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Home-based cognitive behavioural therapy for families of young children with cancer (FAMOS): a nationwide randomised controlled trial

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Short title: Therapy for families of young children with cancer

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Abbreviations and acronyms

CI	confidence interval
FAMOS	FAMILY-Oriented Support
PTSD	post-traumatic stress disorder
RCT	randomised controlled trial
SSCIP	Surviving Cancer Competently Intervention Program
SSCIP-ND	SSCIP Newly Diagnosed

Abstract

Introduction: Evidence-based knowledge is needed to reduce psychological symptoms in families of young children with cancer after treatment ends.

Objective: To evaluate the effect of a psychotherapeutic intervention, FAMily-Oriented Support (FAMOS) on parents of young children after cancer treatment.

Methods: All families of children aged 0–6 years who had been treated for cancer at one of the four paediatric oncology departments in Denmark were invited to participate after ending intensive medical treatment. The families were randomly assigned 1:1 to up to six sessions of FAMOS, a cognitive–behavioural manualised home intervention, for 6 months or to usual psychosocial care. The primary outcome was parents’ symptoms of post-traumatic stress disorder (PTSD) at 6 and 12 months after enrolment. The secondary outcomes were parents’ symptoms of depression and anxiety.

Results: We enrolled 109 families (204 parents). Parents in the intervention group did not show a statistically significant decrease in symptoms of PTSD as compared with the control group at 6 months (predicted mean difference, -0.10 ; 95% CI -0.19 ; 0.01), but a statistically significant decrease was seen at 12 months (predicted mean difference, -0.15 ; 95% CI -0.28 ; -0.02), and they had significantly lower symptoms of depression at both 6 and 12 months. Differences in reductions in symptoms of anxiety were not statistically significant.

Conclusions: The FAMOS intervention reduced parents’ symptoms of PTSD and depression. A next step is to also report on psychological effects in the children and siblings. (clinicaltrials.gov: NCT02200731).

Introduction

Cancer in a child can be a trigger for psychological reactions in the family^{1,2,3,4}, which has been termed pediatric medical traumatic stress⁵. Parents in particular often experience post-traumatic stress symptoms or may meet criteria for a diagnosis of Post-Traumatic Stress Disorder (PTSD) (e.g. fear, re-experiencing, avoidance and physiological arousal)⁶. Depression and anxiety⁷ may also develop throughout the disease trajectory and in a family context⁸. Indeed, sub-groups of children with cancer¹ and their siblings^{9,10} have also been shown to experience cancer-related adjustment difficulties and for some traumatic stress symptoms. Post-traumatic stress symptoms, especially re-experiencing and avoidance, are especially found in siblings of children with cancer⁹.

For some families, psychological distress decreases with time, while others may experience long-term difficulties. The time after ending medical treatment may be one of particular vulnerability as families have to adjust to life after cancer without the structure and support from the hospital clinic^{4,11,12}.

There are a few randomized controlled trials (RCT) of psychosocial interventions for parents of children with cancer either *during* or *after* the end of treatment. We identified three for parents *during treatment*,^{13,14,15} only one of which found a significant effect on symptoms of PTSD, depression and anxiety in mothers three months after diagnosis¹⁵. Additionally, a systematic review of intervention studies revealed nine studies of childhood cancer survivors and their parents *after completion of treatment*¹⁶. However, only one study was in RCT design: The Surviving Cancer Competently Intervention Program (SCCIP), a 1-day cognitive behavioural and family systems intervention that utilizes a multiple family discussion group model examined the effect of the

intervention on adolescents (> 11 years) with cancer, siblings and their parents (N=150) up to 12 years after treatment¹⁷. This is the only intervention to include siblings¹⁷. The intervention had a marginal effect on intrusive thoughts (a PTSD dimension) in fathers, but not mothers and no effect on anxiety. Few studies have addressed young children with cancer aged < 5 years, even though although almost half of all childhood cancers occur in this group¹⁸ and parents of the young children may have special concerns e.g. related to how to communicate with the young child about the disease.

Rationale for a family-focused cognitive-behavioural intervention

Parents' thoughts related to the child's cancer may not always be helpful and realistic, which may amplify negative emotions. This may be modifiable through cognitive behavioural therapy (linking thoughts, feelings and consequences)¹⁹ where parents may e.g. be encouraged to identify and reframe thoughts. Parents' experiences of feeling alone in the situation may be addressed through psychoeducation to help normalise emotions¹⁹ whereas a focus on goal setting and problem solving may improve feelings of empowerment and self-efficacy²⁰. When faced with the same stressful situations, individual family members may have different psychological reactions²¹ and these reactions take place in a family system, where family members affect one another²².

