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Psychological Interventions for Parents of Children with Cancer: A Systematic Review and Meta-analysis

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ABSTRACT

This study provides a systematic review and meta-analysis of randomized controlled trials that analyzed the efficacy of psychological interventions for parents of children with cancer. The search was conducted in the databases PsycInfo, Medline, PsycArticles, and PsycTests. Fourteen studies met the inclusion criteria. Two independent researchers extracted relevant data, and the studies were assessed for methodological quality. The standardized mean difference (d) was used as the effect size index. The meta-analyses, which applied random and mixed-effects models, showed that weighted effect sizes were statistically significant for depression at posttreatment ($d= 1.19$). However, the methodological quality moderated the depression estimate. The weighted effect sizes for the remaining variables were not statistically significant: stress/burnout ($d= 0.90$), quality of life ($d= 1.26$), anxiety ($d= 0.21$), posttraumatic stress ($d= 0.05$), and general indicator of emotional symptoms ($d= 0.33$). This review also highlights several methodological limitations of the studies. Future directions for research that examines interventions targeting primary caregivers of children with cancer are discussed. In conclusion, more high-quality research is needed to establish the efficacy of psychological interventions for parents of children with cancer.

Key words: cancer, children, parents, psychological intervention, meta-analysis.

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Novelty and Significance

What is already known about the topic?

- Parents of children with cancer have to face many difficulties such as uncertainty, anxiety, depression symptoms, posttraumatic stress, and changes caused by the illness that compromise their quality of life.
- Psychological interventions are widely recommended to promote parents' adaptation to their children's illness.

What this paper adds?

- This is the first meta-analysis focused specifically on parents and randomized controlled trial studies.
- The increased homogeneity between the meta-analyzed studies and the evaluation of the methodological quality allows for more accurate assessments of the efficacy of psychological interventions.

Psycho-oncology has mainly focused on adult cancer due to its higher prevalence compared with childhood cancer. Although childhood cancer only represents between 1-3% of human cancer, it is the first cause of death due to illness in children in developed countries. The incidence of cancer in children aged 0-14 years was 140.6 per million person-years, and in those aged 1-19 years, it was 185.3 per million person-years (Steliarova-Foucher *et alia*, 2017). Indeed, mortality due to childhood cancer is only surpassed by accidents and intoxications (Ries, Smith, Gurney, Linet, Tamra, Young, & Bunin, 1999).

Notably, the rates of survival in childhood cancer are usually high thanks to good access to health care and appropriate treatment (Bonaventure *et alia*, 2017). For

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instance, the probability of surviving at least five years after diagnosis for children with precursor-cell acute lymphoblastic leukemia (ALL) was as high as 90%. Also, this probability was 80% for children with acute myeloid leukemia (AML). Despite the high levels of survival, childhood cancer is still related to death, incurability, loss, and suffering (Kohlsdorf & Costa, 2012).

Childhood cancer usually affects the whole family. The diagnosis of cancer is a challenge for the family due to the length and aggressiveness of the treatment, the high risk of mortality, the long-term morbidity experienced by the child, and the numerous changes in family relationships and routines (Gerhardt, Gutzwiller, Huiet, Fischer, Noll, & Vannatta, 2007). Families need to adapt to this new situation. Specifically, parents face several difficulties, including fear of relapse, anxiety, the need to assimilate the information received, the care provided to healthy children, attempts to adapt to the new health condition, and providing care in the event of side effects and for intercurrents (Kohlsdorf & Costa, 2012). The parents' reaction to these difficulties depends on multiple factors such as their personality, the family's previous experience with illness and cancer, the support they receive, their religious beliefs, and the course of the illness and its treatment (Die-Trill, 1993).

