klassen *et al.*, 2008; Ljungman *et al.*, 2014). Furthermore, studies have indicated that mothers of young cancer patients are more vulnerable to distress and its consequences (poorer QoL and psychological health) compared with mothers of healthy children (Eyigor *et al.*, 2011) or to the fathers (Stuber *et al.*, 1996; Quin, 2004). Parental burnout symptoms associated with emotional exhaustion as a result of prolonged and severe stress are largely underreported. Although the median time of presentation is unknown, a previous report has indicated that parental burnout may occur as early as 6 months post-diagnosis (Beheshtipour *et al.*, 2016). It is reasonable to assume that burnout may start to develop early in parents facing pediatric cancer and professionals need to be aware and to draw attention to these symptoms.

Similarly to parents, siblings of children with cancer may exhibit symptoms and negative emotions, as they also have to deal with changed daily routines in the family and decreased physical and emotional availability of their parents (Alderfer *et al.*, 2010). Evidence-based psychosocial standards for children with cancer, which includes psychosocial care for parents and siblings of children with cancer, have been published and substantiate the need for developing interventions targeting the entire family, particularly mothers of children diagnosed with cancer (Gerhardt *et al.*, 2015; Kearney *et al.*, 2015; Wiener *et al.*, 2015).

Familial support through psychosocial interventions plays a crucial role in maximizing welfare and treatment success for the child facing cancer treatment (Kearney *et al.*, 2015). There are several types of such interventions, including cognitive behavioral therapy (CBT), problem-solving skills training (PSST), and family therapy. All interventions aim at changing parent cognition or shifting behavior, or both, with the intention of improving child outcomes (Eccleston *et al.*, 2015). There is an urgent need for personalized approaches that will assist professionals to choose the most appropriate type of intervention that can significantly improve mental/physical health and facilitate behavior to enhance parent's adaptation to their child's cancer diagnosis. CBT includes a range of strategies aiming to modify social/environmental and behavioral factors that may exacerbate or cause symptoms, and by adjusting maladaptive thoughts, feelings, and behaviors reduces symptoms and prevents relapse (Eccleston *et al.*, 2015). PSST typically encompasses several sequential steps: problem definition, solution generation, decision-making, solution implementation, and verification, and aims to increase adaptive coping and behavioral competence and reduce daily stress (D'Zurilla and Nezu, 1999). Early research in using CBT and PSST indicated that they may both reduce depression and anxiety in parents of children with cancer (Sahler *et al.*, 2002; Ljungman *et al.*, 2018). Apart from those principal approaches, relevant studies also experiment with group-based therapeutic interventions that either treat the family as a whole or bring together participants from different families, giving them an opportunity to express their feelings and interact with parents with similar experiences (Stehl *et al.*, 2009; Shekarabi-Ahari *et al.*, 2012). Finally, some studies use technology to enhance the intervention procedures, such as personal digital assistant (PDA)- or web-based resources (Askins *et al.*, 2009; Sigurdardottir *et al.*, 2014).

Regardless of its type, scale, or target group, every intervention is focusing on the ability of parents to maintain their

psychological well-being during their child's treatment. Achieving that is not only a determining factor for their mental and physical health, but may also have an impact on their child's well-being and long-term adjustment to their condition. Despite the development of international guidelines aiming to assist parents to develop coping strategies, it is unclear which interventional programs are supported by evidence and what change may formulate. Thus, the primary purpose of the present paper is to systematically evaluate the evidence of the effectiveness of psychosocial interventions targeting families during their child's active cancer treatment and to make recommendations for the direction of future research.

Methods

Data collection

An initial analyses were carried out in 2014 and included studies published over the previous 5 years (2009–2014). However, for the purposes of this review, the analyses were updated to include studies published up to 2017. We identified relevant studies by searching for interventions published in MEDLINE from January 2009 until July 2017. Only articles in English were included. We used the following combination of keywords: “cancer AND children AND (intervention OR training) AND (mothers OR primary caregivers OR parents OR fathers OR siblings).” Eligible for inclusion was considered any type of psychosocial intervention that targeted families of newly diagnosed children with cancer undergoing therapy. The study aimed to analyze data regarding families with children in the range of 7–12 years of age although some studies may have also included a small number of older patients. We sought to analyze data from interventional studies involving parents/siblings immediately post-diagnosis and aiming to modify distress early in the course of the disease and treatment. More specifically, studies comprised CBT, PSST, relaxation techniques, spiritual care training, and various psychoeducational interventions. Furthermore, the support was provided by individual, family, and group counseling sessions, telephone or web-based approaches. In addition, we included studies that assessed the impact of the intervention on participants (either on psychosocial or educational level) and/or on the cancer patient. Studies not reporting post-intervention results, including parents with children at the terminal stage, comprising less than 15 subjects and qualitative studies were not included in the reviewed list. These studies were exempted as (i) studies nor reporting results would not allow us to reach conclusions on efficacy of the intervention, (ii) we wanted to differentiate the two scenarios between parents facing fear of cancer death immediately after diagnosis and during active therapy from parents facing cancer death of their children in the terminal stage of cancer diagnosis, (iii) we did not want to include studies of small-case series, and (iv) qualitative studies were excluded as they are usually reviews or narrative reports and as such were out of the scope of this analyses. In addition, a snowball technique was utilized in order to include any potential studies not revealed through this process. Issues of related journals, reference lists of included studies, and other relevant papers in the field were rummaged in an attempt to locate possible records. We carefully selected publications by titles and abstracts referring to our aim and then we gained full access to all the relevant studies through open access journals' sites or the university's library.