Misunderstandings and conflicts may arise if the individual family member expects the others to react in synchrony with their own reactions²³. Communication and understanding between parents may be addressed in a family-oriented intervention^{22,24,25}. The timing of the intervention is important, and providing therapy after treatment may target families when they leave hospital support and when they are processing how cancer has affected their everyday life.

Proposed theoretical framework

We developed the FAMOS intervention, targeting psychological symptoms in the whole family after the end of childhood cancer treatment²⁶. The intervention includes promising components of problem-solving from a previous study¹⁵ but was inspired mainly by SCCIP²³ and SCCIP Newly Diagnosed (SCCIP-ND)¹⁴. SCCIP-ND is a 3-session intervention for caregivers and includes a video family discussion group. The FAMOS techniques are based on cognitive behavioural therapy including components to normalise cancer-related thoughts, goal-setting and problem-solving techniques that have been shown effective for targeting PTSD, depression and anxiety²⁷ as well as on family system therapy including techniques that have been shown effective in addressing communication about cancer in the family (Fig. 1)²³. We hypothesised that a family-oriented intervention would reduce psychological symptoms in the whole family. In this study, we report the effect of the intervention on cancer-related PTSD, depression and anxiety in parents at 6 and 12 months of follow-up.

Method

Study design and participants

The FAMOS study was a nationwide RCT with two arms, conducted with all four paediatric oncology departments in Denmark (University Hospital Rigshospitalet, Aarhus University Hospital, Odense University Hospital and Aalborg University Hospital). The study design and feasibility have been described previously²⁶. In Denmark, approximately 185 children below age 18 years are diagnosed

with cancer each year²⁸ of which approximately half are below 6 years of age¹⁸. Because of a concurrent study, we could not include the families of school-aged children (6–18 years) with cancer. A nurse from each of the four paediatric oncology departments screened potentially eligible single- and two-parent families of children aged 0–6 years with any cancer who had received treatment at the department. Further eligibility criteria were: curative intensive treatment completed within 4 months (children with leukaemia could enter when receiving maintenance chemotherapy), at least one parent who spoke Danish well enough to understand the questionnaires, siblings of all ages could participate, and the family was living in Denmark. Between August 2014 and March 2018, a total of 171 eligible families expressed interest in the study.

Randomisation

Families providing informed written consent were randomised to the intervention or usual care by computer-generated randomisation (1:1) stratified to ensure equal distribution by cancer type (leukaemia and lymphoma, central nervous system tumours, and other) and hospital with varying block size, blinded to the project manager and nurses. Allocation could not be blinded, as a behavioural intervention was being tested.

Procedures

The FAMOS intervention includes several techniques inspired by SCCIP (“Adversity, Belief and Consequence” model, the “family survival roadmap”, “4 steps to reframing” and “Unwanted guest”) that were further developed to specifically accommodate the whole

family including siblings and age-appropriate techniques for the younger children (Fig. 1)²⁶.

Techniques were applied that address psychological symptoms in the individual as well as in the family e.g.:

- Using the ABC (Adversity, Belief and Consequence) model, a parent struggling with hypervigilance may e.g. learn new strategies to recognize a fear-inducing situation and how to restructure their thoughts in order to manage the situation without fear.
- Using the “Family’s road through cancer”, family members are asked where they see themselves in the cancer journey. They learn how to communicate with each other about their individual beliefs, to accept un-synchronous psychological reactions and this may enable support within the family system²¹.
- Problem-solving techniques were added as they have been found effective for relieving psychological symptoms (PTSD, depression and anxiety) in mothers of children with cancer¹⁵.

Psychological reactions to cancer vary by children’s developmental stage. Although most children aged < 9 years do not fully understand the concept of mortality, even very young children may sense tension in their family and express their reactions, mainly in bodily reactions, unease, hyperactivity and anger²⁹. The developmental stage was taken into account by adapting the techniques to siblings aged 6–12 and 13–18 years, e.g. by asking about their thoughts and feelings while adjusting the information and use of tools to their responses. Parents of children < 6 years were provided

psychoeducation on normal reactions of children to trauma and on communicating with their child about the reactions.

The intervention comprised up to seven face-to-face 1–1.5-h sessions at home within 6 months of inclusion: an introductory session for the entire family, three sessions for parents, two sessions for siblings aged ≥ 7 years or one for parents with younger childhood cancer survivors and siblings and a session for the whole family. At least three sessions were required for the intervention to be considered completed. As the children with cancer in the study were too young to participate in sessions on their own, only siblings > 6 years were invited to do so. Families completed the intervention within 6 months and received the 6 month follow-up questionnaires shortly after completion. Families whose child had a relapse or died were offered continuation of the sessions.