The way parents cope with the difficulties experienced is essential for the quality of life of the family. For instance, parents might focus on their ill child to the point of ignoring their own needs and the needs of other members of the family (Sloper & While, 1996). In a systematic review (Vrijmoet-Wiersma, van Klink, Kolk, Koopman, Ball, & Egeler, 2008), parents' stress reactions were grouped into four categories called uncertainty, anxiety, depression symptoms, and posttraumatic stress. These authors also found that mothers tend to report more and higher levels of symptoms than fathers, and propose this might be related to the traditional distribution of caregiving tasks and responsibilities.

According to Sloper (2000), the attempts to return to regular routines after the active phase of treatment were usually difficult. Parents perceived that they received enough training for coping with the intervention, but insufficient support in the post-intervention phase. Some parents stated that they put their feelings aside during the active phase of treatment to help their child cope with the situation. Once they returned home, these feelings might surface.

Some of the newly acquired responsibilities during the active treatment phase of cancer, such as the obligation of physical proximity to their child to provide comfort and keep them monitored the whole time (Young, Dixon-Woods, Findlay, & Heney, 2002), might have repercussions at the end of the treatment phase. The problem that remains in 90% of the cases is that parents and family generally overprotect the child with an excess of physical care, hindering the child's development of independence and autonomy after overcoming the illness (Méndez Venegas, 2005).

To cope with these difficulties, psychosocial support is widely recommended to promote the short and long-term family adaptation to the changes caused by their child's illness (SIOP, 2009). Indeed, psychological interventions have been developed for parents of children and adolescents with cancer to improve parents' outcomes. Some studies have reviewed the efficacy of psychological interventions for parents of children with chronic illness in general (e.g., Eccleston, Fisher, Law, Bartlett, & Palermo, 2015; Eccleston, Palermo, Fisher, & Law, 2012). Other reviews focused only on childhood cancer, but they were not meta-analyses (e.g., Muglia Wechsler, Bragado Álvarez, & Hernández Lloreda, 2014). The two meta-analyses about the effects of psychological interventions in pediatric oncology were conducted by Pai, Drotar, Zebracki, Moore, and Youngstrom (2006) and Sánchez Egea, Rubio Aparicio, Sánchez Meca, and Rosa Alcázar (2019). Pai *et alia* (2006) investigated the efficacy of psychological interventions in parents and

children, finding small effect sizes in distress and adjustment for parents. Sánchez Egea *et alia*'s (2019) meta-analysis revealed positive effects of mild to moderate magnitude for anxiety, problem-solving skills, and posttraumatic stress. The selected studies in these meta-analyses included different participants' categories (children, siblings, and parents), therapy methods (face-to-face interventions, written disclosures, and internet-based, guided self-help), study designs (randomized controlled trial -RCT- and quasi-experimental), and a wide range of topics (grieving, venipuncture, radiotherapy, etc.).

Given the increase in the interest in the psychological aspects of childhood cancer and the higher number of studies in this field in the past few years, we decided to conduct a meta-analysis focused only on the efficacy of the interventions for parents of children with cancer. This meta-analysis adds to the literature by providing an updated overview of the field and by evaluating the efficacy of psychological interventions, specifically in parents of children and adolescents with cancer in RCT and face-to-face interventions. In contrast to previous meta-analyses, this approach provides greater homogeneity among studies, which increases the internal validity of the meta-analysis and avoids the potential bias introduced by within-group designs and non-randomized control trials (Knock, Janis, & Wedig, 2008).

METHOD

Study selection criteria

The selection criteria to include studies in this meta-analysis were: (a) face-to-face intervention, (b) designed specifically for parents of children diagnosed with cancer, (c) with a nonactive control group (waiting list or nonintervention), and (d) randomized allocation to the experimental conditions. We excluded studies that analyzed the effect of psychological interventions for parents of children who received medical procedures or treatment (e.g., marrow transplant) and palliative and end-of-life phase treatment. This decision was adopted because these families have to cope with extreme situations that involve different characteristics compared to the remaining studies (e.g., treatments are very aggressive and risky).

