Children with a chronic illness or cancer, their siblings and parents

Psychosocial online group intervention & long-term consequences

Mala Joosten

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Colofon

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Children with a chronic illness or cancer, their siblings and parents: psychosocial group intervention & long-term consequences

Kinderen met een chronische ziekte of kanker, hun broers, zussen en ouders: psychosociale groepsinterventie & langetermijngevolgen

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CHAPTER 1

GENERAL INTRODUCTION

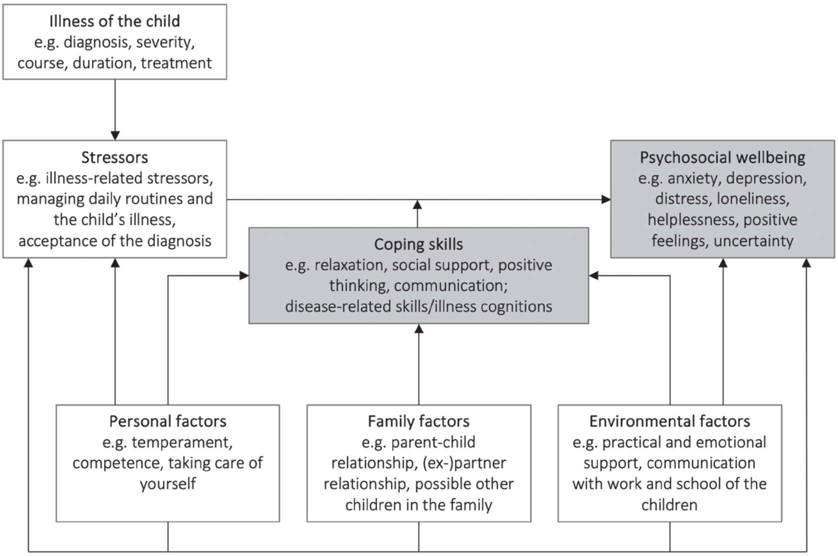
WHEN A CHILD IS ILL

Chronic and life threatening illness

In The Netherlands, around 500.000 children grow up with a chronic illness [1]. This includes approximately 600 children newly diagnosed with cancer every year, of whom around 80% survive with possible late effects [2]. Childhood chronic illness has an onset between the ages 0-18, has a diagnosis based on medical scientific knowledge, is not yet curable and is present for at least three months or has at least three episodes in the last year [3]. The life-threatening aspect of cancer, the intensive treatment that almost all children with cancer have to undergo and the fact there is an endpoint to the treatment is distinctive from chronic illnesses. More common chronic diseases are asthma, eczema, diabetes mellitus type 1, and sickle cell anemia. As medical knowledge improves, children with a chronic illness live longer and overall survival rates for childhood cancer have increased [4, 5]. Even after having successfully completed treatment for childhood cancer, children can experience adverse physical and cognitive effects [6].

Children mostly grow up in a family, and when a child is ill, all family members are impacted. This thesis focuses on the psychosocial impact pediatric illness has on the child itself, the siblings and the parents. The disability-stress-coping model by Wallander and Varni [7] (See an adapted model in Figure 1) illustrates that the relation between the stressors that families have to face and their wellbeing is mediated by coping skills. Coping skills are, in their turn, related to personal, family and environmental factors.

Figure 1. Adapted version of the disability-stress-coping model of Wallander and Varni (1998) to explain psychosocial adjustment in children with an illness, their siblings and their parents.



Stressors

Pediatric illness comes with numerous stressors, related to the illness of the child (e.g. diagnosis) and to psychosocial factors (e.g. managing daily routines) [8]. Some of these stressors are mainly experienced by the child with an illness, such as having to undergo medical procedures, experiencing pain or nausea, use of medication, and restrictions in diet [9]. Especially older children and adolescents experience additional stressors that impact their course of life, including school absence, reduced participation in activities with peers, and changes in appearance [10, 11].

Some stressors however, do not (only) have impact on the sick child, but on siblings and parents and caregivers (further referred to as 'parents'). This applies to for example worrying about the treatment and the future of the child with an illness, accompanying the child to outpatient clinic visits and hospital stays and disruption of daily routines. Because the focus in a family is on the child with an illness, siblings are sometimes described as the forgotten children. Siblings can experience stressors such as lack of parental availability and time, and less attention from other family members and friends. They also report having to take up extra tasks in the household, having to stay at a neighbor or grandparent and absence from school [12]. Most of the time, parents are responsible for managing a child's illness and for taking care of extra needs their child may have. This implies less time for employment and leisure activities and results in challenges in balancing family-, social- and work life. Some parents experience financial problems and sometimes parents are not able to maintain a job at all [5, 6].

Psychosocial wellbeing

Having to face stressors that come with pediatric illness and that are often persistent throughout life, children, siblings and parents are at risk for developing psychosocial problems. Problems in psychosocial wellbeing can include symptoms of anxiety, depression, distress and impaired health-related quality of life (HRQoL).

Even though illness characteristics differ between chronic diseases, psychosocial consequences are mostly comparable [13]. The Integrative Trajectory Model of Pediatric Medical Traumatic Stress describes that although most families recover over time after the diagnosis of a pediatric illness, a small proportion continues to experience problems even after months or years [14]. For families of a child with cancer, the end of treatment may seem like a relieving time point, however children, siblings and their parents often remain vulnerable in the period after finishing treatment. For example, parents report that re-establishing family life is a challenge after being used to the hospital routine and their roles in that environment [15, 16].

Children with an illness sometimes experience medical traumatic stress as a result of their treatment [17]. They also report higher levels of anxiety, depression and distress than peers [9, 18].

Literature on HRQoL of children with an illness is inconclusive. While impaired HRQoL is reported in some studies [11, 19, 20], others indicate no difference in HRQoL between children with an illness and healthy peers [19]. Additionally, adolescents with an illness report problems in the formation of identity, self-image, body-image and self-esteem [11, 21].

Siblings of children with an illness describe feelings of jealousy, embarrassment, guilt, isolation and loss of companionship of the ill child [22-24]. While some studies suggest siblings have worse psychosocial functioning than peers in terms of anxiety and depression [25, 26], others report no difference in anxiety, depression and HRQoL of siblings of children with an illness [27-29].

For parents, the time around diagnosis of their child is accompanied by several emotions including shock, disbelief, denial and anger [30]. Parents of a child with an illness also report feelings of guilt and sorrow [31]. As well as their child with an illness, they report elevated anxiety, depression and distress, and furthermore impaired HRQoL [13, 32-36].

Coping and influencing factors

Coping is central in the disability-stress-coping model because it plays a crucial role in adjusting to stressful situations such as illness of the child. Coping strategies can moderate the effect of influencing factors on psychosocial adjustment. Therefore, it is important to pay attention to coping styles of people dealing with an illness or family member's illness.

A coping style can be described as the way someone reacts to a stressful situation. It consists of both thoughts and actions to handle stressors that are too demanding or overwhelming for the person's abilities [37]. A distinction can be made between engaged and disengaged strategies, or active and passive strategies. Active strategies refer to problem-approaching strategies such as problem solving and cognitive restructuring. Passive strategies refer to problem-avoiding strategies such as social withdrawal [38]. Coping strategies can vary within persons across circumstances, but people tend to apply the same strategies in different situations. Previous research shows that an active coping style is related to better adjustment to illness and higher capability of managing an illness [39-43] and that passive coping is related to poorer adjustment [44].

Coping in itself, is influenced by personal, family and environmental factors, that also have a direct impact on stressors and psychosocial wellbeing. First, personal factors are characteristics of the child with an illness, sibling or parent, such as temperament. For example, an introvert person is more prone to worry a lot [45, 46].

Second, family factors can impact psychosocial wellbeing, directly and indirectly via coping. Adolescents who grow up in a warm and supportive family are more likely to use more active coping strategies compared to adolescents living in an unsecure family [42, 47]. Within family factors, the parent-child relationship is particularly important, since it could be a risk factor or protective factor for problems in psychosocial wellbeing [28, 48]. For parents, practical stressors such as managing daily routines in family life can influence their psychosocial wellbeing. Dividing attention between the child with an illness and healthy siblings in the family might form a challenge as well. Furthermore, the relationship with an (ex-)partner can play a role in how well parents adjust to the situation. Parents who feel supported in their relationship will likely be more resistant to psychosocial distress [49, 50].

Lastly, environmental factors impact psychosocial outcomes. For example, peer support is important for psychosocial adjustment [51]. When support from peers is lacking, adolescents can feel different, lonely and demotivated, which are risk factors for using passive coping strategies [51-53]. This also applies for siblings and parents. Being and feeling supported is another protective factor for good psychosocial adjustment [28]. When parents do not feel understood and supported at work, it can be a stress factor in addition to the already existing distress [49, 50, 54]. Lower income of parents is also a risk factor for poor sibling adjustment to illness [28].

PSYCHOSOCIAL INTERVENTION

Since children with an illness and their parents and siblings are at risk for developing psychosocial problems, it is important that suitable support is offered [55, 56]. Psychosocial care in the hospital setting consists of psychologists, social workers and child life specialists. Outside of the hospital, it is important to have an adequate referral network. Interventions that aim to improve or prevent psychosocial wellbeing could target coping skills, based on the disability-stress-coping model of Wallander & Varni [7].

Op Koers intervention

The relationship between coping skills and psychosocial wellbeing provided the basis for the Op Koers intervention program that was developed in the Emma Children’s Hospital in Amsterdam, the Netherlands over 25 years ago. Op Koers is a group intervention for different members of a family with a child with an illness that aims to teach active coping skills in order to prevent and/or reduce problems in psychosocial wellbeing. The group format of Op Koers provides participants with positive peer contact, which is important because sharing experiences with people that are in a comparable situation is found to be helpful in decreasing distress [57].

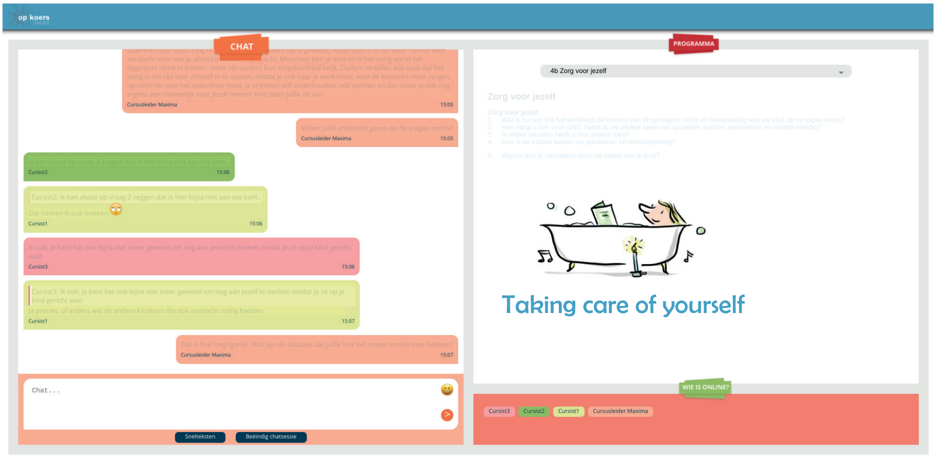
While previous group interventions mainly focused on a specific illness, Op Koers has a more disease-generic character. This is based on the knowledge that psychosocial problems in children with different illnesses are usually similar [13] and allows for (family members of) children with rare diseases to participate. The only distinction is drawn between chronic illness and oncology, given the life-threatening aspect and intensive treatments associated with the latter. The content of the intervention is mostly similar for both categories. However, from a clinical perspective it is not desirable to have children, siblings and parents from the two distinguished categories participate in the same groups.

Initially, Op Koers started as a face-to-face group intervention for siblings of children with cancer. After promising results in that target group [58], modules were developed for and tested in children and adolescents with a chronic illness [59-61]. Then, the originally face-to-face group course was translated into an online module. The idea for an online intervention arose when adolescents showed to be less likely to participate in a face-to-face intervention than younger children [59], while at that time the first e-health interventions were emerging. Combining the content of Op Koers face-to-face with the technology of an existing Dutch chatroom intervention for adolescents and young adults with depressive symptoms [62, 63], the first online module of Op Koers was developed [64]. Online interventions were supposed to be easier for families to participate because an online intervention does not require additional hospital visits.

In Op Koers, coping skills are taught using cognitive behavioral therapy (CBT) techniques, because CBT was previously found to be effective in reducing psychosocial problems [65]. CBT focusses on teaching how to use active coping skills. Op Koers makes use of the Thinking-feeling-doing model that helps participants to realize that thoughts are related to and influenced by both feelings and actions, that are related in their turn as well. Over the years, elements of acceptance and commitment therapy (ACT) were integrated in the Op Koers program. ACT is a third wave of CBT that strives for acceptance of thoughts or situations to reduce their impact on daily life. ACT is an effective psychological intervention for psychological stress [66]. Incorporating ACT in Op Koers is meaningful, because many aspects of living with an illness are not changeable.

The online modules of Op Koers Online all take place in a secured chat room (Figure 2) and consist of six or eight 90-minute sessions on a set day and time. Five to six months after the start of the intervention, a booster session takes place. Every group consists of 3-6 participants and two course leaders, one of whom is an experienced psychologist and the other can be a junior psychologist. Confidentiality is discussed with all participants and maintained by having them agree with several statements before entering the chat room (e.g. “Listen to each other and treat one another with respect” and “What is discussed in the chat remains within this group”). The first session is meant for the participants to get to know each other. In the last session, participants look back on the course and what they have learned. Every session in between covers a specific coping skill or a theme. During the sessions, peer support is stimulated by course leaders motivating participants to have group discussions in order to share experiences and learn from each other. In between the sessions, participants complete homework assignments. Homework exercises cover the theme that was discussed in the previous session and serve as a preparation for the upcoming session. Many of the exercises are based on the Thinking-feeling-doing model. For the modules that are targeted at parents and young adults, in-depth psycho educational reading material is available. This material elaborates on the themes that are discussed in the sessions. For example, after the session about "the family" for parents of children with cancer, tips and tricks are given to support siblings of the sick child.

Figure 2. Chat room of the Op Koers Online intervention.



vaak enerzijds opluchting om … sieve tijd is geweest. Anderzijds is er nu meer ruimte voor aandacht voor wat je allemaal … jaakt. Misschien ben je moe en is het lastig om in het dagelijkse ritme te komen. Soms zijn ouders hun zorgeloosheid kwijt. Ouders vertellen ook vaak dat het lastig is om tijd voor zichzelf in te ruimen, omdat je ook naar je werk moet, voor de kinderen moet zorgen, op controle naar het ziekenhuis moet, je vrienden wilt onderhouden, wilt sporten en dan moet je ook nog ergens een momentje voor jezelf nemen. Hoe doen jullie dit nu?
Cursusleider Maxima 15:05

Willen jullie antwoord geven op de vragen rechts?
Cursusleider Maxima 15:05

Ik kan alvast op vraag 2 zeggen dat ik hier bijna niet aan toe kom..
Cursist2 15:06

Cursist2: Ik kan alvast op vraag 2 zeggen dat ik hier bijna niet aan toe kom..
Dat herken ik ook meteen 🙄
Cursist1 15:06

Ik ook, je bent het ook bijna niet meer gewend om nog aan jezelf te denken omdat je zo op je kind gericht was!
Cursist3 15:06

Cursist3: Ik ook, je bent het ook bijna niet meer gewend om nog aan jezelf te denken omdat je zo op je kind gericht was!
Ja precies, of anders wel de andere kinderen die ook aandacht nodig hadden
Cursist1 15:07

Dat is heel begrijpelijk. Wat zijn de situaties dat jullie hier het meest moeite mee hebben?
Cursusleider Maxima 15:07

Chat...

Zorg voor jezelf

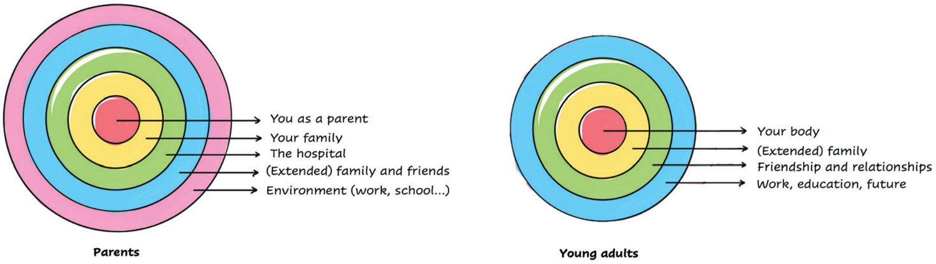
Zorg voor jezelf
1. Wat is nu nog (na behandeling) de invloed van de gevolgen ziekte en behandeling van uw kind op uw eigen leven?
2. Hoe zorgt u ook voor uzelf, naast al uw andere taken als opvoeder, partner, werknemer en vriend/vriendin?
3. In welke situaties heeft u hier moeite mee?
4. Hoe is de balans tussen uw privéleven en werk/opleiding?

5. Waarin ben je veranderd sinds de ziekte van je kind?

Specifically for the modules for children and adolescents with an illness and for siblings, coping skills are translated into five learning goals: 1) information seeking and information giving about the disease ('good to know better' principle), 2) use of relaxation during stressful situations, 3) increasing knowledge of self-management and compliance (not applicable for siblings), 4) enhancing social competence (group discussions, role playing), and 5) positive thinking (use of the Thinking-Feeling-Doing model; replacement of inaccurate thoughts).

For the modules for adults (young childhood cancer survivors and parents with either a child with a chronic illness or cancer), themes are structured around different environments of the participants (Figure 3). Learning goals are either discussed in the chat session, and/or are a part of the homework assignments and the reading material. Learning goals are: 1) use of relaxation during stressful situations; 2) increasing knowledge of self-management and compliance of their child (not applicable for young adults); 3) positive thinking; 4) positive parenting (not applicable for young adults); 5) open communication about the illness and seeking and accepting support.

Figure 3. Environments in which the themes of the Op Koers interventions for parents and for young adults are structured.



Over the past 25 years, the Op Koers program has developed into a group course program with different modules based on different target groups (parents, siblings, children with an illness), diseases (chronic illness and oncology) and format (online and face-to-face). This required many steps in the development and evaluation of the intervention. Although previous research had been done into Op Koers Online, this was limited to survivors of children with cancer. Exploration of applications for other groups was warranted. Therefore this thesis focuses on modules for siblings of a child with a chronic illness (development), for adolescents with a chronic illness (pilot evaluation and feasibility) and parents of children with cancer (efficacy research).

PSYCHOSOCIAL FUNCTIONING OF PARENTS AND SIBLINGS OF SURVIVORS OF CHILDHOOD CANCER ON THE VERY LONG TERM

Thanks to advancement of treatments for childhood cancer, survival rates have increased to approximately 80%, and an increasing number of childhood cancer survivors (CCS) reaches adulthood [67]. Among adult CCS, the prevalence of adverse health outcomes is high [68], and sometimes long-term CCS experience impaired psychosocial wellbeing [69].

As described previously, and following the model of Wallander and Varni [7], an illness of a child could have a major impact on the psychosocial functioning of parents and siblings [48, 55, 70, 71]. Most research results on wellbeing of parents and siblings of CCS stem from studies shortly after treatment or studies among young CCS, below the age of 18. A systematic review into minor siblings showed that they have comparable HRQoL and symptoms of anxiety and depression as peers, but more parent-reported internalizing and externalizing problems [28]. Parents of minor CCS reported psychological distress and poorer HRQoL than comparison groups [71, 72]. Studies showed that (young) adult very long-term CCS were resilient but have (slightly) impaired HRQoL [73-75].

However, few studies have been done into siblings and parents of long-term CCS. Some suggested ongoing psychological distress in parents of adult CCS [76] while others reported similar rates of post-traumatic stress to the general population [77], which has also been found in an adult sibling sample [78]. Previous research into families closer to the cancer diagnosis revealed that, besides negative consequences, siblings can also experience positive impact of having a child or brother or sister with cancer, such as post-traumatic growth [79].

Several factors were found to be associated with psychosocial outcomes of parents and siblings of children with cancer closer to diagnosis and treatment. For example, female sex, lower level of education, central nervous system tumor diagnosis and relapse were identified as risk factors for impaired wellbeing [70, 78, 80, 81]. Another potentially relevant factor might be coping strategies, or cognitions of parents and siblings, again aligning with the disability-stress-coping model previously described by Wallander and Varni [7].

Previous research shows that mothers of children with cancer consistently experienced elevated rates of mental health-related outpatient visits over time compared with controls and that siblings' risk for mental health problems began to increase relative to controls from approximately 15 years after diagnosis [82]. However, since further knowledge on the wellbeing of parents and adult siblings of very long-term CCS so far is limited, it is relevant to do more research on the topic. Furthermore, it is interesting to study whether positive consequences are still visible in siblings and parents of CCS decades after diagnosis.

AIMS AND THESIS OUTLINE

The focus of this thesis is on children with an illness and in particular their family members in the context of a pediatric illness, including siblings and parents of adult long term survivors of childhood cancer. This thesis has two aims: 1) to develop and study the effect of the Op Koers intervention in different populations and 2) to study psychosocial functioning of siblings and parents of long-term CCS. The thesis consists of two parts. An overview of the aims of the different chapters is presented in Table 1.

Part 1: The development and effect of the Op Koers intervention in different populations

In Chapter 2 the online support needs of siblings of children with a chronic illness are identified, in order to develop a sibling-specific module within the existing intervention program Op Koers. Results of an online questionnaire and additional semi-structured interviews, that enquired about wishes for peer support and important themes for an intervention, are reported. In Chapter 3 the feasibility and preliminary efficacy of Op Koers Online for adolescents with a chronic illness is addressed in a pre-posttest questionnaire design without a control group. Chapter 4 presents a randomized controlled trial to study the efficacy of the Op Koers Online intervention for parents of children with cancer. Parents in the intervention condition were compared to a waitlist-control condition at several time points over the course of a year. In Chapter 5 we critically appraise the efforts in 25 years of experience in development, research and implementation of the Op Koers intervention program, based on models for behavioral intervention development and implementation. Important lessons that we have learned are shared, as well as suggestions for future directions.

Part 2: Psychosocial wellbeing of parents and siblings of very long-term survivors of childhood cancer

In the Netherlands, a nationwide cohort study of late effects after childhood cancer treatment was conducted: the Dutch Childhood Cancer Survivor LATER Study [83]. A sub study is LATER-psychology, in which not only long-term CCS but also their siblings and parents participated.

In Chapter 6 the psychosocial wellbeing of adult siblings of very long-term CCS is described. Besides comparing the psychosocial wellbeing of siblings in the sample to the general population, associated factors are studied. Psychosocial wellbeing of parents is studied in Chapter 7. Again, psychosocial wellbeing is compared to the norm population and associated factors are studied.

The final Chapter 8 is the general discussion of this thesis, that presents a summary, followed by reflections on the main findings, clinical implications and future directions.

Table 1. The aims of this thesis.

	Aims	**Design + Outcome measures**	**Sample characteristics**
Part 1: The development and effect of the Op Koers intervention in different populations			
Chapter 2	To identify siblings' online support needs in order to develop a sibling-specific module of the Op Koers Online intervention	Mixed methods: questionnaires, interviews Support needs (self-developed questionnaire) Psychosocial functioning (SDQ) Semi-structured interviews	Siblings (age 12-18) of children with CI, *n*=91
Chapter 3	To assess feasibility and explore preliminary efficacy of Op Koers Online for adolescents with chronic illness	Longitudinal questionnaire assessment; pre-post design without control group (T0, T1 0-2 weeks after intervention); Coping skills (Op Koers Questionnaire) Internalizing and Externalizing problems (YSR) Health-Related Quality of Life (PedsQL)	Adolescents with CI (age: 12-18 years), *n*=29
Chapter 4	To evaluate the efficacy of Op Koers Online for parents of children with cancer	Randomized controlled trial Longitudinal questionnaire assessment (T0, T1 5 months after intervention, T2 12 months after intervention) Anxiety (PROMIS CAT item bank) Depression (PROMIS CAT item bank) Coping skills (Op Koers Questionnaire and CCSS-PF) Distress (DT-P) Emotional reactions (SSER-Q)	Parents of children with cancer, *n*=89 (Intervention *n*=43, Waitlist control *n*=46)
Chapter 5	To share the lessons that we have learned in the process of 25 years of development, research and implementation of Op Koers	Critical appraisal of activities in different stages, described using the National Institutes of Health Stage Model for Behavioral Intervention Development and the Consolidated Framework for Implementation Research CFIR. n/a	n/a
Part 2: Psychosocial wellbeing of parents and siblings of very long-term survivors of childhood cancer			
Chapter 6	To describe psychosocial outcomes among adult siblings of very long-term childhood cancer survivors (CCS), to compare these outcomes to reference populations and to study associated factors.	Cross-sectional questionnaire study (DCCSS-LATER 2 Psycho-oncology Study) Anxiety and depression (HADS) Health-Related Quality of life (TAAQoL) PTSD (SRS-PTSD) Self-esteem (RSES) Benefit and burden (BBSC)	Siblings of CCS (CSS diagnosed 1986–2001) *n*=505
Chapter 7	To describe psychosocial outcomes of parents of long-term survivors of childhood cancer (CCS), to compare these outcomes to reference populations and to study associated factors.	Cross-sectional questionnaire study (DCCSS-LATER 2 Psycho-oncology Study) Health-Related Quality of life (TAAQoL) PTSD (SRS-PTSD) Post traumatic growth (PTGI) Illness cognitions (ICQ)	Parents of CCS (CSS below 30 years and diagnosed 1986–2001) *n*=661

Note. QOK-c = Questionnaire Op Koers – children, YSR = Youth Self Report, PedsQL = Pediatric Quality of Life Inventory, PROMIS CAT = Patient Reported Outcomes Measurement Information System Computer Adaptive Test, SSER-Q = Situation Specific Emotional Reactions Questionnaire, QOK-p = Questionnaire Op Koers – parents, CCSS-PF = Cognitive Coping Strategies Scale Parent Form, TAAQoL = TNO-AZL Adult Quality of Life, Self-Rating Scale for Post-Traumatic Stress Disorder, RSES = Rosenberg Self-Esteem Scale, BBSC = Benefit and Burden Scale for Children, PTGI = Post-traumatic growth inventory, ICQ = Illness cognition questionnaire.

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PART 1.

THE DEVELOPMENT AND EFFECT OF THE OP KOERS INTERVENTION IN DIFFERENT POPULATIONS

CHAPTER 2

HEARING SIBLINGS' VOICES: EXPLORING THE (ONLINE) SUPPORT NEEDS OF SIBLINGS OF CHILDREN WITH A CHRONIC CONDITION

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ABSTRACT

Background Siblings of children and adolescents with a chronic condition are at risk for developing psychosocial problems. It is important, that they receive appropriate support according to their needs. A sibling-specific module of an existing online intervention (Op Koers Online) for adolescents with a chronic condition might be an appropriate way to offer psychosocial support to siblings. The aim of the current study is to identify siblings' online support needs in order to develop a sibling-specific module of the existing Op Koers Online intervention.

Results A total of 91 siblings (mean age 15.2 years, Standard Deviation 2.7) of children with a chronic condition completed an online questionnaire; nine semi-structured interviews were held additionally. Of all participants, 55% would like to initiate or increase contact with other siblings of children with a chronic condition and 46% of those were interested in an online chat course. The themes for online support considered most important were impact on daily life, worrying about brother's/sister's future, handling other people's reactions, and how attention is divided within the family.

Conclusions Siblings are interested in peer contact and online support. Op Koers Online for siblings seems to be a suitable intervention to offer online psychosocial support. The next step is to develop a sibling specific module of the Op Koers Online course, taking into account the identified themes.

BACKGROUND

In the Netherlands, 15–20% of children live with a chronic condition [30]. It is estimated that this concerns around 500,000 children. Many siblings are also affected by chronic conditions during childhood. Children and adolescents growing up as a sibling of a child with a chronic condition, might have to cope with difficult situations. They can experience loneliness [16], worry about the prognosis of the ill child's condition, and their brother's/sister's condition might affect family life and daily life [9]. Siblings also report receiving less attention from their parents and having lost the companionship of the ill child [24]. They are described as being the "forgotten children" [14].

To date, the literature remains inconclusive about the psychosocial functioning of siblings of children with a chronic condition. The mixed findings could probably be explained by diversity in outcome measures, chronic condition of the child and characteristics of the sibling under study, including how long the sibling has been living with the chronically ill child [10, 23, 33]. Two meta-analyses suggest siblings have worse psychological functioning (anxiety, depression) [23], more internalizing and externalizing problems, and fewer positive self-contributions than peers without a chronically ill brother/sister [33]. Some research reports lower scores on several indicators of well-being, even though effect sizes are usually small [4]. Other findings, however, suggest that siblings' levels of depression and quality of life are similar to those of peers without a chronically ill sibling [10, 12, 32].

Even though the findings of different studies are contradictory, siblings of children with a chronic condition deserve attention. For a population as vulnerable as those siblings, it is important to have insight into their support needs. In several studies parents have been asked to report about sibling needs. Research shows that the agreement between proxy-reported outcomes and self-reported outcomes is sometimes low [8]. Hence, sibling participation is of great importance, as siblings are experts by experience. Participation can help better match the care to their needs, and a sibling perspective can add their own values to the values of professionals [27, 29]. In cancer populations, research was conducted on siblings' (unmet) needs [18, 26] and how to screen them [13, 19]. In chronic-condition populations, however, needs of siblings have not been studied extensively. Research about support needs of siblings of special-needs families shows that most siblings do not know where they can get support and that there is not enough support available [17]. The need for a better insight into siblings' support needs is stressed so that suitable interventions can be developed [25]. Interventions directed at siblings fit into the concept of family-centered care, where attention is given not only to the patient but to the well-being of the other family members too.

Specific interventions for siblings of children with chronic conditions are scarce, as are studies looking into the effectiveness of such interventions. A recent systematic review included 17 studies on the effects of psychosocial interventions for siblings [25]: only one study focused on chronic conditions (cystic fibrosis and heart disease), the others focused mainly on cancer and mental illnesses. Findings in this review suggest that interventions aimed at improving psychological outcomes had a positive effect on siblings of children and adolescents with a chronic condition. They lead to improved knowledge about the illness, and to better externalizing and internalizing behavior scores.

As far as we know, only one intervention for siblings has been examined in the Netherlands [11]. It concerned a support group developed at Emma Children's Hospital/Amsterdam University Medical Centers (UMC) that was conceived for siblings of children with cancer. The goal was to improve siblings' coping strategies and reduce anxiety. The group course consisted of five weekly sessions led by two psychologists. Changes in the family situation and emotions as a result of living with an ill brother or sister were discussed. The study with a pre-post design suggested that, on average, 16.5 months after their sibling received a cancer diagnosis, children experienced less anxiety shortly after participation in the support group.

This support group has become the basis of the face-to-face Op Koers program (in English: On Track). The program now consists of group courses for children, parents, and siblings, and has separate modules for cancer and chronic conditions. All group courses are based on cognitive behavioral therapy in order to prevent or reduce psychosocial problems. Cognitive behavioral therapy focuses on recognizing cognitive distortions and teaching coping skills [1]. Sharing experiences with fellow-patients is an important part of the intervention [20]. Effectiveness of the face-to-face Op Koers group course has been studied in chronically ill children with a randomized controlled trial. The group course had a positive effect on coping skills such as positive thinking, and on internalizing and externalizing problems [22].

To better fit into the current online world and to overcome logistic barriers, the Op Koers program was further developed into online Op Koers group courses. Online interventions that use cognitive behavioral techniques seem to have a positive effect on depressive and anxious symptoms and general distress in adults with a chronic condition [28]. Peer support is suggested to have a positive effect on attitudes, beliefs and perceptions [21]. The first online Op Koers group course was developed for childhood cancer survivors (CCS) [15]. After establishing preliminary feasibility for CCS, the module was adapted for adolescents with a chronic condition (ages 12–18) and parents of children with a chronic condition (ages 0–18) [3]. In these online courses, participants log on to a chat box at a set time for eight weekly sessions led by two psychologists. Participants are taught coping skills and share experiences with each other about themes that are related to themselves or their child having a chronic condition.

Although Op Koers Online is available for parents and children, there is no module yet for siblings of children with a chronic condition. An Op Koers Online group course, adapted for siblings (ages

12–18) might be an appropriate way to offer them psychosocial support. An online group course would allow siblings to get in contact with other siblings and share experiences on themes related to having a brother or sister with a chronic condition. It is not clear that such a group course meets siblings' needs in terms of psychosocial support, though. We do not know whether siblings would like to have contact with peers through a chat course and what themes would be important to them. The aim of the current study is to identify siblings' online support needs in order to develop a suitable cognitive-behavioral based chat course led by two psychologists: an Op Koers Online module for siblings.

METHODS

Procedures & participants

An online questionnaire was developed to identify siblings' online support needs. Additionally, in-depth information about online support needs was collected through semi-structured video-call interviews. In order to draw a large, heterogeneous sample of siblings of children with a wide variety of conditions, the questionnaire was published online with open access. Siblings were approached via patient associations' websites, newsletters and social media, and flyers at the outpatient clinics of Emma Children's Hospital/Amsterdam UMC. Information about the survey was also provided via announcements on websites and social media accounts linked to the psychosocial department of Emma Children's Hospital/Amsterdam UMC.

Siblings could access the questionnaire via a link to the Op Koers website (www.opkoersonline.nl) between January and May 2017. Participants did not need a login code to complete the questionnaire. No names were used on the website – the data were stored and analyzed anonymously. Siblings were asked to leave their e-mail addresses only if they wanted to participate in a video call to further discuss their online support needs. Interviews were held between April and May 2017 and were audio-recorded.

Inclusion criteria for siblings were 1) to be 12–18 years old, 2) to have a brother or sister with a chronic condition, and 3) to be able to understand Dutch well enough to complete the questionnaires.

This study was conducted with permission of and in accordance with the regulations of the Medical Ethics Committee of Amsterdam UMC.

Measures

Background characteristics

Background characteristics of participating siblings (age, sex, education) and their brothers or sisters with a chronic condition (diagnosis, age at disease onset, age) were collected with a self-developed questionnaire. The diagnoses were reported by the participating siblings and later categorized by the researcher with the assistance of a medical doctor at Emma Children's Hospital/ Amsterdam UMC. When more than one diagnosis was reported, only the first one listed was taken into account. To gain insight into siblings' psychosocial well-being as a background characteristic, information was gathered using the Dutch self-report version of the Strength and Difficulties Questionnaire (SDQ) [5,6,7]. Siblings were asked to rate 25 items (e.g. Other people my age generally like me, I worry a lot) on a three-point scale ranging from 0 Not true to 2 Certainly true. There are five scales (score range 0–10) consisting of five items, including emotional symptoms, conduct problems, hyperactivity/inattention, peer problems and prosocial behavior. A total difficulties score is calculated by adding the scores of all scales aside from the prosocial behavior scale. A higher score means more problems, except for prosocial behavior, where a higher score means more prosocial behavior. The internal consistencies of the total difficulty, emotional symptoms, conduct problems, hyperactivity/inattention, and prosocial behavioral scales were satisfactory, ranging from Cronbach's α 0.5 to 0.8. Internal consistency of the peer problems scale was insufficient (α=0.32). Therefore, this scale was not taken into account in further analyses. Mean scale scores in a Dutch population of boys and girls aged 11–16 were available [31], as well as cut-off scores with cut-off points chosen so that 80% of children scored normal, 10% borderline, and 10% abnormal [5].

