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PEDIATRIC ADVANCE CARE PLANNING FOR ADOLESCENTS WITH CANCER AND THEIR PARENTS: THE BOOST INTERVENTION AND LESSONS LEARNED

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GENERAL INTRODUCTION

Introduction

This PhD dissertation presents the development and the results of the BOOST pACP trial: **B**enefits of **O**btaining **O**wnership **S**ystematically **T**ogether in **p**ediatric **A**dvance **C**are **P**lanning. This trial aims to evaluate the effectiveness of an advance care planning intervention for adolescents with cancer aged 10 – 18 years old. The BOOST pACP intervention is designed to improve communication between parents and adolescents about what the adolescent values most in maintaining their quality of life, as well as their perspectives on current and future care and treatment. A behavioral theory was used to better understand and explain the behaviors of adolescents with cancer and their parents discussing pACP with each other and with a pediatric oncologist. Ultimately, this approach aims to empower adolescents and to integrate these important discussions into regular care and treatment with healthcare professionals.

In the context of serious illness, advance care planning (ACP) is recognized as a valuable strategy for exploring individual values and preferences [1]. It is grounded in the principles of shared decision-making and should be dynamic, evolving over time, to allow patients and their caregivers to receive information and discuss their concerns, priorities and wishes [2]. The focus of ACP has shifted from merely documenting end-of-life care preferences to discussing preferences and goals of care to achieve better person-centered care [3].

Besides developing and evaluating the BOOST pACP intervention, this dissertation also aims to fill several other key gaps in knowledge. Key factors that describe child development in the context of serious illness are examined, including potential accelerators and decelerators of child development important for a child's involvement in pACP. This thesis also explores the challenges and opportunities in recruiting adolescent cancer patients and their parents for psychosocial intervention studies. Although such studies are rare, they are crucial for significantly improving healthcare outcomes through high-quality intervention research [4]. In this dissertation, the term 'adolescent' refers to individuals aged 10 to 18 years, while 'child' refers to those aged 0 to 18 years [5].

Background

1. Distinct challenges and progress in childhood cancer care

Childhood cancer differs significantly from adult cancer in several ways. The types of cancer affecting children are different, and treatment involves additional considerations due to the developing body and the potentially more harmful long-term impacts of treatments [6]. Although the 5 year-survival rate of cancer has risen to 85% in children [7], cancer is the leading disease-related cause of death in children in the United States [8]. Survival has increased for all childhood cancer types due to, among other factors, a better understanding of the natural behavior of the disease, improved diagnostic methods, more effective drugs, more accurate use of already existing drugs, and better surgery and radiotherapy [9]. Fewer children will die from the cancer itself, however, a higher proportion of death will be treatment-related [10]. Long-term survivors have excess morbidity and late mortality (death beyond 5 years from cancer diagnosis) compared with the general population attributable to late effects of treatment [11].

2. Childhood cancer: the Belgian context

In Belgium, childhood cancer represents less than 1% of the total cancer burden [9]. Each year, approximately 340 children under 15 years old and 180 adolescents (between 15 and 19 years old) are diagnosed with cancer[9]. This equates to approximately one in every 300 young adults who has experienced cancer in childhood [12]. For those diagnosed between 2012 and 2021, the 10-year relative survival rate was 83% for children and 87% for adolescents and young adults (AYAs, ages 16 – 35) [13].

Pediatric hemato-oncology encompasses over 60 rare malignancies, treated exclusively in seven Belgian pediatric hemato-oncology centers, including pediatric university hospitals, pediatric general hospitals, and university or general hospitals with pediatric units that provide care for various diseases [13, 14]. A Royal Decree from 2014 (currently under revision) sets specific standards for pediatric hemato-oncology programs, covering diagnosis, multidisciplinary treatment, rehabilitation, late-effect follow-up and palliative care for all patients under 16 with hemato-oncological conditions potentially requiring stem cell transplantation [9, 13]. Standard care includes participation in multinational academic studies where possible, with a focus on early-phase studies [13]. However, Belgium's medical and paramedical staffing levels for pediatric hemato-oncology are among the lowest in Europe, which poses challenges in maintaining high-quality care amid advancing diagnostic and therapeutic complexities [13]. For adolescents aged 16 and older, treatment generally occurs in adult wards, although they may choose to be treated in the pediatric ward if preferred [13].

3. The impact of cancer on adolescents and their family

Adolescence is a particularly vulnerable period, as it is marked by the process of 'individuation', where identity formation and role-taking ability are central; crucial psychosocial tasks that shape how individuals perceive themselves and form a sense of who they are [15, 16]. A cancer diagnosis can significantly disrupt this process [15], as adolescents diagnosed with cancer often face significant social and emotional challenges both during and after treatment [17]. The demands of cancer treatment and the prioritization of survival can severely limit adolescents' opportunities to achieve typical developmental milestones, such as attending school, pursuing hobbies, and building relationships, all of which are essential for their identity formation [18]. Diagnosis, treatment, and long-term health consequences can

reshape adolescents' future perspectives and goals, deeply influencing how they see themselves and their future [19]. Throughout their cancer journey, adolescents and young adults (AYAs) strive to maintain control, redefine their sense of self, and integrate their cancer experience into their long-term life plans [20].

A cancer diagnosis also affects the entire family [17]. Although many families adapt over time, some experience ongoing difficulties and poor functioning [21]. Parents often feel intense stress and worry about their child's prognosis, treatment duration, and the physical and emotional pain their child may endure [17, 22]. This stress is often compounded by the need to balance work responsibilities, manage financial strain, care for healthy siblings, and maintain social support networks. Many parents report symptoms of post-traumatic stress, uncertainty, anxiety, and depression, especially in the period immediately following the diagnosis [17]. Parental distress can negatively impact family relationships and overall family life satisfaction [23].

Siblings of children with cancer also experience significant effects, including higher levels of depression, anxiety, and challenges with peer relationships compared to siblings of healthy children [21]. They frequently report disruptions in daily routines, difficulties concentrating in school, reduced quality of life, and strong negative emotions [24].

4. Communication between the child and parent during the cancer trajectory

Effective family communication in the context of cancer is increasingly recognized as vital to the quality of life for children and adolescents [25]. Regardless of whether the cancer is expected to be curable [26], this diagnosis creates new communication challenges between parents and children [27]. Persistent communication difficulties can negatively impact the family's adaptability and cohesion during cancer treatment, leading to adverse psychological consequences for both the adolescent and the parent [15].

Effective and transparent parent-child communication can lead to better health outcomes, positive emotional and psychological states, and improved illness management coping skills [28]. A family's ability to communicate their concerns, emotions, and thoughts is a protective factor and a key component of family resilience [23]. However, a major obstacle to open communication in the context of childhood cancer is the mutual desire of parents and children to protect each other from the pain associated with discussing treatment and its risks [28,29].

Adolescents with cancer experience symptoms more frequently than younger children, yet often do not communicate these symptoms to their parents or healthcare professionals, believing they are an expected part of cancer treatment that must be endured [30]. Additionally, parents find it challenging to discuss the illness with their children[23], especially when confronted with decisions about ceasing treatment and discussions about mortality[31]. Even when the prognosis is relatively positive, similar distress may arise during or immediately after active treatment [31].

5. Shared decision-making in treatment planning

Shared decision-making (SDM) is an evidence-based approach that promotes collaboration between patients, family members, and healthcare professionals when making health-related decisions [32]. While shared decision-making can already be challenging among adults, it is even more so in pediatric settings. This is often due to uncertainty about a child's ability to

actively participate in health-related decisions. A child's capacity to engage in these decisions is shaped by several factors, including their developmental stage, experience with the illness, and the attitudes of parents and healthcare professionals toward their decision-making abilities [33]. Additionally, factors such as socioeconomic status, peer environment and culture influence neurocognitive development in children, which subsequently shapes how they can, want to, and should participate in their own healthcare [34,35].

However, several barriers hinder healthcare professionals from effectively exploring a child's perspective. These barriers include insecurity about their own communication skills, time constraints, perceived parental unreadiness and gatekeeping by both families and healthcare professionals [36–39]. As a result, children's voices are often not systematically included in decision-making or discussions about treatment preferences and tools to support their participation are scarce [40].

Engaging in early conversations with children about their health and treatment preferences is crucial for implementing SDM, particularly when there is a possibility of needing to make difficult decisions later in the course of the illness [41]. Thus, pACP initiatives are essential to ensure that children are actively involved in their healthcare decisions.

6. Pediatric advance care planning

Defining the end-of-life phase has become increasingly challenging due to medical advancements that allow more adolescents with previously lethal conditions to survive into adulthood [42,43]. ACP provides an appropriate framework for individuals to plan their future healthcare [44]. While ACP can include palliative care and end-of-life care, it is not limited to these aspects. Instead, it serves as a process for discussing all kinds of potential outcomes related to disease progression, enabling the exploration of possible treatment plans [45]. Important criteria are that ACP discussions are person centered and adapted to the person's concerns and questions [44]. The content, order and number of topics can be changed, and as ACP is a process, these conversations should take place regularly [44].

Previous research has shown that ACP for children differs significantly from that for adults in terms of both content and approach [46], due to the legal and ethical issues with regards to a minor's capacity to consent and the influence of parents and clinicians as surrogate decision makers [47]. Pediatric ACP is defined as *'an ongoing conversation that enables the goals, wishes and treatment plans for the child or young person with life-limiting/life-threatening conditions to be discussed by parents, healthcare professionals and, where appropriate, the young person'* [47]. The phrase *"where appropriate"* highlights the complexity of when and how to involve the child in pACP.

Assessing the appropriateness of involving children in pACP often involves evaluating the child's ability to participate in health-related decisions. However, determining this ability is challenging [33] because decision-making competence is not binary; it can vary depending on the specific decision and context [48]. Engaging in early and ongoing discussions about the child's quality of life as part of pACP can facilitate the involvement of children in a manner that is both preferred and suitable. pACP recognizes the role, voice, and values of the child, and considers the relationship of the child within a family context [49]. While sharing preferences and future care goals is a key element of pACP, previous research has shown that parents benefit from a stepwise approach that begins with understanding the child's illness and current situation as a first step in ACP [50], also lowering the threshold for healthcare professionals to start ACP conversations with the family.

7. Current evidence on pediatric advance care planning

Several pACP programs and tools have been developed and tested at various levels, from face validity to effectiveness [3,51-56]. However, these initiatives often focus primarily on specifying end-of-life care preferences or on equipping healthcare professionals with tools, materials, and training to facilitate ACP conversations initiated by them. They frequently overlook the need to actively engage adolescents and parents in the process themselves.

Although there is a general lack of research on ACP in pediatric settings [47, 50], reports of pACP interventions are increasing [40]. A systematic review on pACP identified 31 articles detailing 18 unique pACP tools [40]. Most of these tools target children with life-limiting conditions, with six specifically focused on oncology patients. The majority of these tools are designed to discuss end-of-life care preferences [51,57,58], only involve parents [57], or train clinicians to use the particular communication tool [57,59-61], with several barriers to wider adoption reported [62]. Additionally, interventions are not typically developed in collaboration with adolescents, as seen with the relatively recent development of the Modular Advance Care Planning (MAPPS) program, on which no evidence on effectiveness is yet available [56].

To our knowledge, the family-centered pediatric advance care planning (FACE) intervention is the only pACP approach that has been studied through randomized controlled trials (RCTs). The intervention was originally intended for adolescents with HIV between 14 – 21 years old, but was adapted to teens with cancer in the same age range (FACE-TC). FACE-TC showed promising results on positive caregiving appraisals reported by caregivers [52], and a 1-year sustainability of the family and adolescents' congruence about end-of-life treatment preferences [53]. Although the results in these domains are generally positive, this intervention focuses specifically on defining end-of-life care preferences and achieving congruence on these between the adolescent and parent [51-53,63-66]. Earlier use of pACP in illness trajectories might be hindered due to this focus [3].

The Implementing Pediatric Advance Care Planning Toolkit (IMPACT) [3] is the first program providing a holistic approach in pACP and was developed together with children and adolescents with life-limiting conditions, parents and clinicians. The program facilitates ACP both early and later in the disease trajectories, addressing both views on living well, as well as views on what is important to them if death is imminent [3]. Although valued as appropriate in a qualitative pilot study, evidence on mechanisms of outcomes and effectiveness is lacking [3].

The scarcity of evidence on the effectiveness of pACP through RCTs is not surprising, given the common challenges faced in conducting these trials in pediatric palliative care settings [67-70]. Known strategies to combat these challenges are often underdeveloped or inadequately applied, necessitating further investigation into best practices for optimizing trial design.

Knowledge gaps addressed within this dissertation

This dissertation addresses pertinent gaps in the knowledge on pACP for adolescents with cancer and their parents.

While there is some evidence supporting interventions aimed at improving congruence on end-of-life care preferences [52, 53], there is no urgency for additional interventions of this nature. Instead, the current gap in knowledge lies in the effectiveness of interventions designed to be integrated earlier in the illness trajectory, regardless of whether a specific scenario of death is (soon) anticipated. This approach may be particularly promising for the pediatric oncology target group, who face a high symptom and treatment burden with uncertainty about the long-term impact [71]. The innovation of the BOOST pACP intervention lies in its focus on enhancing ACP communication by primarily addressing the behavior of both the adolescent and the parents, and by providing the oncologist with a summary that can serve as a starting point for subsequent conversations. Together with relevant stakeholders, we have employed a behavioral theory, as it generally leads to more effective interventions and successful behavior change [72]. To our knowledge, this approach has not yet been used in pACP interventions.

Considering that having cancer during adolescence adds extra challenges to an already difficult developmental period, during which communication is crucial [73,74], this stage seems particularly relevant for receiving such a holistic pACP intervention. Definitions regarding the specific age range in adolescence vary. Generally, adolescence is perceived to begin when a sense of competency is achieved and to end with the development of an adult identity, typically corresponding to the ages of 10 – 18 years [30], which is the age range of the target group of the pACP intervention that was developed and tested as part of this dissertation. Evidence of pACP on this age group is currently lacking.

Additionally, the literature lacks cohesive evidence on the appropriate way to involve children of different ages in medical decision making that align with their developmental abilities, needs and preferences [75]. A systematic review found that none of the existing pACP interventions had comprehensively examined the developmental stages of their target population [40]. However, the relevance of an age-appropriate approach was implicitly mentioned in most articles [40]. To foster developmentally appropriate communication when discussing illness and health with children and adolescents, and to benefit pACP initiatives, an overview of characteristics of child development in the context of serious illness is included in this dissertation.

To further advance pediatric oncology care, key strategies to optimize recruitment and retention in randomized controlled trials (RCT) of psychosocial interventions targeting both the child and parent are outlined. These strategies help improve future studies in this field, as approximately half of these trials require extensions of time and/or budget to successfully recruit their target sample [4]. The experiences of the RCT of this dissertation are integrated with those from other psychosocial intervention studies. By optimizing research protocols and trial-implementation of such studies, we can contribute to better psychosocial care for children with cancer and their parents.

Study objectives and research questions

The main objectives of this dissertation are: 1) to develop a pACP intervention for adolescents with cancer and their parents and to describe the protocol of a randomized controlled trial (RCT) on the evaluation of this intervention; 2) to test the effectiveness of the developed pACP intervention in a multicenter RCT; 3) to provide insights for future interventions on how to further develop tailored interventions aimed at optimizing communication and care for children with various serious illnesses and how to improve the feasibility and quality of RCTs in pediatric populations.

Objective 1: to develop a pACP intervention for adolescents with cancer and their parents and to describe the protocol of a RCT on the evaluation of this intervention.

The research questions are:

1. What are the potential intervention components and current barriers and facilitators for ACP in the context of pediatric oncology?
2. What is the pathway through which the pACP intervention is likely to achieve change, including the selection of proximal and distal outcomes and the required intervention components?
3. How acceptable and feasible are the intervention components and materials for adolescents with cancer, their parents, and healthcare professionals?
4. What is the design, methodology and procedure for conducting the trial?

Objective 2: to test the effectiveness of the BOOST pACP intervention in a multicenter RCT

The research questions are:

5. What is the effect of the BOOST pACP intervention compared to care as usual on parent-adolescent communication?
6. What is the effect of the BOOST pACP intervention compared to care as usual on parents' and adolescents' attitudes towards and self-efficacy in discussing ACP topics with each other?
7. What is the effect of the developed intervention compared to care as usual on the behavior and intention of parents, adolescents and pediatric oncologists to discuss ACP topics with each other?

Objective 3: to provide insights for future interventions on how to further develop tailored interventions aimed at optimizing communication and care for children with various serious illnesses and how to improve the feasibility and quality of RCTs in pediatric populations.

The research questions are:

8. Which prevailing theories and constructs concerning the ongoing development of children with serious illness are identified?
9. What typical developmental aspects are observed in children with serious illness and what factors influence ongoing development?
10. What are the experienced recruitment and retention challenges, and strategies to overcome them, from psychosocial intervention studies conducted among children with cancer and their parent(s)?

Methods

To address the research questions of this dissertation, several methods of data collection were used. First, we described the development process of the pACP intervention and we developed a research protocol that outlines all relevant aspects of the trial (**Chapter 1 and 2**). To assess its' effects on the primary outcome parent-adolescent communication and on the secondary outcomes attitude, self-efficacy, behavior and intention, we conducted a randomized controlled trial (RCT) across four university hospitals in Belgium (**Chapter 3 and 4**). An additional study was conducted to provide an overview of characteristics of different child development phases and factors affecting child development in the context of serious illness (**Chapter 5**). Finally, we summarized the experiences, challenges, and strategies for conducting RCTs of psychosocial intervention studies among children with cancer and their parent(s) (**Chapter 6**). The methods for each study are briefly described in this section.

Study 1: Development of the pACP intervention (Research questions 1 – 4)

A comprehensive iterative phased approach was used to develop and test the pACP intervention, informed by the supplementary guidance for the development of complex interventions by Bleijenberg et al. (2018) [76]. Five steps were used:

1. interviews with pediatric oncologists (n=4), psychologists (n=2) and nurses (n=5) working at a pediatric oncology ward
2. literature search to identify existing components in academic and grey literature
3. development of a logic model using the Theory of Planned Behavior (TPB) via iterative discussions among the core research team (n=6)
4. identification of core components and feedback of an international advisory group (n=11), psychologists (n=8), members of the Pediatric Palliative Care Research Network (PPCRN), and researchers (n=2) to develop prototypes of the intervention
5. semi-structured interviews with adolescents with cancer (n=4), parents (n=6) and healthcare professionals (n=9) to evaluate acceptability, and testing the feasibility with 3 families.

All interviews and feedback sessions lasted approximately 30 – 60 minutes and were audio-recorded and transcribed. Thematic analysis by hand was used to structure the participants' feedback. A detailed overview of the components of the BOOST pACP intervention and methods and design of the trial can be found in **Chapter 1 and 2**. The intervention materials are provided in **Appendix 1 - 5** of this dissertation.

Study 2: Conducting the BOOST pACP trial (Research questions 5 – 7)

We conducted a multi-center parallel-group superiority trial, comparing the BOOST pACP intervention to care as usual (1:1 allocation ratio), recruited through four university hospitals in Belgium. Facilitators external to the medical team were trained before and during the data collection period to perform the pACP conversations with the families. Conversations took place at home, at the hospital or online. Patients were recruited from March 2021 to March 2023.

Outcomes were measured at baseline, 3 months after baseline, and at 7 months in three groups: adolescents, parents and pediatric oncologists. The primary outcome was parent-adolescent communication measured in adolescents using the Parent-Adolescent

Communication Scale (PACS) [77]. Secondary outcomes were anxiety of adolescents and parents (measured by PROMIS Anxiety [78,79]), attitude towards and self-efficacy in discussing care and treatment with each other of adolescents and parents, and behavior and intention to discuss ACP topics with each other of adolescents, parents and pediatric oncologists. A self-developed face-validated questionnaire based on the Theory of Planned Behavior (TPB)[80], was used to measure these behavioral outcomes. Data on clinical characteristics were gathered through pediatric oncologists at baseline, and socio-demographic data were gathered from parents. The complete baseline questionnaires for adolescents, parents and pediatric oncologists can be found in the additional files Chapter 2. We estimated mean differences in the quality of communication between the two groups using a linear mixed model. Our primary analysis followed the intention-to-treat (ITT) principle. In addition, we conducted several sensitivity and subgroup analyses. For the secondary outcomes, we used exploratory factor analysis and computed sum scores of behavior and intention, which served as dependent variables in a linear mixed model. Details on the methods can be found in **Chapter 3 and 4**.

