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REVIEW

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Psychological treatment for family members of children with cancer: A systematic review and meta-analysis

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Abstract

Objective: This meta-analytical study examined the effects of psychological treatments applied to family members of children and adolescents with cancer, as well as the characteristics of the studies that can be associated with their effects.

Methods: Four databases were searched between January 1980 and January 2017; the references of the located studies were reviewed, and emails were sent to experts in this topic. Forty articles fulfilled the selection criteria. The standardized mean pretest-posttest (or pretest–follow-up) change was used as the effect-size index for the treatment and control groups.

Results: The 40 articles included 40 treatment groups and 21 control groups. When treatment and control pretest-posttest mean effects were compared, psychological interventions revealed positive, statistically significant results for anxiety (d_{adj} = 0.339) and problem-solving skills (d_{adj} = 0.385) and, to a lesser extent, for posttraumatic stress (d_{adj} = 0.224). No statistically significant differences were found for mood (d_{adj} = 0.147), acute stress (d_{adj} = −0.010), coping skills (d_{adj} = 0.123), social support (d_{adj} = 0.245), or quality of life (d_{adj} = 0.538).

Conclusions: Positive effects of mild to moderate magnitude were found in the posttests for some outcome measures. Behavioral interventions seem to be the most promising. Interventions achieved the best results when they were long in duration and low in intensity and when they were applied to family members with young children who were undergoing medical treatment. At follow-up, the intervention benefits were diminished. The application of psychological interventions is recommended to mitigate the negative psychological repercussions in this population.

KEYWORDS

adolescents, cancer, children, family members, meta-analysis, oncology, psychological treatment, relatives

1 | BACKGROUND

Current treatments to fight pediatric cancer not only focus on increasing survival but also aim to improve patients' quality of life through prevention of sequelae and treatment of negative consequences, both physical and psychological, which result from the disease.

The relatives of children affected by cancer also suffer greatly because of the psychological distress caused by this experience. Some parents of children with cancer present symptoms and disorders that require clinical attention. The most common effects parents show are psychological distress,[1] anxiety,[2,3] depression,[3,4] acute stress or posttraumatic stress symptoms,[3,5,6] and sleep problems.[7] Similar to

their parents, some siblings of children with cancer may be prone to emotional, behavioral, and social problems, especially feelings of loss, fear, grief, helplessness, insecurity, loneliness, jealousy, anger or guilt,[8,9] sleep problems,[10] anxiety and sadness,[11-13] posttraumatic stress symptoms,[8,13,14] and difficulties in academic and social contexts.[15,16]

Although there is abundant descriptive research on the psychological impact of pediatric cancer on family members,[1,4,14,15,17,18] empirical research on the development and application of psychological interventions that reduce symptoms or disorders is much less extensive. However, an increase in research on this topic has been observed in recent years.

The most common interventions for parents have been based on the cognitive behavioral model, such as problem-solving skills training[19,20]; coping skills training[21-23]; cognitive restructuring or positive self-instruction[24,25]; positive reinforcement or behavioral trials[26-28]; relaxation training,[29-31] and training in communication skills, assertiveness, or guided communication.[32,33] As for siblings, problem-solving skills training,[34-36] cognitive restructuring,[34-36] and coping skills training have been used.[37] In addition to cognitive-behavioral techniques, psychoeducational interventions have been applied to both parents and siblings, focused on providing information on cancer, treatments, and possible long-term sequelae.[37-42]

To date, systematic reviews involving family members of children with cancer have focused on collecting data not only from this group of patients but also from patients with other chronic health problems. Specifically, Pai et al[43] reviewed 12 articles published between 1967 and 2005 that included, among others, treatments for children with cancer. The researchers concluded that there was improvement in the outcomes assessed, with effect sizes of medium-low magnitude for parental distress (d_+ = 0.35) and low magnitude for psychological adjustment (d_+ = 0.23). Law et al[44] evaluated the effects of psychological therapies in parents and relatives of children with various chronic physical illnesses (asthma, cardiovascular diseases, cystic fibrosis, diabetes mellitus, etc). They included 37 investigations, of which seven were focused on studies of children with cancer. The results showed a significant positive effect of interventions on the behavior of parents (d_+ = 0.25), but not on their mental health (d_+ = 0.19) or family functioning (d_+ = 0.05). Eccleston et al[45] analyzed 47 articles assessing the efficacy of psychological therapies in parents of children with several chronic medical conditions. In their meta-analysis, they included 10 studies focused on children with cancer. The outcome variables analyzed were the parents' adaptive behavior, which showed a low-magnitude but significant improvement (d_+ = 0.20), and their mental health, which did not show any significant improvement.