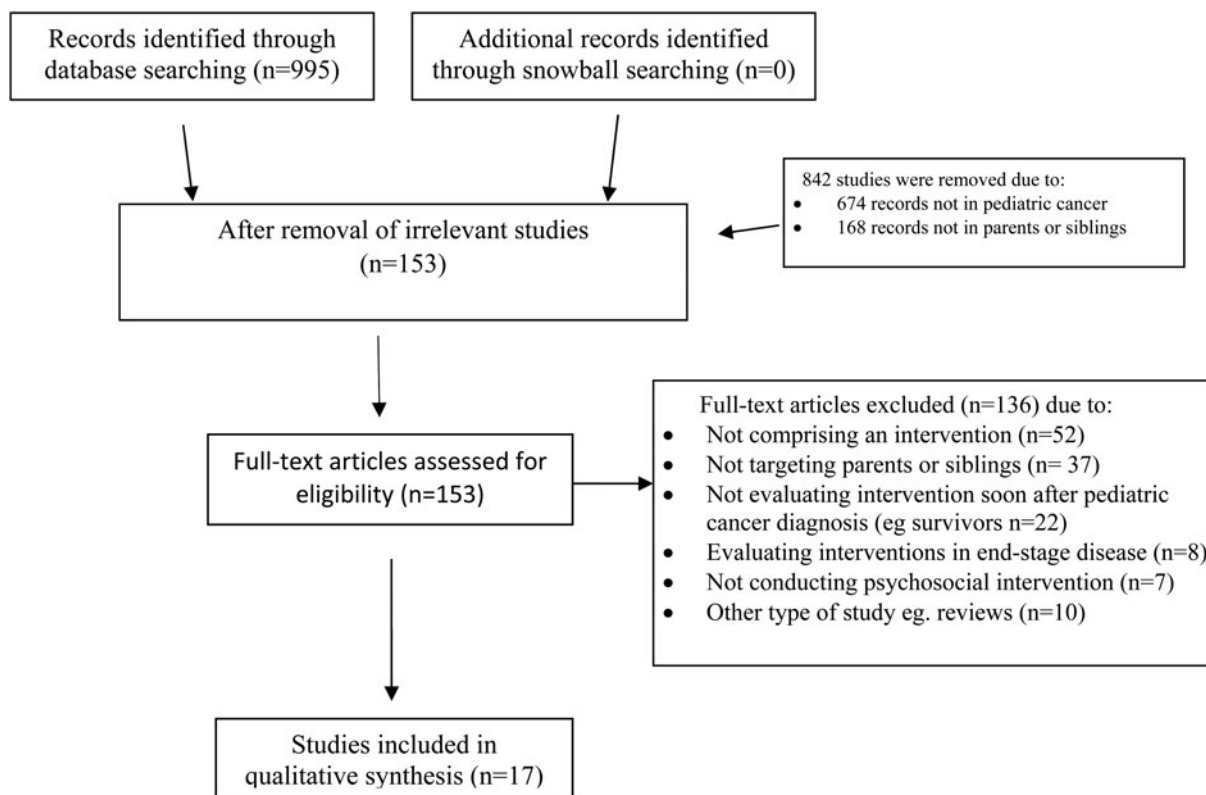


Fig. 1. Flow of information (PRISMA diagram).

Coding process

A.E.S. and A.A.K. participated in the literature search, study selection process, and extraction of studies. Disagreements between the authors were resolved through discussion or by the help of A.K. All authors participated in the appraisal of the extracted studies.

We extracted information pertaining to the following characteristics: “Research design and time points of measurements, type of intervention and duration, measures, study population (size and gender of participants), location and summary of main results.” The flow of information from record identification to inclusion followed the principles of the PRISMA statement (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) (Moher et al., 2009) and appears in Figure 1.

Quality control

In order to assess the research quality of the reviewed papers, we used the Delphi list questionnaire (Verhagen et al., 1998). The Delphi list examines quality defined as a set of parameters in the design and conduct of a study that reflects the validity of the outcome, related to “internal validity,” “external validity,” and “statistical considerations” (Verhagen et al., 1998). The Delphi list includes items to investigate blinding of investigator/patient and other important aspects of clinical trials such as randomization, eligibility criteria, and intention to treat analysis. With respect to the blinding, it entails three separate items: for care provider, patient, and outcome assessor. This allows the evaluation of trials in which participant or care-provider blinding is impossible. Details of Delphi items are shown in Table 1.

Results

Based on the predefined criteria of this systematic review, 995 articles were identified in PubMed from which 17 full-text articles were selected through careful screening. A PRISMA diagram is provided in Figure 1. The scoring of all studies according to the Delphi list is presented in detail (Table 1). The design and results of all studies, such as randomized control trials and quasi-experimental studies, included in this systematic review are described in detail (Table 2).

General characteristics of the study

Overall, 1,387 family members participated in the 17 interventional studies included in this systematic review and details are shown in Table 2.

Study participants

Of the 17 studies included in the present review, six included only mothers, one study comprised patient’s siblings, and 10 involved families and primary caregivers (Table 2). The mean age of parents (regardless of gender) was less than 40 years, the caregivers’ age ranged between 24 and 50 years, and the mean age of siblings was 8.5. The children’s ages in all studies (shown in Table 2) ranged from 7 to 14 years except in one study, where the age of five patients ranged from 11 to 18 years (Svavarsdottir and Sigurdardottir, 2013). All studies involved caregivers of pediatric patients with hematologic and solid malignancies except one study that included only leukemia (Asadi Noughabi et al., 2015). The timing of subjects’ enrollment was specified in most studies and ranged between 2 and 24 weeks post-diagnosis.

Table 1. Score breakdown on the Delphi List for each study by the alphabetical order

Authors (year)	Randomized	Treatment allocation concealed	Similar baseline characteristics	Eligibility criteria specified	Outcome assessor blinded	Treatment provider blinded	Patient blinded	Point estimates/ validity	Intention-to-treat analysis	Total
Askins et al. (2009)	1	0	0	1	0	0	0	1	1	4
Beheshtipour et al. (2016)	1	0	1	1	0	0	0	1	0	4
Borjalilu et al. (2016)	0	0	0	1	0	0	0	1	1	3
Cernvall et al. (2017)	1	0	1	1	0	0	0	1	1	5
Othman et al. (2010)	0	0	0	1	0	0	0	1	1	3
Marsland et al.(2013)	1	0	1	1	0	0	0	1	0	4
Mullins et al. (2012)	1	0	1	1	0	0	0	1	1	5
Asadi Noughabi et al. (2015)	1	0	1	1	0	0	0	1	0	4
Othman et al. (2010)	0	0	0	1	0	0	0	1	1	3
Prchal et al. (2012)	1	0	0	1	1	0	0	1	1	5
Safarabadi-Farahani et al. (2016)	1	0	1	1	0	0	0	1	0	4
Sahler et al. (2013)	1	0	1	1	0	0	0	1	1	5
Shekarabi-Ahari (2012)	1	0	0	1	0	0	0	1	0	3
Sigurdardottir et al. (2014)	0	0	0	1	0	0	0	1	1	3
Stehl et al. (2009)	1	0	1	1	0	0	0	1	1	5
Svavarsdottir and Sigurdardottir (2013)	0	0	1	1	0	0	0	1	1	4
Tsitsi et al. (2017)	1	0	1	1	0	0	0	1	1	5

Table 2. Description of selected studies carried out in newly diagnosed children with malignancy in pediatric tertiary referral centers worldwide