Study 3: Characteristics of child development in the context of serious illness (Research question 8 - 9)

A scoping review was performed using methods from Arksey and O'Malley [81] with further refinement from guidance by the Joanna Briggs Institute [82]. A structured computerized literature search was conducted in four databases: Medline, Embase, PsycINFO and CINAHL, with keywords: serious illness, child, communication, theory. Articles were included until October 2022. Thematic analysis was conducted to present key elements of child development and influencing factors. **Chapter 5** entails more details on how the scoping review was performed.

Study 4: Experienced recruitment and retention challenges and strategies (Research question 10)

We conducted a collective case study consisting of online semi-structured expert interviews with principal investigators and research staff members of a selection of recent or ongoing trials testing psychosocial interventions for children and/or adolescents with cancer and their parents (n=7). To identify the cases, a search on PubMed, ClinicalTrials.gov and ISRCTN.com trial registries was used. Online interviews of approximately one hour with the principal investigators and data collectors took place in March and April 2022, using a topic list including the domains: 1) Actions before the study start; 2) Screening for eligibility; 3) Enrollment; 4) Attrition; 5) Encountered challenges; 6) Additional strategies to enhance recruitment; 7) Advice to other researchers. All interviews were audio recorded and transcribed verbatim. A combination of deductive and inductive thematic analysis was used. A more detailed overview of the methods can be found in **Chapter 6**.

Dissertation outline

First, a general introduction to pACP for adolescents with cancer and their parents is provided. Chapters 1 - 6 of this thesis are based on articles which have either been published or submitted for publication.

The dissertation is structured into three main parts, each addressing specific research questions and aims. **Part 1 and 2** address the first and second aims to develop and evaluate a pACP intervention for adolescents with cancer and their parents through a multi-center RCT.

Part 1 focuses on the development (**Chapter 1**) and trial design (**Chapter 2**) of the BOOST pACP intervention for adolescents with cancer and their parents. It addresses research questions one to four.

Part 2 describes the findings of the BOOST pACP study on the primary outcome (**Chapter 3**) and secondary outcomes (**Chapter 4**), answering research questions five to seven.

Part 3 addresses the second aim of providing insights for future interventions on how to further develop tailored interventions aimed at optimizing communication and care for children with various illnesses and how to improve the feasibility and quality of RCTs in pediatric populations. It addresses research questions eight to ten. **Chapter 5** explores characteristics and factors influencing ongoing development in children with serious illness. **Chapter 6** examines recruitment and retention challenges experienced in psychosocial intervention studies involving children with cancer and their parents, and presents strategies to overcome these challenges.

In the discussion section, the main findings of each study are thoroughly discussed, considering the strengths and weaknesses of their designs. The results of this dissertation are compared with the existing literature on pACP and potential explanations for the results of the BOOST pACP trial are explored. Finally, the discussion concludes by outlining how these findings can inform practice, influence policy and guide future research.

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PART I

THE DEVELOPMENT OF THE BOOST pACP INTERVENTION AND TRIAL

Chapter 1

THE BOOST PEDIATRIC ADVANCE CARE PLANNING INTERVENTION FOR ADOLESCENTS WITH CANCER AND THEIR PARENTS: DEVELOPMENT, ACCEPTABILITY AND FEASIBILITY

This chapter is based on:

van Driessche A, Gilissen J, De Vleminck A, Kars MC, Fahner J, van der Werff Ten Bosch J, Deliëns L, Cohen J*, Beernaert K*. The BOOST paediatric advance care planning intervention for adolescents with cancer and their parents: development, acceptability and feasibility. BMC Pediatrics. 2022;22(1):210. [2022 IF 2.4; Ranking Q2; ranking 58/130 in PEDIATRICS in SCIE edition]

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Abstract

Background: Although advance care planning (ACP) has been widely recommended to support patient and family engagement in understanding the patient's values, preferences and goals of care, there are only a few models in paediatric oncology that capture ACP as a process of behaviour change. We aimed to develop and test the acceptability and feasibility of BOOST pACP (**B**enefits of **O**btaining **O**wnership **S**ystematically **T**ogether in **p**aediatric **A**dvance **C**are **P**lanning) – an intervention to improve ACP in adolescents with cancer, their parents and paediatric oncologists.

Methods: Several methods informed the intervention development process: 1) Problem identification: interviews with 11 healthcare professionals working in paediatric oncology; 2) Identification of evidence: literature review of existing pACP tools and barriers and facilitators in performing pACP; 3) Logic model and 4) Intervention design: collaborative expert meetings with researchers and professionals in pACP; 5a) Acceptability test of the materials: interviews with nine healthcare professionals, four adolescents and young adults with cancer and six parents; 5b) Feasibility test of core intervention components with three families, including interviews about their experiences.

Results: The BOOST pACP intervention was iteratively developed and adapted, based on feedback from families, healthcare professionals, and pACP experts (e.g., components were changed, deleted, and added; formulation of themes and associated questions were amended to enhance acceptability). The core components of the BOOST pACP intervention include: four ACP conversation sessions with the adolescent and/or parent(s) provided by a trained facilitator, structured by interactive conversation cards covering different ACP themes, followed by a transfer of information from the intervention facilitator to the paediatric oncologist. Core intervention components were deemed feasible by all participating families.

Conclusion: The BOOST pACP intervention was developed by close involvement of both adolescent patients and their parents, healthcare professionals and pACP experts. The final intervention and supporting materials are considered appropriate and feasible. Its effectiveness in improving parent-adolescent communication on ACP themes is currently being tested in a multi-centre randomised controlled trial. Researchers aiming to develop a complex psychosocial intervention for a vulnerable target group could use the step-by-step approach described in this paper.

Keywords: Advance care planning, paediatric palliative care, paediatric oncology, intervention development, communication, adolescent, parent-adolescent communication

1. Introduction

Many adolescents with cancer often require multiple medical procedures, hospitalisations or adjusted home care services with the potential to cure the illness and to maintain as normal a life as possible [1]. Families and clinicians must navigate serial uncertainties, from diagnosis through survivorship or end of life [2]. The interface between development, cancer, and treatment means that the impact is often persistent and can affect individual and family for many years [3]. With the complexity of these conditions, clinicians, parents and adolescents frequently face difficult decisions and conversations involving both current and future care and treatment options [4, 5]. Therefore, it is important to support family engagement in understanding the adolescent's goals of care [5]. The lack of open communication between parents, adolescent and healthcare professionals about living with illness has consistently been reported by several studies [6–11], while adolescents have the desire and ability to share their values, beliefs and preferences of treatment [6, 12, 13] and parents indicate that they find it important to communicate about these themes [6]. Talking about cancer with their child has been designated as one of the most significant sources of stress during treatment [14], especially talking about what to do if the adolescent's health should get significantly worse [11].

Advance care planning (ACP) has been widely advocated [15, 16] to support patient and family engagement in understanding the patient's values, preferences and goals of care – regardless of prognosis and disease trajectory [17]. It entails a communication process that is aimed at aligning future medical care and treatment with an individual's values and preferences in a timely manner, not only at the end of life but at any stage in the course of the illness [17, 18]. ACP has been positively evaluated in adults, and studies in paediatrics [18–20] show promise that it can provide an opportunity to address misconceptions, improve understanding of prognosis and prepare families for future situations [21, 22]. Moreover, knowing what is important to the adolescent can be a great relief for both parents and adolescents, leading to an increased sense of control and security [22]. Despite this, exploration of the child's perspectives by healthcare professionals in particular appears to be difficult due to barriers such as insecurity about their own communication skills, a lack of time and perceived parental unreadiness and gatekeeping by both families and healthcare professionals [23–26].

A few paediatric ACP (pACP) programs have been developed and tested on different levels ranging from face validation to effectiveness [5, 18, 22, 27, 28]. However, these initiatives are often predominantly focused on specifying end-of-life care preferences or on providing healthcare professionals with tools, materials and training to support them in performing ACP conversations with their patients instead of the adolescents and parents themselves. This despite the fact that ACP has been widely defined as a broader approach (not limited to end-of-life topics), and that it is a process of behaviour change that is not only initiated by healthcare professionals but by other stakeholders as well [18, 29]. Thus, adolescents and their parents would likely benefit from, and increase their communication about, a broad range of topics through a structured program that empowers adolescents themselves and their parents while simultaneously involving healthcare professionals. However, such a program – including evidence of its effectiveness – does not yet exist.

The primary objectives of this study were to develop and test the acceptability and feasibility of a novel pACP intervention for adolescents with cancer and their parents. In this paper, we present both the development process and the content of the final intervention. The specific objectives of the study were:

- 1) To identify potential intervention components and current barriers and facilitators for ACP in the context of paediatric oncology.
- 2) To specify the pathway through which the pACP intervention is likely to achieve change, including the selection of proximal and distal outcomes and required intervention components.
- 3) To evaluate the acceptability and feasibility of the intervention components and materials with adolescents with cancer, parents and healthcare professionals.

The resulting BOOST pACP (**B**enefits of **O**btaining **O**wnership **S**ystematically **T**ogether in **p**aediatric **A**dvance **C**are **P**lanning) intervention aims to facilitate and improve ACP communication among adolescents between 10 - 18 years old with any type of cancer at any stage, parents, and paediatric oncologists [30].

2. Methods

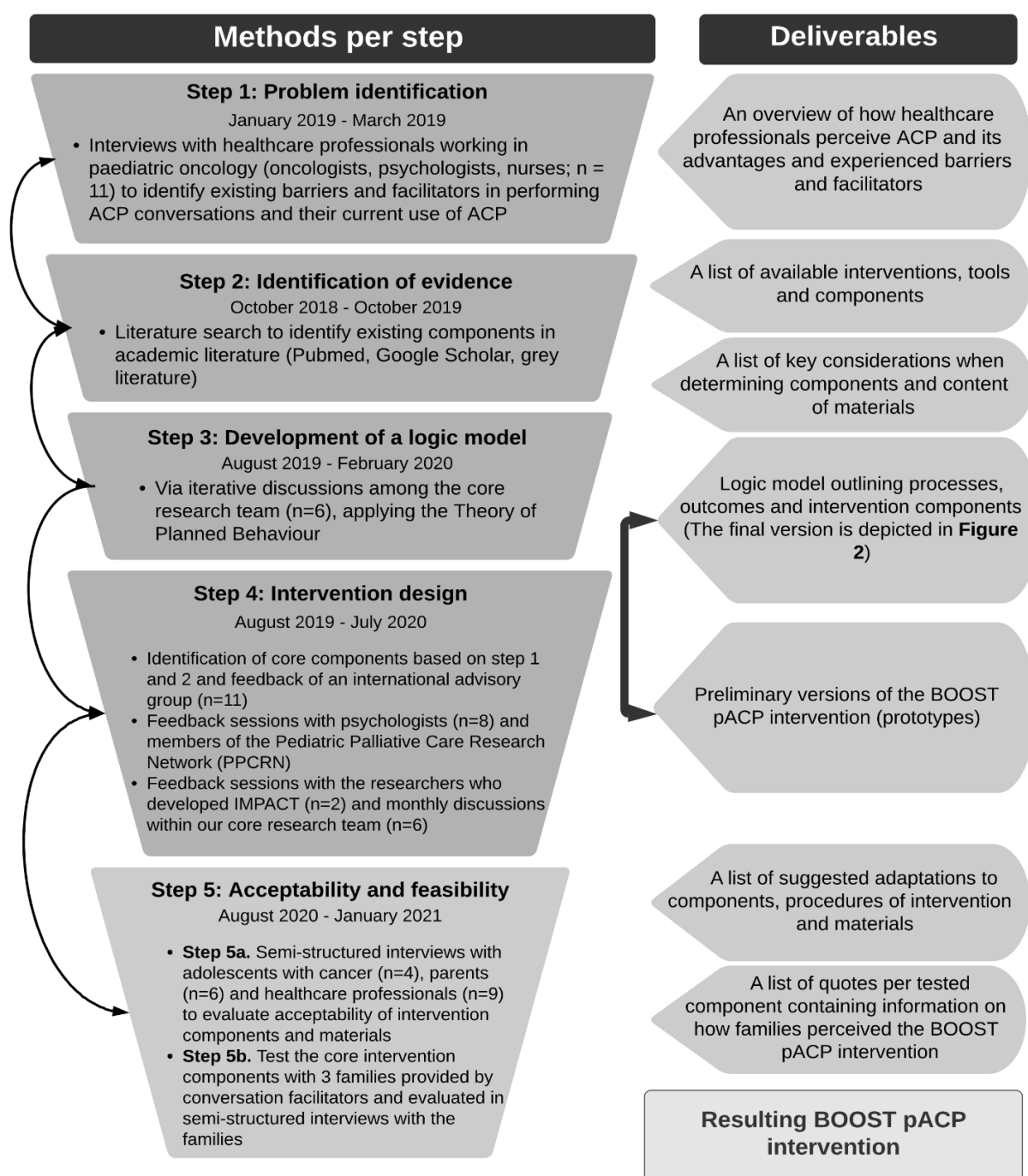
2.1. Study design and setting

We conducted a comprehensive iterative phased approach to develop and test the BOOST pACP intervention, informed by the supplementary guidance for the development of complex interventions by Bleijenberg et al. (2018) [31]. This guidance combines elements from the development phase (phase 0 – 2) stipulated within the Medical Research Council's (MRC) Framework for Complex Interventions [32, 33] with extra elements such as problem identification to enhance the intervention design. We applied several methods to inform the study objectives, resulting in five steps of the intervention development process (**Figure 1**).

The reporting of the intervention development in this paper is compliant with the GUIDED checklist (2019) [34].

The study was performed in Flanders, the Dutch-speaking part of Belgium. In Flanders, there are four University hospitals, each with a paediatric oncology department. These paediatric departments treat children between 0 and 16 years old, and, more exceptionally, children between 16 and 18 years old. In Belgium, every year about 340 children (0-14 years) and 180 adolescents (15-19 years) are diagnosed with a malignancy [35]. In Flanders, the number of new diagnoses in the age group 10 – 18 years was 139 in 2018 (email from the Belgian Cancer Register, Brussels, 30 October 2020).

Figure 1: Flow diagram of the development process of the BOOST pACP intervention



Footnote: The 'core research team' consists of: one PhD student with a background in health intervention development (AvD), two professors (PhDs) in palliative care, one sociologist (PhD), one psychologist (PhD), an assistant professor specialized in paediatric palliative care (PhD), and a paediatric oncologist (MD).

2.2. Study participants and data collection

Step 1: Problem identification

We performed individual semi-structured interviews with healthcare professionals working at a paediatric oncology department in Flanders. Interviews lasted approximately 40 minutes and were structured according to a topic list, covering: knowledge of and experience with ACP, barriers and facilitators, use of ACP on their ward, whether any tools or materials are being used to conduct ACP, desired outcomes, and importance and feasibility of integrating ACP on the ward structurally. We first asked them what they understood ACP to be, and we used the definition of Rietjens et al. [36] to supplement their explanation. In addition, we proposed components of FACE [37] – at that point in time, the only pACP intervention that demonstrated effectiveness in paediatric oncology [5] – to get an impression of the fit of such an intervention in our local context.

Step 2: Identification of evidence

We performed a scoping review of academic and grey literature via PubMed and Google Scholar on existing pACP tools and interventions, barriers and facilitators in performing ACP conversations for families and healthcare professionals. The first author (AVD) performed hand searches using terms such as ‘advance care planning’, ‘goals-of-care conversations’, ‘interventions’, ‘tools’, ‘paediatrics’, ‘adolescents with cancer’ and selected and summarized literature.

Step 3 and step 4: Development of a logic model, including processes, outcomes and intervention components

The process of developing and adapting the logic model (Step 3) ran synchronously with the adaptations made to the intervention components (Step 4). Whenever we adapted the logic model, the components were adapted accordingly. Decisions about adaptations were made by reaching consensus within the core research team through monthly meetings (in total, approximately ten meetings were held). Several activities were performed chronologically to develop and refine both the logic model and, accordingly, the intervention components:

1. Identification of core components and proposing these to an international advisory group: Intervention components are defined as the parts of the complex intervention that are distinct from, but compose the whole of the intervention in full or in part [38]. We first identified five core components of the pACP intervention, based on the results of the interviews with healthcare professionals and the literature review (step 1 & 2). We contacted researchers and healthcare professionals working in the pACP field worldwide and sent them an e-mail asking them to give feedback on our identified components. We included the underlying evidence and rationales for each of the five components and gave selected members the option to give feedback in any way they preferred. Guiding questions presented to them were: “Are any important components missing?”; “Which components do you find most important?”; and “Do you acknowledge and support our findings?”. We included the feedback of this international advisory group in the following phases of the development process. Researchers who were in the process of developing a pACP intervention, or who have studied the effects of pACP, were contacted further by digital meetings. These researchers included the developers of pACP interventions IMPACT [18] and FACE [5, 39].

2. Development of the logic model: After discussions within our core research team, we developed a preliminary logic model to define desired outcomes and to be able to specify pathways through which the pACP intervention would change desired outcomes.

We applied the Theory of Planned Behaviour (TPB) [40] as a guiding framework for the development of the logic model, integrating the results from previous steps 1 and 2. The TPB postulates that intention, the most important determinant of behaviour, is in turn determined by conceptually independent constructs such as attitude and self-efficacy [40]. The TPB was chosen because it has proven to be a useful framework for designing behaviour change interventions and for explicating the mechanisms by which interventions are expected to exert their effects on behaviour [41]. In developing and adapting the logic model, we strove to fulfil three conditions for effective behaviour change: i.e., the target concepts must be: 1) determinants of behaviour; 2) amenable to change via intervention; 3) able to be translated into a practical application in a way that preserves the parameters for effectiveness and fits with the target population, culture and context [42]. The ACP process is complex – for instance, it involves many different actors, such as the patient, informal caregivers, and different kinds of healthcare professionals who ideally engage in different ACP behaviours [43]. This indicates the need for a complex intervention including multiple components, complicated or multiple causal pathways, feedback loops and mediators or moderators of effect, and potentially targeting multiple groups of participants [44].

The preliminary logic model and draft intervention components were proposed to: 1) psychologists purposively recruited via a special Facebook page for psychologists in Flanders, snowball sampling and by contacting the paediatric oncology departments of the hospitals. We decided to include feedback from psychologists due to the psychosocial aspects of ACP and their expertise in facilitating communication, and we met with them individually; and 2) members of the Pediatric Palliative Care Research Network (PPCRN), an interdisciplinary, multi-centre team of researchers and clinicians specialized in paediatric palliative care, set up by the Dana-Farber Cancer Institute (USA).

3. Feedback sessions with researchers experienced in paediatric ACP intervention development: two additional feedback sessions were held with two experienced researchers in paediatric palliative care who developed the IMPACT ACP intervention [18] in the Netherlands (MK and JF). We involved them in the BOOST pACP intervention development process from the moment we noticed that the IMPACT goal and materials represented a good fit with the logic model (see **section 3.2** for more information).

Step 5: Testing of acceptability and feasibility of the intervention

Within this study, the term ‘acceptability’ refers to determining how well an intervention is received by the target population and the extent to which the new intervention, or its components, meets the needs of the target population and organizational setting [45]. To test acceptability of the intervention materials (Step 5a), we performed semi-structured individual interviews with the target groups: i.e., adolescents who are currently being treated for cancer or individuals who finished treatment in their adolescence, parents of adolescents with cancer, and healthcare professionals working at a paediatric oncology department (nurses, psychologists and oncologists). Participants were recruited via paediatric oncologists and psychologists from two University Hospitals and support organizations that posted a flyer on their social media. Interviews took place either at the participant’s home, or online (in conformance with the local COVID-19 measures). During these interviews, intervention

materials were presented on paper or online to the participants for them to review. We discussed in depth the relevance and formulation of the themes and main questions mentioned on the intervention materials with the adolescents, parents and healthcare professionals. If questions were perceived as confrontational, the core research team re-evaluated the risk of formulating questions and phrases that negatively affect the relationship in the conversation, on the one hand, to the degree to which this was important to the goal of the study, on the other hand. This helped us to decide whether to adapt the formulation or remove the text entirely. In addition, two psychologists specialized in working with adolescents gave feedback on the materials.

In this study, ‘feasibility’ refers to the extent to which the intervention will be able to be delivered as intended [32]. We tested the core intervention components with three families in the feasibility test [46] (Step 5b). The families were recruited by healthcare professionals in the University Hospitals of Ghent and Brussels. AVD performed semi-structured interviews regarding their experiences.