Search strategy

Studies regarding psychological interventions in parents of children with cancer were identified using the following strategies. First, in January 2019, we searched the electronic bibliographic databases PsycINFO, Medline, PsycARTICLES, and PsycTESTS, using the following keywords in the abstracts: (Childhood cancer OR children cancer) AND (parents OR mothers) AND (intervention OR randomized trial). The keyword "parents" includes both fathers and mothers, but we also included the keyword "mother" because some interventions are specifically focused on mothers. The selected studies were carried out between 1998 and 2017. Second, the reference lists of existing reviews and meta-analyses on the matter were also reviewed (Eccleston, Palermo, Fisher, & Law, 2012; Fisher, Law, Bartlett, & Palermo, 2015; Muglia Wechsler *et alia*, 2014; Pai *et alia*, 2006).

Coding of moderator variables

To analyze the characteristics of the studies that might influence the magnitude of the effect sizes, treatment, methodological, extrinsic characteristics of the studies, and the main outcome variables were coded. This coding was conducted by two

researchers independently, and inconsistencies were resolved by consensus. The treatment characteristics coded were: (a) child diagnosis, (b) time from diagnosis, (c) treatment intensity, (d) child's and parents' age and gender, (e) mothers' and girls' percentage, (f) parents' educational level, (g) financial incomes, (h) marital status, (i) ethnicity race, (j) family members who receive the intervention, (k) intervention during or at the end of medical treatment, (l) type of psychological intervention, (m) number of sessions, (n) number of reminder sessions, (o) overall duration, (p) individual or group format, and (q) professional who implemented the intervention. The methodological characteristics were coded as follows: (a) design type, (b) statistical techniques, (c) type of control group, (d) last follow-up in months, and (e) outcome measures. The extrinsic characteristics of the studies were: (a) year and (b) type of publication. Finally, the outcomes coded for both experimental and control groups were: (a) number of participants and (b) mean and standard deviations at pre-intervention, post-intervention, and follow-up.

Additionally, each study included in the systematic review was rated for methodological quality using the checklist suggested in Botella and Sánchez Meca (2015). The checklist includes the following items: random assignment to groups, equivalent groups on relevant variables at pre-intervention, pretest measurements of dependent variables, psychological placebo control group, pharmacological placebo control group, evaluator blinded study, validated assessment tools, large sample size, 10% or less dropout at post-intervention, and intent-to-treat analysis. Each item is scored as 1 if the study accomplished the item's content or 0 if not. Therefore, the range of scores is between 0 and 10 points. The two independent researchers also coded this evaluation.

Effect size calculation

Controlled between-group effect size biases corrected for small samples were computed on all outcome measures at posttreatment and follow-up. This effect size is a difference between the means of the treated group and the control group divided by a pooled estimate of the within-study Standard Deviation (S) corrected by the factor $c(m)$ for small samples (Hedges & Olkin, 1985). Effect sizes and standard errors were computed using the web-based effect-size calculator <https://www.campbellcollaboration.org/escalc/html/EffectSizeCalculator-OR1.php> (DB Wilson, n.d.). Positive effects represent better results for the intervention condition. According to Cohen's rule-of-thumb, effect sizes were interpreted as small (0.20 to 0.49), medium (0.50 to 0.79), and large (0.80 or higher) effects.

In each study, a separate d index was calculated for the six following outcome measures if they were present in the study: depression, anxiety, posttraumatic stress, stress/burnout, general indicator of emotional symptoms, and quality of life. When the study did not report means and standard deviations of the groups, we requested them from the authors, or the d index was calculated from the results of t -tests, ANOVAs, etc. (Glass, McGaw, & Smith, 1981; Lipsey & Wilson, 2001). Lastly, a weighted d index was calculated for each of the six outcome measures.