1.1 | Purpose of the study

The overall aim of the present work was to perform a systematic review and meta-analysis of empirical evidence on the efficacy of psychological treatments applied to family members of children and adolescents with cancer. We wished to investigate the effects of treatment on such clinical variables as anxiety, mood, and stress. Another of our goals was to identify characteristics of the studies that could be statistically associated with their effect sizes. Because of the small number of randomized controlled trials (RCTs) expected in the literature on this topic, we included both RCTs and uncontrolled trials.

2 | METHODS

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations[46] (see the PRISMA checklist in Data S1).

2.1 | Selection criteria

For inclusion in this meta-analysis, studies were required to fulfill the following selection criteria based on the PICOS statement[46]: (*a*) *participants*: family members (parents and/or siblings) of children with cancer at any stage (active treatment, remission, relapse, or grieving relatives); (*b*) *interventions*: psychological treatments exclusively applied to family members of pediatric cancer patients; (*c*) *comparison groups*: active and inactive control groups; (*d*) *outcomes*: anxiety, mood, stress, and coping skills; (*e*) *study designs*: RCTs and uncontrolled trials with pretest and posttest assessments and, optionally, some follow-up. In addition, all studies were required to report sufficient statistical data to calculate effect sizes, to have sample sizes greater than or equal to five participants in the posttest, to be written in English or Spanish, and to have been performed or published between January 1980 and January 2017.

2.2 | Search strategy

Four electronic databases were consulted: *PsycINFO*, *PubMed*, *Cochrane Library Plus*, and *the Turning Research Into Practice (Trip) database* (in this last source, the *evidence-based synopses* were used). A series of keywords in English (child*, adolesc*, pediatric, sibling, parent, family, cancer, oncology, psychological, psychosocial, treatment, intervention, and therapy) and Spanish were combined using the Boolean operators AND and OR and were required to appear in the title, abstract, or both parts of the work. In addition, the references of the three above-cited meta-analyses and seven systematic reviews were consulted.[9,47-52] The references of the located studies were also reviewed. Finally, 84 emails were sent to experts on the topic to try to locate unpublished studies.

2.3 | Data extraction

To examine the potential influence of study characteristics on effect sizes, we extracted a large number of treatment, participant, contextual, methodological, and extrinsic variables from the treatment groups. The *treatment variables* coded were (*a*) psychological approach (cognitive-behavioral treatment, psychosocial/psychoeducational treatment), (*b*)

techniques applied to participants (cognitive, behavioral, problem-solving skills training, coping skills training, relaxation/breathing training, other), (*c*) type of modeling (male, female, coping, mastery, no modeling), (*d*) length of the intervention (number of weeks), (*e*) number of sessions, (*f*) treatment intensity (number of hours per session), (*g*) treatment magnitude (total number of intervention hours per participant), (*h*) frequency of sessions (total sessions divided by weeks of duration), (*i*) inclusion of homework (included, not included), (*j*) inclusion of a follow-up program, (*k*) format of the follow-up program (telephone, email, etc.), (*l*) number of follow-up sessions (booster sessions) applied, (*m*) mode of treatment (individual versus group or mixed), (*n*) name of program, (*o*) professional field of therapist/s (psychologist, nurse, physician, social worker, other), and (*p*) therapist experience (high, medium, low). In addition, two *contextual variables* were extracted: (*a*) country of the study and (*b*) place of application (university, clinic or health center, hospital, leisure center, home).

Several *participant characteristics* were also coded. The coded characteristics of relatives were (*a*) family relationship (father/mother, sibling, other), (*b*) age group of sample (children, adolescent, adult, mixed), (*c*) average age of participants (in years), (*d*) gender (male, female, mixed), (*e*) gender distribution (percentage of males), and (*f*) inclusion or exclusion of grieving relatives (explicitly excluded, did not exclude and appeared, did not exclude and did not appear). The extracted characteristics of the children with cancer extracted were (*g*) average age of child patients (in years), (*h*) gender (male, female, mixed), (*i*) gender distribution (percentage of males), (*j*) phase of disease (newly diagnosed, active treatment, remission, relapse, death, mixed), (*k*) inclusion or exclusion of children with cancer in the psychological treatment, (*l*) existence of medical procedures associated with psychological intervention, and (*m*) duration of illness (mean in months).