All interviews (Steps 1, 4 and 5) were audio-recorded and transcribed. We applied thematic analysis by hand to structure the participants’ feedback. Suggested adaptations were discussed with the core research team in multiple meetings.

2.3. Ethical approval

The methods outlined in Step 5 were approved by the Medical Ethics Committees of the Ghent and Brussels University Hospitals (B1432020000060) in Flanders, Belgium.

3. Results

Throughout the development process, we further specified the content and rationale of the BOOST pACP intervention, which resulted in several prototypes through which the intervention evolved (**Additional file 1**). Given the iterative nature of the work performed, results are described according to the objectives of the study, rather than the chronological steps outlined in the methods section.

3.1. Participant characteristics

During Step 1 (Problem identification), 11 healthcare professionals working at a Flemish paediatric oncology department participated (four oncologists, two psychologists and five nurses). During Step 3 (Development of a logic model) and Step 4 (Intervention design), we contacted 17 healthcare professionals and experts working in the field of pACP worldwide, of whom 11 responded (65% response rate). Feedback on the logic model was provided by eight local psychologists, members of the Pediatric Palliative Care Research Network (PPCRN) and two experienced researchers. During Step 5a (Acceptability of the intervention), four adolescents and young adults (AYAs) who were at that time being treated for cancer or finished treatment in their adolescence, six parents, and nine healthcare professionals (nurses, psychologists and oncologists) working at a Flemish paediatric oncology department (**Table 1**) were involved. During Step 5b (Feasibility of the intervention), two 13-year-old adolescents and one 17-year old adolescent participated together with one parent. The core research team led and supervised the development and testing throughout all steps.

Table 1. Characteristics of stakeholders involved in Step 5a: acceptability of the intervention

Participants	Adolescents and young adults	Parents	Healthcare professionals
Gender			
Male	2	1	-
Female	2	5	9
Age*			
Mean (SD); range	19.25 (2.86); 16 – 23		
<30 years old	-	-	2
30 – 39 years old	-	1	1
40 – 49 years old	-	5	1
>50 years old	-	-	5
Time since diagnosis			
<1 year ago	1	-	-
>3 years ago	3	-	-
Highest education			
Lower secondary education	-	1	-
Higher secondary education	-	2	-
Graduate	-	1	-
Bachelor	-	2	2
Master	-	-	7
Family situation			
Married/living together	-	5	-
Single parent/unmarried	-	1	-
Provider type			
Paediatric oncologist	-	-	2
Clinical remedial educationalist	-	-	1
Clinical psychologist	-	-	4
Specialist in palliative care at home	-	-	2
Work experience within field of paediatric oncology			
<5 years	-	-	4
5-10 years	-	-	1
11 – 20 years	-	-	1
>20 years	-	-	3

Values are numbers

*Age categories are not applicable to young adults and adolescents as they were all younger than 23

3.2. Barriers and facilitators for pACP in the context of paediatric oncology and identification of existing tools and interventions to identify components (objective 1)

The challenges indicated by healthcare professionals are mostly system-, attitude- or parent-related factors (**Box 1**), many of them corresponding with findings from the literature [18, 23, 25, 47]. Findings from the interviews confirm that ACP is complex and not only dependent on healthcare professionals' behaviour, but also on broader patterns that should be targeted within an intervention, such as the way the family has been communicating with the medical team throughout their treatment.

Box 1. Barriers and facilitators for pACP from the perspective of healthcare professionals working in paediatric oncology

Barriers	Facilitators
- ACP is not yet performed structurally - conducting ACP is deemed difficult - lack of time during standard consultations - insecurity about the timing of such conversations - too little training to perform ACP conversations - lack of structure in the way the medical team works hinders involving the other team members - afraid of not being able to deal with the family's emotions - afraid of losing the parents' trust when discussing certain themes with the patient - perceived lack of parental readiness to talk about ACP themes - because the child's situation can change rapidly, professionals do not always see an added value regarding starting a conversation on their current or future preferences - the idea that you are only able to discuss ACP themes when the patient or parent him- or herself opens up the conversation, or that it is necessary to perform ACP in an indirect way to almost hide what they mean, is illustrated by this quote from a participant: <i>"it's an art isn't it, to try and bring it up in a way that they don't notice you want to talk about it."</i> - the idea that, in the oncological target group, ACP is less needed and is done sufficiently due to the relatively clear illness trajectory compared to other groups with complex chronic conditions	- agreement that conducting ACP conversations is important, and that it is essential to start talking about ACP themes rather early in the illness trajectory - the view of ACP as a broader process and not only with the end goal of completing an advance directive - the belief that ACP would lead to more involvement of the adolescent in their treatment, and that the family is better informed about the different potential trajectories - the belief that ACP will give the family peace of mind, as they will have discussed ACP themes and thought about different potential trajectories, making it easier to make difficult decisions when needed. - consensus about the criteria the facilitator performing the BOOST pACP conversations should adhere to: have experience with talking with adolescents with cancer, have good communication skills and have sufficient time to conduct the conversations.

We identified several ACP tools and interventions in the literature: My Choices [48], Voicing My Choices [22, 49], the family-centred advance care planning (FACE) intervention [50], FINK (Family Interaction Nurtures Kids) cards [51] and the Implementing Paediatric Advance Care Planning Toolkit (IMPACT) [18]. In particular, IMPACT followed a rationale that we identified as important as it matched with findings from the interviews with healthcare professionals: namely, aiming to generate an open conversation on a comprehensive set of ACP themes among clinicians, parents and the child. IMPACT consists of a set of materials for both clinicians and families to prepare, conduct and document ACP conversations and a two-day clinician training. IMPACT can be used in early phases of the illness trajectory and is primarily focused on defining shared goals of care and treatment instead of on filling out an advance directive. The pilot evaluation of IMPACT showed that participants perceived that all of the themes mentioned in the materials were appropriate for discussion with children with life-limiting conditions and their families [18], incorporating a holistic person-centred approach and

stimulating the exploration of the voice of the child. These materials also seemed applicable for our specific target group. We selected several IMPACT components with agreement from the developers, such as the preparation booklets, the ACP themes from the conversation guides, the summary sheet and the training and adapted these to the specific target group of the BOOST pACP intervention.

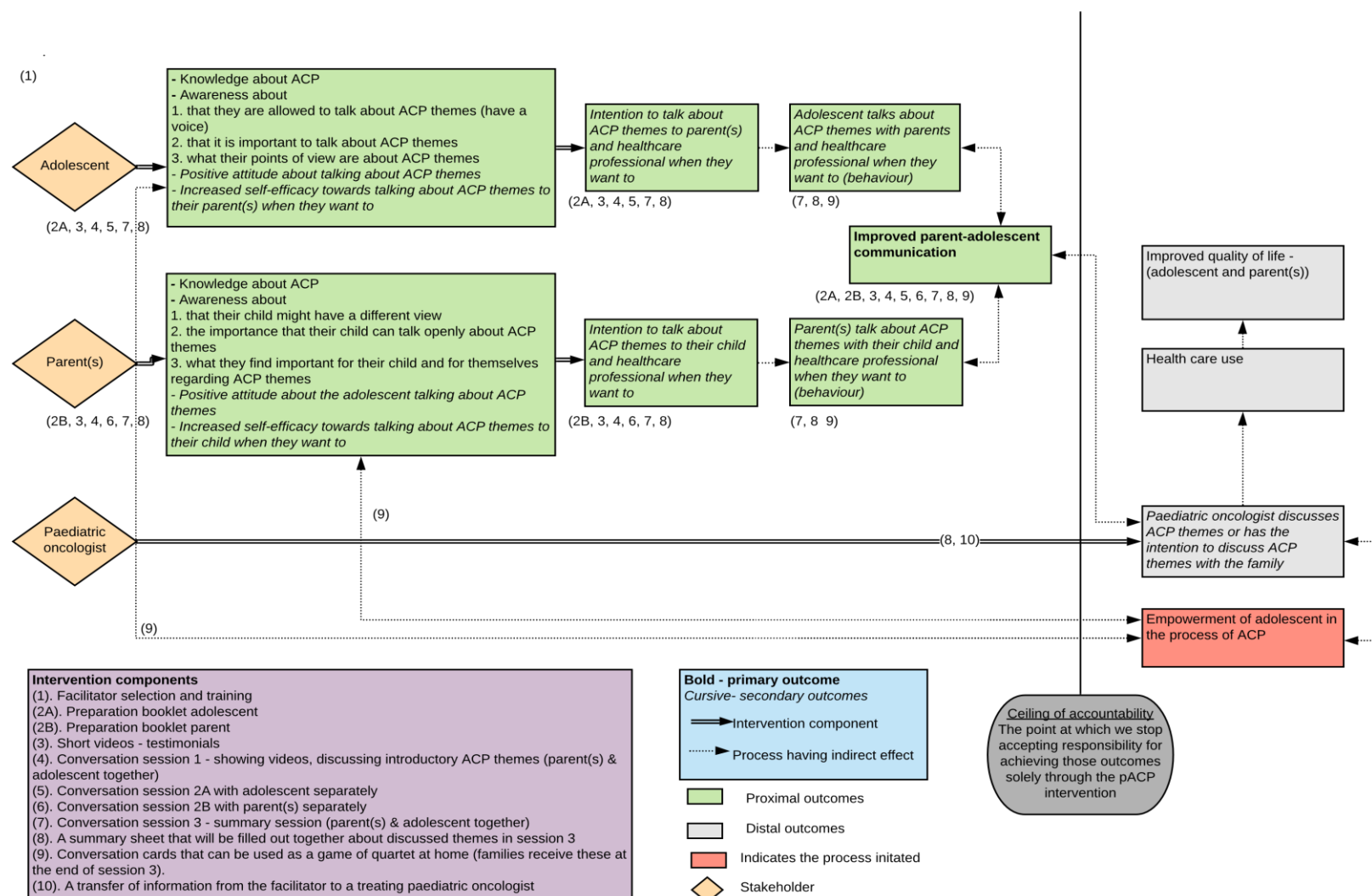
3.3. The BOOST logic model (objective 2)

The logic model of the resulting BOOST pACP intervention is displayed graphically in **Figure 2**.

The main goal and primary outcome of the BOOST pACP intervention is to improve parent-adolescent communication on ACP themes. In turn, improved parent-adolescent communication on ACP themes would lead to improved communication between the family (parents and adolescent) and the paediatric oncologist, further facilitated by the transfer of information derived from the ACP conversations from facilitator to paediatric oncologist.

Following the TPB, important secondary goals of the intervention are: an increased self-efficacy towards, and a more positive attitude about, talking about ACP themes, in combination with more knowledge about ACP and awareness about their own role in the communication process. Based on this logic model, ten different intervention components were constructed.

Figure 2: Logic model of the resulting BOOST pACP intervention



Footnote: Proximal outcome = an outcome that can be realized in a short time. Distal outcome = an outcome that can be realized in the long-term [64]

3.4. The resulting BOOST pACP intervention

The resulting BOOST pACP intervention comprises ten intervention components, which are summarized in **Table 2** according to the TIDieR (template for intervention description and replication) checklist [52]. **Table 3** gives an overview of the rationale for each of the intervention components and their specific content. The rationales are based on existing evidence and feedback from stakeholders throughout the different steps of the development process. **Additional file 2** describes the content of the components and intervention materials in more detail.

A total of four conversation sessions are at the core of the BOOST pACP intervention: two conversation sessions are held with the adolescent with cancer and their parent(s); two of the sessions are held separately. **Figure 3** depicts the conversation cards used in the conversation sessions 1, 2a and 2b.

Conversation session 1 (with adolescent and parent(s)): The goals of this session are to: 1) inform the family about the upcoming conversations and the BOOST pACP intervention; 2) introduce the family to the concept of advance care planning; and 3) positively affect the attitude and self-efficacy of the family regarding talking about ACP themes with one another. In this session, videos with testimonials of two families talking about their personal situation and experienced effects with the BOOST pACP intervention are shown and two introductory themes are discussed, using conversation cards.

Conversation session 2a (with the adolescent): The goals of this session are to: 1) explore the adolescent's point of view on several ACP themes and to what extent he or she has the need and opportunity to talk about these themes with his or her parents; 2) give the adolescent insight into the themes he or she would like to discuss with his or her parents and discuss ways to do this; and 3) normalize talking about ACP themes. Adolescents can choose what themes they want to discuss with the facilitator and the order in which to do so. They may choose to not discuss certain themes.

Conversation session 2b (with the parent(s)): The goals of this session are to: 1) explore the parents' point of view on several ACP themes and the extent they talk about those themes with their child; 2) give the parents insight into themes they would like to discuss with their child and discuss ways to do this; and 3) normalize talking about ACP themes. Parents can choose the themes they want to discuss with the facilitator and the order in which to do so. They may choose to not discuss certain themes.

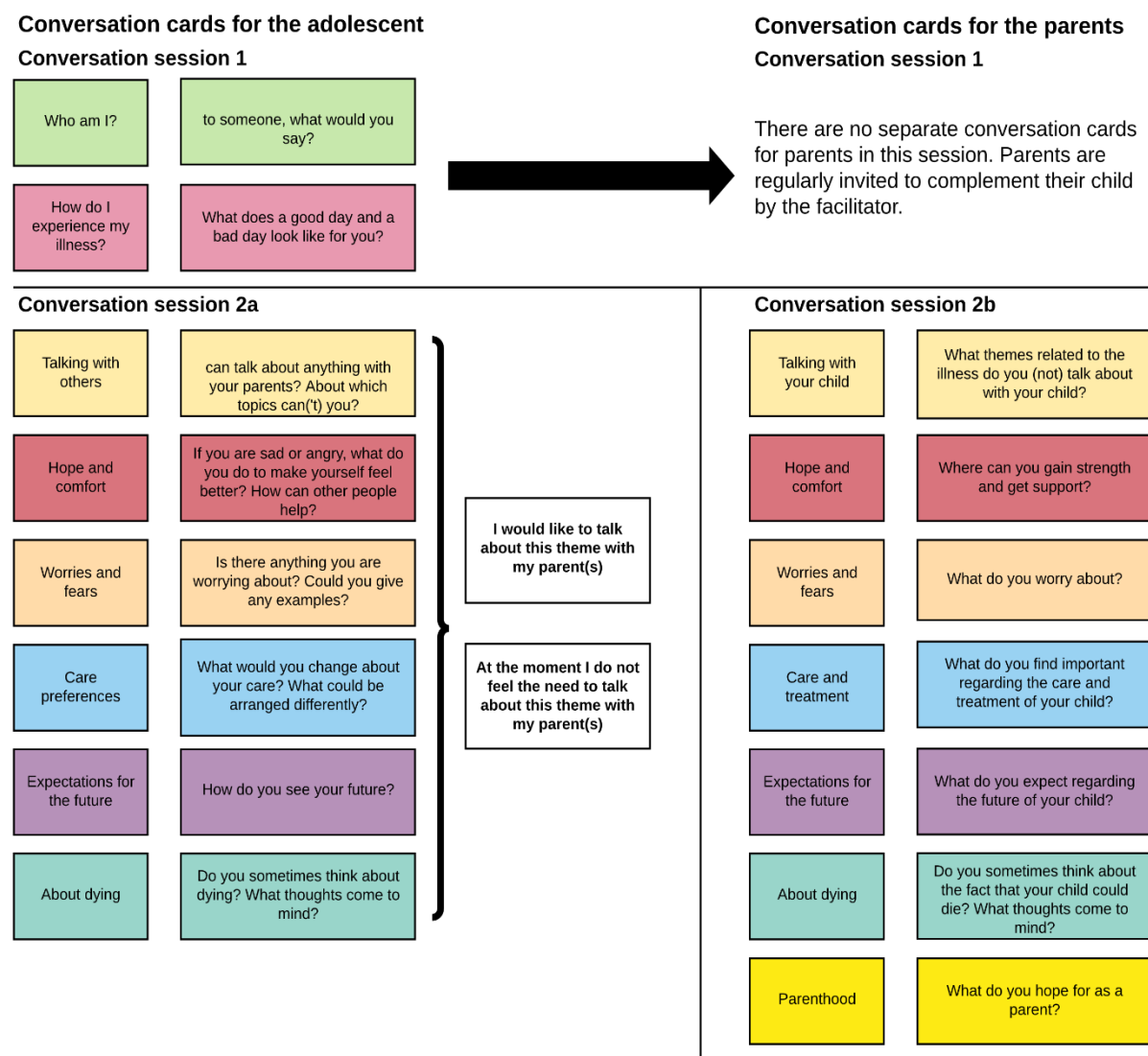
Conversation session 3: The goals of this session are to: 1) give the adolescent and parents the opportunity to discuss ACP themes; and 2) bring together the information from the other sessions and to fill out a summary sheet and discuss whether the facilitator may plan a transfer of information with the paediatric oncologist.

Table 2. Description of the final BOOST pACP intervention according to the TIDieR checklist

Timing	Intervention component (n=10)	Supporting material(s)	Intervention activities, procedures and processes
Prior to start of program and approximately every six months	1. Facilitator selection and training	Facilitator manual outlining all steps of the conversation sessions (including extra follow-up questions for each conversation card)	- Selection of two external facilitators - Preparation of facilitators for the training - Two-and-a-half-day training program for facilitators focused on conversation skills and consisting of theoretical explanation and role plays - Debriefing sessions for facilitators (discussing challenges in case studies) approximately every six months for facilitators (four hours)
At least one week before conversation session 1	2. Preparation booklets for adolescent (2A) and parents (2B)	Separate booklet for parents and adolescent including information about ACP and questions to trigger the thinking process about ACP themes	- Data collectors give preparation booklets to the families that are assigned to the intervention group or send the booklets via e-mail - Adolescent and parent(s) have the option to read their preparation booklet before conversation session 1 takes place
During conversation session 1	3. Short videos of two families talking about their experiences with the intervention	Videos with testimonials of two families talking about their personal situation and experienced effects of the BOOST pACP intervention	- The facilitator introduces the videos that will be shown in conversation session 1. - Adolescent and parent(s) watch the videos during conversation session 1. - The facilitator asks whether the adolescent and parent(s) recognize any aspects from the videos.
One – two weeks after having received the preparation booklets	4. Conversation session 1	Facilitator intervention manual and conversation cards	- The facilitator guides the conversation session and introduces the conversation cards to the adolescent and parent(s)
One – two weeks after conversation session 1.	5. Conversation session 2a	Facilitator intervention manual and conversation cards	- The facilitator guides the conversation session with the adolescent alone, using the structured conversation guide outlined in the intervention manual and conversation cards. The conversation is tailored to the preferences of the adolescent (e.g., to (not) discuss ACP themes and the order).

One – two weeks after conversation session 1. Often planned on the same day as session 2a.	6. Conversation session 2b	Facilitator intervention manual and conversation cards	- The facilitator guides the conversation session with the parent(s) alone using the structured conversation guide outlined in the intervention manual and conversation cards. The conversation can be tailored to the preferences of the parent(s) (e.g., to (not) discuss ACP themes and the order).
One – two weeks after conversation session 2b	7. Conversation session 3	Facilitator intervention manual	- The facilitator guides the conversation session with the adolescent and parent(s), using the structured conversation guide outlined in the intervention manual and gives room for them to discuss ACP themes.
During conversation session 3	8. Summary sheet	Summary sheet on which the same themes discussed during the conversation sessions are covered. If given permission by the family, the facilitator will send the summary sheet to the paediatric oncologist to include in the patient's electronic dossier.	- The facilitator introduces and explains the summary sheet. The facilitator asks whether the family would like the information they write down to be shared with the paediatric oncologist/medical team.
At the end of conversation session 3	9. Conversation cards	Conversation cards that can be used as a game of quartet at home whenever the family members would like to.	- The facilitator explains the purpose of the quartet game and that the cards can facilitate communicating on ACP themes together at home in a playful way.
Within one month after conversation session 3	10. Transfer of information from ACP facilitator to the paediatric oncologist involved in the care of the adolescent	The summary sheet is used during the transfer of information.	- If the family has given permission, the facilitator makes an appointment with the paediatric oncologist involved in the care of the adolescent, indicated by the family. - The facilitator gives a summary of the conversations with the family to the paediatric oncologist and asks whether he or she can add the summary sheet to the patient's electronic dossier.

Figure 3: Conversation cards used by the conversation facilitators during conversation sessions 1, 2a and 2b



Footnote: To integrate structure into the conversations structured by the conversation cards, one main question is printed on the back of the conversation cards. In the intervention manual, the follow-up questions are listed. Two of these follow-up questions will be asked of every participant. The remaining questions in the intervention manual can be used by the facilitator, depending on what course the conversation takes and to allow flexibility.