Study	Type of intervention and duration ^a (specialty of researcher)	Study population arm size (mean age or age range of children ^b)	Time of assessment ^c	Measures	Major findings
Randomized controlled studies					
Cognitive behavioral therapy					
(Stehl et al., 2009)	I: Surviving Cancer Competently Intervention Program – integration of CBT and family therapy approaches. Three weekly, 45-min sessions, and 3 booster sessions monthly (psychologists and nurses) C: Treatment as usual	76 families of children with cancer at one center in the USA I: 38 families (5 y) C: 38 families (7 y)	T1: baseline T2: 1 month post-intervention	- Demographic data and child’s medical information - Acute Stress Disorder Scale (ASDS) - Impact of Event Scale Revised (IES-R) - State Trait Anxiety Inventory (STAI) - Program evaluation	Data indicated no differences in STAI scores at T2 between groups for primary or secondary caregivers. No significant differences in all measures between the two groups. Positive feedback after the completion of the intervention.
(Mullins et al., 2012)	I: 12 weekly, 45-min individual sessions. Interdisciplinary intervention. (psychologists and nurses) C: Treatment as usual	52 mothers of children with cancer at one center in the USA I: 27 (2–16 y) C: 25 (2–17 y)	T1: baseline T2: 1 month post-intervention T3: 3 months post-intervention	- Demographic data and child’s medical information - Intensity of Treatment Rating (ITR) - Parent Perception of Uncertainty Scale (PPUS) - Symptom Checklist 90-Revised (SCL-90-R) - Impact of Events Scale-Revised (IES-R) - Care of my Child with Cancer Scale (CMCC) - Participant’s Satisfaction Survey	Pre-to-post slopes for SCL-90-R and IES-R demonstrated significant decreases in distress outcomes PTS symptoms, and perceived burden of care. Improved distress measures and adjustment post-intervention. Post-intervention slopes were not significant for any measure. Sessions were rated as highly beneficial.
(Prchal et al., 2012)	I: Two family sessions lasting 50 min focusing on: (1) medical information, (2) coping with stressful situations, and (3) information for parents and three sibling assessment sessions of 45 min at home (psychologists) C: Treatment as usual	29 siblings of children with cancer at two centers in Switzerland I: 14 (8.5 y; 6–14 y) C: 15 (11.5 y; 6–17y)	T1: baseline T2: 6 post-intervention T3: 7 months post-intervention	- Demographic data and child’s medical information - Medical knowledge scale - A list with people providing social support - KIDSCREEN-27 - UCLA PTSD Reaction Index (UCLA RI) - Spence Children’s Anxiety Scale (SCAS)	At T3, data showed increased psychological well-being, social support, and medical knowledge. No significant effects on PTS symptoms, anxiety, and siblings’ Health-Related QoL post-intervention.

(Continued)

Table 2. (Continued.)

Study	Type of intervention and duration ^a (specialty of researcher)	Study population arm size (mean age or age range of children ^b)	Time of assessment ^c	Measures	Major findings
(Shekarabi-Ahari et al., 2012)	I: Therapy on hope and depression entailing CBT techniques. Eight group sessions (psychologists) C: Control group	20 mothers whose child recently completed chemotherapy treatment for cancer at one center in Iran I: 10 (7.2 y) C: 10 (5.1 y)	T1: baseline T2: 6 post-intervention T3: 2 months post-intervention	- Demographic data and child's medical information - Beck Depression Inventory - Snyder Hope Scale	Results indicated that Hope therapy increased hope significantly and decreased depression also significantly.
(Fedele et al., 2013)	I: 12 weekly individual sessions, alternating 45-min sessions with 15–30 min phone call every other week. Interdisciplinary clinic (psychologists and nurses) C: Treatment as usual	52 mothers of children with cancer at one center in the USA (children's age in both groups: 8.2 y; 2–17 y) I: 27 C: 25	T1: baseline T2: 6 post-intervention T3: 3 months post-intervention	- Demographic data - Symptom Checklist 90-Revised (SCL-90-R) - Behavior Assessment System for Children 2nd edition—Parent Report Scale (BASC-2-PRS)	Maternal distress was associated with child adjustment disorder. Psychological intervention in mothers reduced child internalizing symptoms at the follow-up time point.
(Marsland et al., 2013)	I: Stress management and coping enhancement intervention named “Connections to Coping.” Six 30–60 min individual sessions every two to three weeks, six telephone contacts in-between the sessions and access to study's website (physicians and psychologists) C: Treatment as usual	45 primary caregivers of children with cancer at one center in the USA (42 mothers, 2 fathers, and 1 grandmother). I: 30 (13.2 y; 8–17 y) C: 15 (12.9 y; 7–17 y)	T1: baseline T2: 6 post-intervention	- Demographic data and child's medical information - Beck Depression Inventory (BDI) - State Trait Anxiety Inventory (STAI) - Perceived Stress Scale (PSS) - Impact of Event Scale (IES) - Client Satisfaction Questionnaire-8 (CSQ-8)	Caregivers who perceived lower social support demonstrated greater levels of distress at baseline and greater intervention-related decreases in depression, anxiety, and perceived stress. On the contrary, caregivers with greater perceived social support benefited less from the intervention. Distress, depression, and anxiety levels at T2 were not significantly impacted by the intervention.
(Cernvall et al., 2017)	I: Web-based guided self-help intervention for PTS symptoms. 10 weeks (psychologists) C: Wait list condition, served as the control group	58 parents of children with cancer at five centers in Sweden. I: 31 (6 y) C: 27 (4 y)	T1: baseline T2: 6 post-intervention	- Demographic data and child's medical information - PTSD Checklist Civilian Version (PCL-C) - Beck Depression Inventory-II (BDI-II) - Beck Anxiety Inventory (BAI)	Significant reduction in PTS, anxiety, and depressive symptoms in the intervention group. Minimal reduction in PTS and depressive symptoms in the control group. Effect on depression and anxiety was maintained in the (I) group at 12 months post-intervention.