The FAMOS intervention is described in a manual with a suggested script for each session's goal, content and techniques (Fig. 1). The intervention was delivered face-to-face at home by one of three psychologists with experience in cognitive behavioural therapy. Adherence to the intervention and consistency among the psychologists was ensured by initial 2-day and continuing training in use of the manual and regular 2-h group supervision with an independent cognitive behavioural therapist and the project coordinator. The families in the control group received usual psychosocial care, which during the study period was diverse and consisted of outpatient medical follow-up and management of late effects. During the study period, only two of the four paediatric oncology departments had a psychologist on staff, who offered a 1-h session during treatment as well as at relapse or death, but not after end of treatment. Families in both groups were free to seek professional psychological support elsewhere.

Outcome measures

Parents completed questionnaires at baseline and 6 and 12 months after randomisation. PTSD was assessed with a 17-item childhood Harvard trauma questionnaire,³⁰ which has been validated in Danish³¹ and used for women with cancer³². We adapted the questionnaire to assess “cancer trauma” rather than “a traumatic event”. The questionnaire comprises a total score (suggested cut-off for PTSD, 2.5³¹) and three sub-scales corresponding to PTSD dimensions (intrusion, avoidance and hypervigilance).³⁰ The secondary outcomes, symptoms of anxiety (10 items) and depression (13 items), were measured on subscales of the Symptom Checklist-92-Revised³³. Gender-corrected cut-off scores were used for anxiety (1.15 for mothers and 0.94 for fathers) and depression (1.60 for mothers and 1.29 for fathers).

Statistical analyses

The sample size was planned to be 300 families and which would allow detection of a small-to-medium effect on symptoms of PTSD (Cohen $d=0.32$)³⁴. To accommodate a concurrent trial, we reduced the number to 100 families and 185 parents, an assumed power of 80% and a significance of 5%, which we estimated would allow detection of a medium effect (Cohen $d = 0.42$) and was considered acceptable. The final sample comprised 109 families and 204 parents (Fig. 2).

Descriptive analyses were used to compare the baseline characteristics of the intervention and control groups. Mean change scores were calculated for symptoms of PTSD, depression and anxiety by time (baseline and 6- and 12-month follow-up) and intervention group from the numbers and

percentages of parents who scored above predefined cut-off values. To investigate the effects of the intervention at 6 and 12 months, we fitted linear mixed-effects models for baseline and 6 and 12 months, assuming no difference between the intervention and control groups at baseline but allowing different effects of the intervention at 6 and 12 months. Two covariance structures were considered for each outcome: a random subject and family effect or a random family effect with unstructured covariance for subjects. The model that showed the smallest Akaike information criterion was considered to have the best fit and was used initially. To account for potential residual confounding, parents' gender and child's cancer diagnosis were included as covariates in a second model. Finally, to explore potential differences in effect according to mothers versus fathers, we added parent gender as an interaction term to the model. Underlying model assumptions were evaluated by visual inspection of residual plots. Intention-to-treat analyses were performed. Estimates were presented with 95% confidence intervals (CIs); and the size of the intervention effect (Cohen d) was estimated from the standard deviation of the control group at baseline³⁵.

In secondary analyses, we examined the effect of the intervention on three PTSD symptom dimensions, intrusion, avoidance and hypervigilance. Logistic regression models were fitted, the correlation being taken into account with two random effects (subject and family) to examine the parents' odds of exceeding the cut-off scores for symptoms of PTSD, depression and anxiety³⁶ with the same covariates as in the linear mixed models. We used cut-off scores and a covariance structure similar to those in the main analyses to determine whether the intervention effect was stronger in parents with high or low symptom scores at baseline. Differences between parents who did and who did not attend the 12-month follow-up were analysed descriptively according to treatment hospital, cancer type and the age and sex of the child with cancer. Finally, we conducted

sensitivity analyses of the three outcomes with two forms of multiple imputation. On the assumption that data were missing at random, we used fully conditional specification methods to impute missing values for the outcome of interest (at baseline, 6 and 12 months, with values for the same person imputed together) by intervention group, education (elementary or high school, ≤ 9 years; short, 12 years; medium, 12–13 years; and long (> 13 years) education), marital status (which was associated with missing data in the outcome) and including the two other outcomes as auxiliary variables³⁷. Secondly, to model the situation in which parents' missing data were associated with their levels of PTSD, depression and anxiety symptoms, we shifted all imputed data upwards by a value from a normal distribution with mean 0.1 (about one sixth of a standard deviation) and variance 0.005, corresponding to higher symptom scores for parents with missing data. The analyses were conducted in SAS version 9.4.