Several aspects of the intervention can be tailored according to the family's personal preferences: 1) they can decide what ACP themes they do or do not want to discuss during the conversation sessions with the facilitator; 2) they can decide on the location of the conversation sessions: either at their home, at the hospital, or online. The last option was offered taking the persisting COVID-19 measures into account. We have developed a structure to perform the conversations in a similar way online as in real life and tested this during the feasibility test; 3) planning/timing of the conversation sessions: according to our protocol, we anticipated a maximum of two weeks between the conversation sessions. However, due to the child following treatment and experiencing side effects and parents juggling responsibilities at work, school and hospital appointments, we allow flexibility in the

planning of the conversation sessions while aiming to finalize all conversation sessions within four months.

Table 3. Specification of, and rationale for, the identified intervention components and materials throughout the development process

Intervention components	Rationale/evidence for the component	Illustrative quote
Facilitator	Should be external to the medical team, because the goal is to test the effectiveness of the BOOST pACP intervention in a randomised controlled trial – and otherwise there is a risk of contamination. None of the parents and adolescents we interviewed disliked the idea of discussing ACP themes with a facilitator they do not personally know yet.	“We have children in our hospital that have five different treating oncologists. Which of these oncologists should be involved in the intervention and in what way? They don’t have time.” (Healthcare professional 4)
A training program for facilitators	Ongoing training of facilitators is important, both regarding conversation skills and steps necessary for the study. We added at least two debriefing sessions.	“An initiation training is important, but it is also essential to provide ‘coaching on the job’ sessions.” (Researchers who developed IMPACT– respondent 1)
Multiple conversation s structured by a conversation guide	ACP is a process, tailored to the needs and readiness of parents and adolescent. The conversation guide is therefore not rigid. However, it provides the necessary structure. Four conversations within three months was considered feasible by parents and adolescents. Healthcare professionals doubted whether 60 minutes per conversation would be sufficient.	“You don’t win trust in one conversation and ACP is a process so it’s good you are proposing several conversations.” (International advisory group – respondent 3)
Patient tools (suitable for adolescents)	We added conversation cards to give structure to the conversations. Adolescents and parents liked the idea of using conversation cards and that they are able to decide themselves what themes to discuss or not to discuss. This gave them a structure but at the same time a certain freedom and opportunity to identify their own needs. Optional person-centred exercises for facilitators to use were added in case the adolescents find it difficult to respond to the questions. Conversation cards that can be used as a game of quartet were added to give the family the opportunity to continue ACP communication whenever they want to.	“Conversation cards work very well to involve children in a playful way. You get different conversations when using these kinds of tools.” (Healthcare professional - respondent 11)
Documenting the outcomes of the conversation s	Introducing an advance directive in the last conversation session would not fit with the goal of improving parent-adolescent communication and the step-by-step approach and broad target group of the intervention. Therefore, the content of the summary sheet matches the content of the conversation sessions.	“It is very difficult for parents to put end-of-life preferences on paper in a concrete way. They associate it with giving up and think that nothing will be done to help their child anymore.” (Healthcare professional 7)
Transfer of information	The participants stressed the importance of a link between this external facilitator and the medical team to ensure continuity of care. Responsibility for transferring the information from the ACP conversations should not lie with the families themselves, but should be built into the intervention. If given permission by the	“If your aim is to get a result concerning ACP, you will have to make sure a healthcare professional is involved in some way in your

	family, the summary sheet is sent directly to the paediatric oncologist, and the facilitator has 30 days to plan the transfer of information with the paediatric oncologist.	intervention." (Researchers who developed IMPACT–respondent 2)
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3.5. Important adaptations for enhancing acceptability and feasibility of the BOOST pACP intervention (objective 3)

Adaptations to enhance acceptability: specific changes to the conversation/ intervention materials changes

We implemented several adaptations in the formulations of the text in the materials. For example, one of the categories was called “Parenthood” in the parents’ session. The main question formulated was “what kind of parent would you like to be?”, which was perceived as confrontational by several parents, illustrated by this quote:

“As a parent, you completely ignore your own needs. You just want to try your best to improve your child’s situation. It’s not relevant what kind of parent you would like to be.

That question would be offensive to me.” [Parent 3]

To avoid immediate resistance from the parents, we decided to rewrite that question to: “what do you as a parent hope for regarding your child?”. This question elicited similar responses – namely, that they hoped their child would recover and experience few long-term effects. However, this question proved to be an appropriate opening question for this theme and was therefore retained. Similarly, regarding the questions meant for the adolescent, one healthcare professional warned to be careful regarding the question “Did you have symptoms for a long time before your diagnosis?”, because it was thought to potentially lead to feelings of guilt about why they did not go to the doctor sooner. We therefore removed that question.

In other cases, there was disagreement about whether questions were perceived as confrontational or useful. An example is: “Suppose the situation of your child worsens, what do you find important regarding his or her care?”. Due to some participants explaining that they recognized themselves in struggling with that question and therefore confirmed its relevance for the study, we retained that question. Healthcare professionals, as well as AYA’s and parents, indicated that the theme “Fears” should be changed into “Fears and worries”. Furthermore, the separate theme “Decision-making” was removed in the conversation sessions 2a and 2b, due to the participants’ explanation that they feel that they do not have many opportunities to ‘make decisions’ because they are following a treatment plan. Several questions that were still relevant were merged into the theme “Care and treatment”. For some ACP themes, the questions that were listed as follow-up questions at first proved to be more appropriate for eliciting responses compared to the main question. Therefore, in those cases, the order of the questions was changed.

Feasibility outcome: Families were positive about the tested BOOST pACP intervention components

In the feasibility test, the families received the preparation booklets a week before the first and only ACP conversation, including the videos and filling out the summary sheet. The facilitator performed the transfer of information with the paediatric oncologist. The three families who participated in our feasibility test reported appreciation of the components and found the materials applicable to paediatric oncology as illustrated by direct quotes (**Additional file 3**). Although we tested only a part of the intervention, some family members indicated that they experienced added value and thought it was a pleasant conversation. We did not make further considerable changes to the content of the materials.

4. Discussion

The BOOST pACP intervention is developed for adolescents with cancer and their parents to improve parent-adolescent communication on ACP themes and to increase the adolescents' involvement in their own care and treatment. We applied an iterative step-by-step approach during which adolescent (ex)patients, their parents, healthcare professionals and pACP experts were involved to develop and test the acceptability and feasibility of the intervention. The resulting 'BOOST pACP' intervention considers ACP as a broad concept to be initiated early in the illness trajectory. Using a structured format of pre-specified ACP conversation sessions, the intervention targets ACP communication behaviour between the adolescents and their parents, but involves paediatric oncologists in the process. Involving these three important stakeholders in a systematic way has not been tested in previously developed pACP interventions. The final BOOST pACP intervention consists of ten components: 1) facilitator selection and training, including a manual; 2) preparation booklets for the adolescent and parents; 3) short videos with testimonials; 4 – 7) facilitated ACP conversation sessions; 8) a summary sheet; 9) conversation cards that can be used as a game of quartet; 10) transfer of information from facilitator to the paediatric oncologist).

The BOOST pACP intervention is deemed suitable for the particular population of children and adolescents between the ages of 10 and 18 years old by the involved experts, healthcare professionals, adolescents and parents. Evidence about effects of ACP on the younger age group (10 – 13 years old) has not yet been evaluated. We specifically include this younger age group as there is evidence that they are willing to engage in conversations about care and treatment [53, 54]. Their willingness and ability to talk about their care and treatment are known to be variable though, depending on the stage of the illness and maturity of the individual child [53–55], which was also emphasized by the psychologists who were involved in the intervention design. It is a particular requirement that the facilitators who will guide those conversations should be experienced and trained in performing conversations with children of this age. In the intervention manual, we offer person-centered planning exercises [56] for younger adolescents that can be used if facilitators notice the adolescent has problems with responding to the facilitator's questions. We do not only include adolescents with an unfavourable prognosis, as we believe that every adolescent with cancer might benefit from looking ahead to the future in light of uncertainties they might have experienced or will experience in the future [2]. That is why the BOOST pACP intervention regards ACP as a communication process not only about care and treatment preferences, but also about broader themes, such as what they find important in their life and what aspects of their illness they find most cumbersome. The intervention is set up in such a way that themes that are addressed within these conversations can be tailored to the adolescent's individual situation and readiness.

As outlined in the logic model, the primary outcome of the BOOST pACP intervention is to improve parent-adolescent communication on ACP themes to eventually contribute to normalizing ACP conversations in the illness trajectory. This might seem unconventional because better parent-adolescent communication does not necessarily directly lead to a better match between the treatment and care and the adolescent's preferences, and thus it has not been previously tested as a result of a pACP intervention. However, literature suggests that ACP is relational – meaning that it is enacted less as an individual directive and more as a

family-centred and social process [57], especially in the paediatric setting [58]. Moreover, there is evidence that there is significant room for improvement in parent-adolescent communication about themes related to the illness, treatment and living with the illness – and this was also indicated by the adolescents and parents we interviewed. Parent-child communication concerning prognosis and goals of care specifically is associated with various positive outcomes, such as positive adaptation [14], lower withdrawn/depression scores [59], and patient and family well-being [60]. A broad array of themes influence goals of care, such as how the illness and treatment are experienced, what their fears and worries are, what helps them in coping and what their expectations for the future are [18]. These themes are represented in the BOOST pACP intervention in the form of conversation cards.

The BOOST pACP intervention was constructed following two guiding principles:

- 1) ACP is an ongoing communication process [6, 29, 57] rather than sporadic conversations when there is bad news. We therefore aimed to either initiate ACP communication early or build further on existing ACP communication, recognizing that, to be able to think about and talk about future care preferences, this must be discussed in relation to the present and the past [61].
- 2) ACP should be tailored to the needs and readiness of the adolescent as well as the parents. The conversation cards give them the stage to talk about ACP themes by triggering the thinking process. At all times, participants can indicate verbally that they want to stop. Although contemplating sensitive issues regarding the future – like hopes, fears and worries – is a demanding and sometimes burdensome endeavour for parents, it is important to consider that this parental unease does not reflect unwillingness to talk about these issues [61].

We have invested a considerable amount of time in identifying interventions and tools that have been developed elsewhere that have the possibility of being adapted to our local paediatric oncology context, as emphasized in the update of the framework for developing and evaluating complex interventions of the Medical Research Council [33]. Within this research study, we used the Theory of Planned Behaviour (TPB). In research regarding advance care planning and other themes related to end-of-life care, the use of behavioural theories has been reported to be still limited (although use is increasing) [62]. As many behaviours can determine the quality of care, the more extensive use of underlying behavioural theories may be warranted if we want to better understand and influence behaviours and normalize ACP. The development of the logic model has helped us to define desired outcomes and to specify pathways through which the BOOST pACP intervention can potentially achieve change [40]. Reviews of research on changing a variety of health behaviours have shown that interventions based on theory or theoretical constructs are more effective than those not using theory [63]. Before we tested the acceptability and feasibility of the BOOST pACP intervention with the end-users, we processed feedback on the formulation of ACP themes and questions in the intervention manual from the two psychologists specialised in working with adolescents who we hired as intervention facilitators. Their involvement supported a feeling of ownership and familiarization with the BOOST pACP intervention, which increases the chance of high motivation to perform an intervention that they support and to enhance implementation fidelity.

Our detailed overview of the development process of the BOOST pACP intervention can serve as an example for other researchers that aim to develop a complex intervention in a limited timeframe of two years. We have experienced that applying a step-by-step approach in

different stages – during which the intervention is increasingly taking shape – and collecting feedback from a variety of suitable experts and the end-users is a time-efficient and appropriate approach, which allowed us to dive deeper into the core of which behaviours are targeted and likely to change. The combination with the use of a logic model facilitates the process of composing components that match predefined goals. This can increase the chance of an intervention having desired effects and improves the sustainability of those effects.

The study has several limitations. First, due to BOOST pACP being a complex intervention focusing on communication, eligibility is limited to Dutch-speaking participants – and so our study lacks cultural diversity and its generalisability is limited. In the participating hospital wards, there are many families that do not speak Dutch and are thus unable to participate in ACP supported by BOOST. Second, we experienced difficulties in recruiting adolescents with cancer within the age range of our target group. We had hoped to interview more adolescents regarding the acceptability of the components and intervention materials and we included two individuals who had cancer in their adolescence instead. The inclusion of these two individuals does not necessarily have to be a disadvantage, because they have the ability to consider what ACP themes they would have found important to discuss in hindsight and what formulations are preferred. Although we did not use participatory methods to include adolescents with cancer in the early conceptualization of our BOOST pACP intervention, we integrated knowledge and experience of development projects with a comparable target group: namely, adolescents with a life-threatening illness. We will have to research applicability and required adaptations for adolescents with other complex chronic conditions and younger and adult populations.

In the next steps, the intervention will be tested in a multi-centre parallel-group randomised controlled trial, with an embedded mixed-methods process evaluation in paediatric oncology in Belgium[30]. This will result in more knowledge of the effectiveness of improving ACP communication between adolescents, parents and paediatric oncologists and on other potentially positive or negative effects. We will gain insight into how adolescents with different types of cancer in various stages and parents value advance care planning and shape this communication process in the semi-structured BOOST pACP format, leading to a better understanding of ways to facilitate a tailored ACP approach. Furthermore, we will improve the components and materials according to the participants' experiences and recommendations. In the future, if the BOOST pACP intervention proves to have positive effects, the task of facilitator could be carried out by a member of the medical team.

5. List of abbreviations

ACP advance care planning; pACP Paediatric advance care planning; PACS Parent-Adolescent Communication Scale; RCT Randomised controlled trial; MRC Medical Research Council; TIDieR Template for intervention description and replication; AYA Adolescents and young adults

6. Declarations

Ethics approval and consent to participate

All methods were carried out in accordance with the relevant guidelines and regulations. This study was approved by the Medical Ethics Committee of two hospitals in Flanders, Belgium

(University Hospital of Ghent and Brussels), where we recruited adolescents with cancer and parents for testing intervention components and materials in Flanders, Belgium (B1432020000060). Adolescents and parents were given ample time to consider participation and were assured that they were completely free to withdraw from participating in the study without any effect on their care. Before participating, written informed consent from both parents, if applicable, and written assent from the adolescent was obtained without any coercion.

Consent for publication

Written informed consent and assent forms also notified about, and included a statement about, consent to publication of anonymized non-identifiable and summarised data.

Availability of data and materials

The data are not publicly available because they are containing information that could compromise the privacy of research participants in this study.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

Conception and design of the work: AvD, ADV, MK, JF, JvdWtB, LD, JC, KB.

Ethics approval: AvD, ADV, JvdWtB, LD, JC, KB, MK

Drafting the work: AvD, JG, KB

Critical revision for important intellectual content: AvD, ADV, JG, MK, JF, LD, JC, KB

All authors have read and approved the final manuscript.

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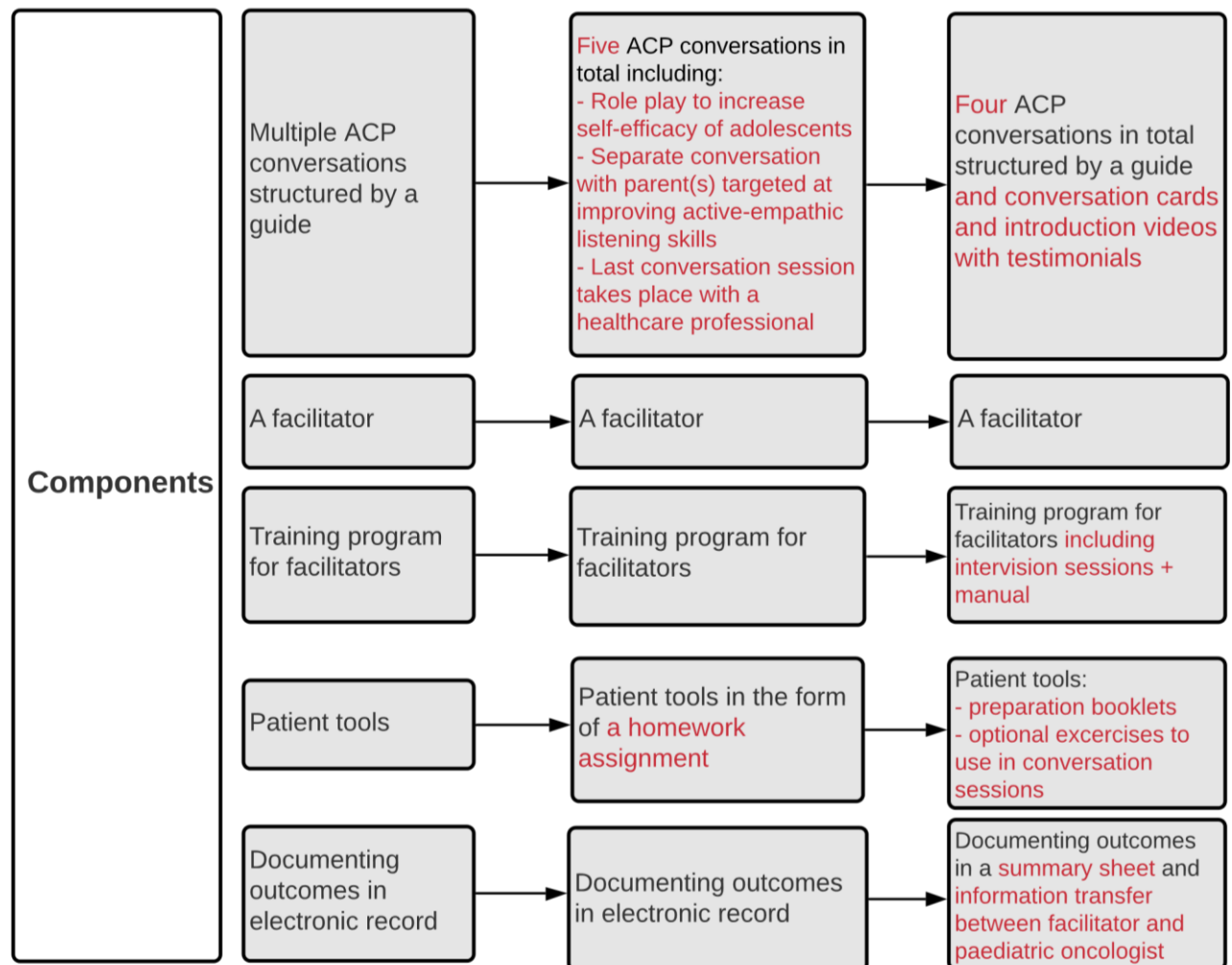
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Additional file 1. Evolution of specifications and adaptations to the BOOST pACP intervention components



Text in red highlights the specifications/adaptations to the BOOST pACP intervention components