The *methodological variables* coded were (*a*) method of assigning participants to groups (random, nonrandom, nonrandom but controlled) in the case of between-group design, (*b*) the longest follow-up assessment (in months), (*c*) sample size in pretest (15 or greater, between 8 and 14, less than 8), (*d*) sample size in posttest, (*e*) sample size in follow-up, (*f*) attrition from pretest to posttest, (*g*) attrition from pretest to follow-up, and (*h*) methodological quality of the study (on a scale of 0-5 points).* For control groups, two characteristics were extracted: (*a*) activity level of control group (active, inactive) and (*b*) type of activity in case of active control group (modified psychological care, standard psychosocial care).

Three *extrinsic variables* were coded: (*a*) year of publication, (*b*) professional background of the first author of the study (psychologist, nurse, physician, other), and (*c*) presence or absence of overlap between the author/s of the study and the treatment facilitator/s.

A codebook and a protocol for registering the variables were previously produced†. In order to assess the reliability of the data extraction, 25% of the studies were randomly selected and subjected to a double coding process by two previously trained coders (AIRA and RSE). The results showed very satisfactory interrater reliability, with κ coefficients ranging from 0.95 to 1 for the categorical variables and intraclass correlations between 0.99 and 1 for the continuous variables.

2.4 | Computation of effect sizes

For maximal comprehensiveness, both studies with and without a control group (RCTs and uncontrolled trials) were included. This circumstance dictated the choice of the effect-size index. In this meta-analysis, the analysis unit was the group, not the study, and the effect-size index was the standardized mean change index, defined as the difference between the pretest and posttest means divided by the pretest standard deviation: $d = c(m)(\overline{y}_{Pre} - \overline{y}_{Post})/S_{Pre}$, with $c(m)$ being a correction factor for small sample sizes.[53] A *d* index was calculated for each of the 40 treatment groups as well as for each of the 21 control groups included in the selected studies. To calculate effect sizes in the follow-ups, we used the same formula with the follow-up mean instead of the posttest mean. Positive values for *d* indicated a favorable change in the group from the pretest to the posttest (or to the follow-up). Although effect sizes based on one-group pretest-posttest change face challenges with internal validity, this type of effect size is recommended in the meta-analytic literature when most of the studies on a given topic do not include a control group.[53,54] However, as a complementary analysis, effect sizes from RCTs were also calculated with the uncontrolled trials excluded. In particular, the standardized mean change index was calculated for each RCT; this index was defined as the difference between the pretest-posttest mean changes in the treatment and control groups, divided by a pooled estimate of the pretest standard deviations.

Separate effect sizes were calculated for each outcome measure: anxiety, mood, acute stress, posttraumatic stress symptoms, coping skills, social support, problem-solving skills, and quality of life.

For an assessment of the reliability of the effect size calculations, the same random sample of studies used in the coding-reliability study was subjected to a double process of effect-size calculations; excellent interrater reliability was achieved, with intraclass correlations equal to 1.

2.5 | Statistical analysis

Separate meta-analyses were carried out with the effect sizes for each outcome measure. To accommodate the variability exhibited by the effect sizes, we assumed random-effects models, such that in the statistical analyses, each individual effect size was weighted by its inverse variance.[53] For each outcome measure, a forest plot was constructed, and a weighted mean effect size with a 95% confidence interval (CI) was calculated with the improved method proposed by Hartung and Knapp.[55,56]

The first analysis consisted of comparing the mean effect size of the treatment groups with that of the control groups using the *F* statistic developed by Knapp and Hartung.[57,58] This comparison was carried out separately for each outcome measure and for the pretest-posttest and the pretest–follow-up effect sizes. In addition, an adjusted average effect size was calculated for each outcome measure as $d_{adj} = d_T - d_C$, d_T, and d_C being the pooled standardized pretest-posttest mean changes in the treated and control groups,

respectively. The same formula was used to calculate the adjusted average effect size for pretest–follow-up effects. With this strategy, we were able to ameliorate the internal validity problems of pretest-posttest (pretest–follow-up) effect sizes by obtaining an average effect estimate that takes into account the average pretest-posttest (pretest–follow-up) change determined experimentally in the control groups. Sensitivity analyses were also carried out to examine whether including *d* indices for treatment and control groups from the same studies (ie, from RCTs) might be a dependence problem that threatens the validity of the results.