Results

A total of 204 parents (109 mothers and 95 fathers) in 109 families (64% of those invited) consented and were randomised (Fig. 2). Three families experienced relapse or death of a child. All parents continued in the study, 161 (79%) provided a 6-month follow-up assessment (82 in the intervention and 79 in the control group), and 109 (53%) parents provided a 12-month assessment (62 in the intervention and 47 in the control group). Families received an average of 5.5 sessions. Three families who received less than three sessions due to relapse or death of a child remained in the analyses.

Descriptive characteristics

The intervention and control groups were comparable in terms of demographic characteristics: the mean age was 36.5 years, 53% were mothers, 90% cohabited, 7% were single and 3% were divorced (Table 1). Mean age of the children was 4 years (range, 0–6 years); 50% had been treated for leukaemia or lymphoma, 15% for a central nervous system tumour and 35% for other cancers; mean time since diagnosis was 1.26 years, and mean time since the end of treatment was 3.4 months. Demographic characteristics of the parents did not differ between baseline and follow-up, suggesting that missing data were distributed randomly during follow-up (data not shown). At baseline, parents in the control group had slightly higher scores for symptoms of PTSD, depression and anxiety (Table 2). The observed mean scores for symptoms at 6 and 12 months of follow-up were lower than those at baseline in both groups.

Effects of the intervention

Scores for symptoms of PTSD at 6 months were not significantly different in parents in the intervention and control groups (predicted mean difference, -0.10 ; 95% CI -0.21 ; 0.01 ; Cohen d , -0.18), but large significant decreases were seen at 12 months (predicted mean difference, -0.15 ; 95% CI -0.28 ; -0.02 ; Cohen d , -0.28) (Table 3), and parents in the intervention group had larger decreases in symptoms of depression at both 6 and 12 months than the control group (predicted mean difference, -0.16 ; 95% CI -0.30 ; -0.03 ; Cohen d , -0.20 and -0.15 ; 95% CI -0.30 ; -0.00 ; -0.18 , respectively). Reductions were also seen in symptoms of anxiety at 6 and 12 months, but the effects did not reach statistical significance. Similar results were observed in models further adjusted for

gender and cancer diagnosis. We did see slightly higher effect effects for mothers compared to fathers, however the differences were not statistically significant (results not shown).

In secondary analyses, we found that significant effects on symptoms of PTSD were mainly accounted for by hypervigilance (Table 3). We found no significant difference between the groups in dichotomised scores for symptoms of PTSD, depression and anxiety (Table 4). The effect on symptoms of PTSD and depression appeared to be stronger for parents with higher baseline scores, while an opposite tendency was seen for symptoms of anxiety; however, the differences were not significant (Supplementary appendix 1). Only small non-significant differences were seen between participants and non-participants in terms of treatment hospital, diagnosis, gender and age of the child with cancer. Attrition in terms of non-submission of the questionnaire was greatest at 12 months' follow-up, and in families in the control group (Figure 2). Sensitivity analyses with multiple imputations and assuming random missing data gave results similar to those with the main model, although the estimates for all outcomes were slightly closer to zero (Supplementary appendix 2). In sensitivity analyses based on the assumption that data were not missing at random, the intervention had a similar but stronger effect for all outcomes (Supplementary appendix 2).

Discussion

The study shows that a home-based psychotherapeutic intervention for families of young children with cancer can improve parents' symptoms of PTSD and depression. A significantly larger decrease in symptoms of PTSD was seen with the intervention at 12 months and in symptoms of depression at 6 and 12 months. Reductions in symptoms of anxiety at 6 and 12 months were not significant. The

finding that the effect of the intervention on symptoms of PTSD was stronger and significant only after 12 months' follow-up may suggest that the effect increases when the intervention techniques have been internalized and used as needed. The techniques taught during the programme may be used mainly at the time of stressful events or developmental milestones in family life, such as starting school or the birth of a new baby; however, we were unable to explore the mechanisms.

Our results add substantially to those of the four previous RCTs^{13-15,17} where only two studies found significant intervention effects^{38 17}. The FAMOS intervention differs from those used in the previous studies in the combination of: (i) targeting the whole family, which may help each member to understand the others' perceptions of life after cancer; (ii) offering the intervention at home, where families are in a secure environment that may make it easier to have difficult discussions and practice new skills; and (iii) offering the intervention immediately after the end of treatment, which is a vulnerable time, as families no longer have access to support in a hospital and a time where medical treatment is no longer the main focus³⁹. Further studies are needed, however, to explore the mechanisms of psychological change with interventions such as the FAMOS programme.