Additional file 2. Content of BOOST pACP intervention materials

Component and accompanying supporting material(s)*	Content of the material(s)
1. Facilitator a) Facilitator training	Core training: Start-training program and accompanying PowerPoint presentations used for the 2.5-day training of the ACP facilitators. The training sections: - Relevant context – 1 day: - o Introduction to ACP - o The BOOST pACP intervention and its components - o Family adjustment and coping strategies when facing paediatric cancer [External speaker – Marieke Van Schoors] - o Paediatric advance care planning by using IMPACT [Speaker co-author JF] - o Oversight of general course of events in the Flemish hospitals (local context) - Training conversation skills [External communication experts – Wilde Kastanje Training and Education, the Netherlands] – 1.5 days Intermediate debriefing sessions - goals: - Exchange of experience by discussing selected fragments of conversations - Reflecting on the goals of the intervention and on behaviour: what should I maintain, what can I do differently? How did I cope with challenges? - Discuss in-depth what happened in the conversations and how the way facilitator's response may have impacted these situations
b) Facilitator manual	A manual for trained ACP facilitators who will perform the ACP conversations with adolescents and parent(s), including a description of steps to follow during and between the structured ACP conversation sessions. The sections of the manual: - Timeline of the study procedure for families in the intervention group - Preparation of the conversations - Steps to follow during the different conversation sessions - Transfer of information - Using person-centred exercises - General communication tips (summary of literature and from the training) - Extra suggestions for difficult conversations
2. Preparation booklets a) For adolescents	Adolescents can choose to fill out these booklets or only read them in preparation for the BOOST pACP conversation session. Title: Advance Care Planning What do you find important and how can we best take care of you? • About you - o What are your hobbies or interests? What do you love to do? - o What is important to you? And who are important people to you? - o What does your situation look like at the moment? Has your situation changed? What are you missing at the moment? What would

	you like in the future? • About your illness ○ What would you like to know about your illness? Do you have sufficient information? ○ Are there things about your illness you would like to know or would not like to know? ○ What do you dislike most about your treatment? ○ Are there any pleasant moments or experiences during your illness? ○ Are there things you are uncomfortable with or things you are dreading? ○ Do you sometimes worry about the treatment? • About how we can help you ○ How can your parents and the healthcare professionals help you? Is there anything they should take into consideration? ○ How can the people in the hospital help you? Is there anything they should take into consideration?
b) For parents	Parents can choose to fill out these booklets or only read them in preparation for the BOOST pACP conversation session. Title: Advance Care Planning What do you find important for your child? • About your child ○ What makes your child happy? ○ What is important to your child? ○ What is difficult for your child? • About your child's illness ○ What would you like to know about your child's illness? ○ Do you want to know more about the future? ○ Should the treatment not have the positive results you hoped for, what things do you want to be prepared for? • What do you wish for your child ○ What do you want for your child? ○ What do you worry about? ○ Do you want to know more about the future? • Care and treatment ○ What do you find important with regard to the care and treatment of your child? What does your child find important with regard to his/her care and treatment? ○ What do the healthcare professionals need to know about your child that could be important regarding the care and treatment? ○ If the treatment would not work well, what do you want or don't you want for your child?
3. Two short videos to be shown during the first ACP conversation session	Two families talk about their personal situation and experienced effects of the ACP intervention. Both scenarios describe that communication with each other about the illness and treatment was difficult for them and how several intervention components helped them in talking about such themes more. Two cases: - The first case is about a mother and her 13-year-old daughter who has been diagnosed recently - The second case is about a mother, father and their 16-year-old son

	who was diagnosed a few years back and has relapsed.
4. Summary sheet	The summary sheet covers similar themes that are covered in the conversation sessions. The facilitator guides the family in filling out this summary sheet and the family may decide whether this is shared with the medical team. If agreed, the facilitator schedules a transfer of information with the paediatric oncologist. We ask families to fill out their response on the summary sheet existing of the following statements: - I am someone who... - The illness means to me that... - The illness means to our family that... - As a family, we generally talk about the following themes... - We need to keep in mind to continue talking about... - I sometimes worry about... - Regarding my care and treatment, it is important to me that... - My expectations for the future are... - If my health deteriorates, it is important to me that... - Sometimes, these thoughts about dying come to mind... - I would like to schedule a conversation with my oncologist: - o Yes - o No, at this moment I don't feel the need to - Healthcare professionals are allowed to receive this information: - o Yes - o No - I would like to add that...
5. Conversation cards that can be used as a quartet	Conversation cards that can be used as a game of quartet at home whenever the family wants. Families will receive these cards at the end of session 3. Each theme consists of four questions. The different themes covered by the game of quartet are: - How do I experience the illness - Talking to others - Hope and comfort - Worries and fears - What care and treatment do you want? - Expectations for the future - About dying - Do it yourself (category with different active assignments)

This overview excludes the conversation cards used in sessions 1, 2a and 2b. These are presented in **Figure 3 in the main paper.*

Additional file 3. Illustrative quotes from adolescents and parents who participated in the feasibility test (families n=3), on the BOOST pACP core components

	Illustrative quotes
Adolescents	
Videos	"I recognized myself in the videos, because I cannot talk very well about certain themes with my father. And also in the second video about the boy who decided not to have further treatment. This was also recognizable because I don't want immunotherapy." [17-year-old girl with acute lymphoblastic leukaemia]
Conversation cards and themes discussed	"In the beginning I thought it was a bit strange, using the conversation cards. I thought, you can also just ask the question. But it was not very disturbing for me." [17-year-old girl with acute lymphoblastic leukaemia]
	"I really liked being asked how we saw my future. I don't discuss this with my doctors." [17-year-old girl with acute lymphoblastic leukaemia]
About the added value of the conversation	"For children that do not talk a lot with their parents and are guarded, I think this is of added value. But I talk about anything." [17-year-old girl with acute lymphoblastic leukaemia]
Parents	
Preparation booklets	"I liked the preparation booklets. They made me think about certain themes. It was a good preparation for the conversation." [Father of 13-year-old girl with acute lymphoblastic leukaemia]
	"The preparation booklet was a good tool to think about what themes I wanted to discuss and not discuss." [Mother of 13-year-old girl with diffuse large B-cell lymphoma]
Videos	"It's not like they were acting in the videos. These were real emotions, which is important I think." [Father of 13-year-old girl with acute lymphoblastic leukaemia]
	"After seeing the videos, I had this epiphany 'maybe I should be more concerned about that'." [Mother of 13-year-old girl with diffuse large B-cell lymphoma]
Conversation cards and themes discussed	"The questions on the conversations cards completely opened up the conversation, so in my opinion that was very positive." [Mother of 13-year-old girl with diffuse large B-cell lymphoma]
Summary sheet	"Sometimes it was difficult for me that the paediatric oncologist was not present. In the summary sheet, it was difficult to nuance and sometimes it seemed that we were criticizing the medical team, although we didn't mean to. However, the facilitator guided us very well." [Mother of 13-year-old girl with diffuse large B-cell lymphoma]
	"I hope the doctors already know, but we often repeat things – for example that our daughter prefers her medication in pills instead of syrup. I'm not sure if this is in her medical file or not. A lot of communication is going very well, but I have the feeling that there is also a lot of miscommunication. The more that is in the medical dossier, the better – also for the psychologists' follow-up in the future. However, they don't have a lot of time to read it." [Father of 13-year-old girl with acute lymphoblastic leukaemia]
About the added value of the conversation	"After our conversation, I think we realized we were all on the same page. I've always had that feeling. But in that week, we talked about some things that we would normally not specifically discuss. Not about heavy themes, but more about how [name child] was feeling. I'm glad we participated. For example, I had the feeling that their [referring to his partner and his child] visits to the psychologist were not that useful. Maybe because I never visit them and I don't feel the need to. But now I've talked about that with them and now I know that this visit is really useful for them and they really feel better. Without this conversation, I would have never asked them." [Father of 13-year-old girl with acute lymphoblastic leukaemia]
	"The most important message for me was that it is important to talk to

	each other about these themes and that I could indicate to my child that I'm concerned but that I'm always there to talk, and that we should not hide such things from each other." [Mother of 13-year-old girl with diffuse large B-cell lymphoma]
	"We are not really thinking about the more difficult themes yet. But talking about the easier themes has also contributed. These may not be the most essential or earth-shattering things, but it was still useful." [Father of 13-year-old girl with acute lymphoblastic leukaemia]

Chapter 2

ADVANCE CARE PLANNING FOR ADOLESCENTS WITH CANCER AND THEIR PARENTS: STUDY PROTOCOL AND PROCESS EVALUATION OF THE BOOST pACP MULTI-CENTER RANDOMIZED CONTROLLED TRIAL

This chapter is based on:

van Driessche A, De Vleminck A, Gilissen J, Kars MC, van der Werff Ten Bosch J, Deliens L, Cohen J, Beernaert K. Advance care planning for adolescents with cancer and their parents: study protocol of the BOOST pACP multi-centre randomised controlled trial and process evaluation. BMC Pediatrics. 2021;21(1):376 [2021 IF 2.567; Ranking Q3; ranking 68/130 in PEDIATRICS in SCIE edition]

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Abstract

Background: Research has highlighted the need for evidence-based interventions to improve paediatric advance care planning (pACP) in adolescents with cancer. Although adolescents express the desire and ability to share their values, beliefs and preferences for treatment, there is a lack of structured multicomponent interventions to improve parent-adolescent communication on different ACP themes including those not limited to end-of-life care. The aim of this study is to evaluate the effectiveness and implementation, context and mechanisms of impact of a novel ACP program in paediatric oncology.

Methods: We will conduct a multi-centre parallel-group randomised controlled superiority trial with embedded mixed-methods process evaluation in Flanders, Belgium. Adolescents aged 10 – 18 who have cancer, and their parent(s) will be recruited via all four university hospitals in Flanders, Belgium, and support groups. Families will be randomised to receive care as usual or the multicomponent BOOST pACP program, consisting of three conversation sessions between an external facilitator and the adolescent and parent(s).

The primary endpoint is improved parent-adolescent communication from the perspective of the adolescent. Secondary endpoints are adolescents' and parents' attitudes, self-efficacy, intention and behaviour regarding talking about ACP themes with each other, parents' perspective of shared decision making in the last clinical encounter, and the paediatric oncologist's intention and behaviour regarding talking about ACP themes with the family.

Measurements will be performed at baseline, at three months and at seven months using structured self-reported questionnaires. We will perform a process evaluation in the intervention group, with measurement throughout and post-intervention, using structured diaries filled out by the facilitators, interviews with facilitators, interviews with involved paediatric oncology teams, and audio-recordings of the BOOST pACP conversations.

Discussion: The BOOST pACP program has been developed to stimulate conversations on ACP themes between parent(s) and the adolescents, simultaneously lowering the threshold to discuss similar themes with healthcare professionals, initiating a process of normalization and integration of ACP in standard care. This combined outcome and process evaluation aims to contribute to building the necessary evidence to improve ACP in paediatric oncology.

Trial registration: The study is registered at ISRCTN.com (no. 33228289). Registration date: January 22, 2021.

Keywords: Advance care planning, paediatric palliative care, paediatric oncology, multi-centre randomised controlled trial, communication, adolescent, parent-adolescent communication

1. Background

1.1. Background and rationale

In Europe, cancer is one of the leading causes of death in children and adolescents [1]. A recent study from the Netherlands [1] found that the overall cancer incidence increased by an average of +0.6% annually over a 28-year period (from 1990 – 2017). This increase was seen particularly in infants and young adolescents [1, 2]. In Belgium, every year about 340 children (0 – 14 years) and 180 adolescents (15-19 years) are diagnosed with a malignancy [2]. Although survival rates for childhood cancer have steadily improved over the last few decades from 58% in the mid-1970s to over 80% today [3], disclosure of the diagnosis and subsequent treatment can still have a significant emotional impact on adolescents and parents and poor psychosocial outcomes that may in turn impact the well-being of the entire family [3].

In paediatrics, treatment decisions are routinely made by surrogates, in most cases parents [4]. Therefore, it is important that parents are aware of their child's preferences for care and their underlying values. The process of advance care planning (ACP) has been promoted as a successful strategy for communication between patients, surrogate decision-makers and healthcare professionals [5]. It is defined as a voluntary process of discussion and review enabling patients to express their views, values and specific treatment choices to inform their future care [6]. Studies in adults demonstrate a range of positive outcomes, including increased congruence between treatment preferences expressed by the patients and their caregivers and increased likelihood that these preferences will be honoured at the end of life [7]. Limited evidence in adolescents with serious illnesses has demonstrated that they have the desire and ability to share their values, beliefs and preferences for treatment at the end of life [8, 9]. In addition, although parents report finding it difficult to engage in ACP with their child, they consider it important, arguing for a sensitive, individualized and gradual approach where hope and quality of life issues are paramount [10].

Although international guidelines and medical societies such as The American Academy of Paediatrics, the Institute of Medicine, and the World Health Organization (WHO) strongly recommend ACP in paediatrics [11], research on specific ACP tools or programs is scarce. The few tools and programs concerning paediatric ACP that do exist [12–18], either lack robust evidence of their effectiveness, or are focused at documentation of end-of-life care preferences; c.q. advance directives, ignoring recent recommendations about ACP being a comprehensive communication process focusing on current and future care [19].

Engaging in ACP can provide an opportunity to address misconceptions about values, preferences and goals regarding current and future care, can improve understanding of the adolescent's prognosis, can contribute to preparing for future situations [20–22], and can lead to an increased sense of control and security in adolescents [10]. The limited evidence available suggest that families benefit from enhanced communication around ACP and the end of life, both among family members and between the family and the medical team [23]. However, we currently lack robust studies that have evaluated the effectiveness of pACP interventions that do not primarily address end-of-life care preferences.

We developed the BOOST pACP program (Benefits of Obtaining Ownership Systematically Together in paediatric Advance Care Planning) to improve parent-adolescent communication on pACP themes for a heterogeneous population of adolescents (age 10-18) with cancer, by

discussing a broad array of ACP themes not limited to end-of-life care and applying a structured format.

1.2. Objectives

We aim to evaluate:

- 1) The effectiveness of the BOOST pACP program on parent-adolescent communication about ACP themes, self-efficacy towards and attitude on talking about ACP themes with each other.
- 2) The implementation process of the BOOST pACP program, important contextual factors and mechanisms of action.

In reporting the study protocol, we followed the Standard Protocol Items of the Recommendations for Interventional Trials (SPIRIT) 2013 Checklist [24].

2. Methods

2.1. Study design

A multi-centre parallel-group randomised controlled superiority trial [25] (RCT) with embedded mixed-methods process evaluation, comparing the BOOST pACP program to standard care (control group). Adolescent patients and their parent(s) will be randomised with a 1:1 allocation ratio to the intervention arm or the control arm after baseline assessment. The mixed-methods process evaluation is structured according to the Medical Research Council (MRC) Framework by Moore et al. [26].

2.2. Study setting and population

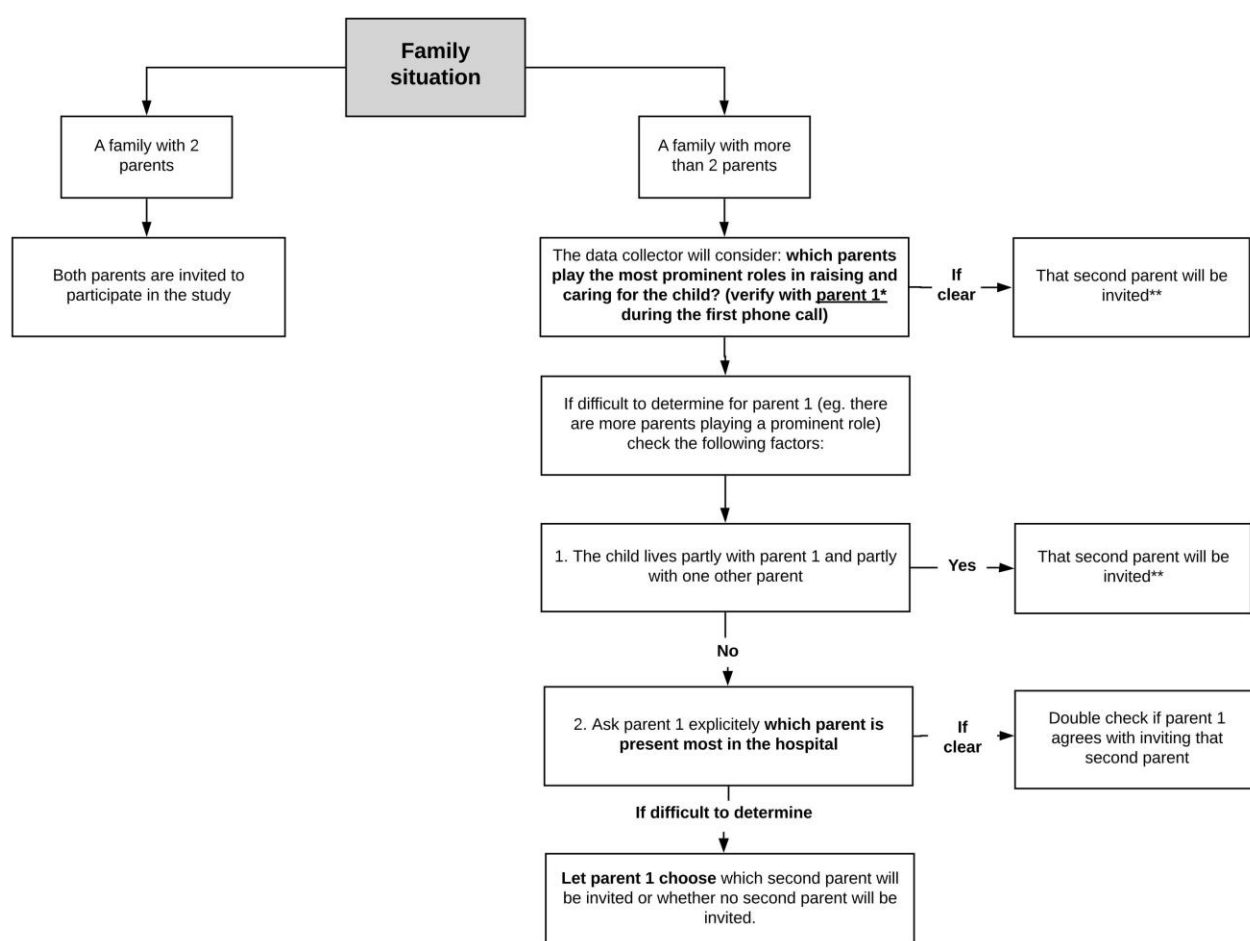
The study will take place in four participating university hospitals in Flanders, Belgium. Families in the intervention group have the choice of having the ACP conversations and visits from the data collector at home, in the hospital or online due to COVID-19 measures. The BOOST pACP program is targeted at adolescents, their parent(s) and involved paediatric oncologists. Inclusion- and exclusion criteria can be found in **Table 1**. Adolescents should be age 10 – 18, diagnosed with any type of cancer at any stage and currently receiving (active) oncology treatment. ‘Active treatment’ encompasses adolescents: 1) who are currently receiving treatment; 2) for whom treatment is planned; 3) for whom the last treatment took place maximally three months ago.

A maximum of two of the most involved parents will be invited to take part; the term “parent/s” includes legal guardians and stepparents. To determine which parents are to be invited into the study, data collectors will follow a flow diagram (**Figure 1**). In case there is only one parent, he/she will automatically be included. If there are more than two parents in the adolescent’s life (e.g. due to blended families), the two parents with the most prominent role in raising and caring for the child will be invited to take part in the study. If the latter is difficult to determine, the most prominent parent will decide which second parent will be invited to participate in the study. The most prominent parent is the one that is usually present and accompanies the adolescent to the hospital and during oncology care and treatment, and also identifies himself or herself as the most prominent parent.

Table 1: Inclusion and exclusion criteria of adolescents, parent(s) and paediatric oncologists

Inclusion criteria (combined by 'AND')	Exclusion criteria (combined by 'OR')
Adolescent	
Aged between 10 and 18 years	Participated in the feasibility test
Diagnosis of cancer $\geq$ 3 months prior to inclusion	Intellectual disabilities to an extent that general communication is very difficult, or serious mental health problems to an extent that the extra effort of participating in the study is not justified (estimated by the paediatric oncologist and psychologist)
Aware of, or informed about, cancer diagnosis according to parent(s)	Life expectancy $\leq$ 3 months
Receiving active treatment in a paediatric oncology ward	Not receiving active treatment (last treatment was more than 3 months ago)
Fluent Dutch language understanding	
Parent(s)	
Aware of, or informed about the diagnosis of their child according to the clinician	Participated in the feasibility test
Fluent Dutch language understanding	Intellectual disabilities to an extent that general communication is very difficult, or serious mental health problems to an extent that the extra effort of participating in the study is not justified (estimated by the paediatric oncologist and psychologist)
Paediatric oncologist	
Medically involved in the treatment of the adolescent, indicated by the family to be the oncologist with whom the family has most contact about treatment	
Fluent Dutch language understanding	

Figure 1: Flow diagram to identify and invite parents for the BOOST study



*parent 1 – parent with whom the data collector had contact about the study

**except when parent 1 does not want to participate together with that second parent

2.3. Intervention and control arm

Intervention: The BOOST pACP program

The “BOOST pACP” (**B**enefits of **O**btaining **O**wnership **S**ystematically **T**ogether in **paediatric Advance Care Planning**) program will be provided alongside any standard care in the intervention group. The main goal of the program is to improve communication about ACP themes between adolescents with cancer and their parents.

The program was developed by following a comprehensive iterative approach, informed by the supplementary guidance for the development of complex interventions by Bleijenberg et al. [27], in addition to the MRC Framework [28]. Using input from interviews with healthcare professionals and a review of the grey literature and the academic literature via PubMed, we developed a conceptual framework outlining the pathways through which the intervention would change desired outcomes. We then identified a pACP program in the Netherlands, called IMPACT (Implementing Paediatric Advance Care Planning Toolkit) [16], that matched the direction of the BOOST pACP program as defined by the conceptual framework. The IMPACT preparation booklets, the summary sheet and conversation structure were integrated into and adapted to the BOOST pACP program, in close collaboration with the developers of

IMPACT (MK, JF). All components were adapted in language and content to match the Flemish context and the specific goals and population of the program. Conversation cards were developed to structure the conversations, integrating a method that has been shown to facilitate open communication [29–31]. All materials were tested for acceptability and feasibility with adolescents and young adults (AYAs) with cancer (n=4), parents (n=6) and healthcare professionals (n=9), and adapted accordingly. The first BOOST pACP conversation session and transfer of information to the paediatric oncologist was tested with three families.