The clinical relevance of the adjusted average effect sizes was assessed by comparing them with the 25%, 50%, and 75% percentiles of the distribution of effect sizes obtained in a synthesis of 50 meta-analyses on the efficacy of psychological treatments.[59] In particular, these percentiles corresponded to *d* values of 0.25, 0.41, and 0.70, respectively, such that d_{adj} < 0.25 was considered practically irrelevant, d_{adj} values between 0.25 and 0.41 reflected mild clinical relevance, d_{adj} values between 0.41 and 0.70 reflected moderate relevance, and d_{adj} > 0.70 reflected large clinical relevance. These guidelines were considered more realistic than those of Cohen.[60]

Publication bias was examined by constructing funnel plots with Duval and Tweedie's trim-and-fill method and by applying Egger's test.[61] These analyses were performed on the effect sizes obtained from the treatment groups and separately for each outcome measure, provided it contained at least 10 effect sizes, as these techniques are not reliable with smaller data sets.

To assess the heterogeneity of the effect sizes, we calculated the *Q* statistic and the I^2 index. The search for moderator variables was accomplished for I^2 indices larger than 25%.[62] The influence of moderator variables was performed by assuming mixed-effects models and was conducted only for outcomes with at least 20 effect sizes. The *F* statistic developed by Knapp and Hartung[57,58] was applied to test the significance of the moderator variables. Q_W and Q_E statistics were computed to assess model misspecification for ANOVAs and meta-regressions, respectively. In addition, an estimate of the proportion of variance accounted for by the moderator variable (R^2) was calculated.[63] The statistical analyses were carried out with the statistical package metafor in R.[64]

3 | RESULTS

3.1 | Search results and study characteristics

The search strategy produced a total of 9063 references. Figure **S1** presents a *PRISMA flow diagram*[46] summarizing the complete screening and selection process of the studies. Forty articles met the selection criteria, 22 being RCTs and 18 being uncontrolled trials.[19-42,65-80] The 40 articles produced a total of 40 treatment groups and 21 control groups. Of those 40 treatment groups, 35 applied cognitive-behavioral interventions (87.5%), four performed interventions from a psychosocial or psychoeducational framework (10%), and one did not specify enough information to deduce the approach ascribed (2.5%).

Most of the studies were performed in the United States (18 studies, 43%), followed by Iceland (four studies, 9.5%), and Canada (three studies, 7%). The effect sizes and characteristics of each individual study included in the meta-analysis are shown in Appendix S1.

3.2 | Comparing pretest-posttest effect sizes from treatment and control groups

Forest plots of the effect sizes obtained in the treatment and control groups for each outcome measure are presented in Figures S2 to S9. Table 1 presents the average effect sizes (with 95% CIs) and I^2 indices for each outcome variable in the treatment and control groups. For anxiety measures, treatment groups showed a statistically significant average effect size (d_+ = 0.532), unlike control groups (d_+ = 0.193). In addition, the difference between these two average effect sizes was statistically significant, $F_{1,32}$ = 11.39, P = 0.002, with 29.3% of variance accounted for. To control potential overestimations of the pretest-posttest *d* indices for treatment groups, an adjusted mean

TABLE 1 Results of ANOVAs for pretest-posttest effect sizes according to the outcome variable

			95% CI		
Outcome Variable	***k***	d_+	d_l	d_u	I^2
Anxiety					
Treatment group	21	0.532	0.409	0.654	55.36
Control group	13	0.193	−0.000	0.387	68.99
Mood					
Treatment group	22	0.621	0.274	0.969	88.10
Control group	9	0.474	−0.309	1.256	95.71
Acute stress					
Treatment group	5	0.088	−0.222	0.399	53.15
Control group	4	0.098	−0.155	0.350	0.0
Post-traumatic stress					
Treatment group	12	0.453	0.328	0.578	48.87
Control group	9	0.229	0.082	0.377	68.26
Coping skills					
Treatment group	4	0.254	−0.044	0.552	0.0
Control group	2	0.131	−0.691	0.952	0.0
Social support					
Treatment group	12	0.142	−0.024	0.307	58.31
Control group	4	−0.103	−0.325	0.119	0.0
Problem-solving skills					
Treatment group	5	0.404	0.156	0.651	78.07
Control group	3	0.019	−0.334	0.372	61.63
Quality of life					
Treatment group	5	0.449	0.122	0.777	42.19
Control group	2	−0.089	−1.410	1.230	93.63