Problem-solving skills training					
(Askins et al., 2009)	I: PSST combined with a PDA supplement (cognitive-behavioral problem-solving practice). Eight individual sessions (psychologists) C: PSST eight individual sessions	197 mothers of children with cancer at four centers in the USA (children's age in both groups: 8.1 y) I: 104 C: 93	T1: baseline T2: 6 post-intervention T3: 3 months post-intervention	<ul style="list-style-type: none"> - Demographic data and child's medical information - Social Problem-Solving Inventory Revised (SPSI-R) - Profile of Mood-States Scale (POMS) - Total Mood Disturbance Scale (TMD) - Beck Depression Inventory (BDI-II) - Impact of Event Scale -Revised (IES-R) 	In both groups, improved problem-solving skills, distress, depression, and PTS symptoms. Overall positive evaluation for the PDA approach by mothers.
(Sahler et al., 2013)	I: PSST applying cognitive-behavioral practice. Eight weekly 1-h individual sessions (psychologists) C: Non-directive support intervention (NDS). Eight weekly 1-h sessions	191 mothers of children with cancer at four centers in the USA I: 93 (8.2 y) C: 98 (9.4 y)	T1: baseline T2: 6 post-intervention T3: 3 months post-intervention	<ul style="list-style-type: none"> - Demographic data and child's medical information - Social Problem Solving Inventory Revised (SPSI-R) - Profile of Mood-States Scale (POMS) - Total Mood Disturbance Scale (TMD)-Beck Depression Inventory (BDI-II) - Impact of Event Scale -Revised (IES-R) 	Significant improvement of problem-solving skills from T1 to T2 was only observed for the PSST group. From T1 to T2, both groups showed significant but comparable improvements in mood disturbance, anxiety, depression, and PTS symptoms. At T3, (I) group maintained improvement in the measures of distress, depression, anxiety, and PTS, while the NDS showed no further gains.
Other methods					
(Beheshtipour et al., 2016)	I: Educational-spiritual intervention aiming to decrease the burnout of parents. Six weekly group sessions (psychologists and nurses) C: Control group	135 parents of children with cancer at one center in Iran (children's age not reported) I: 65 C: 70	T1: baseline T2: 6 post-intervention T3: 1 month post-intervention	<ul style="list-style-type: none"> - Demographic data - SMBQ (Shirom and Melamed Burnout Questionnaire) 	Post-intervention measurements at the follow-up time point showed maintained in time differences in burnout symptoms between the (I) and (C) groups ($p < 0.0001$)
(Safarabadi-Farahani et al., 2016)	I: Brief psychosocial intervention focusing on the improvement of parents' QoL. Five weekly individual sessions and five phone call (follow-up) (social worker) C: Treatment as usual	65 primary caregivers (age range: 24-47 y) of children with cancer (95% were mothers) at one center in Iran I: 32 (6.42 y) C: 33 (5.65 y)	T1: baseline T2: 6 post-intervention T3: 1 month post-intervention	<ul style="list-style-type: none"> - Demographic data and child's medical information - Caregiver Quality of life Index-Cancer - Persian Version (CQOLC-P) 	Significant improvement over time on QoL ($p < 0.001$) and on subscale outcomes of mental, emotional burden, disruption, and positive adaptation was recorded for the intervention group. Improved disease and treatment information post-intervention.

(Continued)

Table 2. (Continued.)

Study	Type of intervention and duration ^a (specialty of researcher)	Study population arm size (mean age or age range of children ^b)	Time of assessment ^c	Measures	Major findings
(Tsitsi et al., 2017)	I: Relaxation intervention with PMR and GI techniques in individualized and supervised sessions. 25 min/week for three weeks (nurses) C: Psychological intervention without PMR/GI	54 parents of children with cancer at two centers in Cyprus and Greece I: 29 (8.11 y) C: 25 (10.2 y)	T1: baseline T2: ^c post-intervention	<ul style="list-style-type: none"> - Physiological measures for anxiety (blood pressure, heart rate, and skin temperature) - Demographic data and child's medical information - Sources of participant's support - Hamilton's Anxiety Scale (HAM-A) - Profile of Mood-States Brief Scale (POMS Brief) 	In the intervention arm, it is noted: A statistically significant difference in the mean score of stress symptoms. Decrease of anxious mood, tension, breathing, and gastrointestinal symptoms. Reduction in systolic blood pressure, heart rate, and body temperature right after the intervention.
Quasi-experimental studies					
(Othman et al., 2010)	I: Psychoeducational sessions on cancer information, adjustment to diagnosis, and effective coping strategies. Four group sessions (physicians and psychologists) C: control group: wait list	79 parents of children with cancer at one center in Malaysia (children's age in both groups 8.03 y) I: 41 C: 38	T1: baseline T2: ^c post-intervention	<ul style="list-style-type: none"> - Knowledge acquisition questionnaire - Perceived Acquired Knowledge (KA-p) - Anxiety Test (subscale of STAI) - Strain Questionnaires (SQ) - Parents' Activities with Children (PA) - Strength and Difficulties Questionnaires (SDQ) 	Intervention showed no significant effects at reducing participants' anxiety and stress symptoms. No other differences appeared either in their symptoms of stress or in their report on children's psychological problems from T1 to T2. Data revealed increased cancer-related knowledge post-intervention ($p=0.01$).
(Svavarsdottir & Sigurdardottir, 2013)	I: Brief FAM-CHI focusing on cognitive, emotional, and/or behavioral domains of family functioning and its strengths. Two or three sessions (nurses) (one group)	19 caregivers (10 primary and 9 partner) of children with cancer at one center in Iceland (children's age range: 1–16 y)	T1: baseline T2: ^c post-intervention	<ul style="list-style-type: none"> - Demographic data and child's medical information - Iceland Family Perceived Support Questionnaire (ICE-FPSQ) - Iceland Expressive Family Functioning Questionnaire (ICE-EFFQ) 	Higher perceived family support, higher expressive family functioning, and higher emotional communication after the intervention were succeeded for the primary caregivers, whereas these were not observed in partner caregivers.

<p>Sigurdardottir et al. (2014, Iceland)</p>	<p>I: WEB-ESI on cancer that aimed to provide families with valuable information in three sections: (i) cancer, (ii) family, (iii) living with cancer (physicians, psychologists, nurses, and social worker) (one group)</p>	<p>38 families (15 mothers, 12 fathers, and 11 children) of children with cancer at one center in Iceland (children's age range: 1–18 y)</p>	<p>T1: baseline T2: ^cpost-intervention</p>	<ul style="list-style-type: none"> - Demographic data and child's medical information - 10-item scale for the favorability of the website - PedsQL 3.0 cancer module 	<p>Mothers rated most favorable the website than fathers but not by a high margin, whereas children's favorability scores were significantly lower than both the mother's and father's score. Enhanced cancer knowledge post-intervention.</p>
<p>(Asadi Noughabi et al., 2015)</p>	<p>I: Care Program Training for cancer through discussion. Eight group sessions (nurses) C: Control group</p>	<p>41 parents of children with leukemia at one center in Iran (children's age not reported) I: 21 C: 20</p>	<p>T1: baseline T2: 2 months post-intervention</p>	<ul style="list-style-type: none"> - Demographic data and child's medical information - SF-36 for parents' QoL 	<p>Significant differences occurred from pretest to post-test in the intervention group in six areas of QoL including bodily pain, general health, emotional health, role limitations due to emotional problems, social functioning, and vitality.</p>
<p>(Borjalilu et al., 2016)</p>	<p>I: Spiritual care training package targeting parents' mental health. Seven group sessions (physicians and psychologists) C: Control group: waiting list</p>	<p>42 mothers (21–52 y) of children with cancer at one center in Iran (children's age range: 7–12 y) I: 21 C: 21</p>	<p>T1: baseline T2:^cpost-intervention T3: 3 months post-intervention</p>	<ul style="list-style-type: none"> - Spirituality and Spiritual Care Rating Scale (SSCRS) - DASS-21 	<p>In the intervention group, anxiety, depression, and stress scores were significantly reduced. Differences between groups in anxiety scores remained in the follow-up period. Religiosity scores increased in the intervention group.</p>

Abbreviations: I: interventional arm; C: control arm; CBT: cognitive behavioral therapy; FAM-CHI: Family Therapeutic Conversation; GI: guided imagery; PSST: problem solving skills training; PMR: progressive muscle relaxation; m: months; PTS: post-traumatic stress; QoL: quality of life; WEB-ESI: web-based educational and support intervention; y: years old.