The program is described in **Table 2**, according to the TIDieR (template for intervention description and replication) Checklist[32].

The BOOST pACP program consists of ten key components:

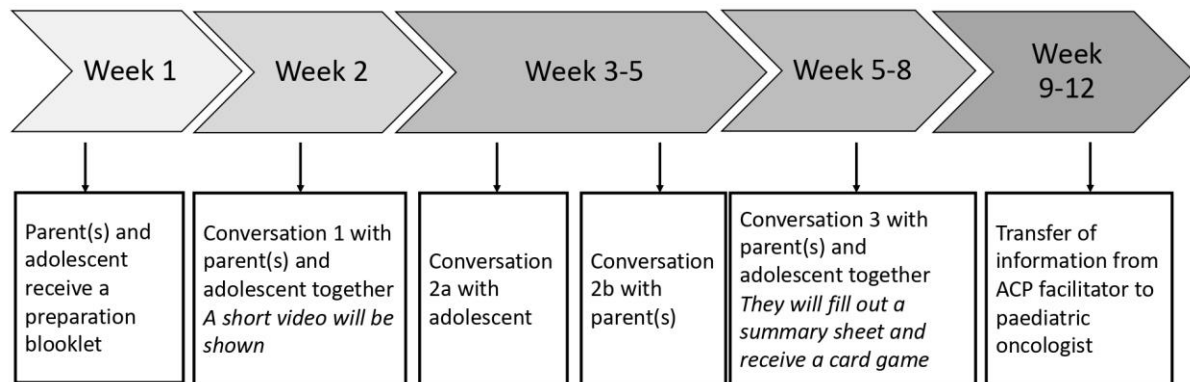
- 1) facilitator training, including manual
- 2) preparation booklets, sent to the home address of the parent(s) and adolescent
- 3) a video of two families talking about the experiences with the program, which will be shown during the first conversation session
- 4) facilitated conversation session 1 (involvement of both the adolescent and parent(s)), aimed at informing the family about ACP and the BOOST program, and stimulating a positive attitude and self-efficacy towards talking about ACP themes with each other. The session is partly structured by using conversation cards.
- 5) facilitated conversation session 2a (involvement of the adolescent), aimed at exploring the adolescent's views on ACP themes and what themes he or she would like to talk about with his or her parent(s) and how to talk about them. Session 2a is structured by using conversation cards.
- 6) facilitated conversation session 2b (involvement of the parent(s)), aimed at exploring the parents' views on ACP themes and what themes they would like to talk about with their child. Session 2b is structured by using conversation cards.
- 7) facilitated conversation session 3 (involvement of both the adolescent and parent(s)), aimed at revisiting ACP themes by filling out a summary sheet and leaving room for further discussion of ACP themes if preferred by the family.
- 8) a summary sheet that will be filled out together by the adolescent and their parent(s), during conversation session 3.
- 9) conversation cards that can be used as a game of quartet at home.
- 10) transfer of information from the ACP facilitator to the paediatric oncologist involved in the care of the adolescent.

Box 1. Themes discussed during structured ACP conversations session 1 to 3 - For adolescents: 1) identity; 2) experiences with the disease and treatment; 3) talking with others; 4) help and comfort; 5) worries and fears; 6) preferences for care and treatment; 7) expectations for the future; 8) dying. - For parent(s): 1) talking with your child; 2) parenthood; 3) help and comfort; 4) worries and fears; 5) care and treatment; 6) expectations for the future; 7) dying. - Adolescents and parents can choose not to discuss certain themes they may prefer not to talk about.

Figure 2 shows the timeline of the BOOST pACP program, graphically displaying the different components. Some components coincide in time. There will be approximately one to two weeks in between the three conversation sessions, so that adolescents and parents have time to reflect on the themes discussed. The transfer of information from the facilitator to the

paediatric oncologist involved in the care of the adolescent will take place within one month after conversation session 3.

Figure 2. Timeline of the BOOST pACP program with adolescents that have cancer and their parents



External facilitators will be hired by the research team to deliver the BOOST pACP program. These facilitators will receive a 2.5-day training, partly provided by a communication expert from an external firm (Wilde Kastanje Training and Education, the Netherlands) in performing ACP conversations with the adolescent and parent(s) separately and with the family members together. The facilitators meet the following criteria: Master's degree in Psychology, advanced communication skills, and experience in working with adolescents.

Table 2. Summary of BOOST pACP program according to the Template intervention description and replication (TiDieR) checklist

TiDieR number	TiDieR item	BOOST pACP program
1.	BRIEF NAME (name or a phrase that describes the intervention)	BOOST pACP (Benefits of Obtaining Ownership Systematically Together in paediatric advance care planning) program
2.	WHY (any rationale, theory, or goal of the elements essential to the intervention)	A more positive attitude and improved self-efficacy towards communicating about ACP themes between adolescents and their parent(s) may result in an intention to talk more about ACP themes. This in turn may lead to improved parent-adolescent communication.
3.	WHAT Materials (any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers)	The BOOST pACP program includes 8 supporting materials: 1. Training program and accompanying PowerPoint presentations used for the 2.5-day training of the ACP facilitators 2. A manual for trained ACP facilitators who will perform the ACP conversations with adolescents and parent(s), including a description of steps to follow during and between the structured ACP conversation sessions. 3. Preparation booklets for both the adolescent and parent(s), including information about the program, why ACP is relevant and questions to trigger the thinking process about ACP themes. 4. A video in which two families talk about their personal situation and experienced effects of the ACP program. 5. Conversation cards to structure the ACP conversation sessions with the adolescent covering the following ACP themes: 1) Who am I?; 2) How do I experience my illness? 3) Talking with others; 4) Help and comfort; 5) Worries and fears; 6) What care do you want?; 7) Expectations for the future; 8) About dying. Adolescents are asked to divide the themes into two categories: "I would like to talk about this theme with my parent(s)" and "at the moment I do not feel the need to talk about this theme with my parent(s)" 6. Conversation cards to structure the ACP conversation session with parent(s) covering the following ACP themes: 1) Talking with your child; 2) Parenthood; 3) Help and comfort; 4) Worries and fears; 5) Care and treatment; 6) Expectations for the future; 7) About dying 7. A summary sheet that will be filled out by the parent(s) and adolescent together in session 3 to stimulate conversation about ACP themes. 8. Conversation cards that can be used as a game of quartet at home. Families will receive these cards at the end of session 3.
4.	WHAT Procedures (each of the procedures, activities, and/or processes used in the	The BOOST program entails 10 program components that can be carried out via 17 activities: As part of "Facilitator training (including manual)" component (1) Activity 1: Selection of two external facilitators Activity 2: Preparation of facilitators for the training

	intervention, including any enabling or support activities) Activity 3: Two-and-a-half-day training program for facilitators Activity 4: Intervention sessions (discussing challenges in case studies) approximately every 4 months for facilitators (2 - 5 hours) As part of "Preparation booklets" component (2) Activity 5: Data collectors give preparation booklets to the families that are assigned to the intervention group Activity 6: Adolescent and parent(s) read their preparation booklet before conversation session 1 takes place As part of "Video" component (3) Activity 7: The facilitator introduces the videos that will be shown in conversation session 1. Activity 8: Adolescent and parent(s) watch the video during conversation session 1. Activity 9: The facilitator asks whether the adolescent and parent(s) recognize any aspect from the video. As part of "Conversation session 1" (4) Activity 10: The facilitator guides the conversation session and introduces the conversation cards to the adolescent and parent(s): As part of "Conversation session 2a" (5) Activity 11: The facilitator guides the conversation session with the adolescent alone and uses conversation cards to discuss ACP themes. As part of "Conversation session 2b" (6) Activity 12: The facilitator guides the conversation session with the parent(s) alone and uses conversation cards to discuss ACP themes. As part of "Conversation session 3" (7) Activity 13: The facilitator guides the conversation session with the adolescent and parent(s) and allows them to discuss ACP themes. As part of "Summary sheet" (8) Activity 14: The facilitator introduces and explains the summary sheet. The facilitator asks whether the family would like the information they write down to be shared with the paediatric oncologist. As part of "Conversation cards that can be used as a game of quartet at home" (9) Activity 15: The facilitator explains the purpose of the quartet game and that the cards can facilitate communicating on ACP themes together at home in a playful way. As part of "Transfer of information to a treating paediatric oncologist" (10) Activity 16: In case the family gave permission, the facilitator makes an appointment with the paediatric oncologist that the family indicated. Activity 17: The facilitator gives a summary of the conversations with the family to the paediatric oncologist and asks whether the paediatric oncologist can add the summary sheet to the electronic dossier of the patient.
5.	WHO PROVIDED (intervention provider, their expertise, External facilitators are hired by the research team to perform the BOOST pACP program, more specifically to facilitate the structured ACP conversations with the families. Facilitators (psychologists) will receive a 2.5 day training and ongoing 4-monthly debriefing session to respond to different scenarios

	background and any specific training given)	and situations (such as strategies when there is little response, dealing with resistance, and emotional feelings of the participants).
6.	HOW (modes of delivery)	All ACP conversation sessions are provided face-to-face (at home or at the hospital) or online by video call, depending on the family's preference. The transfer of information with the paediatric oncologist/ medical team will take place by (video) call or in real life.
7.	WHERE (the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features)	The conversation sessions can take place either at the home address of the family, in the hospital or online by video call (because of the COVID-19 measures).
8.	WHEN and HOW MUCH (the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose)	The intervention period per family is three months (from receiving the preparation booklets to the transfer of information with the paediatric oncologist). Each conversation session will take approximately 60 minutes. There will be at least one week in between the conversation sessions, due to the importance of time to reflect on ACP themes and potentially discuss certain ACP themes at home if participants want to. The debriefing sessions for the facilitators will take maximally five hours and will be planned every 4 months.
9.	TAILORING (if the intervention was planned to be personalized, titrated or adapted, then describe what, why, when, and how)	Within the conversation sessions, participants have freedom and flexibility in choosing certain ACP themes to discuss and the facilitator will clarify that participants are not obligated to talk about all ACP themes. The conversation sessions are structured in the sense that per topic, there is a key question and two follow-up questions that will be asked always. Apart from that, facilitators can ask other questions or decide to zoom in on the participant's story whenever they want. Families can choose the mode of delivery of the conversation sessions (face-to-face at home or in the hospital or online by video call). Furthermore, the facilitator will ask paediatric oncologists how they would like to organize the transfer of information (if family permitted sharing a summary of the conversations with healthcare professionals).
10	FIDELITY - HOW WELL (planned)	As part of the process evaluation, we will record audio recordings of all structured ACP sessions 1, 2a, 2b and 3 from eight dyads in total (after consent) to evaluate fidelity. We will use a fidelity checklist that is based on the steps described in the manual of the facilitators.

Control

The control group will not receive the BOOST pACP program. Adolescents in the hospitals are seen by different oncologists and nurses. Families that are recruited via four participating university hospitals will have access to contact with psychologists whenever they request it. Paediatric ACP is not implemented as standard care within these hospitals. The conversation cards that can be used as a game of quartet at home are offered to the families in the control group after study completion.

Criteria for discontinuing or modifying allocated interventions

Families can withdraw from the study at any moment. Where a participant experiences psychological distress the facilitator, being an experienced psychologist by background, will discuss their feelings and ask if they want to continue. In addition, if a participant displays signs of psychological distress, the ACP facilitator will discuss and facilitate contact with the psychologist from the involved paediatric oncology wards. Where patients are recruited through support organizations, the facilitator will ask the family which psychologist from their facility they can contact.

A bereavement protocol will be in place for when a patient or parent dies during the study period. When the data collector is notified about the death of a participant, he/she will then notify the trial manager and ACP facilitator. The bereaved participant will receive a phone call from the data collector outlining condolences and where they can access support if required. Bereaved participants will not be asked or expected to complete follow-up study questionnaires.

Strategies to improve adherence to the intervention protocols

The research team also developed an implementation protocol outlining all intervention components and associated procedures, in collaboration with the facilitators that they use throughout the delivery of the BOOST pACP program. Next to the 2.5-day training, the ACP facilitators will participate in 4-monthly (or more, depending on need) debriefing/comeback sessions ('coaching on the job') with a researcher (AVD) and a specialist trainer (in communication) from the research group. Debriefing sessions are aimed at providing facilitators with additional knowledge and skills required to successfully implement the program, based on a discussion of the challenges they experience, and implementation approaches and strategies to deal with these challenges.

Relevant concomitant care and interventions that are permitted or prohibited during the trial

There are no restrictions regarding concomitant care or interventions during the trial.

2.4 Outcomes

Outcomes are measured at baseline (T0), three months after baseline (T1), and at seven months (T2) in three groups: adolescents, parents and paediatric oncologists. The outcome measures used for the primary and secondary endpoints are shown in **Table 3**. The full questionnaires used at T0 in these three groups are provided in **Additional file 1**.

Table 3. Outcome measures of the primary and secondary endpoints of the BOOST pACP program

Outcomes	Measurement instrument	No. of items	Unit of analysis	Timepoint		
				T0	T1	T2
Primary endpoint						
1. Quality of Parent-Adolescent Communication	Parent-Adolescent Communication Scale (PACS) (33)	20 items	Adolescent		x	
Secondary endpoints						
2. Quality of Parent-Adolescent Communication	PACS	20 items	Adolescent	x		x
3. Attitude on talking with the other (parent(s)/ their child) about what the adolescent finds important regarding his/her care and treatment	Created by the research team	8 items*	Adolescent	x	x	x
		7 items*	Parent(s)	x	x	x
4. Self-efficacy towards talking with the other (parent(s)/ their child) about different ACP themes	Created by the research team	9 items*	Adolescent	x	x	x
4a. if the child initiates the conversation	Created by the research team	9 items*	Parent(s)	x	x	x
4b. to initiate the conversation his/herself	Created by the research team	9 items*	Parent(s)	x	x	x
5. Self-efficacy towards talking with their child and letting their child talk in different situations	Created by the research team	6 items*	Parent(s)	x	x	x
6. Behaviour: talking with the other (parent(s)/ their child) about different ACP themes	Created by the research team	9 items*	Adolescent	x	x	x
		9 items*	Parent(s)	x	x	x
7. Intention to talk with the other (parent(s)/ their child) parent(s) about different ACP themes	Created by the research team	9 items*	Adolescent	x	x	x
		9 items*	Parent(s)	x	x	x
8. Behaviour: talking with paediatric oncologist about different ACP themes	Created by the research team	9 items*	Adolescent	x	x	x
9. Intention to talk with paediatric oncologist about different ACP themes	Created by the research team	9 items*	Adolescent	x	x	x
10. Anxiety	PROMIS Anxiety 8a Short version (38) †	8 items	Adolescent	x	x	x
	PROMIS 7a Short version (39) †	7 items	Parent(s)	x	x	x
11. Level of shared decision making	CollaboRATE Scale (36,37) ‡	3 items	Parent(s)	x	x	x
12. Satisfaction items for the intervention group	Created by the research team	14 items	Adolescent and parent(s)		x	x
13. Behaviour & intention to discuss ACP with the family	Created by the research team	3 items	Oncologist	x	x	x

14. Quality of Life	EQ-5D-Y(35)	6 items	Adolescent	x	x	x
Background characteristics						
15. Demographic and background information	Created by the research team	3 items	Adolescent	x		
		14 items	Parent(s)	x		
16. Disease & treatment information about adolescent	Created by the research team	7 - 10 items	Oncologist	x	x	x

* The following procedure was followed: 1) The Theory of Planned Behaviour instructed ways items were formulated regarding the four key constructs operationalizing ACP as a health behaviour: attitude, self-efficacy, intention and actual behaviour; 2) the prototype instrument was linguistically improved and made age appropriate by a literacy expert agency; 3) cognitive interviews with adolescents who were diagnosed with cancer (n=4) and parents (n=6) were then performed; 4) feedback using thematic analysis and discussions with the researchers informed refinements. Response categories: 'Strongly Disagree', 'Disagree', 'Neither Agree Nor Disagree', 'Agree' or 'Strongly Agree'

† Response categories: 'Never', 'Rarely', 'Sometimes', 'Often', or 'Always'

‡ Response categories: 10 – point Likert scale, ranging from 'No effort was made' (=0) to 'Every effort was made' (=10)

Primary endpoint

The primary endpoint is dyadic ACP communication (between adolescent and parent) at three months (T1), using the Parent-Adolescent Communication Scale (PACS) [33], a validated questionnaire to measure the adolescent's perception of their communication, as applied to pACP themes with (both of) the parent(s). The Parent-Adolescent Communication Scale [33] entails two subscales: 1) openness in communication subscale; 2) problems in communication subscale, including 20 items, that can be rated from 1 to 5 and produce factor-derived scores (range: 10 – 50). Items are summed for each scale, so that higher scores indicate more openness and more problems. The scores for items on the Problems subscale are reversed in value. The score ranges from 20 – 100 on the full scale. Both subscales have demonstrated strong internal consistency ($\alpha = 0.87 - 0.78$) and test-retest reliability ($r = 0.78 - 0.77$) [34]. The questionnaire was translated to Dutch following a forward-backward translation procedure, in collaboration with an independent translation agency. The adolescent will fill out the PACS about both parents, if applicable.

Secondary endpoints

One of the secondary endpoints is dyadic communication (between adolescent and parent(s) at seven months (T2). The other secondary endpoints will be measured at baseline (T0), T1 and T2 and include:

- adolescent's/parents' attitudes to talking about ACP themes with his/her parent(s)/child (self-developed items)
- adolescent's/parents' self-efficacy towards talking about ACP themes with his/her parent(s)/child (self-developed items)
- parents' self-efficacy towards talking with their child and letting their child talk in different situations (self-developed items)
- adolescent's/parents' behaviour of talking about ACP themes with his/her parent(s)/child (self-developed items)
- adolescent's/parents' intention to talk about ACP themes with his/her parent(s)/child (self-developed items)
- adolescent's behaviour of talking about ACP themes with his/her paediatric oncologist (self-developed items)
- adolescent's intention to talk about ACP themes with his/her paediatric oncologist (self-developed items)
- adolescent's quality of life (EQ-5D-Y (38))
- parents' perception of shared decision making in the last clinical encounter (Collaborate Scale [36, 37])
- adolescent's/parents' level of anxiety in the past week (PROMIS Anxiety [38, 39])
- paediatric oncologists' behaviour of talking about ACP themes with the family (self-developed items)
- paediatric oncologists' intention to talk about ACP themes with the family (self-developed items).

Participant characteristics

We will collect demographic and relevant background information from adolescents (i.e. gender, data and country of birth) and from parents (i.e. gender, date of birth, highest education). From paediatric oncologists, we will gather relevant clinical information about the adolescent (i.e. main diagnosis, recurrence, metastasis and type and line of treatment).