Data Analysis

Separate meta-analyses were carried out for each outcome measure according to the effect sizes calculated in each study. The meta-analysis was conducted with JASP Version 0.8.4 (JASP Team, 2019). A random-effects model was used to calculate the weighted effect sizes and 95% confidence intervals (CI) because we expected significant heterogeneity across the studies. This model assumes that the studies are different from

each other due to random error within the studies and true systematic variation in effect sizes across them (Borenstein, Hedges, Higgins, & Rothstein, 2009). The heterogeneity of the effect sizes was assessed with the Q statistic. The I^2 index was used as an indicator of the degree of heterogeneity across effect sizes around the mean effect (Cooper, Hedges, & Valentine, 2009). Following the suggestion of Higgins, Thompson, Deeks, and Altman (2003), values of 0%, 25%, 50%, and 75% in the I^2 statistic were considered as indicative of no, low, moderate, and high heterogeneity, respectively.

RESULTS

Figure 1 shows the flowchart of the search conducted. The search produced 925 references, and 21 articles fulfilled the selection criteria. Of them, 7 studies were excluded during the full-text review: in 1 of them, both conditions received the intervention, but there was no control condition to compare the efficacy of the intervention; 2 had questionable descriptive statistics; 1 reported the effect of parents' interventions only on child adjustment; and 3 studies had an active control group. The remaining 14 studies were included in the review and meta-analyzed.

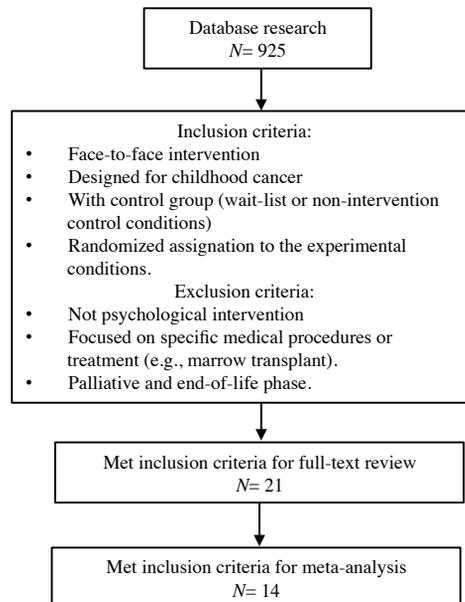


Figure 1. Study inclusion flowchart.

The selected studies were carried out between 1998 and 2017. The total sample size of the meta-analysis involved 1,561 individuals, of which 809 subjects formed the 14 treatment groups (Mean sample size= 57.79 participants, SD = 55.48, range= 10-217 participants) and the remaining 752 participants constituted 14 independent control groups (Mean sample size= 53.71 participants, SD = 53.96, range= 10-213 participants). Attrition rates ranged between 0% and 32.5%. The main characteristics of the studies are presented in Table 1.

Table 1. Summary of the Studies Included in the Meta-Analyses.