^aThe exact timing and duration of intervention was not always reported.

^bIn some studies, data on age, standard deviation (SD), or range were partially reported or unreported as indicated.

^cThe exact time of assessment post-intervention was not reported.

Intervention, tools, and measurements

The duration of intervention sessions ranged from 25 to 120 min, and these were repeated every 2–12 weeks. An exception was the case of web-based educational and support intervention (ESI), where the site resources were available to participants for 16 weeks. Different psychological variables of parents and siblings of children with cancer, such as distress, related psychological traits, and coping strategies were assessed in the selected studies by a variety of tools (Table 2). These included Beck depression inventory (five studies), Impact of Event Scale-Revised (IES-R, four studies), State Trait Anxiety Inventory (two studies) Total Mood Disturbance Scale (two studies), Profile of Mood-States Scale (two studies), and others. In eight studies (47%), two measurements were obtained; a baseline (T1) prior to the intervention and a post-interventional (T2); most commonly at 1 month. In the remaining nine studies, a third measurement (T3) took place at a later date, most commonly at 3 months post-intervention (range 1–7 months) (Table 2).

Study location and investigators

In 11 (65%) studies, participants were recruited from a single center, whereas six studies were multicenter (details shown in Table 2). The country location of the sites varied, including six in the USA, five in Iran, two in Iceland, one in Switzerland, one in Sweden, one in Greece/Cyprus, and one in Malaysia.

The researchers delivering the intervention were nurses (three studies), psychologists (five studies), both psychologists and nurses (four studies), social worker (one study), psychologist and physician (three studies), and multidisciplinary team (one study) (details shown in Table 2).

Delphi score

The studies' Delphi score ranged between 3 and 5 and is described criterion by criterion in Table 1.

Types of intervention and outcomes

Randomized controlled trials

Of the 12 randomized controlled trials (RCTs) included in this systematic review, seven employed CBT, two PSST, one educational–spiritual group sessions, one brief psychosocial intervention (including five weekly individual counselling sessions and five phone calls), and one relaxation intervention with progressive muscle relaxation (PMR) and guided imagery (GI) (Table 2).

Cognitive behavioral therapy. All seven CBT interventions were carried out by at least one psychologist as a primary investigator and comprised at least five 45 min sessions. Measurements assessing outcomes at three time points (baseline, post-intervention, and 2–3 months post-intervention) were carried out in four out of seven studies.

Distress. Distress levels were assessed in three CBT studies. In two studies, distress levels were measured in mothers before and after 12 weekly individual sessions and found to be significantly reduced and associated with improved adjustment outcomes (Mullins et al., 2012; Fedele et al., 2013). A third study treating caregivers (93% mothers, 4.5% fathers, and 2.5% grandmothers) with six individual sessions of CBT, followed by six telephone contacts and access to a dedicated web site, showed benefit in decreasing psychosocial distress, particularly in those with lower perceived social support at the time of their child's diagnosis (Marsland et al., 2013).

Depression. Depression was assessed in three CBT studies. The first study applied 10 web-guided self-help sessions (Cernvall et al., 2017) and the second study eight group therapies on hope and depression (Shekarabi-Ahari et al., 2012). Both studies reported a significant decrease of depressive symptoms in the intervention group that was maintained also in the long-term follow-up (T3) (Shekarabi-Ahari et al., 2012; Cernvall et al., 2017). The third study, employing six individual CBT sessions, six telephone contacts, and access to a dedicated website did not result in significant reduction of maternal depressive symptoms (Marsland et al., 2013).

Anxiety. Three CBT studies assessed anxiety. The first was a web-based guided self-help intervention lasting for 10 weeks, and the effect was retained at the follow-up at 12 months (Cernvall et al., 2017). The second was a stress management program involving six individual sessions, six telephone contacts, and access to study's website that resulted in reduction of anxiety (Marsland et al., 2013). The third study investigating CBT in two and three family sessions did not diminish anxiety levels (Prchal et al., 2012).

Post-traumatic stress (PTS). Four studies investigated the effect of CBT on PTS. Two studies reported a positive effect induced by the intervention, one with 10 web-based and one with 12 individual sessions (Mullins et al., 2012; Cernvall et al., 2017). Two studies employing, however, an inferior number of CBT family sessions (two and three sessions) showed no benefit and no differences in PTS between siblings or parents in the investigational and control groups (Stehl et al., 2009; Prchal et al., 2012).

Other outcomes. Children adjustment and its relation to maternal distress were examined in the context of one study applying 12 weekly individual CBT sessions in mothers of children with cancer (Fedele et al., 2013). The study showed that post-intervention, there was a significant reduction of maternal distress and this in turn associated with improved downstream effects on child internalizing symptoms (Fedele et al., 2013).

One study aimed to educate families of children with cancer about cancer treatment and was reported to increase knowledge (Othman et al., 2010; Prchal et al., 2012; Sigurdardottir et al., 2014; Safarabadi-Farahani et al., 2016). Finally, one study employing two family sessions focusing on medical information, coping with stressful situations through a cognitive behavioral approach, resulted in a better medical knowledge score in siblings at 7 months post-intervention, but did not result in the improvement of PTS symptoms, anxiety, or HRQoL (Prchal et al., 2012).

Problem-solving skills training. Both PSST interventions included in this analysis were carried out by a psychologist as a primary investigator and comprised eight 60 min sessions. Measurements assessing outcomes at three time points (baseline, post-intervention, and 3 months post-intervention) carried out in both studies indicated significant improvement of problem-solving skills of mothers and the decrease of negative affectivity following intervention.

Distress, Depression, Anxiety and PTS symptoms. The first study indicated that PSST significantly decreased maternal distress and, in a mediational model, that an increase in problem-solving skills accounted for 27%, 20%, and 26% of the decrease in anxiety, depression, and PTS symptoms, respectively (Sahler et al., 2013). The effect was maintained also in the follow-up measurement (T3).

The second study indicated that PSST with or without a PDA supplement improved problem-solving skills, distress, depression, and PTS symptoms (Askins et al., 2009)

Other methods. Apart from CBT and PSST, other methods have been investigated in the context of RCT to improve the mood of parents of children with cancer. These included a spiritual intervention to decrease burnout (Beheshtipour et al., 2016), a brief psychosocial intervention to improve parents' QoL (Safarabadi-Farahani et al., 2016), and relaxation techniques to reduce anxiety and improve the mood (Tsitsi et al., 2017). With the exception of one study reporting on a significant decrease of parental anxiety following relaxation techniques (Tsitsi et al., 2017), specific results on distress, depression, anxiety, and PTS symptoms were not recorded in these studies.