Online support needs

Data on online support needs, and themes for online support were collected with a questionnaire, tailored for siblings of children with a chronic condition. The questionnaire was developed by the researchers, to identify whether siblings are interested in online peer support, with whom, in what form and discussing what themes. The themes included in the questionnaire were identified by clinical psychologists from the Psychosocial department of Emma Children's Hospital/Amsterdam UMC, and based on existing literature and clinical experience. The questionnaire consisted of nine items, partly open (e.g. What themes would you like discuss in online support) and partly multiple-choice (e.g. In what form would you like online support). All multiple-choice questions are listed in Table 2.

In addition to administering the questionnaire, semi-structured interviews were conducted. Every interview was held with a fixed sequence of topics, to check for potential missed needs in the questionnaire. The topics were: 1) Do you talk to others about your brother's or sister's condition, and would you like support? 2) What themes do you find important concerning your chronically ill brother or sister? 3) What should an online intervention look like? Within these topics, siblings were free to talk about anything they found important.

Data analysis

All analyses were conducted using The Statistical Package for Social Sciences 24 (SPSS Inc., Chicago). Descriptive analyses were performed on background characteristics and online support needs. Siblings’ mean SDQ scale scores were compared with weighted (by gender) mean scores from the Dutch norm population, using a one-sample t-test. Effect sizes (d) were calculated for the differences in mean scores between the siblings and the norm group, dividing the difference by the standard deviation in the norm group. Effect sizes (d) of up to 0.2 were considered to be small, effect sizes around 0.5 medium and effect sizes around 0.8 large [2]. In addition, binomial tests were performed to assess whether the percentage of siblings with scores in the abnormal or borderline range differed from the percentage (20%) with equivalent scores in the Dutch population.

To explore whether any themes in the online-support-needs questionnaire were missed, the audio tapes of the interviews were listened to.

RESULTS

Participants

A total of 104 siblings of a child with a chronic condition completed the online questionnaire in the broad age range of 4–35 years, even though the provided information about the survey mentioned the eligible age range of 12–18 years. The researchers then decided to widen the eligible age range to 11–21 years so they could take data of more participants into account. A total of 91 participants fit that range (including six 11-year-olds and ≥ 19-year-olds).

Twenty-three siblings left their e-mail address in order to be contacted for a video call. Fourteen of them did not participate in an interview, due to either non-response at follow-up or planning difficulties. Nine interviews were held.

Background characteristics

Background variables of participants are shown in Table 1. Of the 91 siblings, 61 (67.0%) were female. Mean age of participating siblings was 15.2 years with a Standard Deviation (SD) of 2.7. Mean age of their brother or sister with a chronic condition was 13.8 (SD 4.4) years. As the variety of medical diagnoses was large, only the most frequently reported diagnoses are presented in Table 1.

Regarding psychosocial well-being, Table 1 shows the percentage of siblings scoring in the borderline/abnormal range of the scores on the different scales and total difficulty scale of the SDQ: borderline

3.3–15.4%, abnormal 5.5–28.6%. The percentages of siblings with abnormal or borderline scores were significantly higher than the 20% in the Dutch population on the emotional symptoms, hyperactivity/attention and total difficulties scales. Compared to the Dutch weighted norm, siblings in our sample also had significantly higher mean scores on these scales, indicating more problems. Regarding conduct problems, the percentage of siblings with abnormal or borderline scores was significantly lower than the 20% in the Dutch population, while their mean scores did not differ from the Dutch population. Siblings also had higher scores on prosocial behavior (mean as well as percentage) than the Dutch population, indicating more prosocial behavior.

Online support needs

Table 2 presents results on multiple-choice questions on online support needs and important themes for an online group intervention. In our sample, 39.6% of siblings does have contact with other siblings, mostly through friends and/or family (25.3% of the total sample). In addition, 55% answered yes or maybe to the question of whether they would like to initiate or increase contact with other siblings of children with chronic conditions. These 55% in turn were asked additional questions about who they would like to get in contact with and how they would prefer online support. This is described next.

Siblings were asked what characteristics they would find important in other siblings for online support. Comparable age (68%) and similar diagnosis of the brother/sister (52%) were regarded important for group meetings. Gender was regarded as less important – only 6% indicated preferring to get in contact with siblings of their own gender. Siblings were then invited to share their thoughts about how they would like to get in contact with other siblings, by asking them an open question. Key words that came up from at least 10% of respondents were through an activity (39%), via the internet (24%), just have a talk and share experiences (18%), and casual, laid back (14%).

For modes of online support, 32% reported not being in need of any form of online support at all; 28% reported that they would like an online message board, 46% an online chat course, and 14% an online Skype course. Concerning time of the day that they would like an online intervention, 82% of participants answered in the evening. When asked about important themes for an online intervention, respondents were initially invited by open question to name the themes that are most important to them. A wide variety of answers were given, the most common themes being how others cope with the situation in general (28%) and parent’s attention (10%). Next, participants were asked to indicate whether a set of listed themes appealed to them. All themes (see Table 2) were considered appealing by at least one third of respondents. Four out of seven themes were considered appealing by more than half of respondents: impact on daily life (66%), worrying about brother’s/sister’s future (64%), handling other people’s reactions (64%) and how attention is divided within the family (56%).

The interview data revealed no additional important themes for online support for siblings. Just as in the survey data, some of the siblings stated they were not in need of support, as they weren't experiencing many difficulties growing up with a ill brother or sister. Most siblings however, did elaborate on the different themes that were already listed in the questionnaire, and were very willing to share their thoughts and feelings with the interviewer. They appreciated the sincere attention the interviewer gave to their experiences, feelings and needs.

Table 1. Background characteristics.

	%	**Mean (SD)**			
Participating siblings (*n*=91)					
Age in years		15.2 (2.7)			
Sex (Female)	67				
Current education					
primary school	9.9				
secondary school	65.9				
advanced education	18.7				
None anymore	5.5				
Strengths and difficulties (SDQ)[1]		Siblings (*n*=91)		Norm[2] (*n*=1353)	
	Borderline/ Abnormal (%)	Total of Borderline/ Abnormal (%)	Mean (SD)	Weighted mean (SD)	Effect size
Emotional symptoms	7.7 / 22.0	29.7*	3.5 (2.6)	2.4 (1.9)	0.58**
Conduct problems	4.4 / 6.6	11.0*	1.8 (1.5)	1.9 (1.5)	-0.06
Hyperactivity/inattention	12.1 / 28.6	40.7***	4.7 (2.7)	3.8 (2.3)	0.37**
Prosocial behavior	3.3 / 5.5	8.8**	8.2 (1.8)	7.3 (2.3)	0.41**
Total difficulties	15.4 / 19.8	35.2**	11.9 (5.9)	10.0 (4.9)	0.39**
Child with chronic condition	%	Mean (SD)			
Mean age child (*n*=90)		13.8 (4.4)			
Age at disease onset (*n*=91)					
during or shortly after birth	46.2				
0-5 years old	27.5				
6-12 years old	19.8				
13-18 years old	6.6				
First named diagnosis					
neurological disorder	12.1				
cardiovascular disorder	11.0				
cystic fibrosis	11.0				
chromosomal/syndromal disorder	8.8				
metabolic disorder	8.8				
connective tissue disorder	7.7				
disorder in the locomotor system	6.6				
Crohn's disease	6.6				
other	27.5				

Note: SD standard deviation

[1] Higher scores indicate more problems, except for the prosocial behavior subscale

[2] Norm population is 11-16 years old. Sample participants age range: 11-21. Analyzing only the 11-16 year-olds did not yield different results.

* p<0.05, **p<0.01, ***p<0.001: siblings differ significantly from the norm.

Table 2. Results of multiple-choice questions about online support needs and themes for online support

	Yes		Maybe		No	
	n	*%*	*n*	*%*	*n*	*%*
Are you in contact with siblings of someone with a chronic condition? (*n*=91)	36	39.6			55	60.4
via Friends/family	23	25.3				
via Patient association or similar	13	14.3				
via Hospital	3	3.3				
Would you like to initiate/increase contact with other siblings? (*n*=91)	11	12.1	39	42.9	41	45.1
Suppose there was online support. What would be your preferred form? (*n*=50)						
I am not in need of online support	16	32				
Via a message board where messages can be exchanged with siblings and therapists	14	28				
Via an online chat course	23	46				
...with a fixed group of siblings and therapists	15	30				
...with a changing group of siblings and therapists	8	16				
Via an online Skype course	7	14				
...with a fixed group of siblings and therapists	5	10				
...with a changing group of siblings and therapists	2	4				
Do you find it important that the siblings you would get in contact with: (*n*=50)						
...are of my own age	34	68				
...are of my own gender	3	6				
...have a sibling with a similar diagnosis to my sibling's	26	52				
Are the following themes appealing to you? (*n*=50)						
Worrying about sibling's treatment	18	36				
Worrying about sibling's future	32	64				
Division of attention within the family	28	56				
Dealing with/planning time for yourself	14	28				
Impact on daily life	33	66				
Your relationship with your parents	18	36				
Handling other people's reactions	32	64				
Say there was an online chat course. At what time of the day would you like to do this? (*n*=50)						
in the morning	4	8				
in the afternoon	11	22				
in the evening	41	82				

DISCUSSION

The aim of this study was to identify siblings' online support needs in order to develop an Op Koers Online intervention for siblings. The needs were assessed with a customized questionnaire supplemented with semi-structured interviews.

Because siblings might have to cope with difficult situations, they might experience psychosocial problems. Hence, psychosocial well-being of participants was assessed as a background characteristic. In our sample, psychosocial well-being of siblings was worse than the norm, except for conduct problems. Siblings also reported more prosocial behavior than the norm. This is in line with what is experienced in clinical practice; siblings of children with chronic conditions tend to be typically friendly and helpful. These results stress the vulnerability of the siblings in our sample. The finding that siblings had more psychosocial problems than peers in some domains but not in all is also in line with previous research [4, 32]. Effect sizes in the present study were moderate, whereas former studies show mostly small effect sizes [4]. The current study provides no information about possible positive effects of being a sibling of a child with a chronic condition. Better understanding of positive effects could provide insight into potential helpful coping strategies that others can benefit from.

An indication of the feasibility of a peer support intervention is given by the result showing that 55% of participants might like to initiate or increase contact with other siblings. This corresponds with findings of a needs assessment conducted by the Netherlands Youth Institute [17].

More in detail, most siblings would like to get in touch with siblings of about the same age, regardless of gender, which is in line with the current design of the Op Koers Online course for children with a chronic condition. This course is aimed at boys and girls of secondary school age. Half (52%) of the participants stated that they find it important that the other siblings they get in touch with have a brother or sister with a similar condition. The current Op Koers Online interventions for parents and adolescents with a chronic condition focus on the similarities between children with different chronic conditions, rather than on the differences between diagnosis groups. It is believed that even though diagnoses may differ, the psychosocial challenges that come with having a chronic condition are mostly the same [20]. A pilot study on Op Koers Online groups with heterogeneous diagnoses among participants or children from participants shows promising results [3]. It is plausible that the heterogeneity of the groups will also work for siblings. Furthermore, heterogeneous groups give siblings of children with rare illnesses the opportunity to participate in a group intervention. It is therefore important that, before introducing Op Koers Online to siblings, psychologists make sure to explain them that having a sibling with a chronic condition has generic consequences for different diagnoses.

Our results additionally indicate that an online intervention fits into the digital environment adolescents live in. Of the participants that stated they would like to get in touch with other siblings, 46% would like to receive online support via an online chat course.

Another interesting result was that siblings appeared to prefer an evening rather than a daytime. So far, Op Koers Online courses for adolescents with a chronic condition mostly take place during daytime. Participation rates might be enhanced if the point of time of the group course fits the adolescents' schedule, thus asking flexibility of the team providing the courses.

On the topic of important themes, the open question yielded a wide variety of answers. The most common answer was (a variant on) how others cope with the situation in general (28%). This suggests that participants were mostly interested in peer contact in general. All pre-listed themes in the multiple-choice question were considered important by at least 30% of participants. It is important to take these themes into account when further developing an intervention for siblings.

The finding that the semi-structured interviews yielded no new information suggests that the questionnaire was appropriate for gaining insight into siblings' online support needs and important themes. The interviews did stress the importance of an intervention for siblings, since most of them reported having trouble with one or more aspects of growing up with a chronically ill brother or sister. It is also important to take into account that some siblings stressed that peer contact should be casual, laid back or just having a talk. This shows that, even though siblings might experience difficulties, they would not like to participate in a group course with too intense of a focus. Finding a balance between giving enough attention to the sibling's difficulties and also "keeping it light enough" are of great importance in developing a course for siblings.

One must keep in mind that this study focuses on online support and provides no insight into support needs other than online ones. The 32% of participants that indicated not being interested in online support may have other support needs. Awareness for siblings' needs is of the utmost importance in pediatrics.

This study had some limitations. The first one is about the sample. The open recruitment strategy had the advantage of being able to include more participants. However, as a consequence of this no information about response rates or differences between non-respondents and respondents is available. In other words, we do not know whether the results are representative for all siblings of children with chronic conditions. One might argue that siblings with more support needs were more likely to complete the questionnaire. This could have led to an overestimation of online support needs and possibly explains why the psychosocial wellbeing of the siblings in our study appeared to be worse than that found in previous studies. Also, two-thirds of the participants were sisters and all the semi-structured interviews were held with girls, since no boys signed up.

Overrepresentation of girls is not uncommon in questionnaire studies. Girls internalize more than boys, so expectedly they are more likely to search for support for their emotional problems. The findings should therefore be interpreted with caution.

CONCLUSIONS

All results taken into account, an Op Koers Online module for siblings seems to be a suitable intervention for part of the sibling population. Siblings appeared to be interested in peer contact and online support. The next step is to develop a sibling-specific module for the Op Koers Online course, taking into account the identified themes. The sibling participation of our study contributed to our process of developing the online course program. Once the intervention is developed, further research should focus on feasibility and effectiveness of Op Koers Online for siblings.

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CHAPTER 3

ONLINE COGNITIVE-BEHAVIORAL GROUP INTERVENTION FOR ADOLESCENTS WITH CHRONIC ILLNESS: A PILOT STUDY

CLINICAL PRACTICE IN PEDIATRIC PSYCHOLOGY, 2019

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ABSTRACT

Objective To assess feasibility and explore preliminary effectiveness of an online cognitive-behavioral group intervention (Op Koers Online) to prevent and/or reduce psychosocial problems by teaching use of active coping skills to adolescents (ages 12 to 18) with chronic illness.

Method Adolescents who signed up for the chat intervention were asked to complete online questionnaires at baseline and post-intervention (after 8 weeks). Feasibility was evaluated based on attendance (missed sessions, dropout rate and homework completion), technological issues and with an evaluation questionnaire. Preliminary effectiveness was evaluated with standardized questionnaires: Op Koers Online Questionnaire (disease-related coping skills), Youth Self-Report (emotional and behavioral functioning), Pediatric Quality of Life Inventory (Health-Related Quality of Life [HRQoL]). Mean scale scores post-intervention were compared with baseline with paired-samples t-tests. Effect sizes were calculated.

Results In total, 33 adolescents participated in the intervention, 29 adolescents completed the questionnaires at baseline. Regarding post-intervention questionnaires, 25 adolescents completed the evaluation questionnaires and 23 adolescents completed all questionnaires post-intervention. Dropout rate was 6%. In 1 session (2%), there were technological issues that caused the session to stop. Participants' overall satisfaction was high. Regarding effectiveness, participants improved significantly in the use of total coping skills and the coping skills "information seeking and giving" and "social competence" after the intervention compared with baseline. Participants also reported significantly fewer withdrawn/depressed behavior and scored significantly better on emotional and psychosocial HRQoL after following the intervention.

Conclusions This pilot study indicates that Op Koers Online is feasible and potentially effective. Further research (a randomized controlled trial) is needed to establish the effects of the intervention.

INTRODUCTION

The number of children and adolescents living with chronic illness (CI) continues to grow due to increased medical knowledge and improved treatments [1, 2]. In the Netherlands, 15-20% of children (ages 0-18) are living with a CI such as diabetes or asthma [3]. Children and adolescents with CI have to live with physical consequences and face difficulties such as hospital visits and/or hospitalizations, activity restrictions and illness-related stressors such as uncertainty about the course of their illness. The stressors are multifaceted and mostly for a lifetime [4].

Children and adolescents with CI show higher levels of stress, internalizing behavior problems and somewhat elevated levels of externalizing behavior problems compared to healthy peers [4-6]. They do not necessarily develop psychopathology, but are constantly confronted with the stressors. Especially during adolescence, with the formation of identity, self-image and self-esteem, a CI constitutes a major challenge [7, 8]. In recent years, psychosocial interventions have become increasingly important in the treatment of psychosocial problems (social, emotional and behavioral problems such as loneliness, depression, aggressive behavior) in adolescents with CI [4, 9]. The psychosocial interventions discussed in the literature are mostly disease-specific [10]. For example, a cognitive-behavioral therapy for adolescents with inflammatory bowel disease (IBD) showed decreased depressive symptoms in participants after treatment [11] and a psychosocial group intervention for young people with epilepsy (PIE) was effective in teaching participants about their illness, how to talk about it and how to cope with difficult feelings [12]. Interventions are available in face-to-face as well as online format. Online interventions are upcoming due to new technologies [9, 13]. An online psychosocial intervention could be a cost-effective way to offer therapy [9, 14, 15].

According to the disability-stress-coping model [16], stressors related to illness and psychosocial adjustment of the child are moderated by coping strategies and cognitive appraisals. The model states that the use of more effective coping strategies can prevent or reduce psychosocial problems in children with CI. Moreover, effective use of coping skills increases patients' abilities to manage illness by improving medical compliance and psychosocial functioning [4, 17-19]. Active coping strategies (e.g. cognitive restructuring, relaxation), learned by transforming negative thoughts into positive, more proactive ones, are proven to be more effective than passive, avoidant coping strategies [19]. To prevent and/or reduce psychosocial problems, appropriate interventions to teach adolescents how to cope with stressors caused by the CI are essential.

Interventions can be offered in individual or group format. Results on the effectiveness of group interventions are promising, particularly on learning to use more active coping skills and improving knowledge about symptom reduction and disease-related problem-solving [20]. Most group interventions are focused on a specific illness, such as diabetes [21]. Compared to individual interventions, psychosocial group interventions enable participants to share emotions and experiences and therapists can treat more patients simultaneously [22]. Sharing emotions and experiences is helpful for adolescents with CI, as peer relationships can positively affect social adjustment and adaption to the disease [7, 20]. This is illustrated by the iPeer2Peer program, where adolescents with Juvenile Idiopathic Arthritis (JIA) are matched to a trained 'peer mentor' for receiving peer support via Skype video calls. Thanks to the online format, the intervention is easily accessible and participants show improvements in perceived ability to manage JIA [23]. In summary, most psychosocial group interventions for children with CI focus on a specific illness. However, even though different diagnoses may have different medical treatments, several of the psychosocial problems are the same [20]. With a generic approach, it is easier for patients with rare illnesses to participate in a group intervention. The group intervention Op Koers (in English: "On Track") was designed with this in mind [24, 25].

Op Koers was primarily developed in a face-to-face format. Through cognitive-behavioral therapy (CBT) techniques, participants are taught to use active coping skills to prevent and/or reduce psychosocial problems [24-26]. CBT focuses on recognizing cognitive distortions and on teaching coping and problem-solving skills [27]. Sharing experiences with fellow patients is an important part of the intervention [20, 28, 29]. In a Randomized Controlled Trial (RCT) of Op Koers face-to-face, positive effects were found on psychosocial functioning [26]. The intervention has weekly sessions at the hospital, which can cause logistical barriers for potential participants.

Online intervention programs eliminate logistical barriers such as travel time and distance [30, 31] and connect to the digital environment in which adolescents live. Offering online interventions has additional advantages of improved accessibility, independence (participation from home) and anonymity (possibility to participate with a nickname). Online interventions without use of a webcam adds the benefit that appearance plays no role which might make it easier to talk about problems [32, 33]. Research has also shown that e-health interventions eliminate the stigma related to participating in mental health services and therefore lower the threshold for participation [34]. To this end, Op Koers face-to-face was translated into a chat version: Op Koers Online. The intervention was first designed for adolescent survivors of childhood cancer (Op Koers Online Oncology). A feasibility study shows promising results: participants and course leaders reported high levels of satisfaction and the dropout rate was very low. Most participants considered chatting appropriate for the intervention and reported to prefer Op Koers Online above Op Koers face-to-face. The intervention was optimized based on feedback from participants and course leaders, the number of sessions was expanded from six to eight, arranging the online intervention by age was recommended and severe learning difficulties became an exclusion criteria for participation [33]. Op Koers Online for adolescents (ages 12-18) with CI was subsequently developed.

The aim of this pilot study was to assess feasibility and explore preliminary effectiveness based on disease-related coping skills and psychosocial functioning (emotional/behavioral problems and Health-Related Quality of Life; HRQoL) of Op Koers Online for adolescents with CI.

METHODS

Study design

This quasi-experimental, pre-post intervention pilot study was conducted between October 2013 and September 2015. Participants were asked to complete online questionnaires before the intervention (baseline; T0) and directly after the intervention (after eight weeks; T1). Participants received an e-mail with a hyperlink to the questionnaires and, when necessary, electronic and/or telephone reminders.

Procedure

Participants were recruited via; 1) healthcare providers, 2) folders at the hospital, and 3) online advertising. A pediatric psychologist informed interested adolescents and parents about the procedure and intervention by phone. Adolescents and parents willing to participate were asked to return the signed Informed Consent form sent by mail. Approval of the Medical Ethical Committee of the Amsterdam University Medical Centers was obtained to conduct this pilot study.

Participants

Inclusion criteria were: age between 12-18 years; CI diagnosis according to the definition of Van der Lee et al.: 1) onset between ages 0 and 18, 2) diagnosis based on medical scientific knowledge, 3) the illness is not (yet) curable, and 4) the illness has been present for at least three months, or at least three episodes have occurred in the last year (3), and receiving treatment in the Emma Children's Hospital (Amsterdam University Medical Centers). Participants also had to have access to a computer with internet connection, be able to read and write in Dutch, and independently complete the questionnaires. Adolescents with severe learning difficulties were excluded.

Intervention

Goal of the intervention is to prevent and/or reduce psychosocial problems by teaching the use of active coping skills (Table 1). Five coping skills are taught with CBT techniques (e.g. relaxation, cognitive restructuring and social skills) [35, 36]: 1) information seeking and giving about the illness, 2) use of relaxation techniques in stressful situations, 3) increasing knowledge of self-management and medical compliance, 4) improving social competence and 5) positive thinking

[24, 25]. The Thinking-Feeling-Doing (TFD) model is used to explain how thought influences feelings and behavior. The focus lies on restructuring negative thoughts about the illness such as worrying about participating in or missing school/sports activities, worrying about what others think of you, etc. Lastly, psychoeducation is used to expand participants' knowledge about the topics used in the intervention, e.g. about sources of information and compliance/noncompliance.

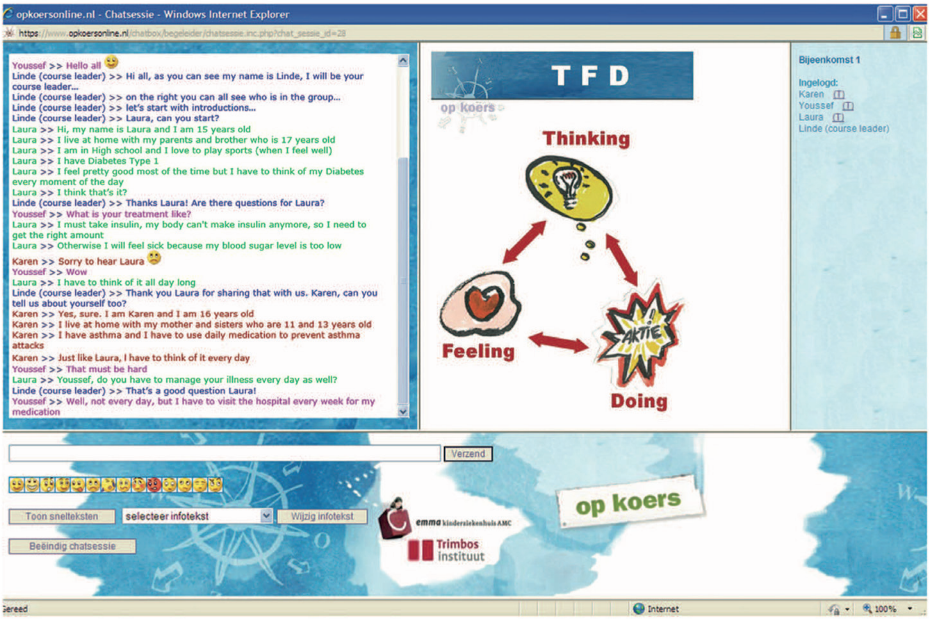
The intervention consists of eight weekly 90-minute sessions that take place at a set time in a secured chatroom (www.opkoersonline.nl) with groups of three to six participants. Participants log on to the website to enter the chatroom (Figure 1) and their personal online environment, where they can view intervention material and submit homework assignments. Sessions are led by two pediatric psychologists (course leaders), who received extensive training in carrying out the intervention based on a detailed manual. To improve adherence, participants receive a small gift (like a memory game) after the last session for participating and completing homework assignments. Four months after the last session, there is a booster session.

The protocol of Op Koers Online protects anonymity. First, participants are asked not to share contact details with each other until the last session. This way, communication between participants during the intervention elapses in the presence of the course leaders. Second, the intervention is designed without a webcam for purposes of anonymity and to keep a low threshold for participation (as participants do not need a webcam).

Table 1. The five basic learning goals of 'Op Koers Online' and examples of learning activities.

		Examples of learning activities	
Learning goals (coping skills)		**Instruction/modelling**	**Practice**
1	Information seeking and giving about the illness	Education about sources of information	Write down questions you have and look for answers
2	Use of relaxation during stressful situations	Relaxation exercise (MP3 fragment)	Practice the relaxation exercise
3	Increase knowledge of self-management and medical compliance	Group discussion about own treatment and compliance/ noncompliance	Write down situations of noncompliance and how to improve compliance
4	Enhancement of social competence	Video and group discussion: how and what do you tell others about your illness	Think of what you CAN (instead of CANNOT) do and write down your story for the other group members
5	Positive thinking	Thinking-Feeling-Doing game	Write down positive adjustments for negative thoughts

Figure 1. Example of a session in the chatroom.



Youssef >> Hello all
Linde (course leader) >> Hi all, as you can see my name is Linde, I will be your course leader...
Linde (course leader) >> on the right you can all see who is in the group...
Linde (course leader) >> let's start with introductions...
Linde (course leader) >> Laura, can you start?
Laura >> Hi, my name is Laura and I am 15 years old
Laura >> I live at home with my parents and brother who is 17 years old
Laura >> I am in High school and I love to play sports (when I feel well)
Laura >> I have Diabetes Type 1
Laura >> I feel pretty good most of the time but I have to think of my Diabetes every moment of the day
Laura >> I think that's it?
Linde (course leader) >> Thanks Laura! Are there questions for Laura?
Youssef >> What is your treatment like?
Laura >> I must take insulin, my body can't make insulin anymore, so I need to get the right amount
Laura >> Otherwise I will feel sick because my blood sugar level is too low
Karen >> Sorry to hear Laura
Youssef >> Wow
Laura >> I have to think of it all day long
Linde (course leader) >> Thank you Laura for sharing that with us. Karen, can you tell us about yourself too?
Karen >> Yes, sure. I am Karen and I am 16 years old
Karen >> I live at home with my mother and sisters who are 11 and 13 years old
Karen >> I have asthma and I have to use daily medication to prevent asthma attacks
Karen >> Just like Laura, I have to think of it every day
Youssef >> That must be hard
Laura >> Youssef, do you have to manage your illness every day as well?
Linde (course leader) >> That's a good question Laura!
Youssef >> Well, not every day, but I have to visit the hospital every week for my medication

Note: Left: chat screen with chat-talk (every participant has his/her own color), smileys to express feelings. Middle: information screen where course leaders can provide information to the participants. At the bottom: menu where course leaders can select information for the information screen. On the far right: listing of the names of participants and trainers.

Measures

Sociodemographic (e.g. gender, age, school-related) and medical information was obtained from adolescents via an online questionnaire. First, feasibility was measured based on attendance (dropouts, missed sessions and homework completion) and technological issues. Online presence was recorded based on entering the chatroom during the session. Participants who explicitly quit the intervention or were absent for four or more sessions were considered dropouts. Course leaders checked if participants completed their homework assignments and recorded technological issues and other particularities in every session log.

Second, an evaluation questionnaire focusing on satisfaction with the content, design and course leaders was completed by participants at T1. The questionnaire consists of two parts with a total of 41 items. The first part has 25 questions (e.g. "What is your opinion about the design of the chatroom?") with different multiple-choice answer options. The second part has 16 statements (e.g. "I liked following the course via a chatroom") with a five-point Likert scale (ranging from 1 "totally agree" to 5 "totally disagree").

Outcome measures of preliminary effectiveness are disease-related coping skills and psychosocial functioning (emotional/behavioral problems and HRQoL), assessed with three specific validated questionnaires. Disease-related coping skills were assessed with the Op Koers questionnaire [24, 33]. Adolescents were asked if they agreed with 26 statements (four-point Likert scale ranging from 1 “always/almost always” to 4 “almost never/never”) on the use of coping skills taught in Op Koers Online (e.g. “I know how to get answers to questions about my disease”). The items are divided into five subscales: information-seeking (6 items), relaxation (3 items), social competence (6 items), positive thinking (3 items) and medical compliance (8 items). All items together form a total scale score. Mean item scores were calculated for the subscales and the total score (range 1-4). Higher scores reflect use of more active coping skills. Subscales had moderate to good internal consistencies (Cronbach’s α=0.46 for social competence T0 to α=0.71 for relaxation T1). The total scale had good internal consistency (T0 α=0.70, T1 α=0.89). The subscale medical compliance was not used in the analyses because of insufficient internal consistency (T0 α=0.10, T1 α=0.40), but the items of that subscale were included in the total scores.

Emotional and behavioral problems were assessed with the Youth Self Report (YSR) [37] consisting of 119 problem items (three-point Likert scale ranging from 0 “not at all” to 2 “often/a lot”). The YSR has two broadband scales each consisting of subscales: internalizing problems (31 items, range: 0-62), including the subscales anxious/depressed (13 items), withdrawn/depressed (8 items) and somatic complaints (10 items), and externalizing problems (32 items, range: 0-64) including the subscales rule-breaking behavior (15 items) and aggressive behavior (17 items). We excluded the subscale somatic complaints from internalizing problems, since all participants have somatic complaints due to their illness (38). On this questionnaire, higher scores indicate more problems. Cronbach’s alphas for the YSR (sub)scales at T0 and T1 were moderate to good (α=0.61 for aggressive behavior T0 to α=0.86 for internalizing problems T0) except for the subscale rule-breaking behavior which was therefore excluded from further analysis (α=0.36, T1). T-scores were used to assess whether participants reported subclinical/clinical symptoms; T-scores in the 90th percentile or higher in the norm population are considered subclinical/clinical, indicating that the adolescent has clinically relevant symptoms and may need professional help [37]. To indicate the percentage of participants scoring within the subclinical/clinical range (T-score 63 or higher), we computed T-scores from the raw scale scores.

HRQoL was measured with the Pediatric Quality of Life Inventory – self report (PedsQL 4.0) [39]. All items state a problem (e.g. “difficulty walking”), and participants indicate to what extent they had difficulties with that problem in the past month (five-point Likert scale ranging from 0 “never” to 4 “always”). The PedsQL 4.0 contains 23 items divided into four subscales: physical functioning (8 items), emotional functioning (5 items), social functioning (5 items) and school functioning (5 items). The psychosocial functioning scale score is the combined score of emotional, social and school functioning, and the total score is the sum of all subscales. Higher scores indicated a better HRQoL (range 0-100). Cronbach's alpha of the PedsQL (sub)scales were moderate-to-good (lowest α=0.66 for physical functioning T0 and highest α=0.89 for physical functioning T1).

Statistical Analyses

Descriptive analyses were performed to characterize the participants. To assess feasibility, we calculated percentages of attendance and analyzed the results on the evaluation questionnaire descriptively. To assess preliminary effectiveness, mean scale scores on disease-related coping skills, emotional/behavioral problems and HRQoL at T1 were compared to T0 by paired sample t-tests ($p<.05$) using SPSS. Given the explorative character of these analyses, we decided not to correct for multiple testing. Between-subject effect size, Cohen's d, was calculated by dividing the difference in mean scores T1-T0 by the standard deviation at T0. Effect sizes d of .2 were considered small, .5 medium and .8 large [40]. The use of between-subject effect size was preferred over within-subject effect size because in small samples as in our pilot study, calculation of within-subject effect size may result in overestimation of the effect size. In addition, the use of between-subject effect sizes is common, which benefits the interpretation of the results [41].

RESULTS

Participants

Divided over six groups, 33 adolescents participated during the pilot period. A total of 29 participants (88%) completed the questionnaires at T0. At T1, 25 (76%) participants completed the evaluation questionnaire and 23 (69%) completed the other questionnaires too.

Table 2 presents the participant characteristics. A majority of the participants was female (62.1%), mean age was 15.1 years. There was a large variability in diagnoses, 31% occurred once. Most common diagnoses were bowel disease (20.7%) and Cystic Fibrosis (17.2%). Ten percent had subclinical/clinical scores on internalizing problems at T0. There were no subclinical/clinical scores on externalizing problems.

Table 2. Characteristics of participants of Op Koers Online (*n*=29).

	n	M	SD or %	Range
Age at T0 (years)	29	15.1	1.85	12.3-18.9
Age at diagnosis (years)	25	5.4	6.44	0-17
Female	18		62.1	
Diagnosis[a]				
Bowel disease	6		20.7	
Cystic Fibrosis (CF)	5		17.2	
Rheumatological disease	4		13.8	
Metabolic disease	3		10.3	
Heart disease	2		6.9	
Other[b]	9		31.0	
Education (current)				
Elementary school (last year)	1		3.4	
Secondary education	26		89.7	
Secondary vocational education	2		6.9	
Treatment[a]				
Use of medication	20		68.9	
Regular hospital visits	28		96.5	
Surgery	4		13.7	
Diet	1		3	

[a] More than one answer is possible
[b] Other diagnoses occurred once and were: eczema, epilepsy, Graves' disease, IL12 deficiency, hereditary motor and sensory neuropathies (HMSN), spherocytosis, Alagille Syndrome and endometriosis.

Feasibility

Attendance

Fourteen out of 33 participants (42%) attended all eight regular chat sessions, 14 participants (42%) missed one session and three participants (10%) missed two sessions, mostly due to illness or hospitalization and sometimes school (homework). Dropout rate was 6%; two participants decided to quit during the intervention (one due to illness/hospitalization, one due to school-related lack of time). They attended less than three sessions. Attendance at the booster session was 88% (two participants who finished the entire intervention did not attend the booster session). Fourteen participants (45%) completed all homework assignments. Six participants (19%) failed to complete one assignment, five participants (16%) failed to complete two assignments and six participants (16%) failed to complete three or more assignments.

Technological issues

In 96% of the sessions, no technological issues occurred. In one session (2%) there was a technological breakdown of the website so that the session had to stop and resume later. In one other session (2%) the chatroom was interrupted a few times, but the session could go on. Sometimes a participant reported technological issues (6%; e.g. interruption of the chatroom, seeing messages multiple times). Course leaders could join the session, and kept contact with participants on how to deal with an issue (e.g. press F5/CMD+R, restart the chatroom).

Evaluation questionnaire

According to the first part of the questionnaire, a majority of participants had previously used chat as a communication tool (52% regularly or often, 20% sometimes). The provided information about the content of the intervention before the start was “enough” according to 84% of participants. Most participants were satisfied with the usability of the chatroom, 64% rated it as “good”. Some participants (12%) thought the design of the chatroom was not attractive. Most participants (84%) were positive about the course leaders. Regarding duration, 20% of participants thought chat sessions were too short and 24% thought they were too long. Most participants (76%) said the number of sessions was enough. Homework assignments were rated as “good” by most participants (92%). All participants rated the intervention as understandable. The intervention was found “quite useful” by 68% of participants and “useful” by the other 32%.