Study	Outcome variable	N	% Attrition Post	Child M age	% of Mothers	Time since diagnosis	During or after treatment	Measures	Control Group
Asadi Noughabi <i>et alia</i> (2015)	Quality of life	50	18%	NS	73.2%	NS	NS	SF36	NI
Beheshtipour <i>et alia</i> (2016)	Stress/Burnout	140	3.57%	NS	56.3%	24-96 w	During treatment	SMBQ	WLC
De la Maza <i>et alia</i> (2015)	Anxiety	102	0%	7.98	96.88%	2-16 w	During treatment	HAM-A	WLC
Delavari <i>et alia</i> (2014)	Depression and Anxiety	30	NS	NS	100%	NS	During treatment	BDI BAI	NI
Hoekstra-Weebers <i>et alia</i> (1998)	Anxiety and General indicator of emotional symptoms	120	32.5%	6.4	50.6%	1-3 w	During treatment	STAI SCL	NI
Kazak <i>et alia</i> (2004)	Anxiety and Posttraumatic stress	244	28.28%	14.64	57.94%	NS	After treatment	STAI IES-R	WLC
Kazak <i>et alia</i> (2005)	Anxiety	38	18.42%	5	50%	4 w	During treatment	STAI BDI	NI
Marsland <i>et alia</i> (2013)	Depression, Anxiety, Posttraumatic Stress, and Stress/Burnout	44	15.91%	13.09	95.65%	4 w	During treatment	STAI PSS IES	NI
Mullins <i>et alia</i> (2012)	Posttraumatic stress, Stress/Burnout and General indicator of emotional symptoms	52	21.15%	8.22	100%	4-16 w	During treatment	IES-R CMCC SCL-90-R	NI
Safarabadi-Farahani <i>et alia</i> (2016)	Quality of life	65	4.62%	6.03	95.15%	NS	During treatment	CQOLC	NI
Sahler <i>et alia</i> (2002)	Depression, Anxiety and General indicator of emotional symptoms	92	NS	8.11	100%	2-16 w	During treatment	POMS	NI
Sahler <i>et alia</i> (2005)	Depression, Posttraumatic stress and General indicator of emotional symptoms	430	5.58%	7.6	100%	2-16 w	During treatment	BDI-II IES-R POMS	NI
Shekarabi-Ahari <i>et alia</i> (2012)	Depression	20	NS	6.15	100%	NS	After treatment	BDI	WLC
Stehl <i>et alia</i> (2009)	Anxiety and Posttraumatic stress	134	31.34%	6	NS	4-6 w	During treatment	STAI IES-R	NI

Notes: BAI= Beck Anxiety Inventory; BDI= Beck Depression Inventory; CMCC= Care of My Child with Cancer Questionnaire; CQOLC= Caregiver Quality of Life Index-Cancer; HAM-A= Hamilton Anxiety Rating Scale; IES-R= Impact of Event Scale-Revised; NI= Non-intervention control condition; NS= Not specified; POMS= Profile of Mood States; PSS= Perceived Stress Scale; SCL= Symptom Checklist; SF36= 36-Item Short-Form Health Survey; SMBQ= Shirom-Melamed Burnout Questionnaire; STAI= State-Trait Anxiety Inventory; w= weeks; WLC= Wait-list control condition.

Depression had a high homogeneity in the selected measure: four out of five studies used the *Beck Depression Inventory-II* (BDI-II; Beck, Steer, & Brown, 1996). In the remaining study, the authors used the *Profile of Mood States* subscale “Depression/Dejection” (POMS; McNair, Lorr, & Droppleman, 1971). The most used measure for anxiety was the *State-Trait Anxiety Inventory* (STAI; Spielberger, Gorsuch, & Lushene, 1970). Five studies reported STAI-State data (one of them reported both subscales data, but we selected the State scale to unify), one study used the *Hamilton Anxiety Rating Scale* (HAM-A; Hamilton, 1959), one used the *Beck Anxiety Inventory* (BAI; Steer & Beck, 1997), and in the remaining study, we selected the POMS subscale “Tension/Anxiety.” Posttraumatic stress was measured with the *Impact of Event Scale-Revised* (IES-R; Weiss & Marmar, 1997) in the five studies. In two studies, data from two different measures were reported, so that we discarded one of them to homogenize. Measures to assess stress or burnout were different in each study: *Perceived Stress Scale* (PSS; Cohen, Mermelstein, & Kamarck, 1983), *Care of My Child with Cancer Questionnaire* (CMCC; Wells et alia, 2002), and *Shirom-Melamed Burnout Questionnaire* (SMBQ; Lundgren-Nilsson, Jonsdottir, Pallant, & Ahlberg, 2012). As a general indicator of emotional symptoms, two studies used the *Symptom Checklist* (SCL; Derogatis, 1983), and two used total scores of the POMS. Finally, quality of life was measured with the *36-Item Short-Form Health Survey* (SF-36; Ware & Sherbourne, 1992) in one study and the *Caregiver Quality of Life Index-Cancer* (CQOLC; Weitzner, Jacobsen, Wagner, Friedland, & Cox, 1999) in the remaining study.