Abbreviations: 95%CI, 95% confidence interval for d_+; d_+, mean effect size; d_l and d_u = lower and upper confidence limits; I^2 = heterogeneity index (in %); *k*, number of studies for each category.

effect, d_{adj}, was computed as the difference between the mean effect of the treatment groups, d_T, and the mean effect of the control groups, d_C. Thus, an estimate of the true treatment effect for anxiety measures was $d_{adj} = d_T - d_C = 0.532 - 0.193 = 0.339$.

In mood state measures, treatment groups presented a statistically significant mean effect ($d_+ = 0.621$), whereas the average effect for control groups did not reach statistical significance ($d_+ = 0.474$). The difference between these two mean effects was not statistically significant, $F_{1,29} = 0.32$, $P = 0.576$, $R^2 = 0\%$. The adjusted mean effect for this outcome was $d_{adj} = 0.147$.

Regarding the remaining outcome measures, two exhibited statistically significant differences between the mean effects for the treatment and control groups, always in favor of the treatment groups. One was posttraumatic stress, $F_{1,19} = 6.63$, $P = 0.019$, $R^2 = 33.4\%$, with statistically significant average effects for both the treatment ($d_+ = 0.453$) and control ($d_+ = 0.229$) groups. The adjusted mean effect was $d_{adj} = 0.224$. The other outcome with statistically significant differences between the average effects of the treatment ($d_+ = 0.404$) and control ($d_+ = 0.019$) groups was problem-solving skills, $F_{1,6} = 8.76$, $P = 0.025$, $R^2 = 49.4\%$. The adjusted mean effect for this outcome was $d_{adj} = 0.385$. No statistically significant differences between the treatment and control groups were found for acute stress, $F_{1,7} = 0.12$, $P = 0.734$, $R^2 = 0\%$, $d_{adj} = -0.010$; coping skills, $F_{1,4} = 0.82$, $P = 0.416$, $R^2 = 0\%$, $d_{adj} = 0.123$; social support, $F_{1,14} = 2.44$, $P = 0.141$, $R^2 = 6.7\%$, $d_{adj} = 0.245$; or quality of life, $F_{1,5} = 2.32$, $P = 0.195$, $R^2 = 0.7\%$, $d_{adj} = 0.538$.

Because of the presence of dependence between the d indices obtained for the treatment and control groups from the same studies, sensitivity analyses were performed. The results, presented in Table S5, showed that this dependence did not affect the findings.

3.3 | Effect sizes from RCTs

Separate meta-analyses for each outcome were carried out with the standardized mean change indices obtained from the RCTs and excluding the uncontrolled trials. The corresponding forest plots are presented in Figures S14 to S20. Statistically significant pooled effect sizes were found for anxiety ($d_+ = 0.621$; 95% CI, 0.128-1.114), mood ($d_+ = 0.470$; 95% CI, 0.125-0.816), posttraumatic stress ($d_+ = 0.216$; 95% CI, 0.048-0.383), and problem-solving skills ($d_+ = 0.276$; 95% CI, 0.081-0.471). Nonsignificant pooled effects were found for acute stress ($d_+ = -0.046$; 95% CI, −0.199 to 0.107), coping skills ($d_+ = 0.759$; 95% CI, −1.584 to 3.102), and social support ($d_+ = 0.251$; 95% CI, −0.149 to 0.650). These results were similar to the adjusted d indices reported in the previous section.