Symptoms of PTSD and depression in parents of children with cancer may include nightmares, avoidance, continuous feelings of fear, anger or guilt (such as feeling responsible for the child having had cancer), fatigue, insomnia and lack of interest in normal activities⁴⁰ and may greatly impact family life. Parents may be at long-term risk of initiating psychotropic medication⁴¹, taking prolonged sick leave⁴² or incurring financial difficulties^{43,44}. We found small-to-moderate reductions in symptoms of PTSD and depression, which are comparable with reductions found in previous

studies of psychosocial interventions for families of young children with cancer⁴⁵. Families in the control group may have sought psychological support independently limiting the between group differences, still, the FAMOS intervention could be further developed, including more powerful techniques to address e.g. fear-inducing situations related to the child's cancer. The FAMOS intervention may nevertheless help parents to readjust to normal life and provide them with skills to help their children cope with life after cancer⁴⁶.

This study has several strengths. We had a participation rate of 64%, which is higher than those in previous studies^{14,15,17} and suggests that the intervention is relevant to a large proportion of affected families. Both parents participated in almost 90% of the families included, which may have contributed support for the functioning of the couple and the family. Our results showed no significant difference in how parents benefited from the intervention, whereas most previous studies included only mothers¹⁵. Our feasibility study showed that 75% of the families in the intervention group were satisfied with the intervention content and found it useful for the whole family²⁶. The intervention manual ensured continuity in the format and therapeutic approach, which may have improved adherence, equality of treatment and internal validity⁴⁷. Participation by all four paediatric oncology departments in Denmark meant that virtually all eligible families in the country were invited, thus improving the generalisability of the results. Relatively high proportions of parents had severe symptoms of PTSD (27%), depression (25%) and anxiety (24%) at baseline and families in both the intervention and control groups were not restricted from using other professional psychological support. Despite limited data, we found that a large proportion (82% of parents from the intervention group and 70% from the control group) of parents across study groups had received psychological support either from the oncology department or from private practices.

This suggests that our results may be generalizable in particular to families with severe symptoms and to families already receiving some degree of support.

We had limited information on the non-participants, and, although we observed no differences in terms of treatment hospital, cancer diagnosis or the age and gender of the child, we cannot exclude selection bias. Our study was limited by attrition regarding the 12-month follow-up questionnaire. The sensitivity analyses with imputation models assuming that data were missing at random indicated that the estimates were slightly closer to zero; however, when we assumed that parents for whom data were missing were more likely to have a higher symptom score, we found a stronger effect of the intervention, perhaps because more data were missing for the control group. Finally, the study was limited by only being able to invite families of young children. Future studies should be conducted to confirm the effect in families of older children, in which different developmental and parent-child communication issues may be present. As a next step, we plan to also analyse the impact of the intervention on the children with cancer and their siblings.

Conclusion

The FAMOS intervention showed benefits over treatment as usual in reducing parents' symptoms of PTSD at 12 months and in symptoms of depression at both 6 and 12 months while reductions in anxiety were not significant. Alleviating the symptoms of PTSD and depression in the parents of children who have had cancer may be important in enhancing family quality of life. Our results are highly relevant for support services, such as providing parent- and family-oriented interventions to

address mental health needs^{48,49}. The effects we observed were small to moderate, and future research should explore further refinement of the intervention as well as an online version for more flexibility.

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Statement of ethics

Participating families (parents on behalf of the children) provided informed written consent. The study protocol was approved by the National Committee for Health Research Ethics in Denmark (reference no: H-1-2013-073), and the study was registered at clinicaltrials.gov (reference no.: NCT02200731).

Disclosure statement

The authors have no conflicts of interest to declare.

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Author contributions

The authors contributed as follows: Hanin Salem: study design, data collection, interpretation of results, drafting, revising and final approval of the paper; Anne E. Kazak: study design, interpretation of results, revising and final approval of the paper; Elisabeth Wreford Andersen: statistical analyses, interpretation of results, revising and final approval of the paper; Federica Belmonte: statistical analyses, interpretation of results, revising and final approval of the paper; Christoffer Johansen: study design, interpretation of results, revising and final approval of the paper; Kjeld Schmiegelow: study design, interpretation of results, revising and final approval of the paper; Jeanette Falck Winther: study design, interpretation of results, revising and final approval of the paper; Peder Skov Wehner: study design, interpretation of results, revising and final approval of the paper; Henrik Hasle: study design, interpretation of results, revising and final approval of the paper; Steen Rosthøj: study design, interpretation of results, revising and final approval of the paper; Pernille E. Bidstrup: study design, data collection, interpretation of results, revising and final approval of the paper.

Availability of data

According to the Danish legislation, data sharing is not available due to privacy or ethical restrictions, data is as presented in this paper. However, collaboration with other researchers using these data are welcomed. The study material can be analyzed according to collaborative study protocols at the Danish Cancer Society Research Center in Copenhagen, Denmark.