On a scale of one to ten, 92% of participants rated a seven or higher for overall satisfaction with the intervention (mean: 8.2), 16% of them rated a ten. More than half of participants (52%) would definitely recommend the intervention to others, some participants (32%) would likely do that and a minority of participants might not (16%). A majority of participants (84%) rated the design of the chatroom a seven or higher. In the end, 72% participants said that given the choice, they would prefer an online group intervention over a face-to-face group intervention.

The results of the second part of the evaluation questionnaire are presented in Table 3. A majority of the participants thought a chatroom is a good format for this intervention and reported that chatting is a good way for them to talk about difficulties related to the illness. Most participants felt understood by other participants. Opinions were divided about the use of smileys (faces with expressions of emotions to use in the chatroom), anonymity and webcam use.

Table 3. Statements about Op Koers Online, evaluation questionnaire (*n*=25).

	(totally) agree	don't agree/ don't disagree	(totally) disagree
The chat box	%	%	%
A chat box is a good format for this intervention	88	12	0
I liked taking part in the intervention via a chat box	76	12	12
I found it hard to take part in the intervention via a chat box [a]	20	8	72
Chatting is a good way for me to talk about the difficulties I have in relation to the consequences of my illness	80	4	16
During the chat sessions…			
… it was hard for me to follow the subject [a]	8	12	80
… a lot of messages appeared on the screen at once	40	32	28
… it was (mostly) clear who responds to whom	68	24	8
… I could (mostly) say what I wanted to say	84	8	8
Interaction	%	%	%
The course leaders responded to what I said	96	0	4
I felt understood by the course leaders	88	8	4
I felt understood by the other participants	92	0	8
Tool for expression of feelings	%	%	%
Smileys helped me express my feelings	28	32	40
Smileys helped me understand participants' feelings	40	32	28
Privacy	%	%	%
I liked the fact that participation was anonymous	36	32	32
I would have liked to see other participants via webcam	36	24	40
I would have liked to see course leaders via webcam	32	12	56

[a] Statement is negative

Preliminary effectiveness

Table 4 shows significant improvement in coping skills: total scale, *t*(21)=-2.83); information-seeking, *t*(21)=-3.07; and social competence, *t*(21)=-2.68. Significant decrease in emotional/behavioral problems was found for: externalizing, *t*(22)=2.36; withdrawn/depressed behavior, *t*(22)=3.27; attention problems, *t*(22)=2.21; and aggressive behavior, *t*(22)=2.47. HRQoL improved on: total scale, *t*(21)=-2.58; emotional functioning, *t*(21)=-4.06; and psychosocial functioning, *t*(21)=-3.42.

Table 4. Effectiveness, T1 versus T0: disease-related coping skills (*Op Koers questionnaire)* and psychosocial functioning (emotional and behavioral functioning; *YSR* and HRQoL; *PedsQL*).

	T0	T1		
	Mean (SD)	**Mean (SD)**	***p*-values**	**Effect size (d)**
Op Koers questionnaire[1] – *n*=22				
Seeking/giving information about the illness	2.72 (0.48)	3.01 (0.53)	**<0.01**	0.60
Relaxation during stressful situations	2.41 (0.65)	2.61 (0.73)	0.16	0.31
Social competence	2.55 (0.48)	2.77 (0.45)	**0.01**	0.46
Positive thinking	2.33 (0.58)	2.62 (0.73)	0.06	0.50
Total	2.83 (0.29)	3.00 (0.43)	**0.01**	0.59
Youth Self Report [2] (YSR) – *n*=23				
Internalizing problems [3]	11.83 (6.67)	10.61 (6.27)	0.17	0.18
Anxious/Depressed	6.13 (4.40)	6.00 (4.25)	0.84	0.03
Withdrawn/Depressed	5.70 (3.01)	4.61 (2.64)	**<0.01**	0.36
Thought problems	4.74 (3.24)	4.30 (3.36)	0.20	0.14
Externalizing problems	5.65 (3.59)	4.30 (3.40)	**0.03**	0.38
Social problems	3.74 (3.11)	3.61 (3.01)	0.81	0.04
Attention problems	6.04 (3.30)	5.09 (3.15)	**0.04**	0.29
Aggressive behavior	3.52 (2.66)	2.26 (2.36)	**0.02**	0.47
Pediatric Quality of Life Inventory – self report [1] (PedsQL) – *n*=22				
Total score	55.93 (14.23)	61.07 (15.19)	**0.02**	0.36
Physical functioning	50.99 (21.87)	54.26 (22.81)	0.37	0.15
Emotional functioning	56.36 (23.41)	67.95 (20.51)	**<0.01**	0.50
Social functioning	69.31 (19.66)	71.59 (15.54)	0.43	0.12
School functioning	50.00 (17.18)	54.55 (18.19)	0.18	0.26
Psychosocial functioning	58.56 (15.13)	64.70 (15.14)	**<0.01**	0.41

Note: Significant differences are bolded.
[1] Higher scores indicate more use of coping skills or better HRQoL
[2] Higher scores indicate more problems
[3] Without Somatic Complaints subscale.

DISCUSSION

The aim of this pilot study was to assess feasibility and explore preliminary effectiveness of Op Koers Online. Regarding feasibility, we found good attendance: the dropout rate was low (6%) compared to dropout rates of other internet-based interventions for adolescents [42]. The technological quality was good; small issues were fixed by course leaders and/or the web developer. Only one time did a technological issue cause the end of a session. Participants reported positive overall satisfaction with the intervention, indicating its feasibility for this population with CI. Regarding effectiveness, we found improvement on disease-related coping skills and HRQoL, and decrease of emotional/behavioral problems.

Feasibility

According to the evaluation questionnaire, participants' opinion about taking part in the intervention anonymously is divided. Regarding webcam use, the difference in percentages between participants who did and did not want to see other participants and course leaders via a webcam is small, which indicates that a considerable portion of participants would have liked more openness. In the pilot study Op Koers Online Oncology, opinion about anonymity was divided too [33]. As discussed, Op Koers Online is intentionally designed without a webcam, and the protocol is set up to ensure anonymity. Furthermore, results of the evaluation questionnaire showed that for a majority of participants the smileys were not specifically helpful to express personal feelings. This could be due to the type of smileys, which are a little outdated. Also, a majority of participants found that the design of the chatroom was not particularly attractive. When optimizing the intervention, a renewed, more attractive design and updates of smileys should be considered.

Among the advantages of offering this intervention online is improved accessibility. The disadvantage is the risk of technological issues which can interrupt with the intervention. Recommendations on what to do when that happens were included in the manual. For example, course leaders can call the web developer for help, and course leaders and participants can press F5 (CMD+R for Apple) to reset the chatroom. Course leaders are advised to call participants when they lose online contact to assist them with resuming the chat.

Preliminary effectiveness

Most results seemed in line with findings on efficacy of the Op Koers face-to-face intervention [26]. However, given the different study designs actual comparison of this pilot study with the RCT is not workable. The coping skill 'use of relaxation' did not improve significantly in participants after following Op Koers Online. This could be explained by the way the relaxation exercise is taught. Participants had to practice with a sound fragment themselves. Though the course leaders asked questions to monitor the performance, it was difficult to check whether participants were performing the exercise correctly. To make the relaxation exercise more attractive for adolescents and increase participant willingness to perform the exercise, we recommend adding a movie to the sound fragment.

So far, studies focusing on online group interventions for chronically ill adolescents in the Netherlands are limited. Studies abroad show promising results on the efficacy of internet-delivered cognitive-behavioral interventions for youth with CI [43-45], but much work remains to be done [46]. The present study's contribution to the field is an evaluation of an online group intervention (chat) for adolescents. Especially the fact that we include adolescents with all kinds of diagnoses is new. In terms of feasibility and preliminary effectiveness, we find comparable results with former research: positive results on preliminary effectiveness and good feasibility [10-12, 21, 23]. The pilot study had some limitations. First, recruitment and enrollment rates are not known because an open recruitment strategy was followed. Second, the data of the assessment after the booster session could not be used for analysis because of too low response rate (10%). Third and fourth limitations are the rather small sample size and a one-group pre/post design. Although the sample size is appropriate for a pilot study, a larger sample and a control group to compare with the results of the intervention group would have expanded our capacity to find evidence for feasibility and potential effectiveness. Notably, effect sizes found in pilot studies should be interpreted with caution as the meaning of hypothesis testing is limited in pilot studies ([47, 48]. Fifth, because of the explorative nature of the analyses, we did not control for multiple testing. Because of these limitations, our findings should be interpreted with caution.

CONCLUSION

First steps into assessing feasibility and effectiveness of Op Koers Online for adolescents with CI were taken. Results are promising; the use of coping skills and psychosocial functioning has improved. The current study shows that an online CBT intervention is feasible for adolescents with CI and that they benefit from the therapeutic techniques used. It also shows that a generic approach is appropriate for these adolescents, which is contributing to the existing knowledge on psychosocial group interventions. As the results of a pilot study should be interpreted with caution, results should be validated in an RCT.

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CHAPTER 4

EFFICACY OF OP KOERS ONLINE, AN ONLINE GROUP INTERVENTION FOR PARENTS OF CHILDREN WITH CANCER: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

PSYCHO-ONCOLOGY, 2024

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ABSTRACT

Objective Parents of children with cancer are at risk for developing psychosocial problems. The present study aims to evaluate the effect of an online group intervention (Op Koers Online, in English: On Track Online) on psychosocial wellbeing and coping skills.

Methods Parents of a child with cancer (diagnosis <5 years ago) participated in a randomized controlled trial. In six consecutive (and one booster-) protocolled sessions in an online chatroom, trained psychologists and social workers taught coping skills using cognitive behavioral and acceptance and commitment techniques. Questionnaires assessed anxiety, depression, distress, situation-specific emotional reactions and coping skills (Op Koers Questionnaire/Cognitive Coping Strategies Scale Parent Form) and evaluated the intervention. Linear mixed-model analyses were performed to detect differences between the conditions in changes over time; T0–T1 and T0–T2 (6-week and 6-month follow-up), and to detect changes in scores T2–T3 (12-month follow-up) for the intervention group only.

Results 89 parents were included in analyses (mean age 41.9 years, 86% female, 62%/38% post/during treatment of their child). Beneficial intervention effects ($p < 0.05$) were found at T1 for anxiety, depression, distress, loneliness and relaxation, and at T2 for anxiety, uncertainty and relaxation. In the intervention condition, scores did not change from T2 to T3, except loneliness that decreased and relaxation that improved. All effect sizes were small to medium ($\beta = -0.21$ to 0.46). Parents were generally positive about the intervention.

Conclusions Op Koers Online for parents of children with cancer has a positive effect on psychosocial wellbeing and the coping skill relaxation. Implementation is recommended to prevent psychosocial problems.

Clinical Trial Registration Dutch Trial Register https://onderzoekmetmensen.nl/en NL73763.041.20

BACKGROUND

Each year, approximately 600 children are diagnosed with childhood cancer in the Netherlands, and around 400,000 children worldwide [1]. Parents and caregivers of children with cancer (further referred to as parents of children with cancer) are confronted with stressful and unpredictable events, such as treatments, hospitalizations and the possibility of long-term health effects in their child. During treatment, posttraumatic stress symptoms (PTSS) are common among parents [2], often preceded by rumination caused by illness uncertainty [3] and uncontrollability. Parents of children with cancer reported increased general distress [4], anxiety and depression [5,6]. Although the end of treatment may seem like a relieving time point, parents are often vulnerable in the period after finishing their child's treatment and PTSS can be persistent [7,8]. Psychosocial problems in parents tend to be correlated to difficulties in management of their child's illness [9], and a significant relationship has been found between parent psychosocial distress and child quality of life outcomes in families of children with cancer [10]. Even though many parents of children with cancer are resilient [11], it is important to offer appropriate interventions, to optimize parent, child and family wellbeing, as is stated in the standards of psychosocial care [12].

The disability-stress-coping model by Wallander and Varni [13] reflects that the relation between the stressors that families of a child with cancer have to face and their wellbeing is mediated by coping skills. Coping skills are, in their turn, related to personal, family and environmental factors. The disability-stress-coping model was adapted for different Op Koers studies previously [14] and refined for this study to explain outcomes for parents of a child with cancer (Supplementary Figure S1). The adapted model shows that both coping skills and the mentioned factors can be targets for intervention. Cognitive coping strategies for stressful events can generate feelings of mastery and control. For example, labeling ordinary events with positive meaning and appraising stressful situations as challenges rather than burden. The ways in which parents cope with the consequences of childhood cancer can be regarded as an important factor for their emotional functioning during and after cancer of their child.

Interventions that are based on cognitive behavioral therapy (CBT) and acceptance and commitment therapy (ACT) could offer parents tools for coping with disease-related stressors and in raising a child with cancer [15]. CBT focuses on recognizing negative thoughts and restructuring them into helpful thoughts, whereas ACT involves reducing the impact of negative thoughts on daily life through acceptance of those thoughts. CBT interventions are effective in reducing distress, depression and anxiety in families of children with cancer [16]. ACT interventions were found to reduce PTSS and emotional symptoms [17]. Group interventions may be additionally helpful because they involve elements of modeling, helping others, joint problem solving and sharing experiences which are associated with a decrease of distress and improvement of resilience and mental health [18–20]. Furthermore, online interventions are on the rise because a digital format has fewer practical barriers, such as traveling distance, when compared to in-person formats [21]. Besides, participating online instead of in person is an opportunity for anonymity, which can encourage participants to self-disclose more easily and to discuss taboos [22].

Internationally, online courses for parents of children with cancer have been studied [23-24], yet such research is lacking in the Netherlands. Op Koers Online is a Dutch group course program with face-to-face and online courses with separate modules for different family members. Research has shown it is an effective group intervention for children and adolescents with a chronic illness and their parents [14, 25, 26]. The originally online intervention was refined for parents of children with cancer, incorporating oncology-specific examples and psychoeducation (e.g., chemo therapy as a form of treatment). The current study aims to investigate the effect of Op Koers online for parents of children with cancer on psychosocial wellbeing and coping skills and additionally, to evaluate the intervention with parent.

METHODS

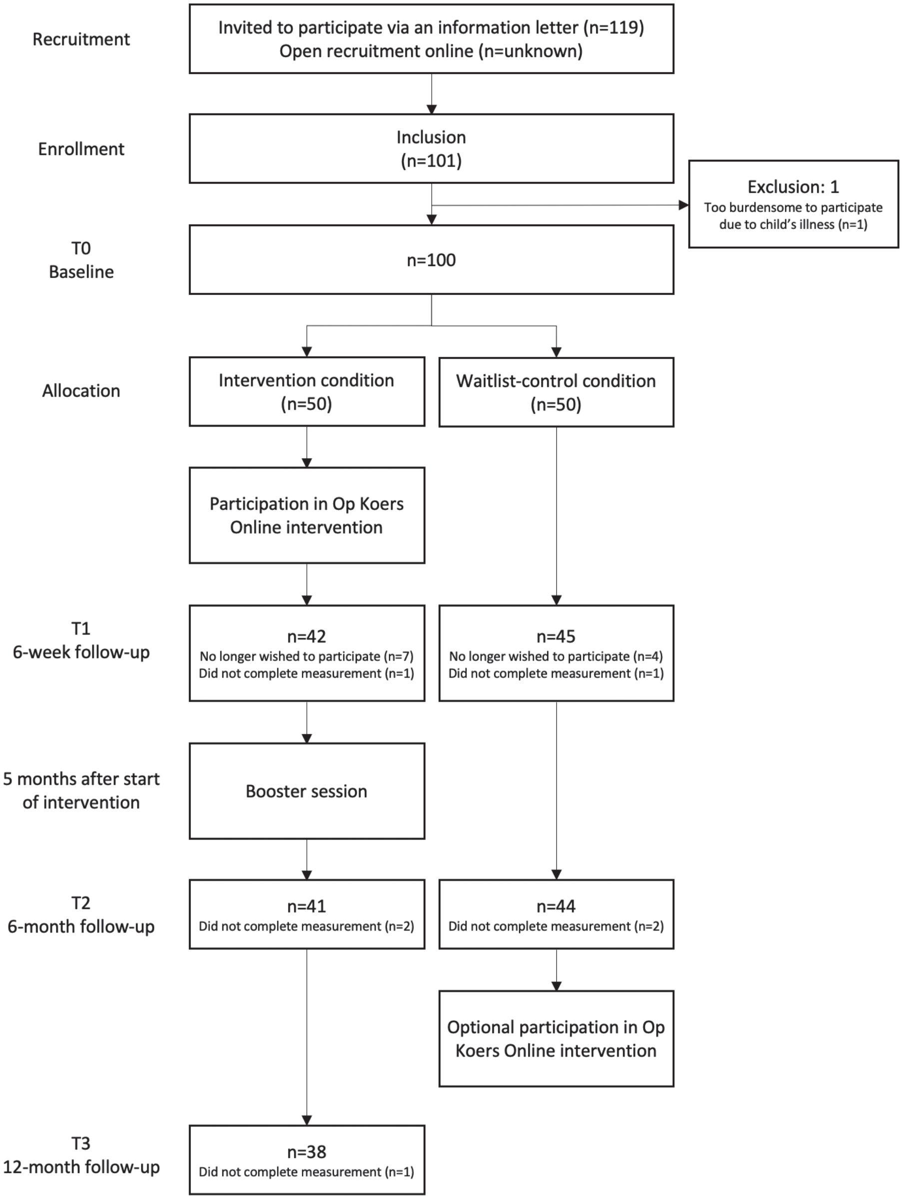
Design

A randomized controlled trial (RCT) with an intervention condition and a waitlist-control condition was performed to assess the efficacy of Op Koers online for parents of children with cancer. Online questionnaires were administered at baseline before randomization (T0), at 6 weeks (T1) and at 6 months (T2) after start of the intervention, and after 12 months (T3) in the intervention condition only (Figure 1). Additionally, parents from the intervention condition completed an evaluation questionnaire (T1). Parents from the waitlist-control condition could participate in the intervention after completion of the questionnaires at T2. The Medical Ethics Board of the University Medical Centre Utrecht approved the study protocol (ref 20/289).

Procedure

Inclusion for this study ran from September 2020 to January 2022. Parents were recruited via (1) calls in the newsletter and on social media of the hospital and parent association, (2) leaflets in the outpatient clinic at the Princess Máxima Center for pediatric oncology, (3) information letters and leaflets via mail. Parents were instructed to leave their contact details on the Op Koers website if they were interested. They were then phoned by the psychologist-researcher for an intake, to assess eligibility and discuss details of participation, after which they signed an informed consent form. Parents were eligible if their child was (1) diagnosed with cancer at the age of 0–18 years, (2) within 5 years from diagnosis (during or after successful treatment), and (3) still living with his/her parent(s). Parents additionally had to have access to a laptop/computer with an internet connection. Parents were excluded if they were not able to follow a group chat course and/or were not able to fill out Dutch questionnaires.

Figure 1. Flowchart participants.



Randomization

Participants were randomized to the intervention or waitlist-control condition with a 1:1 ratio. Randomization was stratified on treatment phase: (1) in treatment, (2) <1 year after treatment, (3) 1+ year after treatment, to ensure that the distribution of treatment phase was similar in both conditions. The randomization was carried out by an independent e-health company who administers the Op Koers website, using block randomization software.

Intervention

The goal of the Op Koers intervention is to teach active coping skills in order to reduce and/or prevent problems in psychosocial wellbeing. The intervention consists of 6 weekly 90-min online chat sessions and a booster session 5 months after the start of the course. Participants and course leaders log into a secured chatroom (www.opkoersonline.nl) on a set day and time every week, either in the morning or the evening. Parents can choose to participate with a nickname, allowing for anonymity. The sessions take place with three-six parents under supervision of a registered healthcare psychologist and a social worker/psychological assistant, who carry out the protocolled intervention. Parents in a group are all in the same phase, either during active treatment or after successful treatment. The sessions focus on different themes: CBT-principles, the hospital, the family, taking care of yourself, and environment/society. In between sessions, parents are provided with in-depth reading material and homework assignments. See Table 1 for a description of the intervention content. Course leaders (*n* = 25) were trained by the researcher in using the detailed intervention protocol as well as in the theoretical background of the course.

Table 1. Content of the intervention.

Session	Content	Home assignments	In-depth information
1. Introduction and Cognitive Behavioral Theory (CBT) principles	• Introduction of the course • Getting to know each other • Introduction to the CBT-model	• CBT exercises (in relationship to self, partner, children) • CBT movie clip • Describing satisfying moments with the family	• Session summary • CBT psycho-education • Hearing the diagnosis
2. The hospital	• Process of the medical treatment • Strengths and difficulties in coping with the medical treatment	• Discuss regulations and restrictions the child has to comply with, together with the child • List strengths and difficulties in adherence. • List questions for the doctor, together with the child • CBT exercises	• Session summary • Dexamethasone • Difficulties in eating and sleeping • Independence of the child
3. The Family	• Impact of child's illness on the family (child, siblings, partner relationship) • Strengths and difficulties of the family	• List family activities • List activities to do with partner • Discuss child's illness with siblings (questions, thoughts, worries) • CBT exercises • Compliment giving exercises	• Session summary • Siblings • Developing a vision with partner about the illness and treatment • Children's quarrels • Family structure • Giving compliments • Thought habits, thinking errors • Ruminating
4. Taking care of yourself	• Impact of child's illness on self • Managing your roles as parent, partner, employee, friend • Balance between private life and work/study	• Relaxation exercise • Giving yourself compliments • List stress increasing/ decreasing moments • CBT exercises	• Session summary • Relaxation • Positive activities • Strategies to cope with negative thoughts
5. Environment/ society	• Who are your support figures • Which forms of support do you like • Difficulties in relationships with other people • Other people's reactions • Relationship with school	• List support figures • Talking to partner • Discuss difficult reactions from other people with partner • CBT exercises	• Session summary • Asking help/being offered help • School
6. Looking back	• Complimenting fellow participants • Looking back at course • Evaluation of course	• Session summary	
7. Booster session (5 months after first session)	• Talk about past months • Looking back at course (what did you learn, what did you use in daily life, what parts did you find useful)		

Measures

Background and illness characteristics

An online questionnaire was used to assess socio-demographic characteristics (parent and child age, gender, educational level, family status and former psychological help) and illness characteristics of the child (diagnosis, date of diagnosis, treatment phase, and if applicable end of treatment date).

Psychosocial wellbeing

Anxiety and depression were measured using item banks of the Patient-reported Outcomes Measurement Information System (www.healthmeasures.net) [27]. Both item banks were administered as Computerized Adaptive Tests (CAT V1.0), where items are selected based on responses to previously completed items, resulting in a reliable score with fewer items than in traditional questionnaires [28]. Items are scored on a 5-point Likert scale, 1 "never" to 5 "always." The CAT's estimate the level of functioning that is reflected by a T-score which has a mean of 50 and standard deviation (SD) of 10 in the U.S. general population. Higher scores represent more anxiety or depression. References for the Dutch population are available [29].

Distress was measured using the Distress Thermometer for Parents. We used only the thermometer on which parents are asked to rate their overall distress regarding physical, emotional, social and practical issues on a scale of 0 (no distress) to 10 (very much distress). Reference values of Dutch parents are available [30].

Disease-specific emotional reactions were measured using the Situation-Specific Emotional Reaction Questionnaire [31]. consisting of 30 items (4-point Likert scale, 1 "almost never" to 4 "almost always") in four subscales: feelings of loneliness, feelings of helplessness, positive feelings and feelings of uncertainty. Higher scores reflect more experience of the emotional reactions. Internal consistency was satisfactory in this study (Cronbach's alpha range 0.82–0.93).

Coping skills

Disease-related coping skills were assessed with the Op Koers Questionnaire for Parents [26]. Parents are presented with 25 statements (4-point Likert scale, 1 "always/almost always" to 4 "never/almost never") in four subscales: open communication, relaxation, social support and positive thinking. Higher scores indicate more use of coping skills. Internal consistency was satisfactory in this study (Cronbach's alpha range 0.76–0.80) except for the social support scale that was low (0.53) and therefore excluded from analyses.

Predictive control was measured with the Cognitive Coping Strategies Scale Parent Form. The questionnaire assesses to what extent parents of children with an illness try to maintain a sense of cognitive control, by relying on cognitive coping strategies [32]. We used the predictive control strategy domain, that consists of five statements (4-point Likert scale, 1 “totally agree” to 4 “totally disagree”). Item scores are recoded so that higher scores indicate that parents are more optimistic about the course of the child’s disease. Cronbach’s alpha was satisfactory (0.68) in this study.

Intervention evaluation

The intervention was evaluated using 18 multiple-choice questions of a self-developed questionnaire. Topics included different aspects of the course (e.g., level and usefulness of homework assignments), practicalities (e.g., amount of sessions) and experience of participating in the intervention in general (e.g., feeling understood by the course leaders).

Statistical analyses

A priori power calculations indicated that with within-subject correlations of 0.5, a sample size of 94 (47 in both conditions), was necessary to achieve 80% power to detect differences of 0.5 standard deviation units on the outcome parameters between the conditions over time at a significance level of 5% [33]. Baseline differences between the conditions on background and illness characteristics and outcome measures were tested with independent sample t-tests (continuous variables) and $\chi 2$-tests (categorical variables). Psychosocial wellbeing at baseline was compared with Dutch norms, if available, using analysis of covariance corrected for age and sex (distress) or one-sample t-test (anxiety and depression). To examine efficacy of the intervention accounting for dependency of data within participants, linear mixed models analyses (SPSS Version 26) were performed. Participants were included in the analyses if their data was available for T0 and for T1 and/or T2 and they attended at least four out of six course sessions. Missing data were not imputed. All continuous variables were standardized expressing deviations from the mean at T0, for meaningful interpretation of regression coefficients.

Linear mixed models were fitted following Twisk et al. [34] with a random intercept and fixed slopes for time (T1 vs. T0 and T2 vs. T0) and the interaction term study condition × time (=intervention effect). Dependent variables were anxiety, depression, distress, disease-specific emotional reactions, and coping skills. All models were corrected for age and sex. To check for confounders, background and medical variables (from Table 2) were added to the model, one by one. If a variable caused >10% change in the intervention effect, it would have been added to the final model, however, this never occurred.

For the intervention condition only, additional linear mixed models were fitted to detect significant changes in scores from T2 to T3, indicating whether levels of wellbeing and coping were maintained, decreased or improved on the long-term. An alpha of 0.05 was used to test the statistical significance of the effects. Descriptive statistics were used to analyze the evaluation questionnaire.

RESULTS

The participant flow from enrollment to follow-up is shown in Figure 1. Recruitment ended when the desired amount of participants signed informed consent and the trial ended when the last parent completed their final measurement in May 2023. In total, 100 parents participated in the study, of whom 89 could be included in analyses, 43 in the intervention condition and 46 in the waitlist-control condition. No differences were found between the intervention and the waitlist-control condition at baseline on characteristics (Table 2) or outcome measures. Participants in both conditions had higher levels of anxiety, depression and distress than Dutch norms at baseline [29], [30]. All participants in the intervention condition attended at least four sessions.

Psychosocial wellbeing

The intervention had a beneficial effect on anxiety ($\beta = -0.35$), depression ($\beta = -0.33$), distress ($\beta = -0.46$) and feelings of loneliness ($\beta = -0.25$) at T1, and on anxiety ($\beta = -0.40$) and feelings of uncertainty ($\beta = -0.32$) at T2 (Table 3, Figure 2). No effects were found on feelings of helplessness and positive feelings. In the intervention condition, wellbeing did not change from T2 to T3, except feelings of loneliness that decreased ($\beta = -0.21$).

Coping skills

The intervention had a beneficial effect on the use of coping skill relaxation at T1 ($\beta = 0.35$) and at T2 ($\beta = 0.32$) (Table 3, Figure 2). No effects were found for coping skills open communication, positive thinking and predictive control. In the intervention condition, relaxation improved from T2 to T3 ($\beta = 0.28$).

Evaluation

Parents rated the intervention with a 7.6 out of 10 on average. 87.8% would recommend the course to peers and 73.2% learned something new. The percentage of parents rating a component useful ranged from 75.6 to 97.5. All logistic aspects of the sessions (e.g., starting time of the sessions) were rated as good/right by at least 82.9% of parents. Reading material and homework assignments were considered (somewhat) useful by all parents. The majority of parents felt understood by both course leaders (90.2%) and fellow participants (92.7%). 47.1% would have rather used videoconferencing than a chatroom, while 24.4% was happy to be able to participate anonymously. Results of the evaluation are further presented in Figure 3 and Supplementary Table S1.

Table 2. Baseline Characteristics of Parents Included in the Analyses: intervention group vs waitlist control group.

	Intervention *n*=43		**Waitlist control *n*=46**		***p*[a]**	**(Cohen's *d* or Cramer's V)**
	Mean or n	**(sd) or (%)**	**Mean or n**	**(sd) or (%)**		
Age parent (years)	41.6	(6.9)	42.2	(8.0)	.678	(*d*=-.09)
Age child (years)	10.5	(5.8)	9.7	(5.5)	.510	(*d*=.14)
Age child (years)					.986	(V=.02)
0-4	6	(14)	7	(15.2)		
5-12	20	(46.5)	21	(45.7)		
12+	17	(39.5)	18	(39.1)		
Gender					.082	(V=.18)
Male	3	(7.0)	9	(19.6)		
Female	40	(93.0)	37	(80.4)		
Educational level					.334	(V=.16)
Low	1	(2.3)	2	(4.3)		
Middle	13	(30.2)	20	(43.5)		
High	29	(67.4)	24	(52.5)		
Family status					.062	(V =.25)
Single parent	6	(14.0)	2	(4.3)		
(Blended) family	37	(86.1)	44	(95.6)		
Former Psychosocial help					.259	(V=.12)
Yes	16	(37.2)	12	(26.1)		
No	27	(62.8)	34	(73.9)		
Diagnosis of child					.398	(V =.14)
Hematology	18	(41.9)	25	(54.3)		
Solid tumors	13	(30.2)	13	(28.3)		
Neuro	12	(27.9)	8	(17.4)		
Time since diagnosis (years)	1.7	(1.1)	1.9	(1.3)	.438	(*d*=-.18)
Treatment status					.815	(V=.07)
In treatment	15	(34.9)	19	(41.3)		
<1 year after treatment	13	(30.2)	12	(26.1)		
1+ year after treatment	15	(34.9)	15	(32.6)		

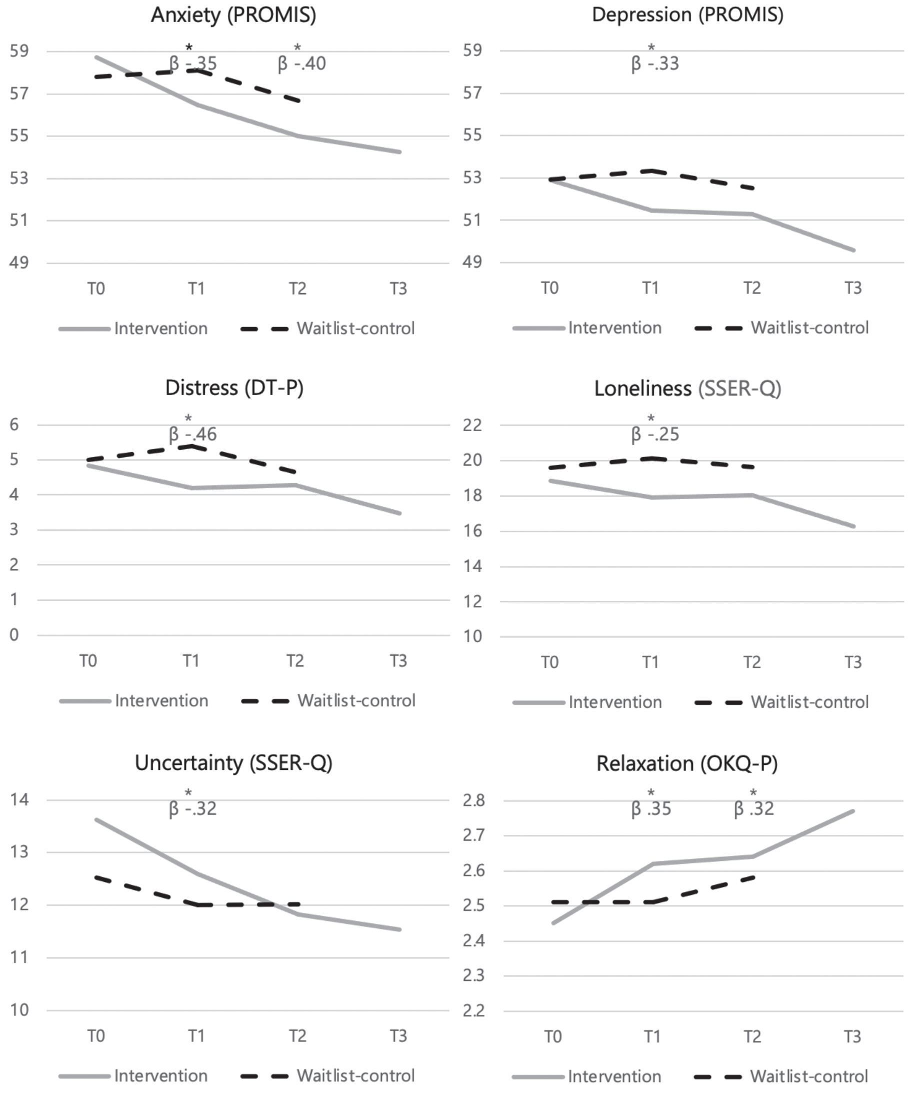
[a] Group differences tested with independent samples *t*-tests for continuous variables and χ2-tests for categorical variables. After Cohen, regression coefficients of dichotomous variables of .2, .5 and .8 and regression coefficients of continuous variables of .1, .3 and .5 were considered small, medium and large [1].

Table 3. Intervention effects: Results of Linear Mixed-Model Analyses, including Means, SD at Baseline (T0), 6-week (T1), 6-month Follow-Up (T2) and 12-month Follow-Up.