The first study involved six weekly group sessions concerning educational and spiritual intervention and was intermediated by a psychologist and a nurse (Beheshtipour et al., 2016). The study investigated parents' "burnout" at 6 months after pediatric cancer diagnosis and found decreased burnout symptoms in parents participating in the investigational arm (Beheshtipour et al., 2016). The second study that investigated five individual sessions targeting psychosocial domains such as mental/emotional burden, lifestyle disruption, and positive adaptation, facilitated by a social worker, resulted in increased cancer-related knowledge and improved the QoL (Safarabadi-Farahani et al., 2016). The third RCT employing PMR and GI, performed by a nurse, reported a significant decrease in anxiety and the improvement of vital sign measurements, such as blood pressure and heart rate post-intervention (Tsitsi et al., 2017).

Quasi-experimental studies

Of the five quasi-experimental (QE) studies, three employed group sessions (one psychoeducational, one cancer care program training, and one spiritual care training), one family therapy sessions, and one web-based ESI sessions. The interventions were carried out by nurses (two studies), psychologists and physicians (two studies), and a group of physicians, psychologists, social worker, and nurses (one study) (Table 2).

Distress, depression, and PTS symptoms

Distress levels, depression, and anxiety were found to be reduced only in one QE study, examining the effectiveness of spiritual care training in seven group sessions, an effect that was retained at the follow-up measurement at 3 months (Borjalilu et al., 2016). Another QE study employed four psychoeducational group sessions on cancer information, adjustment to diagnosis and effective coping strategies, showed no significant effects at reducing parents' anxiety and stress symptoms (Othman et al., 2010).

Other outcomes

Improvement in the QoL was shown in one QE study examining the effect of eight group sessions of cancer care program training on improving the parents' QoL (Asadi Noughabi et al., 2015). Two studies, aiming to educate families of children with cancer about cancer treatment, resulted in increased cancer-related knowledge after the cancer educational intervention (Othman et al., 2010; Sigurdardottir et al., 2014). In addition, the later study evaluated an evidence-based cancer web site that was found to associate with a marginally significant improvement of mothers' communication with health professionals (Sigurdardottir et al., 2014). A fourth study investigated two to three sessions of family therapy focusing on cognitive, emotional, and/or behavioral domains of family functioning and its strengths and the perception of family support by primary and partner caregivers, and found to be

significantly higher post-intervention (Svavarsdottir and Sigurdardottir, 2013). In the later study, significant expressive family functioning was also observed on the overall scale, as well as on the emotional communication subscale.

Patient satisfaction and use of computer- and web-based material

The overall mean acceptance rate for participation in these studies was 64% (range 26–94%), while most participants evaluated the interventions positively. Three studies, two CBT and one QE, included three different but specific scales to evaluate parental satisfaction with the intervention that was rated favorably (Stehl et al., 2009; Mullins et al., 2012; Sigurdardottir et al., 2014).

Two more studies assessed satisfaction by the inclusion of technology-based tools (Table 2). The first study was a multi-institutional RCT examining PSST with or without of a handheld PDA-based supplement for mothers (Askins et al., 2009). Although results were similar between the two interventions, mothers were more willing to recommend PSST without the concomitant use of PDA. In addition, several technical difficulties were encountered that led to periodic loss of data and rendered the data uninterpretable by the investigators (Askins et al., 2009). A second QE study investigated whether an evidence-based web ESI (WEB-ESI) for families of children with cancer could have any impact on the cancer communication aspect (Sigurdardottir et al., 2014). The assessment of the WEB-ESI indicated a very high favorability score, but the increase in mothers' evaluation of cancer communication was not statistically significant.

Discussion

Parents are devastated by a child's cancer diagnosis and may suffer from marked distress, but for those resilient and well-functioning will gradually adjust and achieve psychological growth and good family functioning (Kearney et al., 2015). However, for parents with pre-existing mental health problems or with emotional issues, pediatric cancer diagnosis may be overwhelming leading to high distress levels and disruption of the ill child's cancer treatment and family support system for the ill child (Kazak and Noll, 2015; Kearney et al., 2015). Parents of children are also at risk for poor adjustment outcomes, frequently even more so than their diagnosed child (Pai et al., 2007). Several studies have indicated that parent and child adjustment outcomes are closely interrelated via a transactional process between child and parental variables such as coping, illness, and sociocultural parameters in chronic diseases (Thompson et al., 1993). Consistent with growing literature on the interconnectedness of parent and child mental health, family-centered psychosocial care has been long considered essential in pediatric oncology (Kazak et al., 2006). As intervening with parents has the potential to help children, interventions should include families in an essential and integral manner (Mullins et al., 2016).

According to the National Comprehensive Cancer Network (NCCN) guidelines, and pediatric psychosocial oncology standards of care, psychosocial aspects are of outmost importance and should be integrated into routine cancer care in order to provide the QoL in cancer patients and their families (Gerhardt et al., 2015; Kearney et al., 2015; Wiener et al., 2015; National Comprehensive Cancer Network, 2018). Cognitive psychotherapy, supportive psychotherapy, psychoeducational programs, and family therapy are considered standard of care, as they have been

shown to improve the psychological adjustment of parents of children with cancer; a process defined as ‘post-traumatic growth’ (Wilson *et al.*, 2016). Despite standardization in disease assessments and curative interventions for childhood cancer, psychosocial interventions remain diverse and disparate, hampered by medical care priorities, financial costs, and inadequate healthcare staffing (Selove *et al.*, 2012; Weaver *et al.*, 2016).

Procedures

In this systematic review, we identified 17 studies that explored the effectiveness of short interventions targeting families, mostly mothers, of pediatric cancer patients. The methodological quality of most of the trials that we reviewed was not optimal and their Delphi score ranged from 3 to 5. Grade is a recently introduced more rigorous method in the context of reviews and Cochrane metaanalysis (Ryan and Hill, 2016). At the time of planning this analyses, the Grade was not yet introduced and we chose to apply the Delphi method. None of the studies reviewed used any form of blinding, neither to those conducting the intervention nor to its participants. Blinding of care providers and patients has inherent difficulties in its application in randomized trials assessing non-pharmacological treatments and as a previous study has shown that it may be difficult or impossible to achieve in 78–82% of studies (Boutron *et al.*, 2004). The difficulties in blinding patients and care providers are linked mostly to the difficulties of performing an indistinguishable control intervention (e.g. CBT or PSST) in this setting.

Outcomes

Distress

Distress levels were assessed in four studies (23.5%), including three CBT (Mullins *et al.*, 2012; Fedele *et al.*, 2013; Marsland *et al.*, 2013) and one PSST study (Sahler *et al.*, 2013). A common element of these studies was that were mediated by psychologists, entailed six–eight individual sessions, and distress reduction was sustained in the follow-up period usually at 3 months post-intervention. The results of these RCTs indicate that both CBT and PSST interventions targeting distress may impact parental distress levels significantly and facilitate a faster and easier adjustment process. A typical pattern of adjustment is one of elevations in distress around the time of diagnosis, with decreases over time to normal functioning, 3–6 months post-diagnosis (Pai *et al.*, 2007). Targeting parental distress may have direct positive family impact on several components and is therefore of utmost importance to recognize it early in the course of the disease. For example, a previous study that identified significant associations between parent and child distress indicated that parental distress may associate with poor communication with the child leading to negative adjustment to the disease and later to survivorship (Robinson *et al.*, 2007).