3.4 | Comparing pretest–follow-up effect sizes from treatment and control groups

The follow-up periods had an average length of 4.84 ± 2.77 months (range 1.5-12). The average pretest–follow-up effect sizes for the treatment and control groups are presented in Table 2. No statistically significant differences between the average effects in the treatment and control groups were found for any of the outcome measures: anxiety, $F_{1,10} = 1.36$, $P = 0.270$, $R^2 = 0\%$, $d_{adj} = 0.263$; mood, $F_{1,20} = 0.15$, $P = 0.701$, $R^2 = 0\%$, $d_{adj} = 0.198$; posttraumatic stress, $F_{1,9} = 3.19$, $P = 0.108$, $R^2 = 31.8\%$, $d_{adj} = 0.208$; coping skills, $F_{1,2} = 0.003$, $P = 0.961$, $R^2 = 0\%$, $d_{adj} = -0.020$; social support, $F_{1,3} = 2.43$, $P = 0.217$, $R^2 = 0\%$, $d_{adj} = 0.590$; and problem-solving skills, $F_{1,5} = 4.36$, $P = 0.091$, $R^2 = 21.6\%$, $d_{adj} = 0.277$.

TABLE 2 Results of ANOVAs for pretest-follow-up effect sizes according to the outcome variable

			95% CI		
Outcome Variable	***k***	d_+	d_l	d_u	I^2
Anxiety					
Treatment group	7	0.454	0.126	0.783	75.89
Control group	5	0.191	−0.189	0.572	79.02
Mood					
Treatment group	13	0.817	0.135	1.499	92.67
Control group	9	0.619	−0.191	1.430	95.31
Post-traumatic stress					
Treatment group	6	0.560	0.379	0.740	76.24
Control group	5	0.352	0.162	0.543	36.02
Coping skills					
Treatment group	3	0.123	−0.752	0.999	60.24
Control group	1	0.143	−1.110	1.396	-
Social support					
Treatment group	3	0.377	−0.393	1.147	88.04
Control group	2	−0.213	−1.140	0.713	0.0
Problem-solving skills					
Treatment group	4	0.371	0.145	0.596	79.07
Control group	3	0.094	−0.160	0.349	69.14

Abbreviations: 95%CI, 95% confidence interval for d_+; d_+, mean effect size; d_l and d_u, lower and upper confidence limits; I^2 = heterogeneity index (in %); k, number of studies for each category.

3.5 | Publication bias

Egger's tests and the funnel-plot–based trim-and-fill method were applied to assess publication bias. These analyses were accomplished only for the treatment groups and for outcome measures with at least 10 pretest-posttest effect sizes, ie, anxiety, mood, posttraumatic stress, and social support. Funnel plots, Egger's tests, and the results of applying the trim-and-fill method are described in Figures S10 to S13. In summary, the pretest-posttest effect sizes of the treatment groups for anxiety, mood, posttraumatic stress, and social support showed evidence of publication bias.

3.6 | Assessing heterogeneity

In the treatment groups, pretest-posttest effect sizes exhibited moderate to large heterogeneity, with I^2 indices varying between 42.2% (for

quality of life) and 88.1% (for mood measures). The only exception was for coping skills measures, which yielded I^2 = 0%, but with only four effect sizes (Table 1). Pretest–follow-up effect sizes exhibited large heterogeneity, with I^2 indices ranging between 75.9% (for anxiety), and 92.7% (for mood measures; Table 2). These results led us to search for moderator variables that might be associated with the effect-size variability of the treatment groups. Analyses of moderator variables were performed only for outcome measures with at least 20 effect sizes, ie, on pretest-posttest effect sizes for anxiety and mood measures.

3.7 | Analysis of moderator variables

3.7.1 | Anxiety measures

One of the main objectives of this meta-analysis was to examine the differential effects of the various treatment techniques applied to family members of children and adolescents with cancer. Table **S1** presents the results of applying weighted ANOVAs for the analysis of categorical moderator variables.

The psychological techniques applied were cognitive in five studies, behavioral in two studies, another type of technique in one study (computer-mediated support group), and mixed techniques or multicomponent treatments in 13 studies. Studies applying behavioral techniques showed the highest average effect (d_+ = 1.262), followed by those using computer-mediated support groups (d_+ = 1.015), mixed or multicomponent regimens (d_+ = 0.484), and, finally, purely cognitive techniques (d_+ = 0.321). Therapist training showed a statistically significant association with effect sizes (P = 0.019), with training in psychology achieving the highest results (d_+ = 0.529). Moreover, interventions were significantly more effective (P = 0.023) if applied to parents when the child with cancer was receiving a medical procedure (d_+ = 0.826) than when the child was not (d_+ = 0.471). No relationship with effect size was found for any of the other categorical moderator variables (Table **S1**).