Regarding methodological quality, one study scored 7 out of 10 points, five studies scored 6 points, four studies scored 5 points, two studies scored 4 points, and two studies scored 3 points (see Table 2). All studies analyzed met the following three items of the scale: random allocation of participants to the experimental groups, pretest measurements of dependent variables, and use of validated assessment tools. None of

Table 2. Quality Scale for Assessing the Threats of Bias in the Estimates of the Effect Sizes*.

Item/Studies	Asadi et alia (2016)	Beheshtipour et alia (2016)	De la Maza et alia (2015)	Delavari et alia (2014)	Hoekstra et alia (1998)	Kazak et alia (2004)	Kazak et alia (2005)	Marsland et alia (2013)	Mullins et alia (2012)	Safarabadi-Farahani et alia (2016)	Sahler et alia (2002)	Sahler et alia (2005)	Shekarabi et alia (2012)	Stehl et alia (2009)
1. Random assignment to groups.	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
2. Equivalent groups on relevant variables at pre-intervention.	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓		✓
3. Pretest measurements of dependent variables.	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
4. Psychological placebo control group.														
5. Pharmacological placebo control group.														
6. Evaluator blinded study.														
7. Validated assessment tools.	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
8. Large sample size**.		✓	✓		✓	✓					✓	✓		✓
9. 10% or less mortality at post-intervention.		✓	✓				✓			✓		✓		
10. Intent to treat analysis						✓			✓		✓	✓		✓
Total	4	6	6	3	5	6	5	4	5	5	6	7	3	6

Notes: * = Adapted from Botella & Sánchez Meca (2015); ** = The distribution of the sample sizes of the meta-analyzed studies is dichotomized according to the median and those sample sizes above this value are assigned to the “high” category. The answer “yes” is scored with a 1, the answer “no” is scored with a 0.

them met psychological nor pharmacological placebo control due to those items being considered exclusion criteria.

Table 3 presents the effect sizes for each study and the weighted effect sizes. The only statistically significant weighted effect size was the one for depression at posttreatment ($d= 1.19$) and follow-up ($d= 0.31$). The weighted effect sizes for the remaining variables were not statistically significant, although, for stress/burnout ($d= 0.90$) and quality of life ($d= 1.26$), the effect sizes were large at posttreatment. Null to small weighted effect sizes at posttreatment were found for anxiety ($d= 0.21$), posttraumatic stress ($d= 0.05$), and the general indicator of emotional symptoms ($d= 0.33$). The effect sizes and 95% CIs of the outcome measures for posttreatment and follow-up are plotted at <https://osf.io/jxzh9/>.

Table 3 also shows the heterogeneity of the effect sizes. Statistically significant Q values were obtained for depression (postintervention: $Q= 4.88, p <.05$; follow-up: $Q= 14.37, p <.001$) and quality of life (postintervention: $Q= 5.26, p <.05$). I^2 indexes ranged from 65.70% to 99.75%, which is considered high heterogeneity. A moderation analysis was only conducted with depression at postintervention because there were only two studies in the remaining variables. Methodological quality was the only moderator variable analyzed because the other potential moderator variables (i.e., time since diagnosis, parent's gender, sample size, etc.) did not report data in all studies or had high homogeneity. The analysis showed a negative relationship between methodological quality and the efficacy in reducing depression ($ES= -0.50, p= .049$): the lower the methodological quality, the larger the effect size.

Table 3. Summary Results for the Meta-Analyses Conducted.