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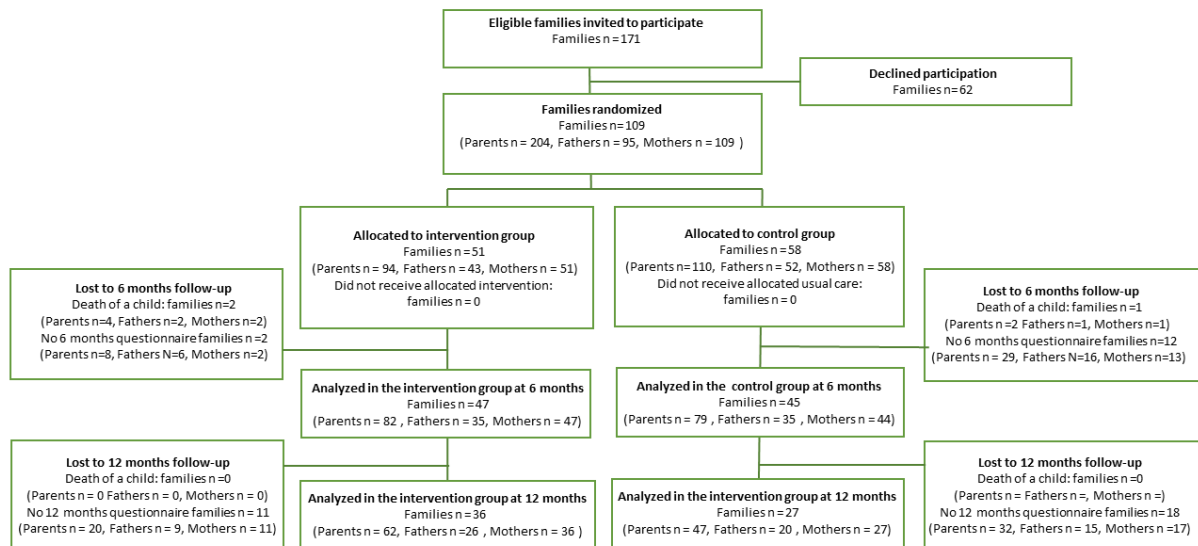
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Legends to figures

Fig. 1. FAMOS session content, goal and technique

Session	Goal	Technique
Introduction	<ul style="list-style-type: none"> Set the FAMOS programme agenda. Review the family's history and experience at diagnosis. Establish goals for the whole programme. 	
Session one: How cancer has affected us as parents and as a family	<ul style="list-style-type: none"> Normalise and reduce cancer-related psychological symptoms. Help parents to identify cancer-related thoughts and behaviour. Strengthen communication between parents, parent and partner or parent and child(ren). 	<ul style="list-style-type: none"> Video 1 ABC model Family's road through cancer
Session two: How we coped with cancer	<ul style="list-style-type: none"> Introduce ways to cope in difficult situations. Learn how to adjust to life after cancer. 	<ul style="list-style-type: none"> Video 2 How situations and thoughts can have different outcomes
Session three: The family's future	<ul style="list-style-type: none"> Understand the association between individual beliefs and family's future. Strengthen family functioning and quality of life. 	<ul style="list-style-type: none"> Video 3 4 steps to reframing family's future Goal-setting techniques Problem-solving techniques
Session four: Children's session: the family before, during and after cancer	<ul style="list-style-type: none"> Normalise children's cancer-related thoughts. Teach the family how cancer can affect each individual in a family differently. 	<ul style="list-style-type: none"> 'Cancer – the unwanted guest' Sky illustration ABC model 'Things I want to change' 'Things I want to throw away' Family road through cancer
Session five: Children's session: how to move on	<ul style="list-style-type: none"> Teach the family how to cope with difficult situations. Strengthen communication between parents and children. 	ABC model and one technique: <ul style="list-style-type: none"> Problem-solving Goal-setting Psychoeducation Registering and identifying feelings chart
Booster: What have we learnt?	<ul style="list-style-type: none"> Summarise the main goals of the intervention. Plan how to continue using the techniques at home. 	<ul style="list-style-type: none"> ABC model 4 steps to reframing Family's road through cancer

Fig. 2. CONSORT diagram of 204 parents (n = 109 families) of children with cancer in the FAMOS study



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Tables

Table 1. Baseline characteristics of 204 parents of children with cancer in the FAMOS study (N = 109 families: 109 mothers and 95 fathers).