	Intervention group								**Waitlist-control group**						**Intervention vs waitlist-control Condition*time**						**Changes from T2 to T3**		
	T0 (*n*=43)		**T1 (*n*=41-42)**		**T2 (*n*=41)**		**T3 (*n*=38)**		**T0 (*n*=46)**		**T1 (*n*=44-45)**		**T2 (*n*=42-44)**		**T0-T1**			**T0-T2**			**T2-T3**		
	M	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**β**	**[95% CI]**	**p**	**β**	**[95% CI]**	**p**	**β**	**[95% CI]**	**p**
Psychosocial outcomes																							
PROMIS																							
Anxiety	58.74	(5.82)	56.49	(3.99)	54.99	(5.97)	54.27	(5.49)	57.81	(6.80)	58.10	(6.91)	56.67	(7.29)	**-.35**	(-.70;-.00)	.05*	**-.40**	(-.75;-.05)	.03*	-.12	(-.43;.19)	.44
Depression	52.88	(6.17)	51.47	(5.80)	51.29	(5.27)	49.59	(6.74	52.91	(6.37)	53.35	(6.24)	52.53	(7.88)	**-.33**	(-.66;-.00)	.05*	-.28	(-.61;.05)	.10	-.26	(-.54;.03)	.07
DT-P Stress score	4.84	(2.61)	4.19	(2.19)	4.27	(2.50)	3.47	(2.19)	5.00	(2.5)	5.40	(2.82)	4.65	(2.72)	**-.46**	(-.85;-.07)	.02*	-.20	(-.59;.20)	.33	-.28	(-.63;.06)	.10
SSER-Q																							
Loneliness	18.86	(6.86)	17.90	(5.97)	18.05	(6.14)	16.26	(5.49)	19.60	(7.37)	20.14	(8.06)	19.65	(7.41)	**-.25**	(-.49;-.01)	.04*	-.20	(-.44;.04)	.10	**-.21**	(-.40;-.01)	.04*
Helplessness	17.33	(5.41)	16.10	(5.03)	14.68	(4.80)	14.63	(5.44)	17.49	(4.40)	16.20	(4.68)	15.81	(4.61)	-.03	(-.30;.24)	.83	-.19	(-.47;.08)	.17	-.04	(-.17;.24)	.73
Positive feelings	15.02	(3.77)	16.07	(3.77)	15.88	(3.67)	15.63	(3.38)	16.07	(4.27)	15.91	(3.78)	15.98	(3.73)	.25	(-.06;.55)	.11	.18	(-.12;.49)	.24	-.04	(-.26;.18)	.75
Uncertainty	13.63	(3.96)	12.60	(4.20)	11.83	(3.86)	11.53	(3.70)	12.53	(3.42)	12.00	(3.82)	12.02	(3.92)	-.08	(-.39;.22)	.59	**-.32**	(-.63;-.02)	.04*	-.07	(-.32;.17)	.55
Coping skills																							
OK-Q																							
Open communication	3.07	(0.53)	3.11	(0.48)	3.08	(0.50)	3.12	(0.52)	3.05	(0.54)	3.05	(0.59)	3.04	(0.55)	.07	(-.23;.37)	.63	.10	(-.20;.40)	.51	.10	(-.16;.36)	.43
Relaxation	2.45	(0.48)	2.62	(0.43)	2.64	(0.47)	2.77	(0.52)	2.51	(0.51)	2.51	(0.58)	2.58	(0.59)	**.35**	(.05-.65)	.02*	**.32**	(.02;.63)	.04*	**.28**	(.01;.55)	.04*
Positive thinking	2.47	(0.47)	2.53	(0.51)	2.66	(0.55)	2.66	(0.58)	2.57	(0.49)	2.64	(0.54)	2.65	(0.56)	-.03	(-.32;.26)	.83	.23	(-.07;.53)	.13	-.02	(-28;.24)	.86
CCSS-P Predictive control	2.50	(0.55)	2.47	(0.64)	2.60	(0.64)	2.6	(0.64)	2.63	(0.52)	2.61	(0.57)	2.65	(0.65)	-.06	(-.35;.24)	.71	.14	(-.16;.44)	.35	.01	(-.28;.29)	.96

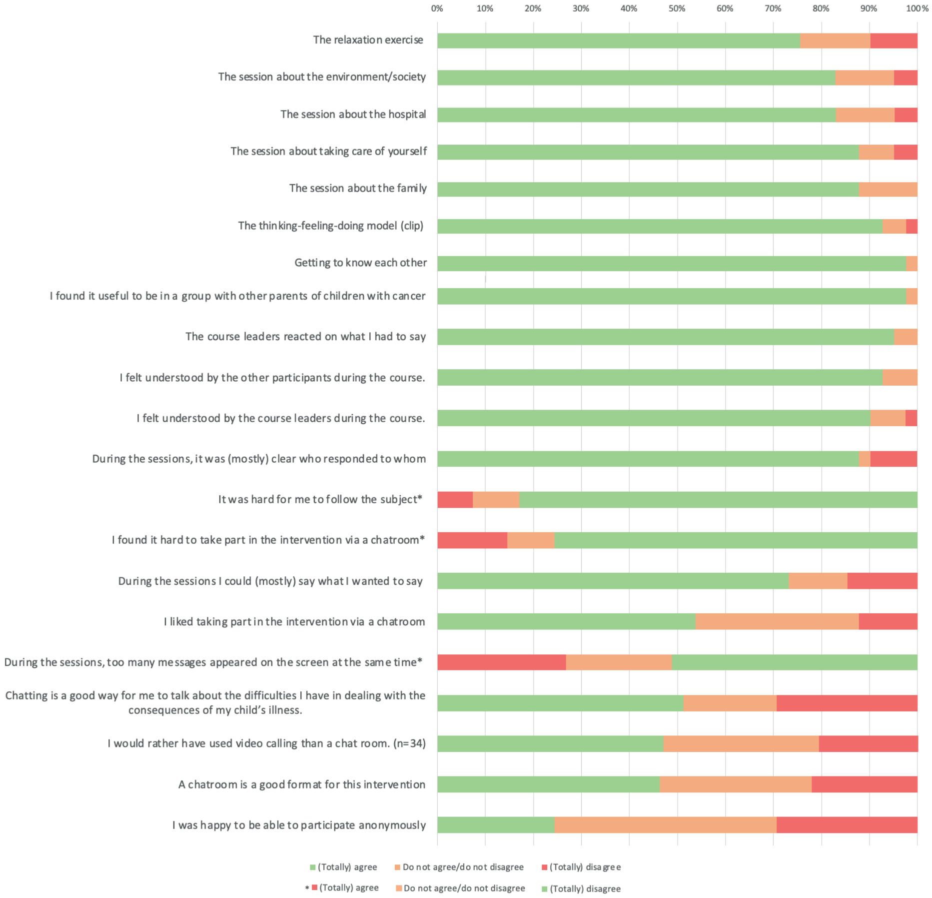
Note: Significant (p < .05) intervention effects (β) are presented in bold.

Figure 2. Effects of Op Koers Online: psychosocial outcomes and coping skill relaxation over time, intervention group vs waitlist-control group.



* significant intervention effect (p<.05)

Figure 3. Agreement of participants on statements about participating in the intervention (*n*=41).



DISCUSSION

This RCT is the first in the Netherlands to study the effect of an online group intervention for parents of children with cancer. We found that it improved psychosocial wellbeing and relaxation as a coping skill. Parents were positive in their evaluation of the intervention.

We found a short-term positive effect of participating in the intervention on anxiety, depression, distress, feelings of loneliness, and the coping skill relaxation after 6 weeks. We also found a longer-term positive effect of the intervention on anxiety, feelings of uncertainty, and coping skill relaxation after 6 months. Reductions in anxiety and depression were previously found after participating in the Op Koers Online for parents of children with chronic illness [14], but not in other online group interventions for parents of children with cancer [23, 24]. However, results of these studies are hard to compare to ours due to differences in participants and study design. Reduction in stress-related symptoms has also been found in online interventions, both in individual settings [35] and in group settings [23]. The finding of a decrease in feelings of uncertainty is important because uncertainty has previously been described as a key element in distress [36]. The previous RCT of Op Koers Online for parents of a child with a chronic illness, that used the same questionnaires, revealed effects on more coping skills (open communication, social support, positive thinking, and predictive control) than just relaxation as in the current study. This may be explained by the fact that characteristics of an oncology diagnosis differ from a chronic illness. For instance, the severity of cancer and the life-threatening aspect might limit the ability to use predictive control and positive thinking as coping skills. Cascade, an intervention for parents similar to Op Koers, did not improve the actual use of coping skills, while a positive effect was found on confidence in using the coping skills [24].

The effects of the intervention seem to be smaller after 6 months than shortly after the intervention but did not disappear completely over time. An explanation might lay in the fact that not all parents completed their homework assignments every week, while doing exercises are thought to strengthen the effect of CBT interventions. We did not structurally register homework completion, which makes it difficult to take the possible impact it had on the outcomes into account. Providing parents with the exercises in a printed handout might make it easier for them to complete the homework. On the long-term, after a year, levels of wellbeing and coping in the intervention condition were the same or slightly better than after 6 months, which suggests maintenance of the intervention effect.

Parents are generally positive about the intervention. The majority of parents (73%) indicated they learned something new, which is comparable to the opinion of parents of children with cancer who participated in a videoconference intervention [35]. Half of the participants (51%) agreed that chatting is a good way to talk about difficulties in dealing with their child's illness and that they liked participating in the intervention via a chatroom (54%). In the intervention Cascade, 92% of parents found the videoconference format easy to use [24]. During the inclusion period of this study, COVID-19 lockdowns were in place, and people became more used to online activities. Both participants and course leaders asked about the possibilities to use videoconferencing instead of a chatroom only. Though there are advantages to typing instead of speaking (e.g., having time for reflection and the possibility for participating anonymously), we consider experimenting with a videoconference format in the future. Parents appreciated the time of the sessions. Offering the course in the evenings is convenient for parents (13 out of 17 courses in this study took place in the evening), but is more burdensome for the course leaders. The vast majority of parents found it useful to be in a group with other parents (97.6%). This is relevant since groups were mixed in terms of age and diagnosis of the child. Parents (and course leaders) sometimes expressed a wish for more homogeneous groups, to have more relatability to other participants' situations. Though this is understandable, forming groups of parents of children in the same age and diagnosis is logistically very challenging.

While difficulties in enrolling parents of children with cancer in an RCT [24, 35, 37] are common, we did not encounter recruitment issues. Announcements on the hospital's social media accounts inviting parents to leave their contact details on the intervention website, resulted in many applications. This may be explained by the centralization of pediatric oncology care in the Netherlands, meaning that every child with cancer is treated in the Princess Máxima Center. This also means that families who live throughout the Netherlands can be reached, underlining the advantage of the online character of the intervention.

Limitations

A strength of this study is the RCT-design to study a protocolled intervention given by trained course leaders, as this is not common in pediatric psycho-oncology [38]. Another strength is the low attrition rate. A high degree of program completion may be explained by the need for peer contact, that is fulfilled through participation in the intervention, and a high degree of questionnaire completion results from efforts of the research team, including reminder phone-calls and e-mails. Limitations of this study include lack of information about non-respondents because of the open recruitment strategy and lack of 12-months follow-up data of the control group, making it impossible to draw conclusions on long-term intervention effect. Since we wanted to give parents in the waitlist-control condition the opportunity to participate in the intervention after 6 months, we could not gather 12-month follow-up data from them. Furthermore, highly educated mothers were overrepresented in this study, which hampers the generalizability of results. We also did not gather specific information on the use of psychosocial support of participants, while that could have confounded the intervention effect.

Clinical implications

According to the literature interventions for parents of children with cancer are needed [12]. Op Koers Online for parents of children with cancer can provide to this need; it is a protocolled group intervention that teaches parents active coping skills and also offers them positive peer support. The general finding that parents are satisfied with the intervention, combined with the positive results on psychosocial wellbeing endorse further implementation. Participating in Op Koers Online for parents of children with cancer has a positive effect on psychosocial wellbeing and the coping skill relaxation, shortly after participating and after 6 months. This is in line with findings from research into other modules of the Op Koers Program. The next step is the implementation of the intervention into the regular care of the psycho-oncology department of the Princess Máxima Center.

CONCLUSIONS

Participating in Op Koers Online for parents of children with cancer has a positive effect on psychosocial wellbeing and the coping skill relaxation, shortly after participating and after 6 months. This is in line with findings from research into other modules of the Op Koers Program. The next step is the implementation of the intervention into the regular care of the psycho-oncology department of the Princess Máxima Center.

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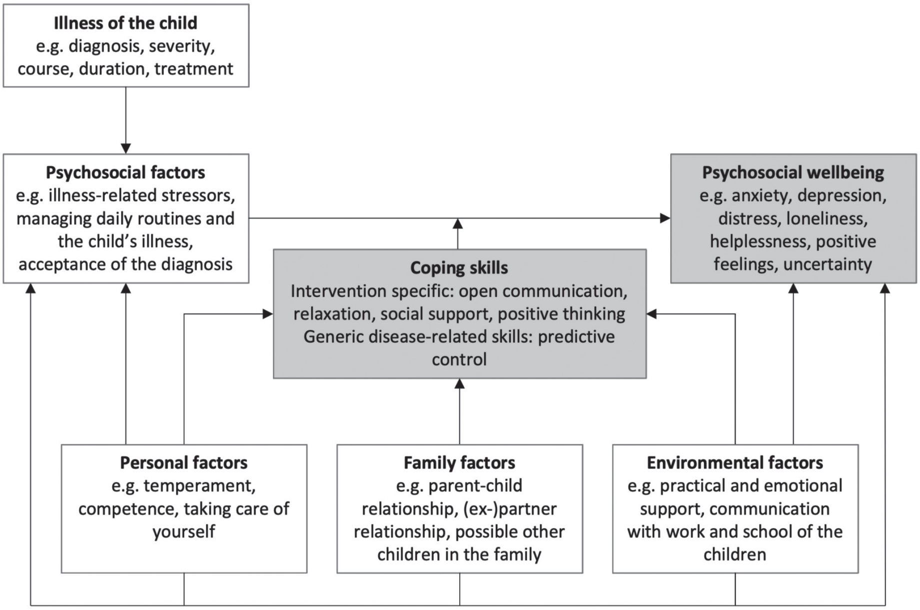
Supplementary Figure 1. Adapted version of the disability-stress-coping model of Wallander and Varni (1998) to explain outcomes of psychosocial wellbeing in parents of a child with cancer.



Supplementary Table 1. Evaluation of Op Koers Online: Statements from the Op Koers Online Evaluation Questionnaire (*n*=41).

<table>
<tr><td>Did you receive sufficient information before starting the course?</td><td colspan="3">Yes
%
87.8</td><td colspan="3">Somewhat
%
2.4</td><td colspan="2">No
%
9.8</td></tr>
<tr><td>Did you look forward to the chat sessions?</td><td colspan="3">Yes, in general
%
68.3</td><td colspan="3">Sometimes
%
31.7</td><td colspan="2">No, in general
%
0</td></tr>
<tr><td>Did you learn something new in the course?</td><td colspan="3">Yes
%
73.2</td><td colspan="3"></td><td colspan="2">No
%
26.8</td></tr>
<tr><td>Do you make use of what you’ve learned in the course?</td><td colspan="3">Yes
%
80.5</td><td colspan="3"></td><td colspan="2">No
%
19.5</td></tr>
<tr><td>I thought … was useful</td><td colspan="3">(Totally) agree
%</td><td colspan="3">Do not agree/do not disagree
%</td><td colspan="2">(Totally) disagree
%</td></tr>
<tr><td>Getting to know each other</td><td colspan="3">97.5</td><td colspan="3">2.4</td><td colspan="2">0</td></tr>
<tr><td>The thinking-feeling-doing model (clip)</td><td colspan="3">92.7</td><td colspan="3">4.9</td><td colspan="2">2.4</td></tr>
<tr><td>The session about the hospital</td><td colspan="3">82.9</td><td colspan="3">12.2</td><td colspan="2">4.8</td></tr>
<tr><td>The session about the family</td><td colspan="3">87.8</td><td colspan="3">12.2</td><td colspan="2">0</td></tr>
<tr><td>The session about taking care of yourself</td><td colspan="3">87.8</td><td colspan="3">7.3</td><td colspan="2">4.9</td></tr>
<tr><td>The relaxation exercise</td><td colspan="3">75.6</td><td colspan="3">14.6</td><td colspan="2">9.8</td></tr>
<tr><td>The session about the environment/ society</td><td colspan="3">82.9</td><td colspan="3">12.2</td><td colspan="2">4.9</td></tr>
<tr><td>What grade would you give the intervention? (10 – excellent, 1 – worthless)</td><td>Mean
7.6</td><td>0-4
%
0</td><td>5
%
4.9</td><td>6
%
14.6</td><td>7
%
29.3</td><td>8
%
26.8</td><td>9
%
14.6</td><td>10
%
9.8</td></tr>
<tr><td>Would you recommend the course to other parents of children with cancer?</td><td colspan="3">Yes
%
87.8</td><td colspan="3">I’m not sure
%
9.8</td><td colspan="2">No
%
2.4</td></tr>
<tr><td>What did you think of the following aspects of the course?</td><td colspan="3"></td><td colspan="3"></td><td colspan="2"></td></tr>
<tr><td>Duration of the sessions</td><td colspan="3">Too short
%
7.3</td><td colspan="3">Right
%
92.7</td><td colspan="2">Too long
%
0</td></tr>
<tr><td>Amount of sessions</td><td colspan="3">Too little
%
17.1</td><td colspan="3">Right
%
82.9</td><td colspan="2">Too many
%
0</td></tr>
<tr><td>Time between the sessions</td><td colspan="3">Too little time between
%
14.6</td><td colspan="3">Right
%
85.4</td><td colspan="2">Too much time between
%
0</td></tr>
<tr><td>Starting time of the sessions</td><td colspan="3">Good
%
82.9</td><td colspan="3">Sufficient
%
7.3</td><td colspan="2">Moderate/poor
%
9.8</td></tr>
<tr><td>Day of the sessions</td><td colspan="3">Good
%
92.7</td><td colspan="3">Sufficient
%
4.9</td><td colspan="2">Moderate/poor
%
2.4</td></tr>
<tr><td>Size of the group</td><td colspan="3">Too small
%
9.8</td><td colspan="3">Right
%
85.4</td><td colspan="2">Too big
%
4.9</td></tr>
<tr><td>What did you think of the in depth information for every session?</td><td colspan="3"></td><td colspan="3"></td><td colspan="2"></td></tr>
<tr><td>Amount</td><td colspan="3">Too little
%
14.6</td><td colspan="3">Right
%
80.5</td><td colspan="2">Too much
%
4.9</td></tr>
<tr><td>Difficulty</td><td colspan="3">Too easy
%
9.8</td><td colspan="3">Right
%
90.2</td><td colspan="2">Too difficult
%
0</td></tr>
</table>

Was it useful?	Useful % 56.1		Somewhat useful % 43.9		Not useful % 0
What did you think of the homework assignments that you made?					
Amount	Too little % 7.3		Right % 82.9		Too much % 9.8
Difficulty	Too easy % 4.9		Right % 95.1		Too difficult % 0
Was it useful?	Useful % 53.7		Somewhat useful % 41.5		Not useful % 4.9
What did you think of the course leaders?	Good % 80.5		Sufficient % 19.5		Moderate/poor % 0
Did you need more contact with the other participants in your group during the course?	No % 29.3	Yes, after the sessions % 31.7	Yes, in between the sessions % 9.8	Yes, via a forum % 17.1	Yes, talking in real life % 41.5
Did you need more contact with the course leaders in your group during the course?	No % 68.3	Yes, via e-mail % 2.4	Yes, via chat room % 9.8	Yes, via telephone % 7.3	Yes, talking in real life % 14.6
To what extent do you agree with the following statements about participating in the course?	(Totally) agree %		Do not agree/do not disagree %		(Totally) disagree %
It was hard for me to follow the subject*	7.3		9.8		82.9
I was happy to be able to participate anonymously	24.4		46.3		29.3
During the sessions, too many messages appeared on the screen at the same time*	26.8		22.0		51.2
During the sessions, it was (mostly) clear who responded to whom	87.8		2.4		9.7
A chatroom is a good format for this intervention	46.3		31.7		22
The course leaders reacted on what I had to say	95.1		4.9		0
Chatting is a good way for me to talk about the difficulties I have in dealing with the consequences of my child's illness.	51.2		19.5		29.3
I liked taking part in the intervention via a chatroom	53.7		34.1		12.2
I found it hard to take part in the intervention via a chatroom*	14.6		9.8		75.6
During the sessions I could (mostly) say what I wanted to say	73.2		12.2		14.6
I felt understood by the course leaders during the course.	90.2		7.3		2.4
I felt understood by the other participants during the course.	92.7		7.3		0
I found it useful to be in a group with other parents of children with cancer	97.6		2.4		0
I would rather have used video calling than a chat room. (*n*=34)	47.1		32.4		20.6

*Statement is negative

CHAPTER 5

DEVELOPMENT, RESEARCH AND IMPLEMENTATION OF THE PSYCHOSOCIAL GROUP INTERVENTION OP KOERS: LESSONS LEARNED

CLINICAL PRACTICE IN PEDIATRIC PSYCHOLOGY, 2024
(accepted pending minor revisions)

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Douma M, Scholten L, Grootenhuis MA

ABSTRACT

Objective This paper aims to share the lessons that we have learned in the process of 25 years of development, research and implementation of a psychosocial group intervention for children with illness and their family members (called: Op Koers, or On Track in English).

Methods Using the National Institutes of Health Stage Model for Behavioral Intervention Development and the Consolidated Framework for Implementation Research, we critically appraised our activities in the different stages. Over the years, we used basic research to create and modify intervention modules in different populations. Op Koers was pilot-tested several times and found effective in improving coping skills and emotional functioning in multiple larger efficacy studies. Finally, the intervention is part of usual care in the authors' institutions and was disseminated throughout the Netherlands.

Results Important lessons were learned about the characteristics of the intervention, the inner and outer setting, individuals, implementation process and research. Future efforts may be directed towards continuous improvement of the intervention and successful lasting implementation.

Conclusions Op Koers is one of few psychosocial interventions that has been both extensively studied and implemented. The main factor for this achievement is the close collaboration between, and the perseverance of the clinical care and research departments.

Keywords Psychosocial intervention development, pediatric CI, pediatric oncology, coping, emotional functioning.

Implications for Impact This paper presents the efforts and lessons learned from over 25 years of research in psychosocial intervention development, evaluation, and implementation. Important lessons about the characteristics of the intervention, the inner and outer setting, individuals, implementation process and research are described.

INTRODUCTION

Pediatric illness

As a result of advances in pediatrics, an increasing number of children is growing up with chronic illness (CI). In the Netherlands, around 500.000 children have a CI, which is defined as follows: 1) onset between ages 0 and 18, 2) diagnosis based on medical scientific knowledge, 3) illness is not curable, 4) illness has been present for at least three months or at least three episodes have occurred in the last year [1]. This also includes the approximately 600 children that are newly diagnosed with cancer each year [2]. Children and their families face multiple consequences of the illness and treatment, including changes in daily routines and stressful situations, that impact their psychosocial well-being [3-7].

Children, parents and siblings may benefit from psychosocial support in coping with CI. In the Netherlands, this concerns support from a child life specialist, psychologist and/or a social worker, which is provided in the pediatric setting.

The senior authors of this paper (MG and LS), at the time employed at the psychosocial department of Emma Children's Hospital Amsterdam UMC, developed a psychosocial group intervention that aimed to improve psychosocial well-being of families coping with pediatric CI using cognitive behavioral therapy (CBT) techniques: Op Koers (in English: On Track), which is described extensively further in the current paper. The previous clinical staff thought a group intervention could prevent or decrease psychosocial problems in children with CI and their families. With a generic approach, including children with any illness instead of focusing on a specific illness, many children could be reached, which is important in pediatric illnesses with a small number of patients [8]. The group intervention teaches active coping skills by giving information, using relaxation techniques, and encouraging self-management, social competence and positive thinking. After initial development of a group course for siblings of children with cancer, the intervention was adapted to fit other target populations as well, that is children with CI, of different ages, and their parents. Op Koers is currently part of standard care in several health care institutions in the Netherlands.

Although there is a clear need for psychosocial interventions in families with an ill child, and many interventions that have been proven to be effective exist, they often do not reach the targeted population because of barriers that impede their implementation [9, 10]. Publicly sharing implementation experiences could inform and promote future implementation of psychosocial interventions, but publications on the implementation of developed and researched interventions in clinical practice are scarce [11, 12].

The use of an established model can be helpful in structurally observing and reporting the development of an intervention. The National Institutes of Health (NIH) Stage Model for

Behavioral Intervention Development (further referred to as the stage model) is such a model, and it was developed to identify, define, and clarify the activities involved in behavioral intervention development to facilitate the scientific development of potent and implementable interventions [10]. The stage model arranges activities in several stages, that do not occur linearly but in an iterative, recursive manner, and seemed useful to structure our reflections on the development of Op Koers. The stage model describes basic science activities as research that occurred before and informs intervention generation or refinement. Feasibility and pilot testing includes preliminary evaluations of a developed or refined intervention, thus providing valuable information for further development, efficacy testing or implementation. If pilot results are promising, research into efficacy, in research or community settings, is the next step. Ultimately, effectiveness research evaluates an intervention while maximizing external validity. Op Koers is classified as efficacy research in this paper, though developed in real-life community settings of pediatric hospitals, implying a high degree of external validity. The final stage of the model describes implementation and dissemination, the adoption of a new intervention in clinical settings, and the distribution of information and material to relevant groups.

Our psychosocial research and care staff started with Op Koers more than 25 years ago. Over the years we have gained experience with the complex process of development, feasibility and efficacy research and implementation, which resulted in a large number of peer reviewed publications. See Table 1 for an overview. To enable others to learn from our experiences, the current paper aims to critically appraise our efforts guided by the NIH stage model and discuss the lessons that we have learned along the way. We first discuss our activities in development, followed by a description of the intervention as it is now. We continue by presenting activities in evaluation and implementation of the intervention. We finish with the lessons we learned, organized by the categories as used in the Consolidated Framework for Implementation Research (CFIR). The updated CFIR is a widely used framework that helps identify determinants influencing implementation outcomes. The framework was developed by implementation researchers and the framework stems from implementation literature and feedback from users on previous versions of the framework [13].

INTERVENTION DEVELOPMENT, EVALUATION AND IMPLEMENTATION ACTIVITIES

In this section we describe our activities in intervention development, evaluation and implementation. These activities occurred non-linearly, but were clustered in a) basic research, b) generation and refinement of the intervention, c) feasibility and pilot testing, d) efficacy research, and finally e) implementation and dissemination. All studies were approved by the medical ethics board of the concerned hospitals and informed consent was obtained from all participants.

a) Basic Research

Op Koers finds its basis in knowledge from the field of pediatric psychology, which focuses on the impact of pediatric illness, in particular on psychosocial outcomes and risk- and protective factors in children and their family members. Since the late 1990s our research groups have conducted a large number of studies focusing on the health-related quality of life and psychosocial functioning of children with CI including pediatric oncology [14-17], as well as their siblings [18] and parents [17, 19-21]. Overall, these studies, in line with literature, revealed that families can experience less favorable health-related quality of life and psychosocial functioning than reference groups (see cited papers for specific information about the reference groups). Although most families are resilient and only a small proportion is at risk for developing (severe) psychosocial problems [22], standards of care for children with a CI or cancer recommend access to psychosocial interventions for children and family member to facilitate their wellbeing [23, 24].

Wellbeing is impacted by the multiple stressors that families of a child with an illness have to face according to the model presented by Wallander and Varni [25], such as uncertainty about the illness, treatment and future of the child, uncontrollability and disrupted daily routines. The relation between stressor and wellbeing is mediated by coping skills, which in itself are impacted by personal, family and environmental factors. Coping is central in the model because it plays a crucial role in the adaptation to stressful situations such as illness of the child. Coping consists of cognitive and behavioral efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of a person [26]. These theories were translated into a psychosocial support model [27], based on emotions and coping strategies of children and parents who were confronted with childhood cancer.

The foregoing provided the basis for the further development of the intervention. See Figure 2 for an adaptation of the model of Wallander and Varni including outcomes and coping skills that we considered relevant for the Op Koers research. Teaching coping skills became the central element of Op Koers. Coping skills are taught using cognitive behavioral therapy (CBT) techniques, because CBT was previously found to be effective in reducing psychosocial problems [28]. CBT focusses on recognizing and acting upon cognitive distortions and on teaching how to use active coping skills for psychosocial problems. Over the years, elements of acceptance and commitment therapy (ACT) were integrated in the Op Koers program. ACT is a third wave of CBT that strives for acceptance of thoughts or situations to reduce their impact on daily life. ACT is an effective psychological intervention for psychological stress [29]. It can be useful for children with an illness and their family members, to teach them to cope with the situation they are confronted with.

Sharing experiences combined with teaching coping skills became the back bone of The Op Koers intervention. The group format, disease-generic use and possibility for online delivery of Op Koers have benefits. Sharing experiences with people that are in a comparable situation is found to be helpful in decreasing distress [30], therefore peer support plays a central role in Op Koers. Since psychosocial problems in children with different illnesses usually overlap [31], Op Koers was developed as a disease-generic intervention. Thus, it provides an intervention also for families of children with rare illnesses. Op Koers has an universal approach targeting children with a CI (and their families), regardless whether psychosocial problems are present. Universal interventions like Op Koers have a preventative as well as a curative character [32]. Besides face-to-face courses, Op Koers online was developed to remove known potential practical barriers for participating in face-to-face interventions such as travel distance, time and costs [33].

b) Intervention Generation and Refinement

The Op Koers program consists of separate modules for children with CI or cancer, in different age groups, for different family members, and provided either face-to-face or online (Table 2). Currently, 13 different modules are available When different modules are suitable, available and scheduled (e.g. both face-to-face and online), a participant can choose in what course they participate. Costs are covered by the psychosocial departments of the hospitals, families are not billed for participation.

Each new Op Koers module was developed through adaptations of existing modules. For example, the pediatric oncology module originated from the module for patients with a CI, adding cancer-related elements. Adaptations of existing modules relied on research into participant's and health care providers' (HCP) needs [34-36], HCP experiences or participant feedback. For example, experiences with the parent component of Op Koers for children with CI uncovered the need to pay attention to the psychosocial needs of parents themselves [37].

The idea for an online intervention arose when adolescents showed to be less likely to participate in a face-to-face intervention than younger children [37], while at that time the first eHealth interventions were emerging. Combining the content of Op Koers face-to-face with the technology of an existing Dutch chatroom intervention for participants with depression symptoms [38, 39], the first online module of Op Koers was developed for survivors of childhood cancer. After pilot testing this module including surveys and focus groups, we developed online modules for parents, adolescents and siblings of children with a CI, for parents and siblings of children with cancer, and young adult survivors of childhood cancer specifically.

Table 2. Different modules of the Op Koers Program.

	Group	Illness	Age	Delivery method	Additional information
1	Patients	CI	8-12	Face-to-face	
2	Patients	CI	12-18	Face-to-face	
3	Patiens	CI	12-18	Chat room	
4	Patients	Oncology	12-18	Chat room	After completion of treatment
5	Parents	CI	Childs' age 0-18	Face-to-face	Add-on to child f2f course (focus on parental support for child)
6	Parents	CI	Childs' age 0-18	Chat room	Focus on overall parent functioning
7	Parents	Oncology	Childs' age 0-18	Chat room	During child's oncology treatment
8	Parents	Oncology	Childs' age 0-18	Chat room	After completion of child's oncology treatment
9	Siblings	CI	8-12	Face-to-face	
10	Siblings	CI	12-18	Chat room	
11	Siblings	Oncology	8-14	Face-to-face	
12	Siblings	Oncology	12-18	Chat room	
13	Young adults	Oncology	18-30	Chat room	After completion of treatment

THE INTERVENTION: ON TRACK (OP KOERS)

Summary of general components of The Op Koers Intervention program:

- Courses consist of five to eight 90-minute group sessions that take place face-to-face (in the hospital or online (in a secured chatroom, no audio or video) on a set time and day of the week.
- Five to six months after the start of the intervention, a booster session takes place.
- Every group consists of 3-6 participants and two course leaders, one of whom is an experienced psychologist and the other can be a junior psychologist or social worker.
- In between the sessions, participants complete homework assignments. Additional reading material is available in the parents and young adults modules
- The first session is meant for the participants to get to know each other. In the last session, participants look back on the course and what they have learned.
- Peer support is stimulated by course leaders motivating participants to share experiences and learn from each other
- Every session in between focusses on a specific coping skill or a theme, both during the courses and in the reading material and homework assignments.
- Confidentiality is discussed with all participants and maintained by having them agree with certain chat rules before entering the chat room.

o Child with illness and siblings

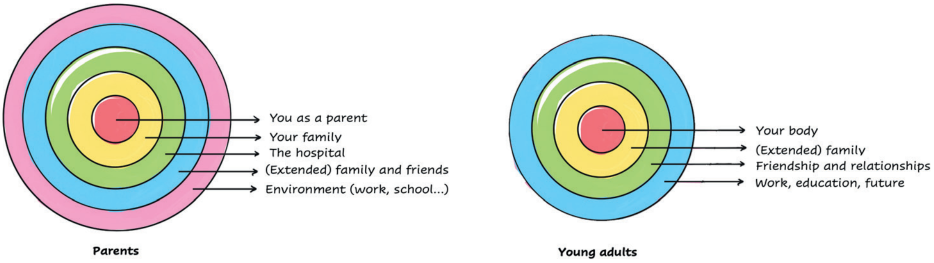
Coping skills are translated into five learning goals: 1) information seeking and information giving about the disease, 2) use of relaxation during stressful situations, 3) increasing knowledge of self-management and compliance (not applicable for siblings), 4) enhancing social competence (group discussions, role playing), and 5) positive thinking (use of the Thinking-Feeling-Doing model; replacement of inaccurate thoughts)

o Young adults and parents

Themes are structured around different environments of the participants (Figure 1). Learning goals are discussed in the chat session, and/or are a part of the homework assignments and the reading material. Learning goals are: 1) use of relaxation during stressful situations; 2) increasing knowledge of self-management and compliance (of their child); 3) positive thinking; 4) positive parenting (not applicable for young adults); 5) open communication about the illness and seeking and accepting support.

- During the group sessions, psycho-education is used to reach the learning goals (through, among others, informative videos and group discussions), and reinforced and practiced through exercises (such as role-play in the face-to-face sessions and games in the online sessions).
- In the courses for patients and siblings in pediatric oncology, an oncologist joins for one session to answer participants' questions about the illness or treatment.

Figure 1. Environments in which the themes of the Op Koers interventions for parents and for young adults were structured.

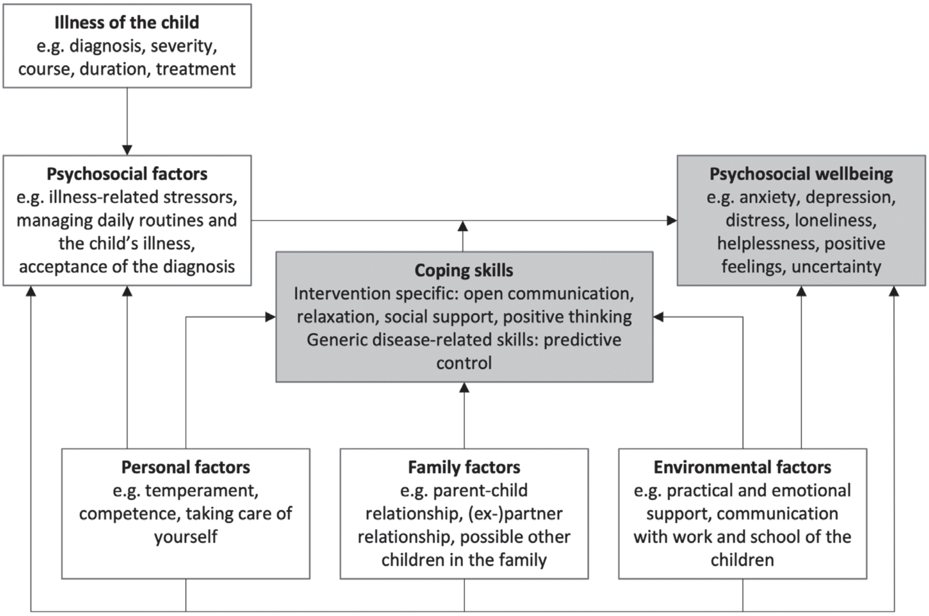


c) Feasibility and pilot testing

The first step in testing an intervention is to study its feasibility in pilot studies. Results of pilot studies were published for four face-to-face modules [8, 40-42] and three online Op Koers modules [36, 43, 44]. Feasibility of Op Koers was evaluated with participants and/or course leaders, and participation rates, e.g. attendance and drop-out, were assessed. Dropout rate was low and satisfaction with the course was high in all studies. Feasibility studies also yielded valuable information for refinement of the content Op Koers, as described above (see b).