The results of simple meta-regressions applied on continuous moderator variables are presented in Table S2. Two moderators presented a statistically significant relationship with the effect sizes. One was the duration of treatment, which presented a positive relationship with the effect sizes (P = 0.042) and explained 65.7% of the variance, such that the highest effect sizes were associated with the longest treatments. Finally, the average age of the children with cancer showed a negative, statistically significant relationship (P = 0.026); therefore, the older the child, the lower the effect size. The remaining continuous variables showed no significant relationships with the effect sizes.

3.7.2 | Mood measures

The analysis of moderator variables for mood measures was carried out with 22 effect sizes from the treatment groups. Tables S3 and S4 present the results of ANOVAs and simple meta-regressions applied for categorical and continuous moderator variables, respectively. As shown in these tables, none of the 31 analyzed moderator variables exhibited a statistically significant relationship with effect size.

Despite not reaching statistical significance, the results of psychological techniques are worth mentioning. Three studies applied cognitive techniques (d_+ = 0.212), four applied problem-solving skills training (d_+ = 1.081), and two applied other techniques, specifically expression and emotional relief through writing and a support group (d_+ = 0.564).[65,66] Twelve studies applied mixed techniques or multicomponent treatments (d_+ = 0.520). Thus, problem-solving skills training showed the highest average effect, followed by other techniques, multicomponent treatments, and, finally, cognitive interventions.

4 | DISCUSSION

The overall aim of the present study was to analyze the empirical evidence regarding the effects of psychological treatments applied to parents and siblings of children and adolescents with cancer.

Given that treatment and control groups were available, the first analysis consisted of comparing the pretest-posttest mean change obtained in the treatment groups with that of the control groups for different outcome variables. For this purpose, an adjusted average effect size, d_{adj}, was calculated for each outcome measure to obtain an effect estimate of interventions on parents and siblings of the children with cancer. Regarding pretest-posttest changes, a statistically significant effect of mild magnitude was found for anxiety and problem-solving skills.[59]

These results allow us to conclude that psychological treatments were effective, although with only mild to moderate magnitude, in improving some symptoms and skills but not others. These results partially coincide with those found in the meta-analyses of Law et al.[44] In particular, the statistical significance revealed in our study for variables related to mental health was not found in these meta-analyses. However, the meta-analysis of Pai et al[43] found improvement, although of medium-low magnitude, in parental distress, including measures of depression, anxiety, and posttraumatic stress symptoms, thus coinciding with the data obtained in our investigation.

Our study confirms the results found in previous systematic reviews: we cannot conclude that there was a significant improvement in all variables involved, since interventions achieved total efficacy in some studies, partial in others and, in some, no effects at all, although this last group constituted a minority. Specifically, the first review on interventions with siblings[49] indicated improvement in depression symptoms and psychological adjustment, but not in anxiety, self-esteem, or behavioral problems. Other reviews[47,48] found that most treatments brought improvements in some variables (anxiety and emotional distress), but with low-magnitude effect sizes. In a review by Wechsler et al,[52] most interventions applied to parents were useful in improving their psychological adjustment (45% of interventions achieved improvement in all variables and 22% in some variables, while the remaining 33% did not achieve any positive effect). Robb and Hanson-Abromeit[50] focused more on the description of the programs than on their results, although they noted that slightly more than half of interventions (60%) caused positive effects in subjects. The most recent review[51] focused on psychoeducational interventions, finding that these improved

knowledge regarding the disease and the locus of health control, while results for other variables such as anxiety, depression symptoms, well-being and self-efficacy were less consistent.

As for comparison between the pretest and the final follow-up in the study, a decrease in the benefits of the interventions was observed in most of the outcome measures and did not reach statistical significance. Although the absence of statistical significance may be because of the scarce number of studies that reported follow-up data, the decrease in the intervention benefits was evident.

The second goal was to examine the presence of possible moderator variables related to participants, interventions, and methodologies used in the studies. The results are presented separately for each outcome measure.

4.1 | Anxiety

Statistically significant differences were found among the psychological techniques applied, with the behavioral techniques achieving the largest effect sizes. In particular, the behavioral techniques used were attentional distraction and positive reinforcement.[26,27] An intervention based on a computer-mediated support group also showed a large effect.[65] The duration of treatment also presented a positive relationship with the effect sizes, with the highest effect sizes being associated with the longest treatments. This result can be explained based on two variables: the duration of the health problem and the consolidation of what has been learned. Parents are faced with a lasting problem and must possess resources to confront all situations that cause anxiety and distress. Extensive training will allow parents to consolidate what has been learned and resolve new situations that may arise.