Outcome/study	<i>k</i>	<i>d</i> (SE)		<i>Q</i>		<i>I</i> ²	
		Post	F-U	Post	F-U	Post	F-U
Depression	Delavari <i>et alia</i> (2014)	2.48 (0.24)	--				
	Marsland <i>et alia</i> (2013)	0.17 (0.12)	--				
	Sahler <i>et alia</i> (2002)	0.50 (0.05)	0.40 (0.04)				
	Sahler <i>et alia</i> (2005)	0.34 (0.01)	0.23 (0.01)				
	Shekarabi <i>et alia</i> (2012)	2.63 (0.37)	--				
	Weighted effect size	5	1.19 (0.54)	0.31 (0.08)	4.88*	14.37***	99.75
Anxiety	De la Maza <i>et alia</i> (2015)	-0.31 (0.04)	-0.42 (0.04)				
	Delavari <i>et alia</i> (2014)	0.47 (0.14)	--				
	Hoekstra <i>et alia</i> (1998)	-0.12 (0.10)	-0.03 (0.10)				
	Kazak <i>et alia</i> (2004)	0.25 (0.15)	--				
	Kazak <i>et alia</i> (2005)	0.78 (0.16)	--				
	Marsland <i>et alia</i> (2013)	0.11 (0.12)	--				
	Sahler <i>et alia</i> (2002)	0.62 (0.05)	0.50 (0.05)				
	Stehl <i>et alia</i> (2009)	-0.01 (0.03)	--				
Weighted effect size	8	0.21 (0.13)	0.02 (0.27)	2.50	0.01	97.32	98.63
Posttraumatic Stress	Kazak <i>et alia</i> (2004)	0.31 (0.06)	--				
	Marsland <i>et alia</i> (2013)	-0.50 (0.12)	--				
	Mullins <i>et alia</i> (2012)	0.87 (0.51)	--				
	Sahler <i>et alia</i> (2005)	0.27 (0.01)	0.32 (0.01)				
Weighted effect size	5	0.05 (0.19)	0.32 (0.01)	0.08	--	99.17	--
Stress/Burnout	Beheshtipour <i>et alia</i> (2015)	1.74 (0.04)	1.74 (0.04)				
	Marsland <i>et alia</i> (2013)	0.14 (0.12)	--				
	Mullins <i>et alia</i> (2012)	0.78 (0.41)	--				
Weighted effect size	3	0.90 (0.50)	1.74 (0.04)	3.25	--	98.03	--
General indicator of emotional symptoms	Hoekstra <i>et alia</i> (1998)	-0.30 (0.10)	-0.22 (0.10)				
	Mullins <i>et alia</i> (2012)	1.03 (0.53)	--				
	Sahler <i>et alia</i> (2002)	0.64 (0.05)	0.45 (0.04)				
	Sahler <i>et alia</i> (2005)	0.32 (0.01)	0.14 (0.01)				
	Weighted effect size	4	0.33 (0.26)	0.13 (0.19)	1.67	0.46	98.79
Quality of life	Asadi <i>et alia</i> (2016)	1.65 (0.13)	--				
	Safarabadi-Farahani <i>et alia</i> (2016)	0.50 (0.67)	0.70 (0.07)				
	Weighted effect size	2	1.26 (0.55)	0.70 (0.07)	5.26*	--	65.70

Notes: *k*= Number of studies; *d*= Effect size; *SE*= Standard Error; *Q*= Heterogeneity Q statistic; *I*²= Heterogeneity index (%); *= $p <.05$; ***= $p <.001$; **= $p <.01$.

DISCUSSION

The current study aimed to review the empirical evidence regarding the efficacy of face-to-face psychological interventions with parents of children with cancer. In so doing, 14 studies fulfilled our selection criteria and were used in the meta-analysis. Twelve studies focused on emotional symptoms and two on quality of life. Most of the studies reported small or moderate effect sizes or did not find a significant effect of the psychological intervention compared to the control group. This is consistent with the literature indicating that effect sizes were small for most comparisons of parental distress and parents' adjustment (Eccleston *et alia*, 2015; Gerhardt *et alia*, 2007; Pai *et alia*, 2006; Sánchez Egea *et alia*, 2019). Depression was the only outcome showing an effect size statistically significantly higher than zero at posttreatment ($d= 1.19$). However, the moderation analysis indicated that this large effect size was due to the effect of the two studies with low methodological quality. Indeed, the effect size at follow-up was considerably smaller ($d= 0.31$) because the two mentioned studies did not report follow-up assessment.