Besides feasibility, most of these pilot studies also addressed preliminary efficacy in a pre-post-test design, see table 1 [8, 40-42, 44]. Coping and emotional functioning were the primary and secondary outcomes, respectively, based on the adapted Model of Wallander and Varni (see Figure 2). Overall, the Op Koers modules showed promising results. Coping skills, such as information seeking behavior, improved in children and adolescents with CI and childhood cancer after Op Koers face-to-face and online [8, 36, 41, 42, 44], and feelings of helplessness in young adult survivors of childhood cancer decreased after Op Koers online [36]. Moreover, at least one aspect of emotional functioning improved in each module. For example, anxiety was lower in siblings after face-to-face Op Koers and young adult survivors of childhood cancer were less distressed after Op Koers online [36, 40].

Figure 2. Adapted version of the disability-stress-coping model (Wallander & Varni, 1998) to explain problems in psychosocial wellbeing in children with an illness and their in family members.



d) Efficacy research

To verify if the positive outcomes of the pilot studies could be attributed to Op Koers, we conducted efficacy research with the help of large research grants. Four modules of Op Koers have been studied in randomized controlled trials (RCT's), see table 1 [37, 45-47]. All modules showed positive effects on both coping skills and emotional functioning, without negative effects on any outcome. Thus, the promising results from the pilot studies were confirmed in the RCT's. We conclude that Op Koers is effective for different family members and diagnoses.

Using the data from one RCT [37], the psychosocial characteristics of children and parents were studied as predictors, moderators and mediators of the intervention effect [48, 49].

e) Implementation & Dissemination

After the first face-to-face modules were developed and studied by researchers from the Emma Children's Hospital Amsterdam UMC in the Netherlands, Op Koers became part of standard care. Furthermore, it was disseminated throughout the Netherlands and the face-to-face module of Op Koers for children with a CI and their parents has been implemented in 30 Dutch hospitals. Thanks to project funding, HCP in those hospitals could be trained and provided with Op Koers materials, e.g. instruction manuals, course materials. We do not have information about the uptake of the intervention: how often the hospitals have provided the course and if these courses are still part of the standard of care. We do know that some of the hospitals who used Op Koers in the context of the RCT's would like to offer the course as regular care, but are unable due to lack of time and money. In the Princess Máxima Center for Pediatric Oncology, where care and research have been centralized in the Netherlands since 2015, implementation of Op Koers was aspired early on and supported by a grant. However, the timing of implementation was inappropriate in the first year of the opening of the hospital because the focus had to be on providing medical care adequately and forming new structures. As a result, implementation activities took longer than anticipated.

We shared our research results in peer-reviewed journals and conferences so that pediatric psychology colleagues can profit from our knowledge and experience. In a commentary on one of these publications, it was suggested that it may be relevant to disseminate Op Koers globally [50]. In addition, over the years, our research team has been contacted several times by international colleagues who were interested in Op Koers. However, international dissemination has been limited so far because translating the intervention and preparing the website for international use is very costly in terms of time and funding. Nevertheless, the manual was translated to Swedish and Op Koers is being implemented at Drottning Silvias barnsjukhus, Göteborg.

LESSONS LEARNED

In this section, we describe the lessons we learned over the past 25 years of Op Koers research, using the updated CFIR.

The CFIR categorizes determinants into five domains: intervention characteristics (e.g. evidence, adaptability), outer setting (e.g. health care system, external funding), inner setting (e.g. implementation climate, culture), characteristics of individuals (e.g. intervention deliverers, recipients), and implementation process (e.g. planning, stakeholders). We present the lessons learned within each domain. In cases where lessons relate to multiple domains, we have categorized them in the most suitable one. Furthermore, we introduce a sixth domain, the research domain, to share insights gained from our research efforts (e.g. study recruitment, choosing instruments).

I. Intervention characteristics

The intervention domain encompasses characteristics that are related to the intervention that is being implemented. Characteristics of the Op Koers intervention that we consider strengths include the robust evidence and the adaptability. There is no comparable group intervention for families of children with an illness and the intervention has been extensively studied (as depicted in Table 1), both in terms of feasibility and effectiveness. The adaptability of Op Koers is showed by the many different modules that were refined and updated to match needs of different target groups of participants. Refinement is still ongoing, and adjustments to the intervention can be made to align with new insights. For example, Op Koers Online was designed as a chatroom intervention. At the time of development, video calls were not very common in the Netherlands. Over the past years, especially during the COVID-19 pandemic, people became more accustomed to online activities, and Op Koers participants seemed to be increasingly interested in an online course that is provided through video calls instead of only a chatroom. Even though we think there are advantages to typing instead of speaking (e.g. having time for reflection and anonymity), we also deem it important to consider new options and are currently experimenting with a video call format. Using videoconferencing could make it easier to further implement and disseminate the course internationally, since the chat platform would not have to be translated.

II. Outer setting

The outer setting domain describes the setting in which the inner setting exists, in our case the Dutch health care setting. Determinants in this domain named by the CFIR relate to for example regulations and funding from external entities.

In the Netherlands, the hospital’s responsibilities primarily extend directly to the patient. For healthcare providers, this results in the challenge of dedicating time to Op Koers courses for parents and siblings of children with an illness.

Over the years, Op Koers has received multiple (mostly research related) grants from external funders. Funding was needed to develop, refine, study and implement the course program. Costs are related to personnel, materials and technical support. Applying for grants is time consuming and several grant applications were rejected. A barrier for funding was the generic approach of Op Koers. Not focusing on a specific illness makes Op Koers unsuitable for many funding agencies targeting only one diagnostic group. Even though costs of research are high, it is important to provide evidence-based care. Also, we believe that preventative group interventions such as Op Koers may in the end be cost-effective in the real world setting, since psychologists can treat multiple participants at the same time and preventing problems may save needed treatment, and thus resources in the longer term [32].

III. Inner setting

The inner setting domain refers to the setting in which the intervention is implemented, within our context, this refers to the hospitals that use Op Koers. Determinants as listed by the CFIR pertain to, for example, the organization of tasks between teams. We learned that the collaboration from the start between pediatric psychologists and the research team, promoted by the integration of research and care in the involved university medical care centers, was a strength and facilitator of the development of Op Koers. Researchers that lead the development and evaluation projects were positioned in the clinical department, rather than universities outside the pediatric clinic. Collaboration between care and research can sometimes lead to challenges in the organization of tasks. It is crucial to make clear agreements about who is responsible for what, especially when the work load in care is high.

IV. Characteristics of individuals

The domain about characteristics of individuals encompasses the roles and characteristics of people that are involved in the delivery of the intervention, in our case the ambassador and coordinator. We learned that it helped to have an ‘ambassador’ or ‘champion’ in the clinical department [51]. Ideally, the ambassador has experience with the program and has gained trust from the intended course leaders, so that they will be more inclined to adopt a positive attitude towards the new intervention. The ambassador could also motivate other HCP such as pediatricians and psychologists, to see the added value of the intervention, and motivate them to invest in recruitment. We also learned that is helpful to appoint an intervention coordinator. This way, a specific person is dedicated to take care of logistics and practicalities, such as schedule management, booking rooms and making sure the intervention supplies are up to date. This coordinator could also hold responsibility for communicating with stakeholders that are needed for tasks beyond our field of expertise, e.g. general data protection regulation laws, designing the course materials’ layout and keeping the website up to date.

V. Implementation process domain

The implementation process domain describes activities and strategies used to implement the innovation.

The recruitment and scheduling of participants for Op Koers have at times proven to be challenging. Op Koers courses occasionally had to be cancelled due to a lack of participants. We found an effective solution in including the courses in the annual planning of psychosocial care. When courses are planned regularly, clinicians can discuss participation with families more easily and patient organizations can add to recruitment by pointing out the course to their members.

Preferably, implementation should be evaluated structurally and guided by an implementation plan, which is grounded on theory and based on a conceptual framework [9]. This requires time and effort (i.e. financial investment), which is a barrier for using such an approach.

We also learned lessons about the implementation process regarding health care providers and recipients of the intervention. HCP should be involved as early as possible to prevent a research-to-practice gap. Doing so results in more commitment, input and effort from clinicians and it leads to a higher chance of successful implementation of an intervention [9]. Engagement of HCP in the dissemination and implementation of Op Koers was a challenge. Firstly, though the multicenter approach in most RCT's was favorable for the inclusion rate and was a first step towards nationwide implementation, it was logistically complicated to prepare the pediatric psychologists for the intervention. It was helpful that we used a very detailed protocol and trained course leaders personally before they started Op Koers. Secondly, as a result of the high work pressure that many psychologists experienced, it was sometimes challenging to introduce this new intervention. We learned that the aforementioned ' ambassador' played an important role.

In terms of recipients of the intervention, we learned that patient and parent participation at an early stage is important in the development of an intervention, as well as for increasing participant rates and reach of dissemination [52]. We encountered that involving patients and parents in the development of Op Koers was difficult, and it was challenging to ensure representativeness. We asked patients and parents either about their support needs before (re)designing the intervention, or about their opinion after participating in the intervention. This often lead to valuable insights, for example that explaining the online course should be available during the evening [35]. It also provided challenges when opinions, literature or clinical experience contradicted each other. For example, when we asked siblings for their ideas about an intervention, they reported to prefer a course group with siblings of children with a similar CI [34], whereas the literature showed that the psychosocial challenges of living with a CI are similar regardless of the diagnosis [31].

VI. Research

We chose to add a category about research to share the lessons we learned in our research projects and that do not directly relate to any of the original categories of the CFIR. These lessons reflect on participant recruitment for studies, study designs and outcome measurement.

Recruitment

In research settings, problems in recruitment lead to problems such as study delay or smaller sample sizes and power. Lack of power makes it difficult to prove effectiveness. This is a typical barrier for psychosocial interventions [53] and complicates implementation. For example, in the

RCT on Op Koers for parents of children with a CI, we did not reach the planned sample size, even after lengthening the inclusion period. Nevertheless, fortunately, power turned out to be sufficient to prove intervention effects [47]. Besides proving effectiveness, it would be interesting to investigate who profits most from the intervention, to make sure the people who benefit get access to it [10]. Unfortunately, the sample sizes of most our RCT's were not sufficient to conduct subgroup analyses, or to examine the working mechanism of Op Koers.

We often used an open recruitment strategy to increase the number of participants. We promoted Op Koers through HCP and social media, in the hospital newsletters or via patient organizations. The downside of this open recruitment strategy is that there is no information available about response rates, nor about the characteristics of non-participants. This hampers drawing conclusions about generalizability of the results. Nonetheless, we consider an open recruitment strategy the best option, using multiple recruitment methods; through social media, leaflets in the outpatient clinics, and to have the psychosocial department in the clinics refer families to Op Koers. To promote Op Koers, we also developed two videos with information for children and adolescents about the Op Koers program (see www.opkoersonline.nl).

Study designs

We have conducted studies with different designs, depending on research aims and opportunities. We started with pilot studies using a pre-post design without a control condition. In addition, multiple RCT's have been conducted over the years, because an RCT is considered to be the gold standard in intervention efficacy research. A recent meta-analysis into group interventions for parents of children with cancer encourages further RCT's [54]. However, attention for the downsides of RCT's is growing [55, 56], which are in line with our own experiences: since an RCT needs a control group, more participants are needed, which makes RCT's very time- and money consuming. Also, such robust but laborious research design makes it difficult to evaluate continuous improvements and adaptations to the intervention, which impacts the validity of research results. This makes RCT's less suitable for intervention development. While some researchers believe RCT's are the only design allowing for conclusions on causality [57], others argue that valid causal inferences can also be drawn from single-case designs because these are also controlled experiments [58]. To date, single-case designs are generally considered to be less valuable and therefore seemingly harder to publish. Thus, we still felt the need to use the RCT design for our efficacy studies.

In our efficacy research, we deliberately opted for a waitlist-control design instead of a control condition consisting of peer support without CBT and ACT elements because peer support is a key element of the Op Koers intervention. Nevertheless, it would be interesting to study the additional effect of CBT and ACT elements on peer support only, but this would require more participants.

Regarding our choice to use a waitlist-control group with ‘care as usual’, it is important to realize that the added value of the intervention may be smaller than compared to a control condition with no care at all. On the positive side, studying Op Koers alongside regular care is actually more informative as this matches with the real-world situation and how it would be implemented. Also, for ethical reasons, the control condition in psychosocial research mostly receives ‘care as usual’.

Outcome measures

The use of appropriate outcome measures is essential to capture intervention effects [59]. Operationalization of intervention effects into outcomes and thereafter, finding sound measures (questionnaires), is crucial but often problematic. If outcome measures are generic, it can be hard to identify intervention-specific outcomes such as coping skills. If outcome measures are more specific, it can be hard to compare the results to other research projects or populations. Therefore, in our research into Op Koers, we used generic as well as specific outcome measures. Regarding generic outcome measures, the Patient-Reported Outcomes Measurement Information System (PROMIS) is recommended. They overcome the lack of comparability between different measurements [60] and are more reliable across a range of functioning than other generic outcomes because they are developed using item response theory [61]. In the RCT with Op Koers for parents online in pediatric oncology that is currently being carried out, we use computer adaptive testing of the PROMIS anxiety and depression item banks. To assess Op Koers specific outcomes, we developed a questionnaire that covers the disease-related coping skills taught through Op Koers. This measure, with variants for children (Questionnaire Op Koers for children [QOK-c]) and parents (QOK-p) has been used in most of our studies (Table 1).

When choosing an instrument, it is important to make sure that the measures are sensitive to change. It sometimes occurs that participants say they gained a lot from the intervention while showing no improvement on the outcome measures. Another factor that complicates demonstrating effects could be the preventative character of Op Koers, which allowed participants to join without reporting significant clinical problems. If the participants’ coping skills were sufficient and participants were not experiencing high levels of psychosocial problems from the start of an intervention, there is little room for improvement and ceiling effects on measures could occur. This is a common problem among studies on preventative interventions [62]. Nevertheless, on average, we found improvements on several outcomes in all evaluation studies of Op Koers. In conclusion, it is necessary to make a well-considered choice of outcome measures and questionnaires for every new research project.

In table 3 the main lessons we learned are summarized into the categories development, evaluation (research) and implementation and dissemination (practice). Though most lessons apply to all categories, they were placed in the categories to which they most apply.

Table 3. Summary of lessons learned.

CFIR Domains	Development	Evaluation	Implementation and dissemination
Intervention characteristics	The adaptability of Op Koers is a strength. e-Health interventions are evolving and technology develops fast. It is important to keep up with new possibilities and opportunities.	The robust evidence of Op Koers is a strength.	The adaptability of Op Koers is a strength. e-Health interventions are evolving and technology develops fast. It is important to keep up with new possibilities and opportunities.
Outer setting	Applying for grants is time consuming but necessary. Funds are needed throughout all three stages: development, evaluation and implementation.	Applying for grants is time consuming but necessary. Funds are needed throughout all three stages: development, evaluation and implementation.	Applying for grants is time consuming but necessary. Funds are needed throughout all three stages: development, evaluation and implementation and dissemination.
Inner setting	Collaboration between care and research team from the start was essential.	Collaboration between care and research team from the start was essential.	Collaboration between care and research team from the start was essential.
Characteristics of individuals		Ambassadors from within the care team are needed	Ambassadors from within the care team are needed, as well as a program coordinator.
Implementation process	– Involving patients was difficult, but lead to valuable insights. – HCP should be involved as early as possible to prevent a research-to-practice gap – patient and parent participation at an early stage is important through all phases	– Engaging HCP in evaluation and dissemination was challenging – patient and parent participation at an early stage is important through all phases	– Including the courses in the annual planning of the care team is helpful for recruitment. – Engaging HCP in evaluation and dissemination was challenging – patient and parent participation at an early stage is important through all phases
Research		– Low recruitment is a barrier in psychosocial intervention research. Open recruitment is considered the best option. – RCT's are very money- and time-consuming and they make it difficult to evaluate continuous improvements and adaptations to the intervention. Feasibility studies including process evaluations are suitable and useful, especially in the development phase of interventions. – Making well-considered choices of outcome measures and questionnaires is important for every new research project. Operationalization of intervention effects into generic and intervention-specific outcomes is challenging. It is essential to take into account that measures should be sensitive to change.	

MAKING UP THE BALANCE

After carrying out so many research projects on Op Koers, pilot studies as well as RCT's, we ask ourselves what the endpoint should be. In all projects so far, the intervention had a positive effect on coping skills and emotional functioning of participants. Still, we keep refining and optimizing the intervention either for existing modules or new ones. Our aspirations include for example new modules for family members of a child with acquired brain injury. Should we invest our time in efficacy research for adapted or new modules or focus on wider lasting implementation of Op Koers? On the one hand, one could argue that efficacy studies are no longer needed, because it is justifiable to trust on the results of our previous research when a module is adapted for a new target population. On the other hand, it is only possible to make statements about the effect of an intervention when it is studied within the appropriate target population. From a researcher's point of view, we would like to continue studying the intervention, for example regarding the working mechanism of Op Koers, or providing the course using videoconferencing. From a more practical point of view, logistical barriers such as time and money sometimes keep us from doing further research. In combination with the often problematic recruitment, this results in having to compromise: only study a new module or refinement of Op Koers when there is a promising grant opportunity and if the number of available participants is expected to be sufficient.

CONCLUSION

In the 25 years of developing the Op Koers intervention, many intervention development and evaluation activities were conducted, partly described in 15 publications in international peer-reviewed journals. The efforts resulted in the availability of 13 separate Op Koers modules that are part of standard care in several Dutch hospitals. In the process, multiple barriers in psychosocial intervention development and research were encountered, regarding characteristics of the intervention and the involved individuals, the inner and outer setting, the implementation process and research. To some of those we have found solutions, and some remain continuous challenges that we will keep trying to cope with in the coming years. We have learned that there is no 'one size fits all solution' to different challenges in different stages, and the most important lesson is that intervention development and implementation require a lot of flexibility, adaptability and perseverance. Op Koers is one of few psychosocial interventions in pediatric psychology that has been both extensively studied and implemented. The main factor for this achievement is the close collaboration between, and the perseverance of the clinical care and research departments.

Table 1. A Summary of all Peer reviewed Research into the Op Koers Online Intervention by development phase (b-d).

Target group and reference	**Focus**	**Methods Outcome (measures)**	**Sample**	**Main Results**
b) Intervention refinement				
Siblings of children with chronic illness (CI), online [34]	To identify siblings' online support needs in order to develop a sibling-specific module	Mixed methods study Questionnaire and semi-structured video interviews on online support needs	Siblings of children with CI (age: 12-18 years) Questionnaire: n=91 Semi-structured video interviews: n=9	Of all participants, 55% would like to initiate or increase contact with other siblings of children with a chronic condition and 46% of those were interested in an online chat course. Important identified themes were: impact on daily life, worrying about brother's/sister's future, handling other people's reactions and how attention is divided within the family.
Parents of children with CI, online [35]	To refine the existing face-to-face module into an online module for parents	Mixed methods study Questionnaire, focus groups and telephone interviews on online support needs	Parents of children with CI (age child: 0-18 years) Questionnaire: n=272 Focus groups: n=15 Telephone interviews: n=7	Important themes for an intervention were identified such as parents' own (emotional) functioning, how to support their child in living with a CI, family functioning, taking care of themselves, relationships with others and practical support. Parents preferred a group with parents of children in the same age category. At first, parents preferred face-to-face contact. After an explanation and demonstration of an online intervention, parents became more positive about online support, mostly because they could participate from home.
Young Adult childhood cancer survivors (YACCS), online [63]	To assess support needs (types and domains) and associated factors in Dutch YACCS	Questionnaire study Questionnaire on support needs	YACCS (age: 18-30 years), n=151	YACCS report the strongest need for support, in particular for concrete information, in the domains lifestyle, fertility, and physical consequences of childhood cancer. Information for YACCS should go beyond the physical consequences of childhood cancer but also focus on emotional and social consequences. Psycho-education should be at the base of survivorship care for YACCS, in order to meet their need for information as well as empower them to take control over their health during the crucial life phase of young adulthood. Survivorship care clinics could specifically consider developing and offering interventions that can be delivered online
c) Feasibility and pilot testing				
Siblings of children with cancer, face-to-face [40]	To study whether the module for siblings reduces anxiety, and to determine predictors of anxiety reduction	Pilot study Longitudinal questionnaire assessment (T0, T1 after intervention) Anxiety (STAI-C)	Siblings of children with cancer (age: 7-18 years), n=24	After group participation, siblings showed less anxiety than before*. Age, sex, treatment phase, survival perspective and time since diagnosis were not related to anxiety reduction.

Target group and reference	**Focus**	**Methods Outcome (measures)**	**Sample**	**Main Results**
Children with CI) face-to-face [8]	To study the efficacy of the course for children with an illness	Pilot study Longitudinal questionnaire assessment (T0, T1 0-6 weeks after intervention, T2 6-8 months after intervention) Disease-related skills (QOK-c) Cognitive coping (CCSS) Behavioral-emotional problems (CBCL) Anxiety (STAI-C) Self-worth (SPPC) Quality of daily functioning (DUX-25)	Children 8-18 year with CI or childhood cancer (age: 8-18 years), n=109	Improvements* in behavioral–emotional outcomes, social competence, information seeking, relaxation and positive thinking were found both in short and medium term.
Adolescents with inflammatory bowel disease (IBD), face-to-face [41]	To investigate efficacy of psychoeducational group intervention for adolescents with IBD	Controlled pilot study Longitudinal questionnaire assessment (T0, T1 6-8 months after intervention) Cognitive coping (CCSS) Self-worth (SPPA) Anxiety (STAI-C) Quality of daily functioning (DUX-25)	Adolescents with IBD (age: 12-18 years), n=40 Intervention group, n=22 Control group, n=18	Positive effect* on: coping (predictive control), feelings of competence (global self-worth and physical appearance), and HRQoL
Children after treatment for childhood cancer, face-to-face [42]	Pilot study into the appropriateness and efficacy of the module for children after treatment for childhood cancer	Mixed methods pilot study Longitudinal questionnaire assessment (T0, T1 0-4 weeks after intervention) and focus group Disease-related skills (QOK-c)	Children after completion of successful childhood cancer treatment (age: 8-12 years), n=11, and their parents	Positive outcomes* on most items concerning disease-related skills. Remarkable improvements with respect to the intervention goals ‘social competence’ and ‘positive thinking’. Parents reported sharing emotions and experiences of their child with other patients/survivors as an important element of the intervention.

Target group and reference	Focus	Methods Outcome (measures)	Sample	Main Results
Adolescents after treatment for childhood cancer, online [43]	Pilot study into the satisfaction with and feasibility of the online module for adolescents after treatment for childhood cancer	Mixed methods pilot study Questionnaire (adolescents) and interview (course leaders) after intervention Questionnaire on satisfaction with and feasibility of intervention	Adolescents after completion of successful childhood cancer treatment (age: 11-17 years), n=11 and course leaders (n=6)	Dropout was very low and high levels of satisfaction were reported by CCS and course leaders. The positive evaluations indicate that OK Onco Online is a promising innovative group intervention.
Adolescents with CI, online [44]	Pilot study into feasibility and efficacy of the online module for adolescents with CI	Pilot study Longitudinal questionnaire assessment (T0, T1 0-2 weeks after intervention) Disease-related skills (QOK-c) Emotional and behavioral problems (YSR) Health-related quality of life (PedsQL)	Adolescents with CI (age: 12-18 years), n=29	High overall satisfaction. Increased use of total coping skills, information seeking and giving, and social competence strategies; significantly fewer withdrawn/depressed behavior and significantly better scores on emotional and psychosocial HRQoL*
Young Adult survivors or childhood cancer (YACCS), online [36]	Pilot study into feasibility and efficacy of the online module for YACCS	Pilot study Longitudinal questionnaire assessment (T0, T1 1-4 weeks after intervention) Evaluation questionnaire Distress (DT) Sense of control over changes in life (MS) Illness cognitions (ICQ) Impact of cancer (IOC-CS) Health-related quality of life (PedsQL)	YACCS (age: 18-30 years), n=10	This first, small pilot study showed short term decrease in distress and feelings of helplessness and, improvement of self-efficacy*. The pilot also indicated that Op Koers Online is a feasible intervention, filling a gap in psychosocial services for YACCS

Target group and reference	Focus	Methods Outcome (measures)	Sample	Main Results
d) Efficacy research				
Children with CI, face-to-face [37, 64]	To investigate the efficacy of the module for children with chronic illnesses and to test the effect of an added parent component.	RCT Longitudinal questionnaire assessment (T0, T1 6 months after intervention, T2 12 months after intervention) Behavioral-emotional problems (CBCL) Disease-related skills (QOK-c, QOK-p)	Children with CI (age: 8-18 years), n=194 and their parents, n=49 Child intervention, n=71 Parent-child intervention, n=49 Wait-list control, n=74	Results show a positive effect* of the intervention on parent-reported internalizing problems, child-reported externalizing problems, information seeking, social competence, and positive thinking. The additional effect* of parental involvement was observed on parent-reported internalizing problems, child-reported externalizing problems, information seeking, and social competence.
Children with CI, face-to-face [48, 64]	To investigate characteristics of children and parents as predictors and moderators of the effect of the module for children with chronic illness	RCT Longitudinal questionnaire assessment (T0, T1 6 months after intervention, T2 12 months after intervention) Child disengaged coping (CSI) Self-worth (SPPC, SPPA) Emotional security of the parent-child relationship (CSS) Parenting stress (PSI)	Children with CI (age: 8-18 years), n=194 Child intervention, n=71 Parent-child intervention, n=49 Waitlist control, n=74	Children with a more disengaged coping style or lower self-worth benefited more from Op Koers, especially as their parents were involved as well. The benefit of parental involvement was dependent on the quality of the parent-child relationship.
Children with CI, face-to-face [49, 64]	To test child coping and parenting stress as underlying mechanisms of the effect of an intervention for children and an additional group intervention for parents.	RCT Longitudinal questionnaire assessment (T0, T1 6 months after intervention, T2 12 months after intervention) Behavioral-emotional problems (CBCL) Disease-related skills (QOK-c) Parenting stress (PSI)	Children with CI (age: 8-18 years), n=120 Child intervention, n=71 Parent-child intervention, n=49	Active coping skills and parenting stress were mediators of the effect of the added parent component on internalizing behavior.

Target group and reference	Focus	Methods Outcome (measures)	Sample	Main Results
Adolescents with CI, online [46, 65]	To evaluate the efficacy of the module for adolescents with a chronic illness.	RCT Longitudinal questionnaire assessment (T0, T1 6 months after intervention, T2 12 months after intervention) Behavioral-emotional problems (CBCL) Disease-related skills (QOK-c) Health-related quality of life (PedsQL)	Adolescents with CI (age: 12-18 years), n=59 Intervention, n=35 Waitlist control, n=24	The intervention had a significant positive effect* on disease related coping skills T1 vs T0 (use of relaxation and social competence) and T2 vs T0 (information seeking), and on HRQoL (social-, school-, psychosocial functioning and total HRQoL) T1 vs T0.
Parents of children with CI, online [47, 65]	To evaluate the efficacy of the online module for parents of children with a chronic illness	RCT Longitudinal questionnaire assessment (T0, T1 6 months after intervention, T2 12 months after intervention) Anxiety and depression (HADS) Disease-related skills (QOK-p) Illness cognitions (ICQ) Cognitive coping (CCSS)	Parents of children with CI (child's age: 0-18 years), n=77 Intervention, n=34 Waitlist control, n=33	The intervention had a significant positive effect* on changes in anxiety, depression, and total score T1 versus T0 and T2 versus T0, the coping skills open communication, relaxation, social support, acceptance, predictive control and helplessness T1 versus T0 and relaxation and positive thinking T2 versus T0.

Target group and reference	Focus	Methods Outcome (measures)	Sample	Main Results
Parents of children with cancer, online [45]	To evaluate the efficacy of the online module for parents of children with cancer	RCT Longitudinal questionnaire assessment (T0, T1 6 weeks and T2 6 months after intervention) Anxiety (PROMIS CAT item bank) Depression (PROMIS CAT item bank) Coping skills (QOK-p and CCSS-PF) Distress (DT-P) Emotional reactions (SSER-Q)	Parents of children with cancer, n=89 Intervention n=43, Waitlist control n=46	The intervention had a significant positive effect* on changes in anxiety, depression, distress and feelings of loneliness and coping skill relaxation T1 versus T0, and anxiety and feelings of uncertainty and coping skill relaxtion T2 versus T0.

**Significant effect: p<.05*

Abbreviations:

CI chronic illness; YACCS young adult survivors of childhood cancer; IBD inflammatory bowel disease; CCS childhood cancer survivors; HRQoL health-related quality of life, QOK-c Questionnaire Op Koers for children; QOK-p Questionnaire Op Koers for parents; CCSS cognitive control strategies scale; STAI-C State Trait Anxiety Inventory for Children; CBCL Child behavior check list; SPPC Self-perception profile for children; SPPA Self-perception profile for adolescents; YSR Youth Self-Report; PedsQL Pediatric Quality of Life Inventory; DT Distress Thermometer; MS Mastery scale; ICQ illness cognitions questionnaire; IOC-CS Impact of cancer – childhood cancer survivors; CSI coping strategies inventory; CSS: child security scale; PSI Parenting Stress Index; HADS Hospital anxiety and depression scale; PROMIS patient reported outcome measurement information system

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PART 2.

PSYCHOSOCIAL WELLBEING OF SIBLINGS AND PARENTS OF VERY LONG-TERM SURVIVORS OF CHILDHOOD CANCER

CHAPTER 6

PSYCHOSOCIAL FUNCTIONING OF ADULT SIBLINGS OF DUTCH VERY LONG-TERM SURVIVORS OF CHILDHOOD CANCER: DCCSS-LATER 2 PSYCHO-ONCOLOGY STUDY

PSYCHO-ONCOLOGY, 2023

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ABSTRACT

Objective To describe psychosocial outcomes among adult siblings of very long-term childhood cancer survivors (CCS), to compare these outcomes to reference populations and to identify factors associated with siblings' psychosocial outcomes.

Methods Siblings of survivors (diagnosed <18 years old, between 1963 and 2001, >5 years since diagnosis) of the Dutch Childhood Cancer Survivor Study DCCSS-LATER cohort were invited to complete questionnaires on HRQoL (TNO-AZL Questionnaire for Adult's HRQoL), anxiety/depression (Hospital Anxiety and Depression Scale), post-traumatic stress (Self-Rating Scale for Post-traumatic Stress Disorder), self-esteem (Rosenberg Self-Esteem Scale) and benefit and burden (Benefit and Burden Scale for Children). Outcomes were compared to a reference group if available, using Mann-Whitney U and chi-Square tests. Associations of siblings' sociodemographic and CCS' cancer-related characteristics with the outcomes were assessed with mixed model analysis.

Results Five hundred five siblings (response rate 34%, 64% female, mean age 37.5, mean time since diagnosis 29.5) of 412 CCS participated. Siblings had comparable HRQoL, anxiety and self-esteem to references with no or small differences ($r = 0.08–0.15$, $p < 0.05$) and less depression. Proportions of symptomatic PTSD were very small (0.4%–0.6%). Effect sizes of associations of siblings' sociodemographic and CCS cancer-related characteristics were mostly small to medium ($\beta = 0.19–0.67$, $p < 0.05$) and no clear trend was found in the studied associated factors for worse outcomes.

Conclusions On the very long-term, siblings do not have impaired psychosocial functioning compared to references. Cancer-related factors seem not to impact siblings' psychosocial functioning. Early support and education remain essential to prevent long-term consequences.

INTRODUCTION

Siblings of children with cancer are impacted by their brother or sister's disease. During treatment, siblings may experience disruptions of daily and academic life, changes in family relations and feelings of worry, loneliness and neglect [1-4]. During this period and even after treatment, siblings may need psychosocial support [5]. The Integrative Trajectory Model of Pediatric Medical Traumatic Stress describes that although most families recover over time after the diagnosis of a pediatric illness, a small proportion continues to experience problems, even after months or years [6]. Most literature on siblings' wellbeing focuses on children below the age of 18. A systematic review shows that emotional and behavioral functioning of adult siblings was similar to references and states that methodological limitations hamper conclusions about health related quality of life (HRQoL) [7]. A more recent study shows lower mental HRQoL in adult siblings than in peers [8]. Regarding post-traumatic stress, adult siblings do not experience more symptoms than controls [9]. Besides generic outcomes such as HRQoL, disease-specific outcomes such as benefits and burden of having a brother of sister with cancer may be relevant. Literature on siblings' burden of and positive experiences with cancer is scarce [10] but post-traumatic growth seems to be higher in young-adult siblings than in controls that were asked about a major stressful event [9]. Minor siblings report higher self-esteem as a positive effect [11].

Previous research into factors associated with psychosocial functioning of adult siblings points out that females and older siblings are at risk [9], as well as adult siblings who were older at diagnosis and older than the childhood cancer survivor (CCS) [12]. Further risk factors are lower income, lower education, nonwhite race, lower perceived social support and health problems, whereas cancer-related factors typically are not associated with wellbeing of siblings [7].

It is especially relevant to study the wellbeing of adult siblings of very long-term CCS since knowledge on very long-term psychosocial functioning in siblings is limited and it was found that siblings' risk for mental health problems starts to diverge from controls from approximately 15 years after diagnosis [12], while the follow-up period of most studies is shorter. The aim of the current study is to describe HRQoL, anxiety, depression, post-traumatic stress, benefit and burden and self-esteem among adult siblings of very long-term CCS and to compare these outcomes to reference populations. Furthermore, we aimed to determine factors associated with siblings' psychosocial outcomes.

METHODS

Participants

This study is part of the Dutch Childhood Cancer Survivor Study DCCSS-LATER study part 2; clinical visit & questionnaire study in which data was collected between 2016 and 2020 [13].

In the DCCSS-LATER 2 psycho-oncology study, siblings (≥18 years old, *n* = 1479) of adolescent and adult CCS (diagnosed <18 years old and between 1963 and 2001, >5 years since diagnosis) were invited to participate in a psychosocial questionnaire study via mail or online if the CCS gave consent. If siblings did not respond, a reminder was sent or they were contacted by phone. The medical ethics board of Amsterdam University Medical Centers, location AMC (ref: 2010/332) approved the study protocol.

Measures

HRQOL was measured with the TNO-AZL Questionnaire for Adult's HRQoL (TAAQoL) that assesses health status problems weighted by their impact. It consists of 45 items covering 12 domains, from which we used 10: cognitive functioning, sleep, pain, social functioning, daily activities, sexuality, vitality, positive-, depressive- and aggressive emotions. Item scores (4-point Likert scale) are added up and transformed to scale scores of 0–100, higher scores indicating better HRQoL. Psychometric properties are satisfactory [14]. Cronbach's α of the scale scores in the current sample was 0.63–0.92. Reference data from the general Dutch population are available [14], to obtain a reference sample with a mean age similar to that of our sample, reference data from adults aged 18–59 years were selected.

Anxiety and depression were measured with the Hospital Anxiety and Depression Scale (HADS), that consists of 14 items (4-point Likert scale). Items are divided over two scales measuring anxiety and depression (range 0–21). Higher scores indicate more symptoms. The cut-off point for (sub)clinical anxiety and depression was eight [15, 16]. Psychometric properties are good [17]. Cronbach's α of the scale scores in the current sample was 0.79–0.81. Reference data from the general Dutch population are available [18].

Post-traumatic stress symptoms related to childhood cancer were measured with the Self-Rating Scale for Post-Traumatic Stress Disorder (SRS-PTSD). The SRS-PTSD consists of 17 items (3-point Likert scale) that correspond to the diagnostic DSM-IV symptoms of PTSD and result in a total scale and three subscales: re-experiencing, avoidance and hyper arousal. Presence of at least one symptom in all three scales is considered subclinical PTSD [19] and presence of at least one re-experiencing, three avoidance and two hyper arousal symptoms is considered symptomatic PTSD [20, 21]. Psychometric properties are adequate [20]. Cronbach's α for the total scale in the current study was 0.70.