Process evaluation

Via a mixed-methods process evaluation in the intervention group, we will assess:

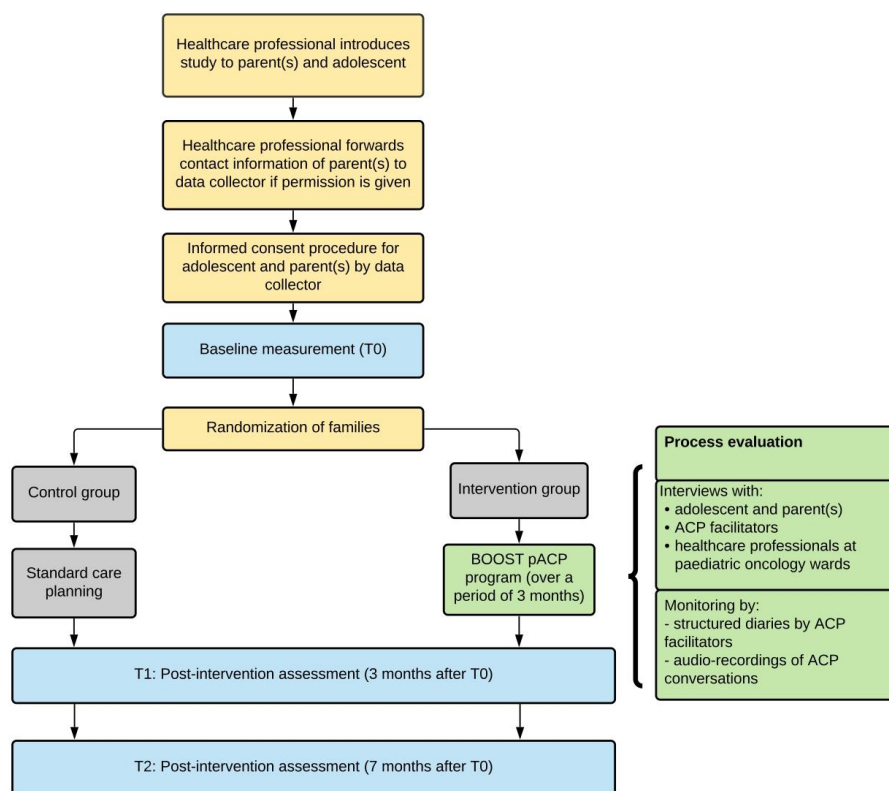
- implementation: the structures, processes and resources through which delivery is achieved, and the quantity and quality of what is delivered [26]. Outcomes involve: a description of how the program activities were implemented, resources and dose, reach, fidelity, adaptations and quality.
- mechanisms of impact: the intermediate mechanisms through which program activities produce intended (or unintended) effects, and how activities, and participants' interactions with them, trigger change [26]. Outcomes involved are responses and interactions with the program, mediators and unanticipated pathways or consequences.
- context: factors external to the program which may influence its implementation, or whether its mechanisms of impact act as intended, and how external factors influence the delivery and functioning of the program [26]. This involves contextual moderators and intention for maintenance.

Additional file 2 provides an overview of all process indicators that are evaluated in the process evaluation, indicating the methods applied and at what time point.

2.5. Participant timeline

The full trial participation of participants takes up to seven months (from baseline to filling out the last questionnaire). The flow diagram of measurements is provided in **Figure 3** and the intervention participant timeline is provided in **Figure 2**.

Figure 3. Flow diagram of adolescent and parent recruitment, randomization and measurements



2.6. Sample size

We consider demonstration of an intervention effect on the primary endpoint as a success. The primary endpoint is the score for the Parent-Adolescent Communication Scale (PACS) [33] at three months (T1). To detect a minimal relevant difference between intervention and control group at T1 of 7 with a pooled standard deviation in both groups of 11.4, with alpha at 0.05 and 80% power ($1-\beta=0.80$), a sample of $n=43$ is needed in each arm. Based on the experiences with the FACE intervention [40], we anticipate a 90% retention rate, similar to the FACE intervention, resulting in an estimation of 96 families in total to be enrolled. Two other studies found a smaller difference in PACS scores between the intervention and control group (e.g. 2.57 [41] and 2.21 [42]). However, both of these intervention studies entailed minimal in-person contact and sending prompts to the parents by mobile phone. The components of the BOOST pACP program entail intensive in-person contact moments, specifically targeted at behavioural constructs to improve parent-adolescent communication on ACP themes. Therefore, we expect to see a larger effect on the PACS scale, compared with the interventions described above.

2.7. Recruitment procedures

The recruitment period will be two years (2021 – 2023). We will recruit adolescents via two different streams:

1. Patients will be recruited in all four participating university hospitals in Flanders, Belgium, via the paediatric oncology wards. Each of the hospital wards will assign one staff member as the main point of contact for the study. The contact person asks each paediatric oncologist to assess which patients would meet the inclusion criteria. The paediatric oncologist or psychologist will ask the parents of these patients whether they would be willing to participate in the study by giving a short explanation and asking whether they agree for a data collector to call them to provide more information about the study. The data collector will then contact one of the parents by phone. If the parent agrees to participate, the data collector will make an appointment with the parent(s) (depending on which parents are considered eligible, see **Figure 1**) and the adolescent. During the appointment, the data collector will explain that both parents are encouraged to join the conversation sessions, but that it is not obligatory for both parents to join all conversation sessions of the program to be able to enrol in the study.

2. We will recruit adolescents with cancer and their parent(s) through support organizations that meet the following criteria: 1) they are non-profit; 2) they are based in Flanders or Brussels; 3) adolescents with cancer or their parents are one of their target groups. Organizations are contacted by the researcher (AVD) and are asked to post an open call using a flyer developed by the research team via their newsletters, website and other social media or share this in other ways that are part of their regular channels of communication with their members and network. Adolescents and/or parents can contact the data collectors (via phone or e-mail) when they are interested in participation in the study or when they have additional questions. Subsequent recruitment procedures are similar to the first recruitment stream.

2.8. Allocation

Randomization will be performed after at least one of the parents has completed the baseline measurement. Block randomization with a 1:1 allocation ratio to either the intervention arm or the control arm will be performed, using a concealed envelope method. To ensure equal allocation of subgroups, we will stratify the allocation by age (10 – 14 years old vs 15 – 18

years old). We have opted for these age strata, because the cognitive development of adolescents between 10-14 years differs from those between 15-18 years [43, 44] which might influence the way they are able to talk about their care and treatment. Allocation concealment will be ensured, as the randomization service will not release the randomization code until the adolescent has been recruited into the trial, which takes place after all baseline measurements have been completed. After randomization, the data collector will then inform the families of their allocation to one of the study arms.

Masking

Researchers will be single blinded as to which arm families belong to including data analyses. Participating families and paediatric oncologists allocated to the intervention group, and ACP facilitators, cannot be blinded, as they will actively participate in some part of the program. Participants in the control group will subsequently be informed about their group allocation. Research staff responsible for data analyses will not receive any information about a family's group allocation.

2.9. Data collection procedures

Quantitative data is collected at baseline (T0), after three months (T1), and after seven months (T2) (see **Figure 3**), using self-reported questionnaires that are pseudonymized using individual identifier codes attributed by the data collector. During a home visit, the data collector will gather written consent from both parents and written assent from the adolescent, immediately after which the baseline questionnaire is provided to the participant (paper-pencil or online using 'LimeSurvey', depending on the choice of the participant). The data collector will fill out the questionnaire together with the adolescent in an interview format. This will be done in a separate room from the parent(s), to avoid that the adolescent is being influenced by their presence. Parent(s) can either choose to fill out their questionnaire independently at the same time or later. The paediatric oncologist mentioned by the family as the one with whom they have most contact about care and treatment will receive a baseline questionnaire about the adolescent via an e-mail link. The data collector will send out one reminder to the parents and paediatric oncologist after one week. Data collection procedures are repeated at T1. At T2, questionnaires are sent to parents and adolescents, either online or via postal mail. To reduce loss to follow-up, improve retention, and encourage adolescents to fill out the questionnaires, retention gifts will be provided after completion of each data collection, at T0, T1 and T2.

Data collection procedures for the process evaluation (**Additional file 2**), include:

- 1) structured diary filled out by facilitators: the facilitators keep track of all activities they perform regarding the BOOST pACP program by filling out a structured diary, including multiple choice and open-ended questions, after each BOOST pACP conversation session. The diary will be completed in a Word template and will be stored in a secure folder.
- 2) semi-structured individual interviews with facilitators; both facilitators will be interviewed for 60 minutes by a researcher at six months, 12 months, 18 months and after the end of the data collection period at 24 months.
- 3) semi-structured individual interviews with a variety of involved paediatric oncology teams after 12 months and after study completion, at 24 months.
- 4) each BOOST pACP conversation is recorded by audio (after informed consent of participants).

All interviews are structured according to a pre-specified topic list and audio-taped for analysis purposes.

2.10. Data management

All questionnaires will contain a pseudonymizing code consisting of a unique number that is linked to the participant's name. Data collectors will keep a record of these codes in a secured folder that is not accessible to the researchers. The data collector is responsible for noting the correct unique number of the paper version of the questionnaires at T0, T1 and T2 or for forwarding the code in the email to participants. For the questionnaires of the paediatric oncologists, the data collector will communicate the name of the adolescent with the corresponding code. The paediatric oncologist will be asked to note down the adolescent's code in the online questionnaire. Data collectors will keep an excel file to indicate to what codes they have sent the questionnaires and share this with researchers. Using this file, the researchers will keep track of responses and will use the unique code to communicate with the data collector to whom a reminder may need to be sent out. Data from paper-and-pencil questionnaires are entered as soon as possible after receipt. Online questionnaires will be automatically saved in a secure open-source web-based survey application (LimeSurvey). Written informed consent files and paper questionnaires are stored in a lockable filing cabinet in a room with restricted access on campus. The file with the participants' names, address and other identifiable information will be stored in one file. This file will be restricted to the data collectors and ACP facilitators only.

Confidentiality

The collected and transferred data will be pseudonymized to ensure that participants' privacy and personal information are protected. In transcriptions of the interviews, all information that can contribute to tracing and identifying the participants will be removed or replaced. We will use sufficient safety measures to protect the data, including a virtual server firewall, back-up systems and sufficient access controls (i.e., ID and ultrahigh password regulator and frequent password changes).

Dissemination

The results of this study will be submitted for publication in peer-reviewed journals and will be presented to the paediatric wards of the participating hospitals and at national and international research and professional conferences. Furthermore, we will disseminate via the website, social media and newsletter of the research group (endoflifecare.be).

2.11. Data analysis

The intervention and control group will be described using descriptive summary statistics (mean, standard deviation, count percentage). We will test for significant differences in the primary and secondary endpoints, between the intervention and control group at baseline and at T1 (three months from T0), and T2 (seven months from T0) while adjusting for baseline scores.

Primary hypothesis testing

The hypotheses related to the primary endpoint, parent-adolescent communication (PACS), will be analysed using a mixed model with the T1 measurement value for parent-adolescent communication as outcome variable and randomization group and baseline measure of parent-adolescent communication as predictor variables. Random effects that we will include

in our mixed model are hospital and line of treatment. We will perform analyses on both intention-to-treat and per-protocol principles, with the intention-to-treat as the primary approach. In the intention-to-treat analysis, all participants who were enrolled and randomised will be accounted for in the main analysis, regardless of whether they completed the BOOST pACP program or not. The linear mixed models we intend to apply handle missing data through maximum likelihood estimation (i.e. assuming data is missing at random), so no missing data imputation should be applied. In case we do decide to apply multiple imputation, predictors for the imputation model will include the baseline measurement, randomization group, age and other possibly confounding variables (e.g. prognosis). In the per-protocol analysis, we will focus on families of which at least one parent was involved in all BOOST pACP conversations. During this analysis, we regard the family as a cluster because it is possible that during some conversation sessions both parents are present, while during others only one parent is present. Therefore, we will add the presence of parents during the conversation sessions as time-varying covariates.

Secondary hypotheses testing

All secondary endpoints will be evaluated by testing the BOOST pACP program against the control group for each participant population separately (adolescents, parents and paediatric oncologists) with random effects being hospital and line of treatment.

For each of the primary and secondary endpoints, subgroup analyses will be performed using formal interaction tests to explore the extent to which the outcomes of the trial differ by gender, working situation and family situation of the parent(s) and gender and prognosis of the adolescent. Interaction terms between gender, working situation and family situation of the parent(s) and gender and prognosis of the adolescent on the one hand and the trial arms on the other hand will be added to the analysis models.

By including the baseline measurement as a predictor variable pre-existing differences will be controlled, enhancing the sensitivity of the analyses. Alpha is set at 0.05. To interpret the magnitude of the effects for the different outcomes, we will estimate effect sizes (Cohen's d). Analyses will be conducted in IBM SPSS and R.

Process evaluation

Process evaluation of the implementation of the program will be analysed following the domains of Moore et al.'s MRC framework for process evaluations of complex interventions [26]: implementation, causal mechanisms and context, guided by pre-defined process indicators outlined in **Additional file 2**. Quantitative data collected via structured diaries (e.g. duration of an ACP conversation session) will be summarized by calculating frequencies and descriptive statistics (mean, median, standard deviation, range) using SPSS. All qualitative transcript data from interviews and audiotaped ACP conversations will be analysed by using thematic content analysis (i.e. deductive coding guided by the pre-defined process indicators, e.g. number of activities delivered as intended) and inductive coding into themes [45, 46]. The inductive approach will enable recognition of unexpected emergent themes. Qualitative data analysis will be managed in NVIVO. One researcher will read the transcripts carefully several times to have a sense of the data, with a 10% random sample of transcripts double coded by another researcher.

2.12. Data monitoring

The main researcher (AVD) and data collectors will continuously monitor trial response using MS Excel sheets. An independent trial monitor will oversee the progress of the trial and ensure it will be conducted in accordance with the protocol and Good Clinical Practice standards. AVD will be the main contact person for participating hospitals to report problems or to ask questions regarding the trial. Data entry will be performed by the data collectors.

Harms

The research team is committed to minimizing risks of harm and maximizing the benefits for potential participants. Participation in this study could be emotionally stressful as it involves coming into contact with themes that might confront them with their illness, prognosis and expectations for the future. We have put in place a procedure to identify and handle any signal of distress in the adolescent or the parents. The facilitators guiding the ACP conversations are experienced psychologists by background. At the beginning of the ACP conversation sessions, the facilitator will explicitly tell the adolescents and parents that they can always take a break when needed or stop participation whenever they want to. In addition, the facilitator will refer participants to the psychologists at the involved paediatric oncology ward if they notice they may need support. In that case, the facilitator will coordinate the contact with the psychologist from the ward. The facilitator will let the research team know and keep into touch with the psychologist to discuss potential continuation or termination of the family's participation and will add this information to the structured diary. Contact details of the psychologists of the ward and of the research team are mentioned on the informational materials.

Discussion

We currently lack robust evidence regarding the effectiveness of advance care planning in adolescents (pACP) who have cancer and their parents which applies randomised controlled trial designs. This study aims to improve, via a novel program, both parent-adolescent communication about advance care planning themes and improved self-efficacy in talking about ACP themes with each other, by contributing to a more positive attitude. The BOOST pACP program is a multicomponent program consisting of three ACP conversation sessions between an external facilitator and the adolescent and their parent(s). In this structured ACP approach, broader ACP themes such as experiences of the disease, preferences for communicating, decision-making by the adolescent and expectations for the future are discussed – hence considering ACP to be relevant from diagnosis onwards and not only targeting the end of life [24,47,48]. Normalizing communication about ACP themes between parents and the adolescent may lead to improved communication with healthcare professionals and trigger a feeling of empowerment of the adolescents in their own care plan and future wishes. The effectiveness, implementation, contextual factors and causal mechanisms will be evaluated in adolescents (age 10 – 18) and their parent(s), applying a randomised controlled trial design and embedded mixed-methods process evaluation.

Several potential limitations to the study design have to be considered. Firstly, the limited use of validated questionnaires to evaluate our selected endpoints; validated measures regarding the outcomes related to communication that are targeted with these kinds of interventions are often non-existent [19, 49]. Options are to either select validated measurement instruments

that match the intervention's goals to a lesser extent and are therefore less relevant, or adapt existing measures matching the desired goals or impact of the intervention, while compromising on validity. After an extensive search and multiple deliberations within the research team, we decided on slightly adapting the PACS to the context of ACP and to construct items based on the Theory of Planned Behaviour [50] regarding our secondary endpoints. We have performed a thorough cognitive testing of the measurement instrument with the target group. Secondly, given our strict inclusion criteria, the number of adolescents with cancer meeting our inclusion criteria might be lower than expected, complicating reaching sufficient sample size for this trial. However, we intend to mitigate this limitation by recruiting adolescents via four hospitals and relevant support organizations.

Mixed-methods results of this study can inform future implementation of ACP in this distinct population. If effective, the BOOST pACP model could represent an ACP approach for paediatric oncology that may also apply to other areas in paediatric care and other paediatric populations with distinct serious illnesses.

Trial status

Recruitment started in January 2021 and is expected to be finalized in January 2023.

List of abbreviations:

ACP advance care planning; pACP Paediatric advance care planning; PACS Parent-Adolescent Communication Scale; RCT Randomised controlled trial; MRC Medical Research Council; TIDieR Template for intervention description and replication; AYA Adolescents and young adults; SD standard deviation

Declarations

Ethics approval and consent to participate

The trial was approved by the Medical Ethics Committee of the four participating hospitals (University Hospital of Leuven, Ghent, Antwerp and Brussels) in Flanders, Belgium (B1432020000060). Important protocol modifications will be communicated to all relevant parties: investigators, trial participants, Ethics Committee and isrctn.com.

Adolescents and parents will be given ample time to consider participation and they will be assured that they are free to withdraw from participating in the study without any effect on their care. Before participating, written consent from both parents, if applicable, and written assent from the adolescent is required and will be obtained without any coercion. Furthermore, an extra box needs to be ticked before the adolescent and parent(s) fill out the questionnaire, indicating that they have understood the information and have given consent to participate in the study. The data collector that fills out the questionnaire together with the adolescent will explicitly verify whether the adolescent understands what participation entails during the assent procedure, and again when filling out the questionnaire together.

Consent for publication

Written informed consent and assent forms also notified about and included a statement about consent for publication of anonymized non-identifiable and summarised data.

Availability of data and materials

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

Conception and design of the work: AvD, ADV, JG, MK, JvdWtB, LD, JC, KB.

Ethics approval: AvD, ADV, MK, JvdWtB, LD, JC, KB

Drafting the work: AvD, JG

Critical revision for important intellectual content: AvD, ADV, JG, MK, LD, JC, KB

All authors read and approved the final manuscript.

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T0 (2 ouders)

Deelnemerscode (in te vullen door onderzoeker, bv AN05J-T1):

Additional file 1: Baseline questionnaires for adolescents, parents and paediatric oncologists



Vragenlijst voor jongeren



BOOST: een studie rond vroegtijdige zorgplanning in de kinderoncologie

Vragenlijst voor jongeren

Uitleg bij deze vragenlijst

Bedankt dat je meewerkt aan ons onderzoek!

Waar gaan de vragen in de vragenlijst over?

Graag komen wij meer te weten over in hoeverre jij hebt nagedacht en gesproken over wat jij belangrijk vindt, als het gaat om de zorg en behandeling. Iemand zal deze vragenlijst met jou overlopen. De vragenlijst gaat over verschillende dingen.

- Deel 1. Praat jij met je ouders of voogd over je zorg en behandeling? En wat vind je van die gesprekken?
- Deel 2. Praat je over je zorg en behandeling met je kinderoncoloog (je arts in het ziekenhuis)?
- Deel 3. Hoe heb je je gevoeld in de afgelopen 7 dagen en hoe voel je je vandaag?
- Deel 4. Wie ben jij?
- Deel 5. Heb je nog opmerkingen?

Hoe vul ik de vragenlijst in?

Iemand zal deze vragenlijst met jou overlopen. Het invullen duurt ongeveer 50 minuten. Je kunt ervoor kiezen de vragenlijst samen in te vullen op papier of digitaal via

<https://tinyurl.com/BoostStudie-J-base2>.

Enkele instructies voor je van start gaat:

1. De meeste vragen kan je beantwoorden door één van de vakjes aan te vinken: .
Indien je meer dan één antwoord aan kunt duiden, staat dit bij de vraag vermeld. Bij de open vragen kun je zelf tegen de persoon met wie je de vragenlijst invult zeggen wat je wilt invullen.
2. Het is belangrijk voor het onderzoek dat je alle vragen in de vragenlijst beantwoordt. Of je nu wel of niet over je zorg en behandeling hebt nagedacht of gepraat, zolang je aankruist wat voor jou geldt is het helemaal goed. Dan help je ons het beste met je antwoorden.
3. De persoon die samen met jou de vragenlijst invult kan je helpen als je vragen hebt. Je kan haar altijd vragen stellen.

Wie krijgt mijn antwoorden?

De antwoorden worden alleen bezorgd aan de onderzoekers die dit onderzoek uitvoeren. We geven jouw antwoorden een code uit letters en cijfers zonder jouw naam, zodat niemand kan weten van wie de antwoorden komen.

Vragen?

Contacteer Anne van Driessche (uitvoerend onderzoeker)

tel: +32(0)456302963

e-mail: Anne.van.Driessche@vub.be

Deel 1: Jouw zorg en behandeling

Welke zorg en behandeling tegen kanker heb je nodig? Misschien is daar met jou en je ouders al veel over gepraat. Maar wat vind jij zelf belangrijk? En met wie praat jij daarover? Daarover gaat dit deel van de vragenlijst.

We hebben het niet alleen over jouw medische behandeling die je krijgt van zorgverleners in het ziekenhuis (zoals de verpleegkundige, arts of psycholoog). We bedoelen met **zorg** ook de hulp of steun die je krijgt van andere mensen, zoals van je ouders, vrienden of familie.