		Intervention	Control
		94 parents	110 parents
Parent age at baseline (mean (SD))		37 (6)	36 (5)
Parent role N (%)	Mother	51 (54)	58 (53)
	Father	43 (46)	52 (47)
Marital status N (%)	Single/separated	8 (8)	12 (11)
	Married/cohabiting	86 (92)	96 (88)
	Other	0 (0)	1 (1)
	Unknown	0 (0)	1 (1)
Parent education N (%)	Elementary/high school	10 (10)	11 (10)
	Short	29 (31)	30 (27)
	Medium	24 (26)	39 (36)
	Long	28 (30)	30 (27)
	Unknown	3 (3)	0 (0)
Employment status N (%)	Full time	72 (78)	81 (74)
	Part time	14 (15)	10 (9)
	Other	7 (7)	19 (18)
	Unknown	1 (1)	0 (0)
Child age at baseline (mean (SD))		4.6 (2)	3.6 (3)
Child gender N (%)	Male	28 (56)	37 (65)
	Female	22 (44)	20 (35)
Child diagnosis N (%)	Leukaemia/lymphoma	27 (53)	28 (48)
	CNS	6 (12)	10 (17)
	Other	18 (35)	20 (36)
Siblings N (%)	0	20 (39)	29 (50)
	1	23 (45)	21 (36)
	2	5 (10)	6 (10)
	≥ 3	3 (6)	2 (4)
Years since diagnosis (mean (SD))		1.3 (0.8)	1.2 (0.8)
Years since end of treatment (mean (SD))		0.3 (0.3)	0.3 (0.3)

*Elementary/high school (up to 9 years), short (12 years), medium (12-13 years) and long education (more than 13 years)

*Percentages may not add up to 100 because of rounding

SD: Standard deviation

Table 2: Number of affected parents who scored above the cut-offs and mean scores on post-traumatic stress, depression and anxiety at baseline, 6 and 12-month follow-up and change from baseline in 204 parents of children with cancer in the FAMOS study.

	Intervention			Control		
	N Total ^a	N affected (%)	Mean(SD) ^b	N Total ^a	N affected (%)	Mean(SD) ^b
Post-traumatic stress						
Baseline	93	21 (23)	1.98 (0.50)	109	34 (31)	2.08 (0.54)
6 months follow-up	82	12 (15)	1.81 (0.49)	79	16 (20)	1.98 (0.54)
Change baseline to 6 months			-0.11 (0.31)			-0.03 (0.38)
12 months follow-up	62	6 (10)	1.81 (0.50)	47	9 (19)	1.94 (0.56)
Change baseline to 12 months			-0.22 (0.39)			-0.05 (0.42)
Depression						
Baseline	82	21 (26)	0.94 (0.72)	98	30 (31)	1.13 (0.81)
6 months follow-up	74	1 (1)	0.33 (0.42)	75	5 (7)	0.55 (0.52)
Change baseline to 6 months			-0.54 (0.57)			-0.43 (0.56)
12 months follow-up	56	2 (4)	0.36 (0.43)	41	2 (5)	0.48 (0.52)
Change baseline to 12 months			-0.59 (0.59)			-0.51 (0.57)
Anxiety						
Baseline	81	18 (22)	0.64 (0.53)	97	32 (33)	0.83 (0.67)
6 months follow-up	74	9 (12)	0.43 (0.55)	75	18 (24)	0.72 (0.68)
Change baseline to 6 months			-0.14 (0.46)			-0.04 (0.60)
12 months follow-up	56	6 (11)	0.47 (0.56)	41	7 (17)	0.63 (0.67)
Change baseline to 12 months			-0.16 (0.46)			-0.11 (0.63)
Post-traumatic stress subscales						
Intrusion^c						
Baseline	93		2.02 (0.51)	105		2.13 (0.61)
6 months follow-up	82		1.90 (0.60)	79		2.06 (0.63)
Change baseline to 6 months			-0.09 (0.47)			-0.00 (0.50)
12 months follow-up	62		1.90 (0.57)	46		1.97 (0.60)
Change baseline to 12 months			-0.18 (0.55)			-0.05 (0.54)
Avoidance^c						
Baseline	93		1.72 (0.54)	109		1.87 (0.62)

6 months follow-up	82	1.58 (0.48)	79	1.75 (0.58)
Change baseline to 6 months		-0.08 (0.35)		-0.02 (0.48)
12 months follow-up	62	1.63 (0.48)	47	1.73 (0.63)
Change baseline to 12 months		-0.11 (0.39)		0.00 (0.57)
Hypervigilance^c				
Baseline	94	2.30 (0.67)	109	2.35 (0.65)
6 months follow-up	82	2.05 (0.66)	79	2.20 (0.68)
Change baseline to 6 months		-0.20 (0.48)		-0.11 (0.55)
12 months follow-up	62	1.96 (0.69)	47	2.18 (0.69)
Change baseline to 12 months		-0.41 (0.54)		-0.15 (0.53)

^a A total of 204 parents provided questionnaire data, however some parents had missing data on certain scales

^b Mean values are calculated given the specific number of respondents for each scale and at each time point

^c No cut-off is available for high symptoms on the sub-scales of intrusion, avoidance, and hypervigilance and thus the number of affected persons are not reported for these.