Self-esteem was measured with the Rosenberg self-esteem questionnaire, which consists of 10 items (4-point Likert scale). A higher score indicates higher self-esteem (range 10–40). Psychometric properties are good.22 Cronbach's α in the current study was 0.90. Reference data from the general Dutch population are available [23].

Benefit finding and disease-related burden of having a sibling CCS were measured with the Benefit and Burden Scale for Children (BBSC [24]), minimally adapted for the use in adults with approval of the original author. The questionnaire consists of two scales with 10 items (see Table 1) on a Likert scale ([1] 'Not at all true for me', [2] 'a little bit', [3] 'somewhat', [4] 'quite a bit', [5] 'Very much true for me'): benefit finding (Cronbach's α 0.90) and disease-related burden (Cronbach's α 0.77) of childhood cancer. Mean item scale scores were calculated. Scores of siblings <4 years old at the time of diagnosis of the CCS were not used.

Table 1. Items of the Benefit and Burden Scale for Children.

***n*-range**	**316-320**		**316-320**
Benefit finding		**Disease-related burden**	
	Mean±SD		**Mean±SD**
Learned what is important in life	3.2±1.4	Afraid to upset others	1.5±0.9
Learned to be happy and enjoy life	3.0±1.5	Cannot enjoy life the way I used to	1.3±0.9
Have become a stronger person	2.7±1.3	Less hopeful about life	1.2±0.7
Family has grown closer	2.7±1.3	Afraid to be a burden to my family	1.3±0.8
Know how much I am loved	2.6±1.5	Less self-confident	1.3±0.7
Learned to be nicer to others	2.1±1.1	Moodier and more irritable	1.2±0.5
Learned to better cope with problems	2.0±1.2	Less happy with my life	1.2±0.5
Know my real friends	2.0±1.4	Less time to spend with friends	1.1±0.4
Learned to be more patient	2.0±1.1	Less time to do fun things	1.1±0.4
Made new friends	1.4±0.8	Feel embarrassed when seen in public	1.1±0.4

Associated factors consisted of demographic characteristics (siblings' age at participation and at diagnosis of CCS, sex, level of education, number of siblings, survivor's age) and cancer-related characteristics of the CCS (primary childhood cancer diagnosis, metastasis and recurrence of primary tumor). Demographic factors were obtained from the DCCSS-LATER 1 or 2 study [25]. Cancer-related factors were obtained from the DCCSS-LATER registry [25].

Statistical analyses

Differences between characteristics of participants and non-participants/LATER cohort were tested with independent t-tests and chi-square tests, having Cohen's d and Cramer's V as effect sizes. Outcomes were analyzed descriptively. In addition, HRQoL, anxiety, depression and self-esteem were compared with references of comparable age for males and females separately, using Mann Whitney-U tests with effect size r, and chi-square tests.

Mixed model analyses were conducted to determine factors associated with psychosocial outcomes, controlled for age and sex. Random intercepts were included to account for dependency of outcomes of siblings of the same CCS.

p-values ≤0.05 were considered statistically significant, except for comparisons between siblings and references, where a Bonferroni correction was applied for the number of scales within the outcomes. Effect size V, effect size r and standard regression coefficients (categorical variables) of 0.2, 0.5 and 0.8 and standard regression coefficients (continuous variables) of 0.1, 0.3 and 0.5 are considered small, medium and large respectively [26].

Table 2. Sociodemographic characteristics of siblings and CCS cancer-related characteristics.

	participants		**non-participants**[a]		
	n	**Mean±SD or %**	**n**	**Mean±SD or %**	**Cohen's d or Cramer's V**
Sibling characteristics					
					Cohen's *d*
Age	505	37.5±10.1 range 17.8-64.6	871	35.3±9.7 range 16.6-76.6	.22**
					Cramer's *V*
Sex	505		871		.17**
Male		36.0		53.7	
Female		64.0		46.3	
Attained level of education [b]	410		427		.08
Low		6.3		9.4	
Middle		42.7		46.1	
High		51.0		44.5	
Number of siblings	422				
1		33.4			
>1		66.6			
Follow-up time since diagnosis (years)	465	29.5±8.4			
Sibling age at diagnosis					
<4		37.0			
4-12		43.7			
12+		19.4			
Age difference	465				
Sibling >2 years younger		50.1			
Difference <2 years		11.8			
Sibling >2 years older		38.1			
CCS cancer-related characteristics				Total CCS Cohort	
Primary childhood cancer diagnosis	465		6159		.12*
Hematologic cancers		55.7		51.2	
CNS tumor		7.7		13.7	
Solid tumor		36.6		35.1	
Metastasis of primary tumor	454	14.6			
Recurrence of primary tumor	465	9.7			

**p-value<0.01, **p-value<0.001, significant differences (p <.05) [a]Non-participants are siblings of CCS that were approached for our study after consent by their CCS but did not participate. [b]Low: primary education, lower vocational education, lower and middle secondary education; middle: middle vocational education, higher secondary education, pre-university education; high: higher vocational education, university.

RESULTS

Participants

In total, 505 of 1479 siblings (34% of siblings invited through their CCS, 64% female, mean age 37.5 years, mean time since diagnosis 29.5 years) of 412 CCS gave informed consent and completed at least one questionnaire. Participants and non-participants differed in sex and age, but not in education (Table 2). CCS' diagnosis differed from the LATER cohort [25]. All effect sizes are small to moderate.

Outcomes

Several small differences ($r = 0.08–0.18$) between siblings and references were found on psychosocial outcomes (Table 3). Regarding HRQoL, females had lower cognitive functioning and higher social functioning and positive and depressive emotions and aggressiveness than references. Males had lower cognitive functioning and sleep than references. Both female and male siblings had less depression and (sub)clinical depression than references, while no differences were found on anxiety. Self-esteem was higher for females compared to references, but not for males. The percentage of siblings reporting subclinical and symptomatic PTSD because of the CCS's disease was respectively 4.4% and 0.4% for females and 4.3% and 0.6% for males. Mean scale scores for benefit and burden were 2.3 ("a little bit" to "somewhat") and 1.1 ("none at all' to "a little bit") respectively, indicating less burden than benefit (Table 1). For benefit, the items with the highest score were "I have learned what is really important in life" (mean 3.2), "I have learned to be happy and to enjoy good things" (mean 3.0) and "I became a stronger person" (mean 2.7). For burden the items with the highest score were "I am afraid to make other people sad or upset" (mean 1.5), "I can't enjoy life like I used to anymore" (mean 1.3) and "I am less hopeful about life" (mean 1.3).

Associated factors

Tables 4 and 5 show the associations of sociodemographic and cancer-related factors with psychosocial outcomes. Age group 12+ at diagnosis had better sleep (compared to 0–4 years) and more perceived benefit (compared to 4–12 years). Having >1 sibling was associated with less pain compared to having 1 sibling. Being >2 years younger or older than the CCS was related to more problems in cognitive functioning and sleep than having a similar age, respectively. Regarding the cancer-related factors, only one significant association was found. Siblings of CCS with CNS tumors reported less pain than other diagnoses. All associations were of small to medium size ($\beta = -0.27–0.41$, $p < 0.05$), except the association between age at diagnosis and benefit ($\beta = 0.67$, $p < 0.001$).

Table 2. Psychosocial outcomes in siblings of CCS.

		Total group	Female siblings	Female references		Male siblings	Male references	
		Median (percentile25;75) or %	Median (percentile25;75) or %	Median (percentile25;75) or %	r[a]/OR	Median (percentile25;75) or %	Median (percentile25;75) or %	r[a]/OR
HRQoL	*n*-range	490-495	311-315	1678-1806		177-180	1362-1399	
Cognitive functioning		87.5 (62.5;100)	87.5 (62.5;100.0)	93.7 (75.0;100.0)	-0.15*[b]	87.5 (56.3;100.0)	93.8 (81.3;100.0)	-0.15*[b]
Sleep		75.0 (50.0;93.8)	68.8 (50.0;93.8)	75.0 (56.3;93.8)	0.05	75.0 (56.3;98.4)	87.5 (68.8;100.0)	-0.10*[b]
Pain		81.3 (62.5;87.5)	75.0 (62.5;87.5)	75.0 (62.5;87.5)	0.01	81.3 (68.8;93.8)	87.5 (68.8;100.0)	0.01
Social functioning		100.0 (87.5;100)	100.0 (87.5;100.0)	93.8 (75.0;100.0)	0.14*[b]	96.9 (81.3;100.0)	93.8 (75.0;100.0)	0.06
Daily activities		100.0 (75.0;100)	100.0 (75.0;100.0)	96.9 (75.0;100.0)	0.01	100.0 (76.6;100.0)	100.0 (81.3;100.0)	0.01
Sexuality		100.0 (75.0;100)	100.0 (75.0;100.0)	100.0 (75.0;100.0)	0.00	100.0 (75.0;100.0)	100.0 (75.0;100.0)	0.00
Vitality		75.0 (50.0;83.3)	66.7 (50.0;83.3)	66.7 (50.0;75.0)	0.03	75.0 (58.3;83.3)	75.0 (58.3;83.3)	0.02
Positive emotions		66.7 (58.3;91.7)	66.7 (66.7;91.7)	66.7 (58.3;75.0)	0.09*[b]	66.7 (58.3;91.7)	66.7 (58.3;75.0)	0.05
Depressive emotions		83.3 (75.0;100)	83.3 (66.7;91.7)	83.3 (66.7;91.7)	0.09*[b]	91.7 (75.0;100.0)	88.9 (75.0;91.7)	0.02
Aggressive emotions		100.0 (88.9;100)	100.0 (88.9;100.0)	88.9 (77.8;100.0)	0.08*[b]	100.0 (77.8;100.0)	88.9 (77.8;100.0)	0.02
Anxiety and depression	*n*	485	307	785		178	811	
Anxiety		4.0 (2.0;6.0)	4.0 (2.0;6.0)	4.0 (2.0;7.0)	0.04	4.0 (2.0;6.0)	3.0 (1.0;6.0)	-0.05
(sub)clinical anxiety		17.5%	18.2%	21.9%	0.80	16.3%	16.2%	1.01
Depression		1.0 (0.0;3.0)	1.0 (.0;3.0)	2.0 (1.0;5.0)	-0.18*[c]	2.0 (.0;4.0)	2.0 (1.0;5.0)	-0.10*[c]
(sub)clinical depression		7.4%	7.2%	14.1%	0.47*[c]	7.9%	14.3%	0.51*[c]
Posttraumatic stress	*n*(-range)	453	282-305			171-177		
Total score		1 (1;2)	1.0 (1.0;2.0)			1.0 (1.0;1.0)		
Symptomatic post-traumatic stress			0.4%			0.6%		
Subclinical post-traumatic stress			4.4%			4.3%		
Symptomatic re-experience			35%			22%		
Symptomatic avoidance			1%			1%		
Symptomatic hyperactivity			1%			4%		
Self-esteem	*n*	494	315	584		179	494	
		33.0 (29.0;37.0)	32.0 (29.0;36.0)	31.0 (29.0;35.0)	0.08*	34.0 (30.0;37.0)	33.0 (30.0;37.0)	0.03
Benefit and burden[d]	*n*-range	319-320	206-207			113		
Benefit		23.0 (16.0;31.0)	23.0 (16,5;31.0)			23.3 (15.0;31.5)		
Burden		11.0 (10.0;13.0)	11.0 (10.0;13.0)			11.0 (10.0;13.0)		

[a] Effect size for differences between siblings and references; calculated with r=Z-score of the difference/(√N).

*Siblings differ significantly from references according to Mann-Whitney-U tests or Chi-Square tests; [b]p<.005 after Bonferroni correction; [c]p<.025 after Bonferroni correction

[d]Only age group >4 years old was used

Table 3a. Standardized coefficients (β) of associations of sociodemographic variables and cancer-related variables with HRQoL (TAAQoL).

	Cognitive functioning	**Sleep**	**Pain**[a]	**Social functioning**	**Daily activities**	**Sexuality**	**Vitality**	**Positive emotions**	**Depressive emotions**	**Aggressive emotions**
n	**403**	**405**	**405**	**405**	**405**	**401**	**405**	**405**	**405**	**403**
					β (95% CI)					
Sibling sociodemographic factors										
Sex (ref: male)	.01 (-.19;.21)	-.15 (-.36;.05)	**-.37***** **(-.57;.17)**	**.27*** **(.05;.48)**	-.17 (-.38;.04)	-.01 (-.22;.20)	**-.36***** **(-.57;-.16)**	.06 (-.15;.27)	-.14 (-.35;.06)	**.23*** **(.03;.43)**
Age	.02 (-.11;.15)	.04 (-.09;.17)	-.04 (-.16;.09)	-.11 (-.24;-.01)	-.01 (-.11;.14)	-.07 (-.20;.06)	-.01 (-.14;.11)	**-.20**** **(-.33;-.07)**	-.06 (-.19;.07)	-.01 (-.14;.11)
Age at diagnosis (years, ref <4)										
4-12	.01 (-.23;.26)	.23 (-.02;.48)	-.07 (-.31;.17)	-.03 (-.28;.22)	-.08 (-.33;.17)	-.01 (-.26;.24)	-.06 (-.30;.18)	-.02 (-.27;.23)	-.003 (-.25;.24)	-.09 (-.33;.15)
12+	-.08 (-.43;.26)	**.39*** **(.04;.74)**	.17 (-.16;.50)	-.07 (-.42;.28)	-.03 (-.31;.37)	.04 (-.31;38)	.31 (-.03;.65)	.10 (-.25;.45)	.26 (-.09;.61)	-.03 (-.36;.31)
>1 sibling (ref: 1 sibling)	.02 (-.20;.23)	-.02 (-.24;.19)	**.28**** **(.08;.48)**	-.03 (-.25;.18)	.04 (-.17;.25)	.11 (-.10;.33)	.03 (-.18;.24)	-.08 (-.29;.14)	.08 (-.14;.30)	.13 (-.07;.34)
Age difference between sibling and CCS (ref: <2 years difference)										
Sibling >2 years younger	**-.39*** **(-.71;-.06)**	-.19 (-.53;.14)	-.19 (-.51;.13)	-.11 (-.45;.23)	-.14 (-.47;.19)	-.23 (-.57;.11)	-.19 (-.51;.14)	-.27 (-.60;.07)	-.23 (-.56;.10	-.01 (-.31;.33)
Sibling >2 years older	-.28 (-.61;.05)	**-.41*** **(-.74;-.07)**	-.28 (-.60;.04)	-.10 (-.45;.24)	-.15 (-.49;.18)	-.34 (-.68;.01)	-.11 (-.44;.21)	.19 (-.53;.15)	-.33 (-.66;.01)	-.0003 (-.32;.32)
CCS cancer-related factors										
CNS (ref: other diagnoses)	-.18 (-.55;.20)	-.17 (-.54;.20)	**.38*** **(.03;.72)**	-.04 (-.42;.32)	.04 (-.33;.40)	-.14 (-.51;.23)	-.07 (-.44;.30)	-.03 (-.40;.34)	-.24 (-.61;.14)	.08 (-.28;.43)
Metastasis (ref: no)	.05 (-.24;.35)	.02 (-.27;.32)	-.02 (-.30;.25)	.09 (-.20;.39)	.21 (-.07;.50)	-.14 (-.15;.43)	.19 (-.10;.48)	-.08 (-.21;.37)	-.09 (-.39;.20)	-.07 (-.36;.21)
Recurrence (ref: no)	-.05 (-.39;.29)	-.04 (-.38;.30)	-.13 (-.45;.19)	.16 (-.18;.50)	-.0002 (-.33;.33)	.03 (-.31;.36)	-.05 (-.38;.29)	-.03 (-.37;.31)	-.04 (-.38;.31)	.10 (-.22;.42)

[a] Model without random intercept, as it was redundant.

*p-value <0.05, **p-value <0.01, ***p-value <0.001

Table 3b. Standardized coefficients (β) of associations of sociodemographic variables and cancer-related variables with anxiety, depression (HADS), PSTSD (PTSD-SRS), self-esteem (RSES), benefit and burden (BBSC).

	Anxiety	Depression	PTSD	Self-esteem	Benefit	Burden
n	**398**	**398**	**371**	**404**	**400**	**400**
Sibling sociodemographic factors			***β (95% CI)***			
Sex (ref: male)	.17 (-.03;.37)	-.12 (-.32;.09)	.17 (-.02;.37)	**-.30**** **(-.50;-.10)**	**.20*** **(.002;.39)**	.14 (-.07;.35)
Age	-.11 (-.23;.02)	.04 (-.09;.18)	**-.19**** **(-.31;-.07)**	.05 (-.07;.18)	**-.19**** **(-.31;-.07)**	-.10 (-.24;.03)
Age at diagnosis (years, ref <4)[a]						
4-12	.01 (-.23;.25)	-.004 (-.26;.25)	-.04 (-.28;.19)	.23 (-.01;.47)	NA	NA
12+	-.08 (-.42;.25)	-.12 (-.47;.24)	.11 (-.22;.43)	.27 (-.06;.61)	**.67***** **(.35;.99)**	.19 (-.16;.54)
>1 sibling (ref: 1 sibling)	-.19 (-.39;-.02)	-.03 (-.25;.19)	-.04 (-.24;.15)	-.06 (-.27;.14)	-.09 (-.28;.11)	-.04 (-.26;.17)
Age difference between sibling and CCS (ref: <2 years difference)						
Sibling >2 years younger	.26 (-.05;.58)	.24 (-.09;.58)	-.22 (.53;.10)	-.30 (-.62;.02)	-.11 (-.42;.19)	-.16 (-.50;.17)
Sibling >2 years older	.27 (-.05;.59)	.12 (-.21;.46)	.08 (-.24;.40)	-.21 (-.53;.11)	.13 (-.18;.44)	-.10 (-.43;.24)
CCS cancer-related factors						
CNS (ref: other diagnoses)	-.06 (-.43;.31)	.13 (-.26;.52)	.04 (-.30;.38)	-.04 (-.40;.32)	.14 (-.20;.49)	.21 (-.17;.59)
Metastasis (ref: no)	.05 (-.34;.24)	.08 (-.22;.39)	.05 (-.32;.23)	-.01 (-.30;.35)	-.14 (-.42;.14)	-.25 (-.56;.05)
Recurrence (ref: no)	-.13 (-.46;.20)	.12 (-.23;.47)	.01 (-.30;.32)	.02 (-.30;.35)	.20 (-.11;.51)	.33 (-.02;.67)

*p-value <.05, **p-value <.01, ***p-value <.001

[a] Age at diagnosis reference category for the Benefit and burden scales is 4-12

DISCUSSION

This study of siblings of the first Dutch nationwide cohort of CCS aimed to gain insight into very long-term psychosocial functioning of adult siblings of CCS and to determine associated factors. Siblings in our sample had comparable outcomes to references. Proportions of symptomatic PTSD were very small and siblings experienced some benefits but hardly any burden of having a brother of sister with childhood cancer. No clear pattern of risk or protective factors for worse psychosocial outcomes could be determined. These results demonstrate that most siblings in our sample seem to have integrated this past experience in their current lives and that they are resilient >17 years after the diagnosis of the CCS. This supports previous results that most families achieve normal wellbeing over time, after a diagnosis of childhood cancer [6].

Outcomes

Overall, HRQoL in our sample was comparable to references. The few differences in the HRQoL domains had different directions and small effect sizes, there was no clear trend. This substantiates existing literature on adult siblings that described similar or better HRQoL in siblings compared to references, but the studies either have methodological limitations such as using unvalidated measures or poorly defined samples [7, 27, 28] or were less long-term after diagnosis [29, 30]. Our outcomes do differ from a recent study that shows lower mental QoL in siblings compared to the general population [8]. However, the population is not comparable since siblings in their sample were different in terms of age, CCS diagnosis and time since diagnosis. Siblings had similar anxiety and less depression compared to references, which is consistent with literature [9, 30]. To our knowledge, no studies have been done into PTSD symptoms of adult siblings on the long-term, but <1% seems very low compared to minor siblings shorter after diagnosis, of whom 22% had PTSD symptoms related to the childhood cancer of their brother or sister [31]. These percentages are based on the DSM-IV criteria, since no measurement based on the DSM V criteria was available at the time of inclusion. Self-esteem was comparable to references for males and slightly higher for females. Higher self-esteem of siblings was also found in minor siblings around 9 years after diagnosis [11].

Siblings reported more benefit than burden of their CCS disease. Items that had the highest means correspond with previously identified themes in growth in family members of CCS (e.g. item “learned what’s important in life” to theme ‘new values and life priorities’) [10]. It suggests that having a brother or sister with cancer leads to positive changes on the very long-term. None of the burden items got a mean higher than 1.5 out of 5. The low specific burden scores are in line with the other generally positive psychosocial outcomes. The generally positive results could be explained by psychosocial care that was widely available in the Netherlands, preventing siblings from developing psychosocial problems. Another factor might be that siblings are resilient, which is supported by the model of medical traumatic stress [6].

Associated factors

No clear trend is visible in the studied associated factors. Effect sizes are small to moderate and no factor impacts more than one outcome, other than being 12+ years old at diagnosis, which is related to better sleep and more perceived benefit. In previous research, being older at diagnosis was only associated with worse health behaviors such as use of tobacco [32]. Furthermore, we found only small effects of birth order, in worse cognitive functioning for younger siblings and worse sleep for older siblings. Previous studies into birth order found that having an older CCS is a risk factor for higher rates of reaching out for mental health support [12] and in siblings of children with a chronic disease, the older siblings seem to be more impacted [33]. Literature about adult siblings is lacking. Concerning cancer-related factors, we expected higher risk for siblings of CCS with CNS tumors, because of worse outcomes for CCS with CNS themselves. However, having a child with a CNS tumor was also not related to psychosocial functioning in parents of long-term CCS [34]. Apart from an association of small to medium size between siblings of CNS CCS and pain, we found no associations between the outcomes and cancer-related factors, which is substantiated in literature [8, 11, 35].

Following these results, factors that impact long-term psychosocial functioning of siblings of CCS might not differ from factors that impact the functioning of the general population.

Clinical implications

Literature suggests siblings are at risk for problems in psychosocial functioning closer to diagnosis and the need for sibling support is stressed in the standards of care [5]. The PAT could be used for psychosocial risk screening, which may help providing early intervention to prevent long-term consequences for families at risk [36]. Besides, age adequate information about the diagnosis and treatment is recommended and it is now commonly part of psychosocial support which will further empower the siblings of now diagnosed patients who will be the CCS in the future. Nonetheless, the current findings are reassuring and can be used in psycho educating families and potentially in comforting families.

Study limitations

This study is one of the first to report on very long-term psychosocial functioning of siblings of CCS in a nationwide cohort. Besides generic outcomes such as HRQoL we looked into benefit and related burden of siblings. Our sample is large, which is of added value to the shortage of research on big samples [7]. To date, research on long-term functioning has been limited to approximately 20 years after diagnosis, whereas our sample's mean time since diagnosis is 29.5 years. Some limitations of the study should be taken into account in the interpretation of the results. Information on CCS health impairment, family functioning or psychosocial support that siblings received was not collected, where it could have impacted the current wellbeing [11, 35, 37]. Further research could investigate these factors to identify siblings at-risk. Another limitation is that siblings were compared to the norm populations, so that siblings' functioning might not be accurately contextualized and which makes comparison of results between studies difficult. Concerning methodology, one of the multivariate models could not be adjusted for dependency of siblings of the same CCS, but because the intra-class coefficient was not significant, a non-adjusted model could be used instead [38]. The internal consistency of two HRQOL scale scores were questionable (0.63 for aggressive emotions and 0.68 for pain), which means results should be interpreted with caution. Siblings were only eligible after the CCS gave consent, which may have caused selection bias. Besides, bereaved siblings were outside the scope of the current research question. Findings are mixed in terms of vulnerability of that specific group [12, 36]. The reported response rate (34%) is a reflection of the invited siblings after the CCS gave consent and not of the entire sibling cohort. The exact response rate of the entire sibling cohort is unknown but will be lower than 34%, which may have decreased the generalizability of the results, even though the differences between participants and non-participants are small.

CONCLUSION

On the very long-term, siblings in our sample do not have impaired psychosocial functioning compared to references. Factors related to the disease of their brother or sister seem not to impact siblings' psychosocial functioning.

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CHAPTER 7

PSYCHOSOCIAL FUNCTIONING OF PARENTS OF DUTCH LONG-TERM SURVIVORS OF CHILDHOOD CANCER

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ABSTRACT

Objective To describe health-related quality of life (HRQoL), post-traumatic stress and post-traumatic growth of parents of long-term survivors of childhood cancer (CCS) and study associated factors.

Methods Parents of survivors of the Dutch Childhood Cancer Survivor Study LATER cohort below 30 years and diagnosed 1986–2001 were invited to complete the TNO-AZL Questionnaire for Adult's HRQoL (e.g., sleep and aggressive emotions), Self-Rating Scale for Post-traumatic Stress Disorder, Post-traumatic Growth Inventory, and Illness Cognition Questionnaire. HRQoL domain scores were compared to references using Mann-Whitney U tests. Correlations between post-traumatic stress, growth and HRQoL were evaluated. Medical characteristics of their child and illness cognitions were studied as associated factors of HRQOL, post-traumatic stress and growth. $p < 0.05$ was considered statistically significant.

Results Parents (n = 661 of n = 448 survivors, 56% female, mean time since child's diagnosis: 21.3 [SD: 3.3] years) reported better HRQoL in social functioning and aggressive emotions than references (r = .08–0.17). Mothers additionally reported better HRQoL in pain, daily activities, sexuality, vitality, positive and depressive emotions (r = .07–0.14). Post-traumatic stress was symptomatic in 3%, and associated with worse HRQoL (r = −0.27–0.48). Post-traumatic growth was positively associated to post-traumatic stress and better HRQoL (r = 0.09–0.12). Cancer recurrence was associated to better HRQoL (β = 0.37–0.46). Acceptance illness cognitions were associated to better (β = 0.12–0.25), and helplessness to worse outcomes (β = 0.14–0.38.

Conclusions HRQoL of parents of young adult survivors of CCS is comparable to references or slightly better. Only a small proportion reports symptomatic post-traumatic stress. Improving acceptance and reducing feelings of helplessness may provide treatment targets for parents with psychosocial problems.

BACKGROUND

The diagnosis of cancer of their child has a major impact on the psychosocial functioning of parent [1, 2]. Stressors change from the initial shock of diagnosis, to the disruption of daily life because of treatment, fear of recurrence [3] and late effects that may await their child after treatment [4]. These stressors may affect the mental and physical health of parents, that is, cause psychological distress. As described in the integrative trajectory model of pediatric medical traumatic stress and substantiated in empirical studies in pediatric oncology, psychological distress is typically high around diagnosis and decreases over time to normal some years after treatment ends [2, 5, 6]. However, some parents continue to report elevated psychological distress [1].

The psychological distress caused by their child's cancer diagnosis and treatment was found to impact parents' health-related quality of life (HRQoL) [2, 7]. Parents sometimes experience the diagnosis and treatment of their child to be traumatic [8], causing post-traumatic stress problems in 6%–30% of parents [1], but also resulting in post-traumatic psychosocial growth [1]. Post-traumatic growth and stress were previously described to be related [9] and both can impact HRQoL [6, 10]. However, most research results stem from studies including parents of a child during active treatment or young survivors of childhood cancer (CCS) (aged <18 years). A rather small study suggested ongoing psychological distress in parents of adult CCS [11]. On the other hand, parents of Swiss CCS 24 years after diagnosis reported post-traumatic stress rates similar to the general population [12]. Systematic knowledge of psychosocial functioning of parents of CCS on the very long-term is lacking.

Several factors were found to be associated to psychosocial outcomes of parents of children with cancer closer to diagnosis and treatment. Mothers of children with cancer were described to have more psychological distress [13] and more post-traumatic growth than fathers [14]. Also, parents with a lower level of education were found to have lower psychological function [2]. Previous research identified relapse and central nervous system (CNS) tumor diagnosis of their child as indicators for potentially impaired psychosocial functioning of parents [2, 15]. Finally, parents' cognitions are important to consider, following the model that Wallander and Varni proposed, where coping skills (e.g., cognitions) mediate the relation between a stressful event and the psychosocial outcomes [5, 16, 17].

To improve knowledge on parents' psychosocial functioning on the long-term, we aimed to describe HRQoL, post-traumatic stress and post-traumatic growth of parents from a large nationwide cohort of Dutch long-term CCS, compare HRQoL to a general population reference sample and study associations between post-traumatic stress and growth, and between these constructs and HRQoL. To be able to identify and help the parents that continue to experience elevated stress, we aimed to identify which sociodemographic factors, medical factors of the child and parental illness cognitions are associated with HRQoL, post-traumatic stress and post-traumatic growth.

METHODS

Participants

The cohort of Dutch survivors diagnosed between 1963 and 2001 has been studied in the Dutch Childhood Cancer Survivor Study (DCCSS) LATER 1 (registry linkage and questionnaires) and LATER 2 (clinical visit and questionnaires) studies [18]. This paper presents results from the psychosocial substudy of LATER 2, in which we invited parents of adolescent and young adult CCS (aged <30 years) who were diagnosed between 1986 and 2001 (cohort of CCS *n* = 1362) for a psychosocial questionnaire study. Parents of survivors younger than 18 years (*n* = 49) were directly approached via an attachment to the patient information regarding their child's participation in the DCCSS LATER 2 study. Parents of survivors 18–30 years were invited to participate by mail if their child gave consent and provided the address of their parents. In total, 996 parents (of 588 CCS) were invited. The medical ethics board of Amsterdam University Medical Centers, location AMC (ref: 2010/332) approved the study protocol.

Psychosocial outcomes and measures

Participants could complete questionnaires on HRQoL, post-traumatic stress and post-traumatic growth digitally or on paper. Additional questionnaire information can be found in Table A1.

Health-related quality of life: TNO-AZL Questionnaire for Adult's HRQoL (TAAQOL)

The TAAQOL was developed by the departments prevention and health and the pediatric department of the Leiden university Medical Center to assess HRQoL in people aged 16 years and older [19]. The TAAQOL measures health status problems weighted by their impact on well-being in the past month in 12 domains, each represented by 2-4 items. We included 10 domains: cognitive functioning, sleep, pain, social functioning, daily activities, sexuality, vitality, positive emotions, depressive emotions, and aggressive emotions, but we left out fine and gross motor functioning. Domain sum scores range from 0 to 100, and higher scores indicate better HRQoL (e.g., less pain, better social function). The TAAQOL has been validated in a random general population sample and a sample of people with chronic illness. Conceptual, convergent and criterion validity and reliability of the TAAQOL are satisfactory [19].

Dutch general population reference data from 2004 are available from the TAAQOL reference study in two samples from the general population, that were randomly drawn from the national telephone registry [19]. To obtain an age-matched sample we included reference data from adults aged 48–64 years for this study (*n* = 1221, 48% female, mean [SD] age: 55.4 [5.0] years).

Childhood cancer-specific post-traumatic stress: Self-rating scale for post-traumatic stress disorder (SRS-PTSD)

The Self-rating scale for post-traumatic stress disorder (SRS-PTSD) assesses post-traumatic stress symptoms that correspond to the diagnostic DSM-IV symptoms in three subscales: re-experiencing (range: 0–5 symptoms), avoidance (range: 0–7 symptoms), and hyperarousal (range: 0–5 symptoms), adding up to a total score (range 0–17). Parents were instructed to think of the childhood cancer that their child had when answering questions on symptom occurrence over the past 4 weeks. Psychometric properties are adequate [20].

Childhood cancer-specific post-traumatic growth: Post-traumatic growth inventory (PTGI)

The PTGI assesses post-traumatic growth (i.e. positive change) in 21 items from the subscales: relating to others (range: 0–35), new possibilities (range: 0–25), personal strength (range: 0–20), spiritual change (range: 0–10) and appreciation of life (range: 0–15). Parents were asked to think of the childhood cancer that their child had when answering questions. Total scores range from 0 to 105, and higher scores reflect more growth. Psychometric properties are adequate [21].

Associated factors and measures

Sociodemographic and medical characteristics of the child

Parents' age, sex, level of education and number of children were the included sociodemographic characteristics. The latter two were obtained from their survivor child in either DCCSS LATER two or DCCSS LATER 1 [22]. Child medical characteristics were CNS diagnosis (vs. other diagnoses), recurrence, age at diagnosis and time since diagnosis, and were obtained from the DCCSS LATER registry [22].

Sociodemographic and medical characteristics of the child

The 18-item Illness cognition questionnaire (ICQ) assesses parents' cognitions on their child's disease in three scales: helplessness, acceptance and disease benefits. Higher scores indicate a stronger presence of the illness cognitions (range 6–24) [17]. Psychometric properties are good [17].

Statistical methods

Descriptive statistics were used to describe the outcomes and associated factors. Within invited parents, age, sex and level of education of participants were compared to non-participants using a t-test and chi-square tests, with Cramer's V as effect size. Characteristics of the sample of CCS of whom one or both parents participated were compared to the total cohort of survivors <30 years using one-sample t-tests and one-sample chi-square tests. HRQoL scores of the parents were compared to the general population for males and females separately using Mann Whitney U-tests with effect size r, since the assumption of normality was not met. Post-traumatic stress and post-traumatic growth were evaluated in the context of childhood cancer, so they were not comparable to the general population. Associations between post-traumatic stress and growth and the other outcomes were assessed with Pearson's correlation coefficient (r).

To study associated factors of the outcomes, multivariable mixed effects linear regression was used with TAAQOL subdomain scores, and SRS-PTSD and PTGI total scores as dependent variables and sociodemographic characteristics, medical characteristics of the child and illness cognitions as independent variables. A random intercept was included to account for dependency of outcomes of parents of the same child. Age of the survivor and of the parent at time of data collection were not included in the models because of multicollinearity with time since diagnosis and child's age at diagnosis. Other assumptions for mixed effects linear regression models were met. To obtain standardized coefficients (β) with confidence intervals, continuous variables were standardized.

A p-value <0.05 was considered statistically significant. A Bonferroni correction was applied for the comparison of 10 domains of HRQoL to reference values (0.05/10 = 0.005). After Cohen, mean differences between two groups (regression coefficients of categorical variables) of 0.2, 0.5 and 0.8 and correlations (regression coefficients of continuous variables, Cramer's V and r) of 0.1, 0.3 and 0.5 were considered small, medium and large [23].

RESULTS

661 parents of the 996 invited parents (response rate 66%, 56% female, mean age 57 years) of 448 CCS (33% of total cohort) provided written informed consent and participated. Table 1 describes sociodemographic characteristics and child medical characteristics of participants. Participants had somewhat higher levels of attained education than non-participants (low/middle/high: 23%/36%/41% vs. 29%/41%/31%, V: 0.10, p = 0.027), but sex (male/female: 44%/56% vs. 48%/52%) and age (57.0 [3.5] vs. 56.5 [3.6] years) were not significantly different. Table A2 shows the characteristics of survivors of whom one or more parents participated in this study (*n* = 448) and the total LATER 2 cohort <30 years. Characteristics of these groups were not significantly different.

Table 2 shows the psychosocial outcomes and illness cognitions of the total group and of mothers and fathers separately. Compared to sex-specific reference values, mothers of survivors had higher HRQoL in all domains except cognitive functioning and sleep and fathers of survivors also had better social functioning and less aggressive emotions (Table 2). HRQoL was never lower than reference values. Effect sizes of the differences were small (r: 0.07–0.17). 3% had symptomatic post-traumatic stress and the mean PTGI score was 45.9 (SD: 21.2).