Depression

Depression was assessed in six studies (35%) including three CBT, two PSST, and one QE (Table 2). In all cases, the intervention was mediated by psychologists and resulted in the improvement of depression maintained at 3 months post-intervention. A recent study indicated that maternal primary control coping and depressive symptoms predict mothers’ subsequent harsh and withdrawn communication about cancer (Rodriguez *et al.*, 2016). Both theoretical models and empirical research have pointed out to an

association between higher levels of maternal depressive symptoms and more negative mother–child communication and child adjustment leading to both over reactive/harsh and lax/withdrawn styles of interaction with the child (Lim *et al.*, 2008). A recent study indicated that promoting primary control coping skills and intervening to reduce or prevent depressive symptoms following a child’s diagnosis may help mothers communicate more effectively with their children and facilitate adjustment to the disease for children (Rodriguez *et al.*, 2016).

Anxiety

Anxiety was assessed by eight studies (47%), and four CBT, one PSST, two QE, one other methods, mostly facilitated by psychologists (Table 2). Of these studies, only 50% reported the improvement of anxiety, resulting negative mostly those carried out in short time (30 min) or for less than three sessions. Not surprising a recent study indicated that negative self-blame/affect and active coping emerged as significant predictors, indicating that using these strategies was positively related to state anxiety symptoms (Greening and Stoppelbein, 2007). A recent meta-analysis of articles describing the prevalence of anxiety in parents of pediatric cancer indicated a highly heterogeneous prevalence, ranging from 5% to 65% for anxiety (pooled prevalence 21% [95% CI, 13–35%]) (van Warmerdam *et al.*, 2019). In addition to the high prevalence, supporting parents for anxiety may be clinically indicated since research shows that although most parents’ distress steadily declines after the initial diagnosis (Dolgin *et al.*, 2007), some continues to experience heightened anxiety during treatment and even years following (Norberg and Boman, 2008). Therefore, it could be useful to screen all caregivers on a regular basis during the entire course of treatment and follow-up to identify parents with anxiety for supportive interventions.

Post-traumatic stress

PTS was assessed in six studies (35%), and all of these but one study indicated a positive outcome on PTS associated with the intervention. In a recent metaanalysis, the prevalence of PTS was 4–75% (pooled prevalence 26% [95% CI, 22–32%]) (van Warmerdam *et al.*, 2019). This large variability of PTS prevalence among studies was attributed to significant methodological differences in measurement tools and defined thresholds (van Warmerdam *et al.*, 2019). PTS symptoms have received significant attention as studies have indicated parents have more PTS than ill children themselves — and almost all parents report at least one PTS symptom in the first two to four weeks post-diagnosis (Patino-Fernandez *et al.*, 2008). In the same study, 51% of mothers and 40% of fathers met criteria for acute stress disorder in the first two weeks post-diagnosis (Patino-Fernandez *et al.*, 2008). In the same study, anxiety was identified as a strong predictor for the development of acute stress disorder. Beyond the first month, studies have varied with some groups finding PTS rates similar to those of the general population of adults (without children with cancer) (Phipps *et al.*, 2014). It is therefore important to be able to identify clinical or subclinical levels of PTS and to develop more effective interventions for parents to reduce PTS symptoms and improve the QoL.

Type of interventions

The majority of studies in this systematic review were either purely based on CBT or were focused on psychoeducation with PSST. It is, thus, worth discussing the findings of these two

approaches. Although no RCT studies have been carried out to identify the most efficient intervention to improve parental depression and anxiety, this analysis indicated that 10–12 sessions of CBT or eight sessions of PSST resulted in significant improvements of these outcomes. Interestingly, most of these studies scored 5 in the Delphi system as they gained one point for each of the following criteria including randomization, similar baseline characteristic, point of estimates/validity, and intent-to-treat analysis. A recent Cochrane metaanalysis on psychological interventions for parents of children and adolescents with chronic illness such as cancer indicated that CBT and PSST may both improve parenting behavior, but only PSST may improve parental mental health (Law et al., 2019). Nevertheless, several CBT therapies for depression, although not explicitly based on problem-solving principles, are considered to actually increase individual's problem-solving skills. For example, providing social skills training as part of a CBT program to depressed individuals may also serve to increase their problem-solving skills by providing alternative methods of interacting with others. Also, cognitive techniques may serve to help depressed individuals better define and formulate problem situations, as well as to decrease the cognitive distortions that might inhibit effective problem-solving attempts (Nezu, 1987). Conclusively, CBT could support the development of stronger problem-solving skills and improve problem formulation among parents who experience significant levels of negative affectivity.

Furthermore, most studies were conducted on parents of children newly diagnosed with cancer and the rest targeted parents of children with cancer in general. An early study in the field indicated that parental distress tends to decrease from diagnosis to post-treatment period and seems to converge to baseline levels (Dolgin et al., 2007). Even though such findings suggest that parental distress is likely to return to baseline levels, other studies have reported that parents struggle with significant psychological difficulties in the long term (Ljungman et al., 2014). This supports the finding of an early study, indicating that maternal adjustment at the time of diagnosis and up to 2 years post-diagnosis was a predictor of later coping adequacy (Kupst et al., 1995). Thus, targeting parents near the time of their child's diagnosis is a promising approach, as it may address burden and negative affectivity at its peak and prevent long-term consequences. Similar conclusions were drawn by a more recent study that, by introducing parents to active focus on cognitions related to their child's illness shortly after diagnosis, increased positive feelings 5 years post-intervention (Maurice-Stam et al., 2008). Another important detail is that relaxation techniques such as PMR and GI received wide acceptance by parents during this completely new stressful, overwhelming, and burdensome situation (Tsitsi et al., 2017). Due to the simplicity and low cost of these relaxation techniques, they can be further tested alone or in conjunction to psychologic therapies, including CBT and PSST, to reduce stress and anxiety.

Indicators of parental need for intervention

One important finding of this review is that interventions targeting maternal adjustment were directly related to reduction of maternal distress, and more importantly, it was associated with improved child psychological adjustment. Furthermore, the above suggests that a systematic way of assessing which parents would profit more by participating in an intervention would be valuable. To the best of our knowledge, such indicators have not been adequately addressed or discussed by the recent

literature. One study indicated that perceived social support assessed within eight weeks of cancer diagnosis is inversely related to caregiver's distress measurements 4–5 months later (Marsland et al., 2013). More specifically, primary caregivers with low perceived social support, receiving the intervention, were more likely to experience a significant decrease in symptoms of depression, anxiety, and perceived stress at 4–5 months compared with those with high social support (Marsland et al., 2013).