Table 3. Predicted mean difference in change in post-traumatic stress, depression and anxiety and 95% confidence intervals (CI) between intervention and control group at 6 and 12-months follow-up in 204 parents of children with cancer in the FAMOS study.

	Linear mixed model ^a				Adjusted linear mixed model ^b			
	Estimate ^c	95% CI	P	Cohen's d	Estimate ^c	95% CI	P	Cohen's d
Post-traumatic stress								
Intervention 6 months	-0.10	(-0.21; 0.01)	0.08	-0.18	-0.10	(-0.21; 0.01)	0.07	-0.19
Intervention 12 months	-0.15	(-0.28;-0.02)	0.02	-0.28	-0.15	(-0.28;-0.02)	0.02	-0.28
Test for no intervention effect			0.04				0.04	
Sub-dimensions of post-traumatic stress								
Intrusion								

Intervention 6 months	-0.11	(-0.25; 0.04)	0.15	-0.17	-0.11	(-0.26; 0.03)	0.13	-0.18
Intervention 12 months	-0.10	(-0.28; 0.09)	0.29	-0.16	-0.10	(-0.28; 0.08)	0.28	-0.16
Test for no intervention effect			0.33				0.29	
Avoidance								
Intervention 6 months	-0.09	(-0.22; 0.04)	0.18	-0.14	-0.09	(-0.22; 0.04)	0.16	-0.15
Intervention 12 months	-0.11	(-0.26; 0.04)	0.16	-0.17	-0.11	(-0.26; 0.04)	0.16	-0.18
Test for no intervention effect			0.25				0.23	
Hypervigilance								
Intervention 6 months	-0.10	(-0.25; 0.05)	0.20	-0.15	-0.10	(-0.25; 0.05)	0.18	-0.16
Intervention 12 months	-0.24	(-0.42; -0.06)	0.01	-0.37	-0.24	(-0.42; -0.06)	0.01	-0.37
Test for no intervention effect			0.03				0.03	
Depression								
Intervention 6 months	-0.16	(-0.30; -0.03)	0.01	-0.20	-0.16	(-0.30; -0.03)	0.02	-0.20

Intervention 12 months	-0.15	(-0.30;-0.00)	<0.05	-0.18	-0.15	(-0.31;-0.00)	0.05	-0.19
Test for no intervention effect	0.05		<0.05				0.05	
Anxiety								
Intervention 6 months	-0.14	(-0.31; 0.02)	0.08	-0.21	-0.14	(-0.31; 0.02)	0.09	-0.21
Intervention 12 months	-0.13	(-0.32;0.06)	0.17	-0.19	-0.13	(-0.32; 0.06)	0.17	-0.19
Test for no intervention effect			0.21				0.22	

^aModels (using all three time points: baseline, 6 months and 12 months) assuming no difference between intervention and control at baseline, but allowing a different intervention effects at month 6 and month 12, respectively.

^bFurther adjusted for parent sex and cancer diagnosis.

^cEstimate of predicted mean.

^dControl group is reference for all outcomes at 6 and 12 months, respectively

Table 4. Estimated change in probability (odds ratios (OR) and 95% confidence intervals (CI)) for scoring above the cut-offs for post-traumatic stress, depression and anxiety in the intervention as compared with the control group at 6 and 12 -months follow-up in 204 parents of children with cancer in the FAMOS study.

	Unadjusted model ^a			Adjusted model ^b		
	OR	95% CI	P	OR	95% CI	P
Post-traumatic stress						
Intervention 6 months	0.69	(0.27; 1.78)	0.45	0.66	(0.25; 1.72)	0.39
Intervention 12 months	0.36	(0.10;1.28)	0.11	0.35	(0.10; 1.24)	0.10
Test for no intervention effect			0.24			0.21
Depression						
Intervention 6 months	0.19	(0.02; 1.76)	0.14	0.18	(0.02; 1.73)	0.14
Intervention 12 months	0.60	(0.07; 4.96)	0.63	0.58	(0.07; 4.91)	0.61
Test for no intervention effect			0.31			0.30
Anxiety						
Intervention 6 months	0.50	(0.17; 1.49)	0.21	0.47	(0.15; 1.46)	0.19
Intervention 12 months	0.58	(0.14; 2.47)	0.46	0.55	(0.12; 2.47)	0.44
Test for no intervention effect			0.40			0.70

Control group is reference at 6 and 12 months, respectively

^a Adjusted for baseline score.

^b Adjusted for baseline score, gender and cancer diagnosis.