Table 3 presents the associations between post-traumatic stress and growth and the other outcomes. We found a small positive association between post-traumatic stress and post-traumatic growth (r: 0.12). Post-traumatic growth also had small associations with higher HRQoL in social functioning, daily activities and positive emotions (r: 0.09–0.12). Post-traumatic stress had medium to large negative associations with all domains of HRQoL (r: −0.27–−0.48).

Table 4 presents the results of multivariable models. Parents with more than one child had less post-traumatic stress symptoms than parents for whom the survivor child was their only child (β: −0.44, p < 0.01). Regarding medical characteristics, recurrence of their child's cancer related to better HRQoL in social functioning, positive emotions and aggressive emotions with a small to medium effect size (β: 0.37–0.46, p < 0.05). Helplessness related most strongly to post-traumatic stress (β: 0.39, p < 0.001) and more depressive emotions (β: −0.26, p < 0.001), and acceptance to more positive emotions (β: 0.25, p < 0.001) and less post-traumatic stress symptoms (β: −0.23, p < 0.001).

Table 1. Sociodemographic characteristics of participating parents (*n*=661) and medical characteristics of their survivor child.

	% (*n*) or mean (SD)		**Missing cases**
Age (years)[a]	57.0	(3.5)	86
Sex			82
Male	44%	(254)	
Female	56%	(325)	
Attained level of education [b]			128
Low	23%	(122)	
Middle	36%	(194)	
High	41%	(217)	
Number of children	2.5	(0.9)	49
1	10%	(61)	
>1	90%	(551)	
Child medical characteristics			
Survivor age	25.4	(3.5)	4
Follow-up time since diagnosis (years	21.3	(3.3)	4
Age at diagnosis (years)	4.1	(3.0)	4
0-4	68%	(451)	
5-9	25%	(165)	
10-14	6%	(41)	
14-17	0%	(0)	
Recurrence of primary tumor	12%	(77)	4
Primary childhood cancer diagnosis			4
Hematologic cancers	55%	(365)	
CNS tumor	8%	(53)	
Solid tumor	36%	(238)	
Treatment period			4
1980-1989	1%	(4)	
1990-1999	69%	(455)	
2000-2001	30%	(198)	

Table 2. Psychosocial outcomes and illness cognitions of parents of survivors of childhood cancer.

	Total group (*n*=543-581)	**Mothers (*n*=269-294)**^{b}	**Female references (*n*=590)**		**Fathers (*n*=208-226)**^{b}	**Male references (*n*=631)**	
	Mean±SD or % (*n*)	**Mean±SD or % (*n*)**	**Mean±SD**	**r**^{a}	**Mean±SD or % (*n*)**	**Mean±SD**	**r**^{a}
HRQoL							
Cognitive functioning	81.2±23.2	80.4±23.6	79.4±24.9	0.02	82.8±21.1	82.3±22.6	0.005
Sleep	69.0±25.0	63.9±25.4	64.1±28.3	-0.02	75.1±22.2	78.0±25.0	-0.09
Pain	71.5±22.0	69.8±21.4	64.4±27.4	0.07*	73.0±21.9	73.7±24.5	-0.04
Social functioning	86.7±16.9	87.1±17.1	80.0±21.5	0.17*	86.5±16.5	84.0±16.8	0.08*
Daily activities	85.7±22.5	84.3±24.3	78.8±28.9	0.09*	87.2±20.1	86.6±22.5	-0.02
Sexuality	84.3±24.1	86.8±21.8	80.2±28.3	0.11*	79.2±27.2	81.4±28.2	-0.05
Vitality	66.6±21.7	65.1±22.4	59.2±25.6	0.10*	68.6±20.3	68.7±22.4	-0.03
Positive emotions	64.9±20.9	64.1±21.0	59.8±22.2	0.09*	65.2±21.3	63.6±20.8	0.04
Depressive emotions	80.3±17.8	77.8±18.4	71.8±22.5	0.11*	83.4±16.6	81.5±19.0	0.03
Aggressive emotions	92.5±12.7	93.3±11.8	88.5±16.2	0.14*	91.3±14.0	87.3±17.6	0.10*
Posttraumatic stress							
Total score	2.1±2.3	2.3±2.4			1.9±2.2		
Symptomatic post-traumatic stress	3% (19)	3% (9)			2% (6)		
Symptomatic re-experience	60% (357)	64% (188)			53% (118)		
Symptomatic avoidance	4% (26)	5% (13)			4% (9)		
Symptomatic hyperactivity	10% (61)	10% (30)			10% (22)		
Posttraumatic growth^a							
Total score	45.9±21.2	49.1±20.6			42.3±21.8		
Relating to others	17.0±7.9	17.8±7.9			16.2±8.0		
New possibilities	8.5±6.0	9.2±6.1			7.9±5.9		
Personal strength	10.4±5.1	11.5±4.9			9.1±5.2		
Appreciation of life	7.9±3.9	8.4±3.7			7.3±4.1		
Spiritual change	2.0±2.6	2.2±2.6			1.7±2.6		
Illness cognitions							
Helplessness	8.1±2.4	8.1±2.3			8.0±2.4		
Acceptance	19.1±3.6	19.1±3.5			19.2±3.7		
Disease benefits	17.8±4.2	18.1±4.1			17.4±4.3		

[a] Effect size for differences from the reference sample; effect sizes were calculated with r=Z-score of the difference/(√N).

[b] Number of mothers and fathers do not add up to total because of missing values in sex

*Mann-Whitney p<0.005 for difference from the general population sample

Table 3. Pearson's *r* (and 95% confidence interval) of associations between post-traumatic stress and post-traumatic growth, and HRQoL and distress.

	Post-traumatic stress		**Post-traumatic growth**	
Post-traumatic stress	x		0.12**	(0.04;0.21)
Post-traumatic growth	0.12**	(0.04;0.21)	x	
Cognitive functioning[a]	-0.30***	(-0.38;-0.22)	-0.03	(-0.11;0.05)
Sleep	-0.37***	(-0.44;-0.29)	-0.02	(-0.10;0.07)
Pain	-0.34***	(-0.42;-0.26)	-0.05	(-0.14;0.03)
Social functioning	-0.32***	(-0.39;-0.23)	0.09*	(0.001;0.17)
Daily activities	-0.35***	(-0.42;-0.27)	-0.10*	(-0.19;-0.02)
Sexuality	-0.27***	(-0.35;-0.19)	-0.08	(-0.16;0.01)
Vitality	-0.40***	(-0.47;-0.32)	-0.02	(-0.10;0.07)
Positive emotions	-0.31***	(-0.39;-0.22)	0.12**	(0.04;0.21)
Depressive emotions	-0.48***	(-0.54;-0.41)	-0.05	(-0.13;0.04)
Aggressive emotions	-0.33***	(-0.41;-0.25)	-0.03	(-0.12;0.06)

*p < 0.05, **p < 0.01, ***p < 0.001.

Table 4. Standardized coefficients (β) of associations of sociodemographic factors, child disease variables and illness cognitions with HRQoL, distress, posttraumatic stress and posttraumatic growth.

	Cognitive functioning^a	Sleep^a	Pain^a	Social functioning	Daily activities^a	Sexuality	Vitality^a	Positive emotions	Depressive emotions	Aggressive emotions^a	Posttraumatic stress	Post-traumatic growth
Model n	**422**	**420**	**421**	**420**	**421**	**416**	**422**	**422**	**421**	**417**	**407**	**430**
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Sociodemographic variables												
Sex (female vs male)	-0.08 (-0.27;0.11)	-0.48*** (-0.67;-0.30)	-0.09 (-0.28;0.09)	0.06 (-0.13;0.24)	-0.15 (-0.34;0.04)	0.39*** (0.20;0.58)	-0.14 (-0.33;0.05)	-0.07 (-0.26;0.12)	-0.31** (-0.48;-0.13)	0.17 (-0.03;0.37)	0.12 (-0.05;0.29)	0.28** (0.10;0.45)
Level of education (ref: low)												
Middle	-0.19 (-0.45;0.07)	-0.05 (-0.31;0.20)	-0.05 (-0.30;0.20)	0.02 (-0.23;0.28)	-0.18 (-0.44;0.09)	-0.07 (-0.34;0.20)	-0.13 (-0.38;0.13)	-0.004 (-0.26;0.27)	-0.05 (-0.31;0.20)	0.15 (-0.12;0.41)	0.04 (-0.20;0.27)	-0.03 (-0.29;0.24)
High	-0.02 (-0.27;0.24)	0.07 (-0.19;0.32)	0.32* (0.06;0.57)	0.27* (0.02;0.53)	-0.13 (-0.39;0.13)	-0.08 (-0.35;0.19)	0.10 (-0.16;0.35)	0.01 (-0.25;0.27)	0.07 (-0.18;0.33)	0.32* (0.06;0.58)	0.06 (-0.18;0.30)	-0.07 (-0.33;0.20)
Number of children (>1 child vs 1 child)	-0.10 (-0.42;0.22)	0.11 (-0.21;0.43)	0.01 (-0.31;0.32)	-0.15 (-0.47;0.16)	-0.06 (-0.38;0.27)	0.003 (-0.34;0.35)	0.10 (-0.22;0.42)	0.15 (-0.18;0.48)	0.07 (-0.25;0.40)	0.11 (-0.22;0.44)	-0.44** (-0.74;-0.13)	-0.05 (-0.40;0.31)
Child disease variables												
Time since diagnosis	-0.01 (-0.12;0.10)	0.05 (-0.05;0.16)	-0.01 (-0.11;0.10)	-0.02 (-0.14;0.09)	0.002 (-0.11;0.11)	-0.07 (-0.19;0.05)	0.001 (-0.11;0.11)	-0.05 (-0.17;0.06)	-0.03 (-0.15;0.08)	0.02 (-0.09;0.14)	0.02 (-0.09;0.13)	0.06 (-0.06;0.19)
Age at diagnosis (years, ref 0-5)												
5-10	0.05 (-0.18;0.29)	0.17 (-0.06;0.40)	0.10 (-0.13;0.33)	0.25 (0.01;0.49)	0.16 (-0.08;0.40)	0.14 (-0.11;0.40)	0.07 (-0.17;0.31)	-0.10 (-0.35;0.14)	0.20 (-0.04;0.45)	0.28* (0.04;0.52)	-0.10 (-0.33;0.12)	-0.17 (-0.44;0.10)
10-15	-0.15 (-0.56;0.26)	0.28 (-0.12;0.68)	0.20 (-0.20;0.59)	-0.07 (-0.48;0.34)	-0.15 (-0.57;0.27)	0.14 (-0.31;0.60)	-0.35 (-0.75;0.06)	-0.30 (-0.72;0.13)	-0.11 (-0.54;0.32)	0.03 (-0.39;0.44)	-0.09 (-0.48;0.30)	0.31 (-0.17;0.78)
Recurrence (any vs none)	-0.03 (-0.34;0.27)	0.07 (-0.23;0.37)	0.24 (-0.06;0.54)	0.41** (0.10;0.72)	-0.02 (-0.34;0.29)	0.08 (-0.25;0.42)	0.23 (-0.08;0.54)	0.46** (0.15;0.78)	0.18 (-0.14;0.50)	0.37* (0.05;0.68)	-0.05 (-0.35;0.25)	0.12 (-0.23;0.47)

	Cognitive functioning[a]	Sleep[a]	Pain[a]	Social functioning	Daily activities[a]	Sexuality	Vitality[a]	Positive emotions	Depressive emotions	Aggressive emotions[a]	Posttraumatic stress	Post-traumatic growth
Model n	**422**	**420**	**421**	**420**	**421**	**416**	**422**	**422**	**421**	**417**	**407**	**430**
CNS diagnosis (ref: other diagnoses)	0.16 (-0.18;0.49)	0.04 (-0.30;0.36)	-0.13 (-0.46;0.20)	-0.01 (-0.35;0.34)	-0.04 (-0.39;0.30)	-0.33 (-0.69;0.03)	0.02 (-0.31;0.36)	0.15 (-0.19;0.50)	-0.03 (-0.37;0.32)	-0.12 (-0.46;0.23)	0.03 (-0.29;0.35)	0.30 (-0.08;0.68)
Illness cognitions												
Helplessness	-0.07 (-0.17;0.04)	-0.08 (-0.19;0.02)	-0.15** (-0.25;-0.04)	-0.14** (-0.25;-0.04)	-0.15** (-0.26;-0.04)	-0.19** (-0.30;-0.08)	-0.12* (-0.22;-0.01)	-0.07 (-0.18;0.04)	-0.26*** (-0.36;-0.15)	-0.16** (-0.27;-0.05)	0.39*** (0.29;0.48)	0.10 (-0.01;0.20)
Acceptance	0.12* (0.01;0.23)	0.19** (0.08;0.30)	0.14* (0.03;0.25)	0.13* (0.02;0.24)	0.15** (0.04;0.27)	0.05 (-0.07;0.16)	0.19** (0.08;0.30)	0.25*** (0.13;0.36)	0.15** (0.04;0.26)	0.17** (0.05;0.28)	-0.23*** (-0.34;-0.13)	0.14* (0.03;0.24)
Disease benefits	0.03 (-0.08;0.13)	0.01 (-0.09;0.12)	-0.01 (-0.11;0.09)	0.12* (0.02;0.22)	-0.06 (-0.17;0.04)	-0.06 (-0.17;0.04)	-0.04 (-0.15;0.06)	0.11* (0.002;0.21)	0.03 (-0.07;0.13)	0.07 (-0.03;0.18)	0.06 (-0.03;0.16)	b

[a] Model without random intercept, as it was redundant.
[b] Excluded because of overlap with the outcome
*p-value<0.05, **p-value<0.01, ***p-value<0.001

DISCUSSION

We found that HRQoL was comparable to references or slightly better in parents of young adult CCS, who were on average 21 years after their child's cancer diagnosis. Also, the proportion of parents with symptomatic post-traumatic stress seemed low. These results reinforce previous insights that the initially elevated levels of distress experienced around the time of their child's diagnosis and treatment eventually return to normal levels in most parents [2, 6]. A consideration with these generally reassuring results may be that pediatric oncology care in the Netherlands at the time of treatment (largely 1990–2001) likely included availability of child life specialists and social workers; this may have helped and prevented long term psychosocial difficulties [24].

Compared to the literature, our results on HRQoL seem positive. A study in parents who were around 3 years after their child's diagnosis found lower HRQoL in several domains compared to references, and mothers in more domains than fathers [25]. HRQoL of parents was previously found to improve with time since diagnosis [7], and other studies evaluating parents' well-being longer after their child's childhood cancer diagnosis also showed relatively high HRQoL in parents of survivors [26].

A small proportion (3%) of participating parents experienced symptomatic post-traumatic stress, which is similar to that reported for Dutch parents of an ill child (3%) [27]. This seems low compared to 6%–30% that previous research described in parents of a younger survivor child [1], but is in line with the finding that Swiss parents of CCS are not at increased risk for post-traumatic stress on the long-term [12]. Nevertheless, parents who experience these symptoms from their child's cancer on the long-term may be in need of support [6]. This may be especially relevant since we found that post-traumatic stress problems showed moderate associations to HRQoL, and previous research also describes a negative impact on psychosocial functioning [6]. Post-traumatic growth scores were lower than previously reported in parents of children with cancer during treatment (66.1 [19.1]) [28] and around 5 years after end of treatment (69.0 [25.5]) [29]. Post-traumatic growth may decline in the 2 decades after diagnosis, in line with results that were found in survivors [9]. These results of relatively low post-traumatic stress and growth, which are associated, are in line with the theoretical models: a stressor causes struggle (i.e., post-traumatic stress), which stimulates growth, and this process tapers off with time in most people [10].

In line with previous studies, mothers had more post-traumatic growth [14]. A higher level of education related to better HRQoL in some domains, which may be explained by similar associations between education level and HRQoL in the general population [30]. Remarkably, having multiple children was a protective factor for post-traumatic stress symptoms.

Previous medical characteristics of their child did not seem to negatively impact parents' psychosocial functioning this long after diagnosis. Remarkably, recurrence was associated to more positive HRQoL in social and emotional domains. Based on previous research we rather expected a negative impact of factors related to more severe treatment and consequences [7, 31]. The contrast may be explained by the time of assessment: previous results concern well-being closer to the time of childhood cancer treatment [31].

The illness cognition helplessness was associated to worse psychosocial functioning, while the illness cognition acceptance was associated to better psychosocial functioning. Apparently, even this long after their child's cancer, cognitions about that illness were relevant for parents' psychosocial functioning, in line with the model of Wallander and Varni [16]. Helplessness scores were substantially lower and acceptance scores seemed higher in our sample than those from a study on parents of a child during treatment for cancer [17]. In line with this study, these cognitions were associated with most psychosocial outcomes [17]. Similar to results of previous studies, disease benefits only showed small positive associations with positive emotions and social function [17, 32].

Clinical implications

Fortunately, psychosocial functioning of parents of children with cancer on average does not seem to be impaired on the long-term. A few parents of survivors experienced post-traumatic symptoms. Our results suggest that illness cognitions may be a target for interventions, for instance using cognitive behavioral therapy or acceptance commitment therapy [33, 34]. As previous research suggests that maladaptive coping early on predicts later outcomes [24], screening in an earlier phase and offering timely intervention may prevent these long-term problems for this small group of parents [35]. Intervention could for example, be provided using the recently developed module for parents of a child with cancer of the psychosocial group intervention Op Koers (in English: on track), which aims to teach active coping skills using cognitive behavior therapy to prevent psychosocial problems. An effect study of this intervention is currently in progress, but evidence was reported for parents of children with a chronic disease [36].

Study limitations

This study is one of the first describing psychosocial functioning in parents of long-term young adult CCS. Recruiting parents from the national LATER cohort provided a large sample of parents and availability of their child's medical characteristics. Nevertheless, there are some limitations regarding determinants and sample selection. Not-included factors, such as parents' health, their child's current functioning, social support or other stressful events [16], could also have contributed to the psychosocial functioning of the parents. Also, some of the multivariable models could not be adjusted for dependency of parents of the same child. Because the intra-class coefficients of these outcomes were not significant, the non-adjusted models seem acceptable [37]. Furthermore, we estimated parents' age based on their child's age and used reports from their survivor child on education level and number of children, which limited reliability and completeness of these variables. Finally, parents of adult CCS were contacted after obtaining contact information from their child. This may have introduced an unknown selection bias, and consequently, hampers sound conclusions about generalizability of the results. Nevertheless, our sample included at least one parent of a third of the total cohort of CCS with current age 16–30 years, participants had similar characteristics as non-participating parents, their children had similar characteristics as the total CCS cohort and the sample was balanced regarding fathers and mothers.

CONCLUSION

HRQoL of parents of long-term CCS is comparable to references or slightly better. A small proportion of parents experiences symptomatic post-traumatic stress. Improving acceptance and reducing feelings of helplessness related to their child's disease may provide treatment targets for parents with psychosocial problems.

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Appendix 1. Questionnaire information.

Measures	Subscales, items and Cronbach's alpha's from the present study	Example items	Scale score computation
TNO-AZL Questionnaire for Adult's HRQoL (TAAQoL)	- Cognitive functioning (4 items, 2 parts each: limitation and burden), α=.88 - Sleep (4 items, 2 parts each: limitation and burden), α=.89 - Pain (4 items, 2 parts each: limitation and burden), α=.76 - Social functioning (4 items, 2 parts each: limitation and burden), α=.84 - Daily activities (4 items, 2 parts each: limitation and burden), α=.88 - Sexuality (4 items, 2 parts each: limitation and burden), α=.84 - Vitality (4 items), α=.84 - Positive emotions (4 items), α=.91 - Depressive emotions (4 items), α=.76 - Aggressive emotions (4 items), α=.66	Cognitive functioning: '*In the past month, did it happen that you had difficulty concentrating on what other said*?' No – a little – some – a lot If a little or more: '*How much did that bother you*?' Not at all – a little – quite a lot – very much Vitality: *'In the past month, did you feel energetic?'* No – a little – quite – very	One score (0-4) is derived from the two scales; a score of 4 is given when there is no health problem or limitation (indicated on the first Likert scale), a score of 3 when there is a limitation (i.e. a little, some or a lot) but when the person is not bothered by the limitation (indicated on the second Likert scale); a score of 2 when there is a limitation and the person is a "a little" bothered, a score of 1 when there is a limitation and the person is "quite a lot" bothered and a score of 0 when there is a limitation and the person is "very much" bothered. Sum scores are calculated by domain and transformed to range from 0-100
Self-rating scale for post-traumatic stress disorder (SRS-PTSD)	- Re-experiencing (5 symptoms), α=.69 - Avoidance (7 symptoms), α=.50 - Hyperarousal (5 symptoms), α=.43 - Total score (17 symptoms), α=.76	Re-experiencing Symptom intrusive thoughts: a. '*I thought about the event regularly, even if I didn't want to.*' Not at all – less than four times a week – four or more times a week b. '*Sometimes images of the event shot through my mind*' Not at all – less than four times a week – four or more times a week Avoidance Symptom avoidant thoughts or feelings: *'Ever since the disaster I have been avoiding people or things (such as shops, restaurants, movies, airports, parties) that remind me of the event'* Not at all – a little bit – very much Hyperarousal Symptom sleep disturbance: *'Ever since the event, I have had trouble sleeping. I have trouble falling asleep, or I wake up in the middle of the night and can't get back to sleep'* Not at all – a little bit – very much	Symptoms are evaluated with one or two items that are answered on a 3-point Likert scale. It differs by symptom which answers indicate presence of the symptom). Post-traumatic stress is considered symptomatic if 1 re-experiencing, 3 avoidance and 2 hyperarousal symptoms were reported.

Measures	Subscales, items and Cronbach's alpha's from the present study	Example items	Scale score computation
Post-traumatic growth inventory (PTGI)	- Relating to others (7 items), α=.84 - New possibilities (5 items), α=.84 - Personal strength (4 items), α=.82 - Spiritual change (2 items), α=.53 - Appreciation of life (3 items), α=.80 - Total score (21 items), α=.93	Relating to others *'I more clearly see that I can count on people in times of trouble'* I experienced this: Not at all – to a very small degree – to a small degree – to a moderate degree – to a great degree – to a very great degree Appreciation of life *'I changed my priorities about what is important in life'* I experienced this: Not at all – to a very small degree – to a small degree – to a moderate degree – to a great degree – to a very great degree	The Likert scales translate to a 0-5 score, which are summed to compute scale and total scores.
Illness cognition questionnaire (ICQ)	- Helplessness (6 items), α=.71 - Acceptance (6 items), α=.81 - Disease benefits (6 items), α=.86	Helplessness Focusing on the negative consequences of the disease and generalizing them to functioning in daily life *'Because of my illness I miss the things I like to do most'* Not at all – somewhat – to a large extent- completely Acceptance Acknowledging being chronically ill and perceiving the ability to manage the negative consequences of the disease *'I can handle the problems related to my illness'* Not at all – somewhat – to a large extent- completely Disease benefits Also perceiving positive, long-term consequences of the disease *'Dealing with my illness has made me a stronger person'* Not at all – somewhat – to a large extent- completely	The Likert scales translate to a 1-4 score, which are summed to compute scale scores.

Appendix 2. Characteristics of the survivors of participating parents and from the total LATER 2 cohort <30 years.*

	CCS of included parents (*n*=448)[a]	**LATER 2 cohort <30 (*n*=1362)[a]**
	% or mean±SD	**% or mean±SD**
Survivor age	25.2±3.7 years	25.4±3.4 years[b]
Follow-up time since childhood cancer diagnosis (years)[b]	21.2±3.3 years	21.4±3.1 years
Age at diagnosis	4.0±2.9 years	4.0±2.9 years
0-4	70%	69%
5-9	25%	27%
10-14	5%	5%
14-17	0	0
Recurrence of primary tumor	11%	11%
Primary childhood cancer diagnosis		
Hematologic cancers	55%	53%
CNS tumor	9%	12%
Solid tumor	37%	35%
Treatment period		
1980-1989	1%	1%
1990-1999	69%	71%
2000-2001	30%	27%

[a] Characteristics missing for *n*=3

[b] Based on mean participation date of participating parents.

*Characteristics of both cohorts were not significantly different

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CHAPTER 8

SUMMARY AND GENERAL DISCUSSION

When a child is ill, all family members are impacted. They have to face stressors that are related to the illness, and can experience problems in their psychosocial wellbeing. This thesis consists of two parts that focused on 1) the development and effect of the Op Koers intervention for different family members and 2) wellbeing of siblings and parents of very long-term childhood cancer survivors. This final chapter provides a summary of the thesis, followed by reflections on the findings, clinical implications and recommendations for the future, and a conclusion. An overview of the studies and main findings is presented in Table 1.

SUMMARY

Part 1: The development and effect of the Op Koers intervention in different populations

In Chapter 2, a study into the online support needs of siblings of children and adolescents with a chronic illness is presented. In total, 91 siblings (aged 11-21 years) filled out a self-developed questionnaire and 9 semi-structured interviews were held additionally. Of all participants, 55% would like to initiate or increase contact with other siblings of children with a chronic condition and 46% of those were interested in an online chat course. The themes for online support considered most important were ‘impact on daily life’, ‘worrying about brother’s/sister’s future’, ‘handling other people’s reactions’, ‘and how attention is divided within the family’. We concluded that siblings are interested in peer contact and online support, and that Op Koers Online for siblings seems to be a suitable intervention to offer online psychosocial support [1].

Chapter 3 consists of a pilot study into the feasibility and preliminary efficacy of Op Koers Online for adolescents with a chronic illness. In total, 23 adolescents (aged 12-18 years) with a chronic illness completed questionnaires before and after participation in the intervention, addressing feasibility, coping skills and psychosocial wellbeing (Health-Related Quality of Life – HRQoL, emotional and behavioral functioning). Dropout rate (6% of participations) and technological issues (2% of sessions) were low. Participants’ overall satisfaction was high. Regarding efficacy, participants improved significantly in the coping skills ‘information seeking and giving’ and ‘social competence’ after the intervention compared to baseline. Participants also reported significantly fewer withdrawn/depressed behavior and scored significantly better on emotional and psychosocial HRQoL after following the intervention. We concluded that Op Koers Online for adolescents with a chronic illness is feasible and potentially effective [2].

Chapter 4 is the result of a randomized controlled trial to study the efficacy of Op Koers Online for parents of children with cancer on coping skills and psychosocial wellbeing. We also evaluated the intervention with participating parents. In total, 100 parents participated in the RCT of which 89 filled out questionnaires before participation and at six week and/or six months follow up. The intervention had a beneficial effect on anxiety, depression, distress and loneliness as well as on the coping skill ‘relaxation’ after six weeks. Furthermore, after six months, an effect of the intervention was found on anxiety, uncertainty and coping skill ‘relaxation’. No intervention effects were found for helplessness, positive feelings and coping skills predictive control, open communication and positive thinking. In the intervention condition, scores did not change from six months to twelve months, except loneliness that decreased and relaxation that improved. Parents were generally positive about the intervention. We concluded that Op Koers Online for parents of children with cancer has a positive effect on psychosocial wellbeing and the coping skill relaxation [3].

The development of the Op Koers intervention program started over 25 years ago. In Chapter 5, the efforts that were made into developing, evaluating and implementing the intervention are described. Using the National Institutes of Health Stage Model for Behavioral Intervention Development and the Consolidated Framework for Implementation Research (CFIR), we critically appraised our activities in the different stages. Important lessons were learned about the characteristics of the intervention, the inner and outer setting, individuals, implementation process and research. Future efforts may be directed towards continuous improvement of the intervention and successful implementation. We concluded that Op Koers is one of few psychosocial interventions that has been both extensively studied and implemented. The main factor for this achievement is the close collaboration between, and the perseverance of the clinical care and research departments.

Part 2: Psychosocial wellbeing of siblings and parents of very long-term survivors of childhood cancer

In Chapter 6, the psychosocial wellbeing of adult siblings of very long-term childhood cancer survivors (CCS) was studied. We assessed HRQoL, anxiety, depression, post-traumatic stress (PTSD), self-esteem and disease-related benefit and – burden. Additionally, we studied whether sociodemographic characteristics and cancer-related characteristics of the ill child were associated to the outcomes. In total, 505 siblings (17 – 65 years) completed questionnaires. Compared to the general population, siblings in our sample had comparable HRQoL, anxiety and self-esteem and slightly less depression. The proportion of siblings with symptomatic PTSD was very small. No clear trend was found in the associations of sociodemographic characteristics and cancer-related characteristics with the outcomes [4].

Finally, Chapter 7 describes the psychosocial wellbeing of parents of very long-term CCS. Similar to the siblings in chapter 6, we studied HRQoL and PTSD. We also looked at post-traumatic growth and illness cognitions. Again, we looked at factors that were potentially associated with the outcomes: sociodemographic and or cancer-related characteristics, and illness cognitions. In total, 661 parents completed questionnaires. We found that parents in our sample reported better HRQoL in the social domain and they reported less aggressive emotions than the general population. Mothers additionally reported better HRQoL in the domains of pain, daily activities, sexuality, vitality, positive and depressive emotions. Post-traumatic stress was symptomatic in 3%, and associated with worse HRQoL. Post-traumatic growth was associated with more post-traumatic stress and better HRQoL. Cancer recurrence was also associated to better HRQoL. Higher levels of the illness cognition acceptance were associated to better outcomes, and higher levels of helplessness were associated to worse outcomes. We concluded that HRQoL of parents of young adult survivors of CCS is comparable to references or slightly better, and that only a small proportion reports symptomatic posttraumatic stress [5].

REFLECTIONS ON MAIN FINDINGS

The research in this thesis finds its theoretical base in the disability-stress-coping model by Wallander and Varni [16]. An adapted version of the model can be found in Chapter 1 of this thesis. The model illustrates that the relation between the stressors that families of a child with an illness have to face and their wellbeing is mediated by coping skills. Coping skills are, in their turn, related to personal, family and environmental factors.

Different parts of the disability-stress-coping model are studied in Part 1 of this thesis, about the Op Koers intervention. Development of Op Koers started over 25 years ago, and over the course of these years, extensive research has been done into the development and evaluation of the intervention [6-16]. This thesis adds to the body of knowledge on different phases of development of Op Koers Online in different populations: children with an illness, siblings and parents. In chapter 2, we looked at themes that are relevant for the intervention module for siblings and found that they relate to psychosocial factors (e.g. illness-related stressors such as managing daily routines), personal factors (e.g. taking care of yourself), family factors (e.g. parent-child relationship), and environmental factors (e.g. communication). In chapters 3 and 4, that look into the (preliminary) efficacy of Op Koers Online, we studied both psychosocial wellbeing and coping skills.

In part 2, psychosocial wellbeing of siblings and parents of very long-term CCS is studied. Additionally, we looked at factors that might be associated with the wellbeing, mostly related to the illness characteristics of the CCS (e.g. diagnosis, treatment).

Part 1: The development and effect of the Op Koers intervention in different populations

Efficacy of Op Koers Online

For parents of children with cancer, we found a positive effect of participating in the intervention on anxiety, depression, distress, feelings of loneliness and uncertainty, and the coping skill relaxation.

Reductions in anxiety and depression were previously found after participating in Op Koers Online for parents of children with chronic illness [9], but not in other online group interventions for parents of children with cancer [17, 18]. However, results of these studies are hard to compare to ours due to for example differences in participants, study design and use of questionnaires. While similar constructs are often measured in psychosocial intervention research (e.g. anxiety, depression, stress), used questionnaires often differ, which complicates the direct comparison of results.

Intervention condition and waitlist-control condition both improved over time

In our pilot study into Op Koers Online for adolescents with a chronic illness, participants reported more use of coping skills and better HRQoL after following the intervention. In our RCT on parents, even though we found a beneficial effect of the intervention on coping skills and psychosocial wellbeing, we also observed that both the intervention condition and waitlist-control condition improved over time. This finding demonstrates the importance of using a control group in efficacy research, to be able to rightfully attribute an effect to the intervention.

The fact that also the parents in the waitlist-control condition improved over time without participating in the intervention, seems to be in line with the Model of Pediatric Traumatic Stress that suggests that many families improve over time and reach normal levels of distress after a certain amount of time [19, 20]. However, our results differ from previous research into Op Koers for parents of a child with a chronic illness, where symptoms of anxiety and depression decreased in the intervention condition but stayed the same over time for the waitlist-control condition [9]. Furthermore, in the Cascade intervention for parents of children with cancer, there was no evidence that parental scores on anxiety and depression changed over time in either the intervention condition or the waitlist-control condition. In the Cascade study, participants completed treatment (up to 10 years ago), potentially indicating that scores on anxiety and depression had reached a steady state, similar to the study involving parents of children with a chronic illness. This contrasts with our RCT, where parents were required to be within 5 years after their child's diagnosis. It is a positive outcome that we can help parents in reaching better wellbeing sooner by participation in Op Koers, even if they might have naturally reached that state on the long term without participating.

Impact on coping skills

Op Koers focuses on teaching active coping skills. In previous research into Op Koers, improvement of coping skills was always found [10, 12, 14]. This is also the case in this thesis, in the pilot study for adolescents with a chronic illness and the RCT for parents of children with cancer. However, only improvement of the coping skill relaxation was found in the RCT for parents. This is in contrast with the RCT of Op Koers Online for parents of a child with a chronic illness, that used the same questionnaires and revealed effects on more coping skills (open communication, social support, positive thinking and predictive control) than just relaxation [9]. This may be explained by the fact that characteristics of an oncology diagnosis differ from a chronic illness. For instance, the severity of cancer and the life-threatening aspect might limit the ability to use predictive control and positive thinking (operationalized as for example “I am sure everything will work out right for my child“ and “I manage to worry less about the consequences of my child’s illness”) as coping skills.

Another possible explanation lies in the CBT exercises that are part of the Op Koers intervention. The uptake on the homework was not always high in our RCT, while doing exercises is thought to strengthen the effect of CBT interventions. In the pilot study of this thesis, where two-thirds of participants completed the homework for at least five out of six sessions, improvements in several coping skills were observed after participating in the intervention. Furthermore, Cascade, an intervention for parents similar to Op Koers, did also not improve the actual use of coping skills, while a positive effect was found on confidence in using the coping skills [18]. Similarly, confidence in the use of coping skill could have been improved by our intervention but this was not included as outcomes in the RCT.

Representativeness

In the studies into Op Koers of this thesis, we used an open recruitment strategy. This approach not only increases participant numbers but also resembles recruitment methods used in clinical practice. We believe that this facilitated reaching our targeted inclusion number. For example, in the RCT for parents of children with cancer, we sent out letters to 300 randomly selected families, which was rather time consuming and resulted in only a handful of participants. The vast majority of participants enrolled following announcements on the patient association or hospital’s social media platforms, proving to be a more effective and efficient way of engaging parents. The downside of this open recruitment strategy is that there is no information available about response rates, nor about the characteristics of non-participants. However, based on the participants, we now have insight into the characteristics of parents that are attracted to the intervention.

Part 2: Psychosocial wellbeing of siblings and parents of very long-term survivors of childhood cancer

Wellbeing is comparable to the general population

The research in chapter 6 and 7 of this thesis, on the wellbeing of siblings and parents 20 to 30 years after diagnosis of the childhood cancer in their family, revealed that, in our samples, both family members are doing generally well. Differences with wellbeing of reference populations were negligible, and manifested in both positive and negative direction. Also, the proportion of siblings and parents with symptomatic post-traumatic stress seemed low.

For siblings, these findings substantiate existing literature that has described similar or better HRQoL in adult siblings compared to references. Ours was a relevant addition, because previous studies either had methodological limitations such as using unvalidated measures or poorly defined samples [21-23], or were less long-term after diagnosis [24, 25].

For parents, our results on HRQoL seem positive compared to literature on wellbeing of parents rather shortly after diagnosis. A study in parents who were around 3 years after their child's diagnosis found lower HRQoL in several domains compared to references, and mothers in more domains than fathers [26]. HRQoL of parents was previously found to improve with time since diagnosis [20, 27] and other studies evaluating parents' well-being longer after their child's childhood cancer diagnosis also showed relatively high HRQoL in parents of survivors [28].