Acceptability and satisfaction

Acceptability and satisfaction of the interventions by parents of children with cancer demonstrate that it is necessary to find ways to adapt interventions to the needs and schedules of the parents. To this end, one important parameter is the intervention's frequency and duration. In this review, duration varied from 3 to 12 weekly sessions lasting from 30 to 120 min. Brief interventions maybe easier to adapt to heavy parental schedules, and this is considered a critical parameter of participation by parents (Safarabadi-Farahani et al., 2016). The Brief Psychosocial Intervention including five weekly sessions (60–90 min) and five follow-up phone calls (30–45 min) provided evidence that short-term but rigorous interventions may be able to have a positive impact on multiple subscales of the QoL.

This review also showed significant effects on different psychosocial aspects of the family, regardless of the member receiving the intervention. In addition to many studies targeting mothers, one study intervening on patient's siblings provided evidence that improving the siblings' medical knowledge and understanding of the disease had a positive and persistent impact on their psychological well-being (Prchal et al., 2012). Only one study targeting siblings was identified in our analysis. As previous studies carried out in the context of other chronic diseases have indicated, interventions for siblings right after diagnosis is also not practical for most families — many of whom have to travel great distances for their child to receive treatment (Gettings et al., 2015). It has been proposed that interventions targeting one member per family can be replicated to involve the entire family, as they have proved to be effective on an individual level (Meyler et al., 2010).

Technology-assisted interventions

An important information deriving from this review is that an increasing number of studies have recently attempted to mix standard healthcare professional-driven intervention with either web resources or computer-assisted technology. One study, applying PDA-assisted interventions, examined whether participants were familiar with the use of technological gadgets in their everyday lives (Cernvall et al., 2017). What they discovered was that only 15.9% had ever used a PDA and only 4.9% used one on a regular basis (Cernvall et al., 2017). Another study had indicated that previous computer experience did not have a significant effect on the problem-solving or psychological outcomes of the participants (Zeman et al., 2006). However, significant attrition was observed in one study, in which mothers were requested to use PDA during times of their child's medical crisis (Askins et al., 2009). In this study, the average number of treatment sessions completed was only four out of the eight prescribed sessions. As technology is expected to evolve and become more integrated with everyday activities, significant familiarization with computer-aiding appliances will be necessary for parents. As in the study by Askins et al. was shown, an important open issue that needs to be

examined is the compliance of parents in using PDA or internet-mediated interventions under stressful conditions.

Based on the above data, it is anticipated that the adoption of educational and social support web-based interventions may have several disadvantages, but several advantages may also occur (Andersson and Titov, 2014). It can be reached at the time of users' convenience, through smart phones, tablets, or computers, and can at the same time benefit families in adjusting to their new life situation (Sigurdardottir *et al.*, 2014). Based on the principle that this type of intervention improves cancer understanding and communication, it has the potential to positively affect cancer-related QoL (Sigurdardottir *et al.*, 2014). It is also possible that this type of distress intervention proves useful for most families facing childhood cancer, leaving the need for professional face-to-face psychological care to a smaller proportion of families, requiring emotional support interventions such as therapeutic conversation interventions leading to an overall more cost-effective approach (Svavarsdottir and Sigurdardottir, 2013).

Limitations of the intervention studies and future directions

The most common limitation in the majority of studies is the small sample size that reduces the possibility of drawing strong conclusions and indicates the need for testing of these approaches in the context of larger prospective studies. A second limitation is that most studies' samples include only or predominantly mothers. An explanation given is that families facing their child's cancer, which is a very mentally and physically demanding responsibility, usually employ the division of labor (Askins *et al.*, 2009). Thus, limited access to data from fathers may be due to the fact that they are usually busy with securing financial stability. Nevertheless, as previously suggested, the abundance of maternal respondents may have influenced the parental results and may not be characteristic of the attitudes of fathers, but as the majority of primary caregivers are mothers, this was an expected phenomenon and is a limitation of unknown significance (Levine *et al.*, 2017). However, it is reasonable to hypothesize that fathers could benefit from distress interventions, and thus, efforts on their inclusion are a key future challenge. A third limitation noticed in some studies was the questionnaire or session attrition, as a considerable number of participants provided incomplete questionnaires or did not complete the intervention program. Other limitations include different psychosocial domains studied and different measurement tools applied in each study. One study used maximum-likelihood estimation to deal with a 42% attrition rate in collected data (Cernvall *et al.*, 2017). In some of the studies, only one site was used to establish a pool of potential candidates for the interventions, while others were multi-site. In the first case, this factor limits the generalizability of outcomes. Demographical, ethnological, spiritual, or religious confounders may be playing significant roles in the observed differences or similarities between intervention and control groups. As blinding of patients and care providers was not possible in these studies, performance bias (systematic differences in care provided apart from the intervention being evaluated) and ascertainment bias (systematic differences in outcome assessment) can occur (Boutron *et al.*, 2004). More research is required to help determine who will benefit from treatment, as factors relating to diagnosis, prognosis, and other confounders will likely affect which kind of intervention is appropriate for which families.

Limitations of this review study

Two important limitations of this systematic review is that it included only studies from the PubMed database and those in English language. Thus, there is a possibility that important studies from social or behavioral science journals, not found in MEDLINE, were omitted. Another limitation is that data included in the review derived from a limited range of different countries and as such it cannot be evaluated with certainty whether cultural differences may have affected outcome.

Regardless of these limitations, the findings of this systematic review confirm that families dealing with pediatric cancer derive benefit from psychological interventions targeting distress.

Mothers were found to be involved more often in psychosocial care and to derive particular benefit from CBT and PSST sessions with significant reduction of distress and increase of problem-solving skills. Fathers were shown to experience severe distress and to benefit from psychological interventions; however, they are largely underrepresented in studies for distress management. Although scarce, programs improving siblings' medical knowledge and understanding of malignant disease, by CBT, were shown to have a positive impact on psychological well-being; however, further studies are required to assess long-term psychological effects including PTS and anxiety. Overall, more effort is required to involve both siblings and fathers into such supporting programs.

Conclusions

In this study, literature concerning interventions targeting families of children with cancer was reviewed and its quality was evaluated using the Delphi scoring system. Different distress interventions have been examined, and mainly CBT and PSST were found to be beneficial for parents, mainly mothers, as they improved distress measures and adjustment. All the results together indicate that psychosocial interventions are feasible and valuable for parents and siblings of children diagnosed with cancer. More importantly, such interventions have the potential to indirectly impact children's psychological adjustment. These findings indicate the need for increased resources to address distress in families facing childhood cancer. A re-examination of psychosocial intervention protocols and study designs is also considered necessary to deliver more effective and acceptable interventions for each family member not only to reduce PTS but also to enhance post-traumatic growth.

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