The professional training of therapists showed a statistically significant relationship with the effect sizes. The average effect was greater when treatments were applied by psychologists than when they were applied by mixed teams with different professionals. Perhaps this is because psychologists are the most qualified professionals to apply this type of therapy.

Regarding participant characteristics, a statistically significant relationship with effect sizes was found for the mean age of the children with cancer, such that studies applying interventions to family members of older children exhibited smaller effect sizes than those for family members of younger children. This may be because in the case of younger children with cancer, relatives feel obliged to improve their own mental health to focus on and meet the needs of the child, paying less heed to themselves. In addition, improved effect sizes were found when the intervention was applied to family members of children who were receiving a medical treatment. This may be because parents continue to maintain an expectation of improvement for children under intervention and focus on the children's well-being, not on themselves.

4.2 | Mood

Despite the large number of moderator variables analyzed, none of them reached a statistically significant relationship with effect size. However, it is worth noting that interventions based on problem-solving skills seem to be the most promising compared with other cognitive and mixed techniques used to improve mood.

4.2.1 | Clinical implications

Our results have clear implications for clinical practice with family members of children with cancer. First, it is important to intervene with parents and siblings of sick children to reduce emotional distress and psychological disorders caused by the situation they are facing, since the improvements in the recipients, although low, are greater than those in the control groups. Intervention is more effective in earlier than later stages. We recommend the application of techniques from the cognitive-behavioral theoretical framework, either separately or in multicomponent regimens integrating some of the main strategies: cognitive techniques, behavioral techniques, and problem-solving skills training.[9] Second, to evaluate treatment efficacy, it would be necessary to use standardized evaluation instruments rather than those developed ad hoc, since great variability among these instruments has been found in this field, with more than 70 different instruments being used. This can hinder the integration of results. Finally, the intervention benefits declined in the follow-up, such that some new intervention should be applied approximately 3 months after the initial intervention.

4.3 | Study limitations

Some limitations of the current meta-analysis should be mentioned. First, the inclusion of studies without control groups forced us to use an effect size index with low internal validity, restricting the scope of the results. In the balance between internal validity and comprehensiveness, we decided to be as inclusive as possible, not excluding studies that applied any psychological intervention to family members of children with cancer. To ameliorate the problems of internal validity in one-group pretest-posttest (and follow-up) effect sizes, we applied an adjusted average effect size comparing the mean pretest-posttest (follow-up) effect sizes of the treatment and control groups. Second, the small number of studies reporting data for some outcome measures did not allow us to accomplish analyses of moderator variables. Third, our results showed the existence of potential publication bias in the average treatment effects of most outcome measures, necessitating cautious interpretation of the results. Fourth, the wide variety of psychological techniques applied in the studies and the diverse nature of the participants who received the treatments (ie, parents, siblings, and patients) made it impossible to examine in greater depth the efficacy of specific treatment techniques for different family members.

4.4 | Future research

Future research should include control groups in all studies carried out, since the results obtained could be more generalized and achieve greater internal validity than those of the current study. Regarding

treatments, it would be interesting to evaluate the differential efficacy of the different protocols or multicomponent treatments and separate them to identify the specific treatment techniques that offer the best benefits to different family members. Researchers need to improve the methodological quality of studies to avoid confounding effects due to methodological flaws. On the other hand, given the variety of evaluation instruments, researchers should develop new instruments that are sufficiently valid and sensitive to treatments and whose reliability and validity have been established with large samples. Moreover, we consider it important to perform additional studies focused on siblings of children with cancer, as studies centered on this population accounted for only 19.7% of the total (12 of the 61 included groups). Finally, it is necessary to carry out research involving more fathers, since some studies (five in total) included only mothers in their samples.

CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest.

ENDNOTES

*The items comprising the methodological quality scale were as follows: (1) random versus non-random assignment of participants to the groups; (2) type of control group (active control, inactive control, or no control group); (3) sample size in the posttest; (4) one minus posttest attrition in the treatment group; and (5) the use of intent-to-treat analysis. Each item was rated from 0 to 1.

†Both documents can be obtained from the corresponding author upon request.

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