A possible explanation for these generally positive results may lie in the availability of psychosocial care in the Netherlands in general, and the availability of support by social workers in childhood cancer more specifically. This might have played a role in preventing long term psychosocial difficulties [29].

Siblings and parents experience positive consequences

In this thesis, we also looked at positive consequences of being a sibling of a parent of a child with cancer. We found that siblings experienced benefit of their siblings' childhood cancer, in line with previously identified themes in growth in family members of CCS (e.g. item "learned what's important in life" to theme 'new values and life priorities') [30]. This suggests that having a brother or sister with cancer could lead to positive impact even on the very long-term. For parents, we found that they also experience post-traumatic growth, but to a lesser extent than was previously found in studies during treatment or shortly after [31, 32]. The parents from our RCT also experienced relatively low levels of distress compared to literature. This is in line with previously described models, that suggest that posttraumatic stress and posttraumatic growth are related. Stressors that cause struggle could also stimulate growth and that process tapers off with time in most people [33].

Factors associated with wellbeing

To try to identify the siblings and parents who are at lower or higher risk for developing psychosocial problems, we mostly looked at childhood cancer-related characteristics, and at illness cognitions of parents.

For siblings, we found no clear trend in the studied associated factors. Effect sizes were small to moderate and no factor impacts more than one outcome, other than being 12+ years old at diagnosis, which is related to better sleep and more perceived benefit. Apart from an association of small to medium size between siblings of CNS CCS and pain, we found no associations between the outcomes and cancer-related factors, which is substantiated in literature [34-36]. Following these results, factors that impact long-term psychosocial functioning of siblings of CCS might not differ from factors that impact the functioning of the general population.

For parents, a higher level of education related to better HRQoL in some domains, which may be explained by similar associations between education level and HRQoL in the general population [37]. We also found that higher levels of the illness cognition helplessness (e.g. “Because of my child’s illness I miss the things I like to do most”) were associated to worse psychosocial functioning, while higher levels of the illness cognition acceptance (“I can handle the problems related to my child’s illness”) were associated to better psychosocial functioning. Apparently, even this long time after their child’s cancer, cognitions about that illness were relevant for parents’ psychosocial functioning, in line with the model of Wallander and Varni [38].

The generally positive findings of these two studies offer reassurance and can be used in psycho educating families, potentially they can also comfort families. Additionally, the study among parents underlines the importance of targeting cognitions of parents of children with cancer, as they are related to psychosocial outcomes. The Op Koers intervention described in chapter 4 provides this opportunity for parents in the Princess Máxima Center.

Representativeness

A strong point of both studies is that they have relatively large sample sizes compared to other research in the field and the respondents were recruited from the total cohort of long term survivors [22]. However, due to the study design, we cannot be certain about the response rate. Parents and siblings were contacted after obtaining contact information from their child. This may have introduced an unknown selection bias. On one hand, it could be argued that individuals with PTSD symptoms are less likely to participate in research of this nature, potentially leading to an underestimation of the proportion of individuals with PTSD. On the other hand, one could argue that individuals with impaired psychosocial well-being are more inclined to participate, as they may feel more addressed compared to those without well-being issues. Nevertheless, only some small differences were found between participants and non-participants in terms of sociodemographic characteristics, and the CCS had similar cancer-related characteristics as the total survivor cohort.

CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

To enhance the value of both psychosocial research and care, it is crucial that they inform each other. This section discusses how the research findings of this thesis contribute to recommendations for clinical practice on the one hand and future research on the other.

Part 1: The development and effect of the Op Koers intervention in different populations

Collaboration with patient association and the importance of a referral network

In Op Koers, peer support is considered an essential element, as previous research showed that peer support can influence wellbeing of participants [39, 40]. Another essential element is the teaching of active coping skills. Since the coping skills did not improve as much as expected in the RCT for parents of children with cancer, it is possible that improvements in wellbeing are at least partly explained by peer contact. Giving parents the possibility of participating in a guided peer-support group without the CBT elements taught by psychologists, might provide opportunities for cooperation between the hospital's psychosocial team and patient associations in supporting families. After proven to be effective, guided peer-support-only groups, as a form of informal care, could be offered as an addition to the Op Koers groups with CBT elements. The patient association could be trained in leading peer-support-only groups. This might relieve the workload of health-care psychologists.

Furthermore, it is crucial to offer parents and siblings psychosocial support beyond the hospital setting. Technically, parents and siblings are not patients, which restricts the healthcare provider's ability to allocate time for their care. Cooperating with the patient association might be a first step to accessible support for parents and siblings. Furthermore, the use of a referral network is essential in relieving the workload of the health care providers. A study into a new network for pediatric physical therapists working in the Dutch community and trained in pediatric oncology, indicated that such a network could bring added value [41]. Such a network could allow for sharing knowledge and developing skills in psycho-oncology, and might lead to improvement of the accessibility and communication in the psychosocial care for childhood cancer patients and their families outside the hospital.

Implementation

From chat room to video call

The studies in this thesis focused on the online format of the Op Koers intervention, which originally began as a face-to-face program. The transition to an online format started in 2009, by integrating the original Op Koers content with the technology from an existing online platform called 'Grip op je Dip', designed for adolescents and young adults with depressive symptoms [13]. Offering interventions online was new and innovative and a chat room was considered the optimal solution. However, significant changes have occurred in the online world and online health interventions over the past 15 years. For instance, when Op Koers was first developed, smartphones were not widespread and video calls were uncommon in the Netherlands. The COVID-19 pandemic especially accelerated the acceptance of online activities [42]. During the RCT, we encountered that Op Koers participants and course leaders were increasingly interested in an online course that would be provided through video calls instead of only a chatroom. Advantages that were named include not having to wait until others finish typing (especially when someone is typing very slowly), having more lively conversations, increased sense of connection and having to focus on the session exclusively (rather than multitasking). On the other hand, there are benefits to typing instead of speaking (e.g. having time for reflection and anonymity).

Another advantage of a video call format is that it does not demand the same level of writing skills as the chat format. Therefore, so far, we offered only face-to-face sessions to younger children but now we are exploring a video call format for (young) siblings of children with cancer. We are preparing to experiment with the video call format for parents as well. Transitioning from chat room to video calls requires changes to the manual and handling homework exercises as these are now collected through the chat platform environment of Op Koers. Translating to a video call format could make it easier to further implement and disseminate the course internationally, since the chat platform would not have to be translated. Consequently, even though we still see the advantages of the chat room format, these no longer outweigh the disadvantages.

Health care providers

After finishing the trial for parents of children with cancer, Op Koers Online was no longer part of a research project. A project group consisting of health care providers, advisors from the research team and a coordinator was then established to start implementation in regular clinical practice. Even though evaluation with course leaders revealed high levels of acceptance (92-100%), appropriateness (78-100%) and feasibility (96%) of Op Koers, and RCT results demonstrated benefits for parents, implementation is facing challenges in the Princess Máxima Center. Health care providers seem to experience barriers for participating in the intervention, related to work load, planning and compensation of efforts. In general, lack of a coordinator specifically dedicated to running the intervention, as was the case during the research phase of Op Koers, also makes implementation of Op Koers difficult.

Previous literature suggests that having an ambassador is crucial for successful implementation [43]. An ambassador ideally has experience with the program and has gained trust from the intended course leaders, so that they will be more inclined to adopt a positive attitude towards the new intervention. Furthermore, given the complexity and continuous nature of implementation, engaging the expertise of an implementation specialist to oversee and guide this process is recommended.

Planning the group courses

In the Princess Máxima Center, where the RCT for parents of children with cancer of this thesis was conducted, recruitment of participants went smoothly and no problems were encountered. This is remarkable, because recruitment issues are common in psychosocial intervention research [44, 45]. Furthermore, including the desired amount of participants proved a major challenge during the Op Koers RCT's of the online modules for adolescents with a chronic illness and parents of children with chronic illness [8, 9]. The lack of recruitment problems in the Princess Máxima Center might be explained by the centralization of care: all children with cancer in the Netherlands are treated in the same hospital, which makes it easier to reach all parents. Furthermore, no group interventions for parents of children with cancer were available, and Op Koers Online seems to be meeting parental needs. Further development and implementation of Op Koers Online for illnesses other than cancer might profit from a closer collaboration between hospitals. Such collaborations can facilitate cost-sharing, streamline recruitment efforts, and optimize the utilization of course leaders' efforts.

Future research

Peer support

In the Op Koers intervention, peer support and CBT-techniques are two important factors. Since attention of peers and course leaders could be seen as an intervention itself, it could be interesting to study what the added value is of the CBT techniques that are taught by a trained health care provider. Another study into an online intervention for parents of children with cancer found no effects of a peer-support group compared to a control group [38]. However, they also found no effect of the intervention group compared to either the peer-support group or the control group, whereas our RCT did reveal a beneficial effect for the intervention group compared to a waitlist-control group. In order to study the added value of the CBT techniques in Op Koers, a three-arm RCT with allocation to either care as usual, Op Koers Online or a guided peer-support based online intervention is proposed to study this effect. Another possibility is to study the effect of a peer-support-only group in a single-case design, that is less time consuming compared to an RCT where a control group is needed [46].

Inclusiveness of psychosocial care

In our RCT, participation required parents to understand and write in Dutch, thereby excluding those with a language barrier. Furthermore, mostly highly educated mothers participated. The limitation concerning overrepresentation of highly educated parents and underrepresentation of ethnic minorities is common in psychosocial intervention research [47]. We know from literature that low-educated parents are at risk for developing psychosocial problems [48]. Even though Op Koers serves as an addition to the regular psychosocial care services and not all parents have to benefit from Op Koers, it is worth studying options to be more inclusive and gain insight in needs of parents that cannot participate in an online intervention like Op Koers. The transition from a chat room to a video call format may benefit parents who do not have full proficiency in the Dutch language or parents with limited writing skills, as participation in a video call intervention might be more accessible for them.

Implementation research

A key factor of successful implementation of an intervention, is the understanding of barriers and facilitators of the health care providers. Future research about Op Koers should focus on those barriers and facilitators. A systematic approach to achieve better understanding of the implementation process could involve the Consolidated Framework for Implementation Research (CFIR) [49]. The updated CFIR is a widely used framework that helps identify determinants influencing implementation outcomes and categorizes them into five domains: intervention characteristics, outer setting, inner setting, characteristics of individuals, and implementation process. The framework is practical and helps guide systematic assessment of potential barriers and facilitators, which could be helpful in better implementation of Op Koers.

Part 2: Psychosocial wellbeing of siblings and parents of very long-term survivors of childhood cancer

Psychosocial care

The findings in the studies into wellbeing of siblings and parents on the very long-term are positive and reassuring. We also found that factors related to childhood cancer are of little impact on the wellbeing on the very-long term.

Nevertheless, it remains important to pay attention to the family system of childhood cancer survivors. Particularly when a survivor experiences impaired physical or psychosocial wellbeing as a result of their childhood cancer, it is reasonable to presume that siblings and parents may also be affected. Given that psychosocial care for survivors in the hospital setting predominantly focuses on the survivors, with relatively less attention to and no financial resources for their family members, especially on the long-term, it is important that parents and siblings can find appropriate support elsewhere. Similarly to the phase during treatment and shortly after, collaboration with the patient association and availability of a referral network familiar with the consequence of childhood cancer is recommended.

Future research

Between end of treatment and very-long term survivorship

In this thesis, parents and siblings on average 20 to 30 years after diagnosis of the child with cancer, were studied comprehensively. Apart from our study, so far, research mainly focused on the period during treatment and shortly after treatment and revealed impaired wellbeing of both parents and siblings in terms of e.g. HRQoL, distress, anxiety and depression [22, 27, 50]. Future research might look at wellbeing of siblings and parents in the time between end of treatment and very long-term after diagnosis.

Associated factors

As is described in the previously mentioned disability-stress-coping model, psychosocial wellbeing is influenced by illness-related factors as well as personal, family and environmental factors. Unfortunately, the research in this thesis did not explore family and environmental factors, known to be associated with outcomes in siblings and parents, such as family functioning and psychosocial support for both siblings and parents [34, 35, 38]. It is presumed that these associations are not specific to family members of childhood cancer survivors, but also occur in the general population. Other potentially relevant factors not studied in this thesis concern childhood-cancer specific factors, such as current functioning of the survivor (related to late effects of childhood cancer/treatment) and fear of recurrence [35, 39]. Future research could focus on these factors, even though our studies suggest that siblings and parents are doing generally well.

CONCLUSION

This thesis focused on Op Koers Online, an online group course program for children with an illness, their siblings and their parents. Op Koers was studied in different phases of intervention development and evaluation, and reflections on the efforts were made. The fact that Op Koers Online is one of the few psychosocial interventions that has been both extensively studied and implemented, is an addition to both scientific and clinical knowledge. The next step is implementation of the intervention into regular care.

Furthermore, this thesis revealed that overall, siblings and parents of survivors of childhood cancer were doing well two to three decades after diagnosis of childhood cancer in the family. Cancer-related factors did not demonstrate a clear impact on wellbeing of siblings and parents on the very long-term. These findings are reassuring and can be incorporated in psycho education for families of children with cancer.

Table 1. Study overview and main findings.

	Title	Aims	Sample characteristics	Design + Outcome measures	Main findings
Part 1: The development and effect of the Op Koers intervention in different populations					
Chapter 2	Hearing siblings' voices: exploring the (online) support needs of siblings of children with a chronic condition	To identify siblings' online support needs in order to develop a sibling-specific module of the existing Op Koers Online intervention.	*n*=91 siblings (ages 11 to 21) of children with chronic illnesses. Mean age 15.2 years	Mixed methods: questionnaires, interviews Support needs (self-developed questionnaire) Psychosocial functioning (SDQ) Semi-structured interviews	55% would like to initiate or increase contact with other siblings of children with a chronic condition 46% of those were interested in an online chat course The themes for online support considered most important were impact on daily life, worrying about brother's/sister's future, handling other people's reactions, and how attention is divided within the family
Chapter 3	Online cognitive-behavioral group intervention for adolescents with chronic illness: A pilot study	To assess feasibility and explore preliminary efficacy of an online cognitive-behavioral group intervention (Op Koers Online) to prevent and/or reduce psychosocial problems by teaching use of active coping skills to adolescents (ages 12 to 18) with chronic illness.	*n*=29 adolescents (ages 12 to 18) with chronic illnesses Mean age 15.1 years	Longitudinal questionnaire assessment; pre-post design without control group (T0, T1 0-2 weeks after intervention); Coping skills (Op Koers Questionnaire) Internalizing and Externalizing problems (YSR) Health-Related Quality of Life (PedsQL)	The pilot study indicates that Op Koers Online for adolescents is feasible and potentially effective Participants improved significantly in the coping skills "information seeking and giving" and "social competence" after the intervention compared with baseline Participants reported significantly fewer withdrawn/depressed behavior and scored significantly better on emotional and psychosocial HRQoL after following the intervention Participants' overall satisfaction was high
Chapter 4	Efficacy of Op Koers Online, an online group intervention for parents of children with cancer: results of a randomized controlled trial	To evaluate the effect of an online group intervention for parents of children with cancer (Op Koers Online) on psychosocial wellbeing and coping skills.	*n*=89 parents of children with cancer	RCT with assessment at baseline (T0), 6 week (T1) and 6 month (T2) follow up Anxiety (PROMIS CAT item bank) Depression (PROMIS CAT item bank) Coping skills (Op Koers Questionnaire and CCSS-PF) Distress (DT-P) Emotional reactions (SSER-Q)	Op Koers Online for parents of children with cancer has a positive effect on psychosocial wellbeing (anxiety, depression, distress, feelings of loneliness and uncertainty) and the coping skill relaxation

	Title	Aims	Sample characteristics	Design + Outcome measures	Main findings
Chapter 5	Development, research and implementation of the psychosocial group intervention Op Koers: Lessons learned	To share the lessons that we have learned in the process of 25 years of development, research and implementation of a psychosocial group intervention for children with a chronical illness or cancer and their parents and siblings (called: Op Koers).	n/a	Critical appraisal of activities in different stages, described using the National Institutes of Health Stage Model for Behavioral Intervention Development and discussion of lessons learned, described using the Consolidated Framework for Implementation Research	Op Koers is one of few psychosocial interventions that has been both extensively studied and implemented. The main factor for this achievement is the close collaboration between, and the perseverance of the clinical care and research departments.
Part 2: Psychosocial functioning of parents and siblings of very long-term survivors of childhood cancer					
Chapter 6	Psychosocial functioning of adult siblings of Dutch very long-term survivors of childhood cancer: DCCSS-LATER 2 psycho-oncology study	To describe psychosocial outcomes among adult siblings of very long-term childhood cancer survivors (CCS), to compare these outcomes to reference populations and to study associated factors.	*n*=505 siblings of childhood cancer survivors (diagnosis between 1963-2001). Mean time since diagnosis 29.5 years	Cross-sectional questionnaire study Anxiety and depression (HADS) Health-Related Quality of life (TAAQoL) PTSD (SRS-PTSD) Self-esteem (RSES) Benefit and burden (BBSC)	On the very long-term, siblings did not have impaired psychosocial functioning compared to references Cancer-related factors seemed not to impact siblings' psychosocial functioning Early support and education remain essential to prevent long-term consequences
Chapter 7	Psychosocial functioning of parents of Dutch very long-term survivors of childhood cancer	To describe psychosocial outcomes of parents of long-term survivors of childhood cancer (CCS), to compare these outcomes to reference populations and to study associated factors.	*n*=661 parents of childhood cancer survivors (diagnosis between 1963-2001). Mean time since diagnosis 21.3 years	Cross-sectional questionnaire study Health-Related Quality of life (TAAQoL) PTSD (SRS-PTSD) Post traumatic growth (PTGI) Illness cognitions (ICQ)	HRQoL of parents of long-term CCS was comparable to references or slightly better A small proportion of parents experienced symptomatic post-traumatic stress. Improving acceptance and reducing feelings of helplessness related to their child's disease may provide treatment targets for parents with psychosocial problem

Note. SDQ = Strengths and Difficulties Questionnaire, YSR = Youth Self Report, PedsQL = Pediatric Quality of Life Inventory, PROMIS CAT = Patient Reported Outcomes Measurement Information System Computer Adaptive Test, CCSS-PF = Cognitive Coping Strategies Scale Parent Form, DT-P = Distress Thermometer for Parents, SSER-Q = Situation Specific Emotional Reactions Questionnaire, HADS = Hospital Anxiety and Depression Scale, TAAQOL = TNO-AZL Adult Quality of Life, SRS-PTSD = Self-Rating Scale for Post-Traumatic Stress Disorder, RSES = Rosenberg Self-Esteem Scale, BBSC = Benefit and Burden Scale for Children, PTGI = Post-traumatic growth inventory, ICQ = Illness cognition questionnaire.

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CHAPTER 9

NEDERLANDSE SAMENVATTING

SAMENVATTING

Als een kind ziek is, heeft dat invloed op alle gezinsleden. Kinderen, broers en zussen en ouders moeten omgaan met stressfactoren die gerelateerd zijn aan de ziekte en ze kunnen psychosociale problemen ervaren. Psychosociale problemen hebben te maken met gevoelens, gedachten of het omgaan met anderen. In de inleiding van dit proefschrift (Hoofdstuk 1), wordt aan de hand van een model beschreven dat er een relatie bestaat tussen de stressfactoren waarmee gezinnen te maken krijgen en hun psychosociale welzijn en dat deze relatie wordt beïnvloedt door copingvaardigheden. Copingvaardigheden zijn manieren om met de ziekte om te gaan. Die zijn op hun beurt gerelateerd aan persoonlijke, familie- en omgevingsfactoren.

Copingvaardigheden staan centraal in het Op Koers programma, dat bestaat uit groepscursussen voor kinderen met een ziekte, hun broers en zussen en hun ouders. Het doel is het aanleren van actieve copingvaardigheden en het voorkomen of verminderen van psychosociale problemen. Lotgenotencontact is een belangrijk onderdeel van de cursus, die zowel in ziekenhuizen als online wordt gegeven.

Dit proefschrift bestaat uit twee delen die zich richtten op 1) de ontwikkeling en het effect van de Op Koers cursus voor kinderen met een ziekte en hun gezinsleden en 2) het psychosociaal welzijn van broers en zussen en ouders van zeer langetermijnoverlevenden van kinderkanker. Een overzicht van de verschillende studies is te vinden in Tabel 1 van de *General Discussion* op pagina 167.

Deel 1: De ontwikkeling en het effect van de Op Koers cursus in verschillende populaties

In Hoofdstuk 2 wordt een onderzoek besproken dat gaat over de online ondersteuningsbehoeften van broers en zussen van kinderen en adolescenten met een chronische ziekte. Voor dat onderzoek vulden 91 broers en zussen (van 11-21 jaar) een vragenlijst in die we zelf hebben gemaakt, daarnaast werden er 9 interviews gehouden waarin we wat dieper op de vragen ingingen. Van alle deelnemers gaf 55% aan (meer) behoefte te hebben aan contact met andere broers en zussen van kinderen met een chronische aandoening, en van die groep had 46% interesse in een online chatcursus. De belangrijkste onderwerpen voor steun via een chatcursus waren ‘hoe de ziekte het dagelijks leven beïnvloedt’, ‘zorgen over de toekomst van de broer of zus’, ‘omgaan met reacties van andere mensen’ en ‘aandachtsverdeling binnen het gezin‘. We concluderen dat broers en zussen interesse hebben in contact met leeftijdsgenoten en online ondersteuning, en dat Op Koers Online voor broers en zussen een goede optie lijkt te zijn voor het bieden van dit soort online hulp [1].

In Hoofdstuk 3 wordt gekeken naar de haalbaarheid en voorlopige effectiviteit van de Op Koers Online cursus voor tieners met een chronische ziekte. In totaal hebben 23 deelnemers (van 12-

18 jaar) met een chronische ziekte vragenlijsten ingevuld over hun psychosociaal welzijn en hun copingvaardigheden. Dit deden ze zowel voorafgaand aan als na afloop van de cursus. Slechts een paar deelnemers (6%) stopten voortijdig, en er waren maar weinig technische problemen (2%). De tieners waren over het algemeen heel tevreden. Na de cursus waren copingvaardigheden (‘informatie geven en zoeken’ en ‘sociale competenties’) beter geworden, en teruggetrokken/somber gedrag verminderd en kwaliteit van leven verbeterd. We concluderen dat Op Koers Online voor tieners met een chronische ziekte haalbaar is en vonden aanwijzingen voor effectiviteit [2].

Hoofdstuk 4 is het resultaat van onderzoek naar het effect van Op Koers Online voor ouders van kinderen met kanker. Ouders die meededen werden geloot over de cursusgroep (meedoen aan de cursus) en een controlegroep (niet meedoen aan de cursus). We vroegen beide groepen vragenlijsten in te vullen over copingvaardigheden en psychosociaal welzijn, voor de loting, en nogmaals zes weken en zes maanden later. De cursusgroep vulde daarnaast de vragenlijst nog een keer in na twaalf maanden. Ook evalueerden we de cursus met de deelnemende ouders. In totaal vulden 89 ouders de vragenlijsten in. De resultaten van het onderzoek laten zien dat de cursus een gunstig effect had op angst, depressie en eenzaamheid, evenals op de copingvaardigheid ‘ontspanning’ na zes weken. Verder werd na zes maanden een effect van de cursus gevonden met vermindering van angst, onzekerheid en verbetering van de copingvaardigheid ‘ontspanning’. Er werd geen effect van de cursus gevonden op gevoelens van hulpeloosheid, positieve gevoelens en copingvaardigheden ‘voorspellende controle’, ‘open communicatie’ en ‘positief denken’. In de cursusgroep vonden we geen verschil in scores van zes maanden naar twaalf maanden, behalve een afname van eenzaamheid en een toename van ontspanning. Ouders waren over het algemeen positief over de interventie. We concluderen dat Op Koers Online voor ouders van kinderen met kanker een positief effect heeft op psychosociaal welzijn en de copingvaardigheid ontspanning [3].

De ontwikkeling van de Op Koers cursussen begon meer dan 25 jaar geleden. In Hoofdstuk 5 worden de stappen beschreven die zijn gemaakt om de interventie te ontwikkelen, te onderzoeken en te implementeren. We hebben onze activiteiten in de verschillende stadia kritisch beoordeeld, aan de hand van twee modellen (National Institutes of Health Stage Model for Behavioral Intervention Development en Consolidated Framework for Implementation Research). Belangrijke lessen die werden geleerd gaan over de kenmerken van de cursus, de context waarin de cursus bestaat, mensen die de cursus geven of krijgen, het implementatieproces en onderzoek naar de cursus. Toekomstige stappen kunnen zich richten op verbetering van de cursus en succesvolle implementatie. We concluderen dat Op Koers een van de weinige psychosociale cursussen is die uitgebreid is bestudeerd en geïmplementeerd. De belangrijkste factor voor dit succes is de nauwe samenwerking en volharding van de klinische zorg- en onderzoeksafdelingen.

Deel 2: Psychosociaal welzijn van broers en zussen en ouders van zeer langetermijnoverlevenden van kinderkanker

In Hoofdstuk 6 hebben we het psychosociaal welzijn van volwassen broers en zussen van zeer langetermijnoverlevenden van kinderkanker onderzocht. We hebben gekeken naar hun kwaliteit van leven, gevoelens van angst en depressie, posttraumatische stress (PTSS) en zelfwaardering. Ook hebben we gekeken naar zowel positieve als negatieve gevolgen van het hebben van een broer of zus met kanker, zoals versterking van relaties of minder hoopvol zijn over het leven. Daarnaast hebben we onderzocht of sociodemografische kenmerken (bijvoorbeeld het aantal kinderen in een gezin) en ziektegerelateerde kenmerken van het zieke kind (bijvoorbeeld type kinderkanker) samenhingen met de uitkomsten. In totaal hebben 505 broers en zussen (17-65 jaar) de vragenlijsten ingevuld. Uit de resultaten bleek dat broers en zussen in onze steekproef vergelijkbare kwaliteit van leven, gevoelens van angst en zelfwaardering en iets minder depressieve klachten vertoonden dan de algemene bevolking. Het percentage broers en zussen met symptomen van PTSS was zeer klein. Verder leken de uitkomsten niet te verschillen op basis van sociodemografische kenmerken en ziektegerelateerde kenmerken [4].

Tot slot beschrijft Hoofdstuk 7 het psychosociaal welzijn van ouders van zeer langetermijnoverlevenden van kinderkanker. Net als in hoofdstuk 6 hebben we onder andere gekeken naar kwaliteit van leven en PTSS. We keken ook naar posttraumatische groei, zoals versterking van relaties, en overtuigingen over de ziekte, zoals verwachtingen over het verloop van de ziekte. Opnieuw hebben we gekeken naar factoren die mogelijk samenhingen met de uitkomsten: sociodemografische en/of ziektegerelateerde kenmerken en overtuigingen over de ziekte. In totaal hebben 661 ouders vragenlijsten ingevuld. Uit onze resultaten bleek dat ouders in onze steekproef iets betere kwaliteit van leven rapporteerden op sociaal gebied en minder agressieve emoties ervaarden dan de algemene bevolking. Bovendien rapporteerden moeders een betere kwaliteit van leven op de gebieden van pijn, dagelijkse activiteiten, seksualiteit, vitaliteit, positieve en depressieve gevoelens. Posttraumatische stress was ernstig bij 3% en hing samen met een slechtere kwaliteit van leven. Posttraumatische groei hing samen met meer posttraumatische stress en een betere kwaliteit van leven. Als bij een kind de ziekte een keer terug was gekomen hing dit samen met een betere kwaliteit van leven. Hogere niveaus van de ziektegerelateerde overtuiging ‘acceptatie’ hingen samen met betere uitkomsten, en hogere niveaus van ‘hulpeloosheid’ hingen samen met slechtere uitkomsten. We concluderen dat de kwaliteit van leven van ouders zeer langetermijnoverlevenden van kinderkanker vergelijkbaar is met de algemene bevolking of iets beter, en dat slechts een klein deel symptomen van posttraumatische stress rapporteert [5].

CONCLUSIE

Dit proefschrift richtte zich op Op Koers Online, een online groepscursus voor kinderen met een ziekte, hun broers en zussen en hun ouders. We hebben Op Koers onderzocht in verschillende fasen van ontwikkeling en evaluatie, en we hebben gereflecteerd op de stappen die daarin zijn ondernomen. Het feit dat Op Koers Online een van de weinige psychosociale cursussen is die uitgebreid is bestudeerd en geïmplementeerd, is een aanvulling op zowel wetenschappelijke als klinische kennis. De volgende stap is de implementatie van de interventie in het reguliere zorgaanbod.

Hiernaast liet het onderzoek in dit proefschrift zien dat het over het algemeen goed gaat met broers en zussen en ouders van zeer langetermijnoverlevenden van kinderkanker, twee tot drie decennia na de diagnose. Ziektegerelateerde kenmerken lieten geen duidelijke langetermijneffecten zien op het welzijn van broers en zussen en ouders. Deze geruststellende bevindingen kunnen worden gebruikt in psycho-educatie voor gezinnen van kinderen met kanker.

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3. Joosten, M.M.H., et al., Efficacy of Op Koers Online, an online group intervention for parents of children with cancer: Results of a randomized controlled trial. *Psycho-Oncology*, 2024. *33*(1).
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5. van Gorp, M., et al., Psychosocial functioning of parents of Dutch long-term survivors of childhood cancer. *Psycho-Oncology*, 2022.

APPENDICES

LIST OF PUBLICATIONS
CURRICULUM VITAE
PHD PORTFOLIO
DANKWOORD

LIST OF PUBLICATIONS

Publications in this thesis

Joosten, M. M. H., Maurice-Stam, H., Scholten, L., & Grootenhuis, M. A. (2019). Hearing siblings' voices: exploring the (online) support needs of siblings of children with a chronic condition. *Journal of patient-reported outcomes*, 3(1), 1-9.

Douma, M., Joosten, M. M.H., Scholten, L., Maurice-Stam, H., & Grootenhuis, M. A. (2019). Online cognitive-behavioral group intervention for adolescents with chronic illness: A pilot study. *Clinical Practice in Pediatric Psychology*, 7(1), 79.

Joosten, M. M. H., Maurice-Stam, H., van Gorp, M., Beek, L. R., Stremler-van Holten, D., Scholten, L., & Grootenhuis, M. A. (2024). Efficacy of Op Koers Online, an online group intervention for parents of children with cancer: Results of a randomized controlled trial. *Psycho-Oncology*, 33(1), e6284.

Joosten, M. M. H., van Gorp, M., Maurice-Stam, H., Douma, M., Scholten, L.*, & Grootenhuis, M. A.* (2024). Development, Research and Implementation of the Psychosocial Group Intervention Op Koers: Lessons learned. *Clinical Practice in Pediatric Psychology,* accepted pending minor revisions. *contributed equally

Joosten, M. M. H., van Gorp, M., van Dijk, J., Kremer, L. C., van Dulmen-den Broeder, E., Tissing, W. J., ... & Schellekens, A. (2023). Psychosocial functioning of adult siblings of Dutch very long-term survivors of childhood cancer: DCCSS-LATER 2 psycho-oncology study. *Psycho-Oncology*, 32(9), 1401-1411.

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Other publications

Luijten, M. A., Terwee, C. B., van Oers, H. A., Joosten, M. M., van den Berg, J. M., Schonenberg-Meinema, D., ... & Haverman, L. (2020). Psychometric properties of the pediatric Patient-Reported Outcomes Measurement Information System item banks in a Dutch clinical sample of children with juvenile idiopathic arthritis. *Arthritis care & research*, 72(12), 1780-1789.

Limperg, P. F., Joosten, M. M. H., Fijnvandraat, K., Peters, M., Grootenhuis, M. A., & Haverman, L. (2018). Male gender, school attendance and sports participation are positively associated with health-related quality of life in children and adolescents with congenital bleeding disorders. *Haemophilia*, 24(3), 395-404.

CURRICULUM VITAE

Werkervaring

Prinses Máxima Centrum voor Kinderoncologie

Promovendus 2019 - 2024

Onderzoek naar

- de ontwikkeling en het effect van de groepsinterventie Op Koers Online bij gezinnen waarin een kind ziek is
- de lange termijn psychosociale effecten van kinderkanker op ouders en broers en zussen van survivors

Projectcoördinator zorginnovatie 2019 - 2022

Zorginnovatieproject *Brussen in Beeld* met aandacht voor broers en zussen binnen het Prinses Máxima Centrum, door o.a. informatievoorziening, evenementen en groepscursussen

Projectmedewerker ontwikkelingsgerichte zorg 2017 - 2018

Implementatie van online groepsinterventie Op Koers Online en KLIK-project in opstartfase van het Prinses Máxima Centrum

Emma Kinderziekenhuis/AMC

Projectmedewerker psychosociale afdeling 2015 - 2018

Ontwikkeling Op Koers Online voor broers en zussen en ondersteuning KLIK-project

Onderzoeksstagiaire psychosociale afdeling 2014 - 2015

Thesis: The effectiveness of an online group intervention for adolescents with a chronic physical illness: a case-series analysis

Klinisch stagiaire psychosociale afdeling 2014

Opleiding

Universiteit van Amsterdam

MSc Pedagogische Wetenschapen: Orthopedagogiek	2013 - 2015
Premaster Pedagogische Wetenschappen	2012 - 2013
BA Taalwetenschap	2008 - 2013

PHD PORTFOLIO

Courses and workshops	year
Qualitative Interviewing	2018
Basic Course Legislation and Organization for Clinical Researchers (BROK)	2019
Managing your Supervisor	2019
Research Planning & Time Management	2019
Working Effectively and Consciously	2019
Supervising Research of MSc Students	2021
Writing a Scientific Paper	2021
This Thing Called Science	2021
Intervention Development	2021
Introduction Course Clinical and Translational Oncology	2021
Basic Methods and Reasoning in Biostatistics	2021
Multilevel Modelling and Longitudinal Data Analysis	2023

Teaching	
Supervision of students (MSc/BSc/HBO)	2020 - 2022
Teaching nurses (Maximaal op Maat program)	2020

Presentations	
55th Congress of Society for Paediatric Oncology	2023
Oral presentation and poster presentation (Ottawa, Canada)	
Landelijke Vereniging van Medische Psychologie Symposium	2023
Poster presentation (Utrecht, Netherlands)	
Landelijke Vereniging van Medische Psychologie Wetenschappelijke dag	2023
Oral presentation, invited (Utrecht, Netherlands)	
Congres Nederlands Vereniging voor Psychosociale Oncologie	2023
Poster presentation (Utrecht, Netherlands)	
54th Congress of Society for Paediatric Oncology	2022
Poster presentation (Online)	
Society of Pediatric Psychology Annual Conference	2020
Oral presentation (Dallas, United States - Online)	
Association of Researchers in Psychology and Health	2020
Oral presentation (Egmond aan Zee, Netherlands)	

Quality of Life Symposium Princess Máxima Center	2020
Poster presentation (Utrecht, the Netherlands)	
51st Congress of Society for Paediatric Oncology	2019
Poster presentation (Lyon, France)	
Siblings symposium Stichting Kind&Ziekenhuis	2018
Oral presentation, invited (Utrecht, Netherlands)	
Amsterdam Pediatrics Symposium	2017
Poster discussion (Amsterdam, Netherlands)	

Awards	year
Young Investigator Award	2023
55th Congress of Society for Paediatric Oncology	
Poster award	2023
Landelijke Vereniging van Medische Psychologie Symposium	
Pediatric Psychology Travel Award	2020
Society of Pediatric Psychology Annual Conference	

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