Kazak *et alia* (2004) reported that more distressed families were more likely to drop out of the intervention, but paradoxically, the intervention effect should be stronger for these families. One reason pointed out is the avoidance of distressing memories and upsetting components of the intervention. In this sense, assessing the psychosocial risk of the families is crucial to reduce the dropout of the most distressed families. Indeed, families of children with cancer were generally resilient during cancer treatment (Gerhardt *et alia*, 2007), suggesting that not all parents would benefit from a psychological intervention to reduce distress. Experiencing emotional symptoms after diagnosis of childhood cancer is a normal response in parents. According to Kazak, Schneider, Didonato, and Pai (2015), one-half to two-thirds of parents are at low risk, one-quarter to one-third presented a medium risk, and up to 15% are at high risk and are considered clinical population. Thus, it is crucial to identify which parents are truly in need of a psychological intervention due to severe, escalating, or persistent distress. This is consistent with Sheard and Maguire's meta-analysis about the effect of psychological interventions on anxiety and depression in cancer patients, which found that targeted interventions at those identified as at risk of or suffering significant psychological distress were associated with strong clinical effects (Sheard & Maguire, 1999). Also, it is essential to identify parents who can cope and adapt to their child's process but who experience subclinical symptomatology that should be monitored. These parents might benefit from services such as psychoeducation and family support.

Most interventions were implemented with the mothers because they are considered at high risk. From this point of view, the emotional response to the diagnosis of cancer would be associated with gender. Other psychological interventions take all family as the target regardless of the risk or distress that each one presents. As gender differences in stress reactions have not been well established in the literature and the primary caregiver is the one most exposed to the repercussions of caring for a child with cancer, it seems more appropriate to address psychological interventions to primary caregivers, which may include parents, step-parents, grandparents or guardians of the pediatric oncology patient.

Several limitations of this meta-analysis related to the characteristics of the conducted studies and methodological aspects are worth mentioning. Firstly, most of the studies have a relatively small number of participants. Childhood cancer is considered a rare disease, and obtaining a large sample is not always an easy task. Secondly, the

meta-analysis contains a reduced number of studies. The absence of a control group and randomized assignation were the reasons not to include many of the studies obtained in the first search. However, it is a necessary criterion to attribute the improvements to the psychological intervention and not to the effect of time or other extraneous variables. Thirdly, nine studies had more than 10% attrition, with five showing more than 20%. Schulz and Grimes (2002) argue that loss to follow-up of 5% or lower is usually of little concern, whereas a loss of 20% or higher can threaten the trial validity. Fourthly, nine out of sixteen studies did not include intent-to-treat analysis, which could affect the effect sizes obtained. Sixthly, six studies did not include follow-up. Only one study included a long-term follow-up (1-year follow-up), and the remaining studies conducted follow-ups of a maximum of three months. Therefore, further research should examine the long-term effect of psychological interventions in comparison to control conditions.

In conclusion, there is little evidence of the efficacy of psychological interventions for parents of children with cancer according to randomized controlled trials. In this regard, it is relevant to highlight that within-group designs and non-randomized control trials tend to overestimate the effect size of the intervention (Knock *et alia*, 2008). It is recommended that further studies (a) analyze the effect of psychological interventions for the most distressed parents, (b) develop assessments of the psychosocial risk of the family to provide personalized attention, (c) conduct longer follow-ups, and (d) implement the psychological interventions to the primary caregivers.

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