Wil je alsjeblieft ook de datum van vandaag invullen?

1. De datum vandaag is: _____ (dag)/_____ (maand)/_____ (jaar)

2. Wie van jouw ouders of verzorgers is het meest aanwezig als je afspraken hebt in het ziekenhuis?

- ☐ Mijn moeder
- ☐ Mijn vader
- ☐ Beiden evenveel
- ☐ Iemand anders (vul in): _____

Ga verder op de volgende pagina

Deel 1a: Over praten met je moeder

Geef aan de hand van onderstaande schaal aan in welke mate je het eens of oneens bent met ELK van de volgende zinnen.

3. De zinnen gaan over in hoeverre jij met je moeder kan praten over wat jij belangrijk vindt in jouw zorg en behandeling.	Helemaal oneens	Oneens	Niet eens en niet oneens	Eens	Helemaal eens
a. Ik kan mijn mening bespreken met mijn moeder zonder dat ik het gevoel heb dat ik me in moet houden of dat ik me ongemakkelijk voel.	☐	☐	☐	☐	☐
b. Ik vind het soms moeilijk om alles te geloven wat mijn moeder me vertelt.	☐	☐	☐	☐	☐
c. Mijn moeder luistert altijd goed.	☐	☐	☐	☐	☐
d. Ik ben soms bang om iets wat ik graag wil aan mijn moeder te vragen.	☐	☐	☐	☐	☐
e. Mijn moeder zegt soms dingen tegen mij die beter niet gezegd zouden worden.	☐	☐	☐	☐	☐
f. Mijn moeder weet hoe ik me voel zonder iets te vragen.	☐	☐	☐	☐	☐
g. Ik ben heel tevreden over de manier waarop mijn moeder en ik met elkaar praten.	☐	☐	☐	☐	☐
h. Als ik in de problemen zou zitten, zou ik het aan mijn moeder kunnen vertellen.	☐	☐	☐	☐	☐
i. Ik toon openlijk dat ik mijn moeder graag zie.	☐	☐	☐	☐	☐
j. Als mijn moeder en ik een probleem hebben, dan praat ik niet meer tegen haar.	☐	☐	☐	☐	☐
k. Ik ben voorzichtig in wat ik mijn moeder zeg.	☐	☐	☐	☐	☐
l. Als ik met mijn moeder praat, zeg ik soms dingen die ik beter niet zou zeggen.	☐	☐	☐	☐	☐
m. Als ik vragen stel, krijg ik een eerlijk antwoord van mijn moeder.	☐	☐	☐	☐	☐
n. Mijn moeder probeert mijn mening te begrijpen.	☐	☐	☐	☐	☐
o. Er zijn onderwerpen waarover ik liever niet praat met mijn moeder.	☐	☐	☐	☐	☐
p. Ik vind het gemakkelijk om problemen te bespreken met mijn moeder.	☐	☐	☐	☐	☐
q. Het is heel gemakkelijk voor mij om al mijn echte gevoelens uit te drukken bij mijn moeder.	☐	☐	☐	☐	☐
r. Mijn moeder zeurt/werkt op mijn zenuwen.	☐	☐	☐	☐	☐
s. Mijn moeder beledigt me soms als zij boos op me is.	☐	☐	☐	☐	☐

4. De volgende zinnen gaan over praten met je moeder over wat je belangrijk vindt in je zorg en behandeling. Hoezeer ben je het eens met elke zin? Kruis aan.	Helemaal oneens	Oneens	Niet eens en niet oneens	Eens	Helemaal eens
a. Ik vind het belangrijk om met mijn moeder te praten over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐
b. Ik vind het oké als mijn moeder wil praten over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐
c. Ik ben bang dat ik mijn moeder verdrietig maak als ik praat over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐
d. Ik weet te weinig over mijn ziekte of behandeling om met mijn moeder te praten over wat ik belangrijk vind.	☐	☐	☐	☐	☐
e. Ik denk dat mijn moeder mij te jong vindt om mee te praten over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐
f. Ik denk dat er toch niets verandert als ik praat met mijn moeder over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐
Denk aan de zorg die je nu krijgt.	☐	☐	☐	☐	☐
g. Ik vind het makkelijk om met mijn moeder te praten over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐
Denk aan de zorg die je later kan krijgen.	☐	☐	☐	☐	☐
h. Ik vind het makkelijk om met mijn moeder te praten over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐

5. Als ik dat zou willen, zou het mij goed lukken om met mijn moeder te praten over...	Helemaal oneens	Oneens	Niet eens en niet oneens	Eens	Helemaal eens
a. wat ik belangrijk vind in mijn leven	☐	☐	☐	☐	☐
b. hoe ik me voel door mijn ziekte en behandeling	☐	☐	☐	☐	☐
c. waarover ik veel nadenk of pieker	☐	☐	☐	☐	☐
d. waarvoor ik bang ben	☐	☐	☐	☐	☐
e. waarop ik hoop	☐	☐	☐	☐	☐
f. wat ik verwacht van de toekomst	☐	☐	☐	☐	☐
g. het wel of niet starten van een nieuwe behandeling, als de behandeling die ik nu krijg niet meer zou werken	☐	☐	☐	☐	☐
h. het stoppen van de behandeling, als die niet meer zou werken	☐	☐	☐	☐	☐
i. de kans dat ik zou sterven	☐	☐	☐	☐	☐

6. Ik heb in de afgelopen maand met mijn moeder gepraat over...	Ja	Nee
a. wat ik belangrijk vind in mijn leven	☐	☐
b. hoe ik me voel door mijn ziekte en behandeling	☐	☐
c. waarover ik veel nadenk of pieker	☐	☐
d. waarvoor ik bang ben	☐	☐
e. waarop ik hoop	☐	☐
f. wat ik verwacht van de toekomst	☐	☐
g. het wel of niet starten van een nieuwe behandeling, als de behandeling die ik nu krijg niet meer zou werken	☐	☐
h. het stoppen van de behandeling, als die niet meer zou werken	☐	☐
i. de kans dat ik zou sterven	☐	☐

7. Ik wil binnenkort met mijn moeder praten over...	Ja	Nee
a. wat ik belangrijk vind in mijn leven	☐	☐
b. hoe ik me voel door mijn ziekte en behandeling	☐	☐
c. waarover ik veel nadenk of pieker	☐	☐
d. waarvoor ik bang ben	☐	☐
e. waarop ik hoop	☐	☐
f. wat ik verwacht van de toekomst	☐	☐
g. het wel of niet starten van een nieuwe behandeling, als de behandeling die ik nu krijg niet meer zou werken	☐	☐
h. het stoppen van de behandeling, als die niet meer zou werken	☐	☐
i. de kans dat ik zou sterven	☐	☐

Ga verder op de volgende pagina

Deel 1b: Over praten met je vader

Geef aan de hand van onderstaande schaal aan in welke mate je het eens of oneens bent met ELK van de volgende zinnen.

8. De zinnen gaan over in hoeverre jij met je vader kan praten over wat jij belangrijk vindt in jouw zorg en behandeling.	Helemaal oneens	Oneens	Niet eens en niet oneens	Eens	Helemaal eens
a. Ik kan mijn mening bespreken met mijn vader zonder dat ik het gevoel heb dat ik me in moet houden of dat ik me ongemakkelijk voel.	☐	☐	☐	☐	☐
b. Ik vind het soms moeilijk om alles te geloven wat mijn vader me vertelt.	☐	☐	☐	☐	☐
c. Mijn vader luistert altijd goed.	☐	☐	☐	☐	☐
d. Ik ben soms bang om iets wat ik graag wil aan mijn vader te vragen.	☐	☐	☐	☐	☐
e. Mijn vader zegt soms dingen tegen mij die beter niet gezegd zouden worden.	☐	☐	☐	☐	☐
f. Mijn vader weet hoe ik me voel zonder iets te vragen.	☐	☐	☐	☐	☐
g. Ik ben heel tevreden over de manier waarop mijn vader en ik met elkaar praten.	☐	☐	☐	☐	☐
h. Als ik in de problemen zou zitten, zou ik het aan mijn vader kunnen vertellen.	☐	☐	☐	☐	☐
i. Ik toon openlijk dat ik mijn vader graag zie.	☐	☐	☐	☐	☐
j. Als mijn vader en ik een probleem hebben, dan praat ik niet meer tegen hem.	☐	☐	☐	☐	☐
k. Ik ben voorzichtig in wat ik mijn vader zeg.	☐	☐	☐	☐	☐
l. Als ik met mijn vader praat, zeg ik soms dingen die ik beter niet zou zeggen.	☐	☐	☐	☐	☐
m. Als ik vragen stel, krijg ik een eerlijk antwoord van mijn vader.	☐	☐	☐	☐	☐
n. Mijn vader probeert mijn mening te begrijpen.	☐	☐	☐	☐	☐
o. Er zijn onderwerpen waarover ik liever niet praat met mijn vader.	☐	☐	☐	☐	☐
p. Ik vind het gemakkelijk om problemen te bespreken met mijn vader.	☐	☐	☐	☐	☐
q. Het is heel gemakkelijk voor mij om al mijn echte gevoelens uit te drukken bij mijn vader.	☐	☐	☐	☐	☐
r. Mijn vader zeurt/werkt op mijn zenuwen.	☐	☐	☐	☐	☐
s. Mijn vader beledigt me soms als hij boos op me is.	☐	☐	☐	☐	☐

9. De volgende zinnen gaan over praten met je vader over wat je belangrijk vindt in je zorg en behandeling. Hoezeer ben je het eens met elke zin? Kruis aan.	Helemaal oneens	Oneens	Niet eens en niet oneens	Eens	Helemaal eens
a. Ik vind het belangrijk om met mijn vader te praten over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐
b. Ik vind het oké als mijn vader wil praten over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐
c. Ik ben bang dat ik mijn vader verdrietig maak als ik praat over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐
d. Ik weet te weinig over mijn ziekte of behandeling om met mijn vader te praten over wat ik belangrijk vind.	☐	☐	☐	☐	☐
e. Ik denk dat mijn vader mij te jong vindt om mee te praten over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐
f. Ik denk dat er toch niets verandert als ik praat met mijn vader over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐
Denk aan de zorg die je nu krijgt.	☐	☐	☐	☐	☐
g. Ik vind het makkelijk om met mijn vader te praten over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐
Denk aan de zorg die je later kan krijgen.	☐	☐	☐	☐	☐
h. Ik vind het makkelijk om met mijn vader te praten over wat ik belangrijk vind in mijn zorg en behandeling.	☐	☐	☐	☐	☐

10. Als ik dat zou willen, zou het mij goed lukken om met mijn vader te praten over...	Helemaal oneens	Oneens	Niet eens en niet oneens	Eens	Helemaal eens
a. wat ik belangrijk vind in mijn leven	☐	☐	☐	☐	☐
b. hoe ik me voel door mijn ziekte en behandeling	☐	☐	☐	☐	☐
c. waarover ik veel nadenk of pieker	☐	☐	☐	☐	☐
d. waarvoor ik bang ben	☐	☐	☐	☐	☐
e. waarop ik hoop	☐	☐	☐	☐	☐
f. wat ik verwacht van de toekomst	☐	☐	☐	☐	☐
g. het wel of niet starten van een nieuwe behandeling, als de behandeling die ik nu krijg niet meer zou werken	☐	☐	☐	☐	☐
h. het stoppen van de behandeling, als die niet meer zou werken	☐	☐	☐	☐	☐
i. de kans dat ik zou sterven	☐	☐	☐	☐	☐

11. Ik heb in de afgelopen maand met mijn vader gepraat over...:	Ja	Nee
a. wat ik belangrijk vind in mijn leven	☐	☐
b. hoe ik me voel door mijn ziekte en behandeling	☐	☐
c. waarover ik veel nadenk of pieker	☐	☐
d. waarvoor ik bang ben	☐	☐
e. waarop ik hoop	☐	☐
f. wat ik verwacht van de toekomst	☐	☐
g. het wel of niet starten van een nieuwe behandeling, als de behandeling die ik nu krijg niet meer zou werken	☐	☐
h. het stoppen van de behandeling, als die niet meer zou werken	☐	☐
i. de kans dat ik zou sterven	☐	☐

12. Ik wil binnenkort met mijn vader praten over...:	Ja	Nee
a. wat ik belangrijk vind in mijn leven	☐	☐
b. hoe ik me voel door mijn ziekte en behandeling	☐	☐
c. waarover ik veel nadenk of pieker	☐	☐
d. waarvoor ik bang ben	☐	☐
e. waarop ik hoop	☐	☐
f. wat ik verwacht van de toekomst	☐	☐
g. het wel of niet starten van een nieuwe behandeling, als de behandeling die ik nu krijg niet meer zou werken	☐	☐
h. het stoppen van de behandeling, als die niet meer zou werken	☐	☐
i. de kans dat ik zou sterven	☐	☐

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Deel 2: Praten met een kinderoncoloog uit het ziekenhuis

13. Heb je in de afgelopen maand nog een afspraak gehad in het ziekenhuis bij de kinderoncoloog?

- ☐ Ja, één afspraak
- ☐ Ja, meerdere afspraken
- ☐ Nee
- ☐ Ik weet het niet meer

14. Ik heb in de afgelopen maand met een kinderoncoloog gepraat over...:	Ja	Nee
a. wat ik belangrijk vind in mijn leven	☐	☐
b. hoe ik me voel door mijn ziekte en behandeling	☐	☐
c. waarover ik veel nadenk of pieker	☐	☐
d. waarvoor ik bang ben	☐	☐
e. waarop ik hoop	☐	☐
f. wat ik verwacht van de toekomst	☐	☐
g. het wel of niet starten van een nieuwe behandeling, als de behandeling die ik nu krijg niet meer zou werken	☐	☐
h. het stoppen van de behandeling, als die niet meer zou werken	☐	☐
i. de kans dat ik zou sterven	☐	☐

15. Ik wil binnenkort met een kinderoncoloog praten over...:	Ja	Nee
a. wat ik belangrijk vind in mijn leven	☐	☐
b. hoe ik me voel door mijn ziekte en behandeling	☐	☐
c. waarover ik veel nadenk of pieker	☐	☐
d. waarvoor ik bang ben	☐	☐
e. waarop ik hoop	☐	☐
f. wat ik verwacht van de toekomst	☐	☐
g. het wel of niet starten van een nieuwe behandeling, als de behandeling die ik nu krijg niet meer zou werken	☐	☐
h. het stoppen van de behandeling, als die niet meer zou werken	☐	☐
i. de kans dat ik zou sterven	☐	☐

Deel 3: Hoe heb je je gevoeld in de afgelopen 7 dagen en hoe voel je je vandaag?

16. Deze vragen gaan over hoe jij de afgelopen 7 dagen gevoeld hebt.	Nooit	Bijna nooit	Soms	Vaak	Bijna altijd
a. Ik had het gevoel dat er iets verschrikkelijks zou kunnen gebeuren.	☐	☐	☐	☐	☐
b. Ik voelde me zenuwachtig.	☐	☐	☐	☐	☐
c. Ik voelde me bang.	☐	☐	☐	☐	☐
d. Ik maakte me zorgen.	☐	☐	☐	☐	☐
e. Ik maakte me zorgen als ik thuis was.	☐	☐	☐	☐	☐
f. Ik werd echt gauw bang.	☐	☐	☐	☐	☐
g. Ik maakte me zorgen over wat er met me zou kunnen gebeuren.	☐	☐	☐	☐	☐
h. Ik maakte me zorgen als ik 's avonds naar bed ging.	☐	☐	☐	☐	☐
i. Ik voelde me gelukkig.	☐	☐	☐	☐	☐
j. Ik voelde me opgelucht.	☐	☐	☐	☐	☐
k. Ik voelde me mentaal sterk.	☐	☐	☐	☐	☐

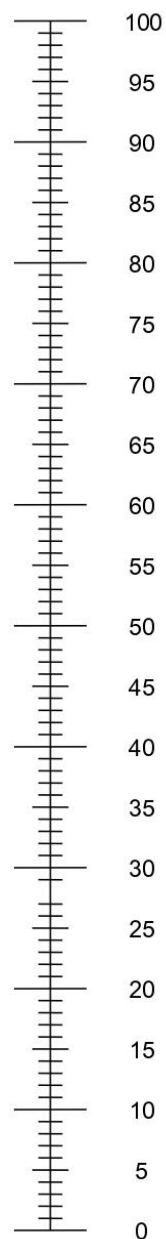
17. Zet bij iedere groep hieronder een kruisje in het ENE hokje dat het best past bij je eigen gezondheid VANDAAG	Nee	Een beetje	Veel
a. Ik heb problemen met rondwandelen.	☐	☐	☐
b. Ik heb problemen met wassen of aankleden.	☐	☐	☐
c. Ik heb problemen met mijn dagelijkse activiteiten (bijvoorbeeld naar school gaan, hobby's, sporten, spelen, dingen doen met familie of vrienden).	☐	☐	☐
d. Ik heb pijn of andere ongemakken.	☐	☐	☐
e. Ik ben bezorgd, verdrietig of ongelukkig.	☐	☐	☐

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18.

- We willen graag weten hoe goed of slecht je gezondheid VANDAAG is.
- Daarvoor hebben we deze genummerde lijn van 0 tot en met 100 getekend.
- 100 geeft de beste gezondheid aan die je je kunt voorstellen.
0 geeft de slechtste gezondheid aan die je je kunt voorstellen.
- Plaats een X op de lijn om aan te geven hoe goed of slecht je gezondheid VANDAAG is

De beste gezondheid die je je kunt voorstellen



De slechtste gezondheid die je je kunt voorstellen

Deel 4: Wie ben jij?

19.

a. Ik ben een

- ☐ Jongen/ man
- ☐ Meisje/ vrouw
- ☐ Anders

b. Dit is mijn geboortedatum: _____ (dag – maand – jaar)

c. Ik ben in _____ geboren

(. geef jouw geboorteland bijvoorbeeld: België, Marokko, Spanje)

Deel 5: Heb je nog opmerkingen?

20. Schrijf het hier:



Onderzoeker
Anne van Driessche

DANK JE!

Vragen of opmerkingen? Stuur een mailtje naar
Anne.van.Driessche@vub.be of bel op +32(0)456302963



Vragenlijst voor ouders

(TO)



BOOST: een studie rond vroegtijdige zorgplanning in de kinderoncologie

Vragenlijst voor ouders

Uitleg bij deze vragenlijst

Bedankt dat u meewerkt aan ons onderzoek!

Waarover gaat het onderzoek?

Dit onderzoek wordt uitgevoerd door onderzoekers van de Vrije Universiteit Brussel (VUB) en Universiteit Gent (UGent) en is gefinancierd door het Fonds Wetenschappelijk Onderzoek (FWO) en het Kinderkankerfonds. Het doel van het project is om in de toekomst de zorg beter af te stemmen op de wensen en noden van adolescenten en ouders.

Waar gaan de vragen in de vragenlijst over?

Graag komen wij meer te weten over in hoeverre u met uw kind praat over welke zorg en behandeling uw kind wilt. De vragenlijst gaat over verschillende dingen.

- Deel 1. Wat uw kind belangrijk vindt in zijn of haar zorg of behandeling
- Deel 2. Over uw laatste contact met een kinderoncoloog
- Deel 3. Hoe heeft u zich de afgelopen 7 dagen gevoeld?
- Deel 4. Demografische gegevens
- Deel 5. Heeft u nog opmerkingen?

Hoe vul ik de vragenlijst in?

Het invullen duurt ongeveer 30 - 40 minuten. U kunt ervoor kiezen de vragenlijst in te vullen op papier of digitaal via <https://tinyurl.com/BoostStudie-ouderbase>.

Enkele instructies voor u van start gaat:

4. De meeste vragen kunt u beantwoorden door één van de vakjes aan te vinken: ☒. Indien u meer dan één antwoord aan kunt duiden, staat dit bij de vraag vermeld. Bij de open vragen kunt u zelf iets neerschrijven.
5. Het is belangrijk voor het onderzoek dat u alle vragen in de vragenlijst beantwoordt. Goede of foute antwoorden zijn er niet. Communicatie tussen kind en ouder(s) is uniek voor elk gezin en loopt bij iedereen anders. Wij willen enkel inzicht krijgen in hoe jullie communicatie verloopt. De vragen in deze vragenlijst zeggen niets over de kwaliteit van de communicatie of de kwaliteit van de relatie tussen jullie beide. Soms kan het moeilijk zijn om een precies antwoord te geven. Vink dan het vakje aan dat zo dicht mogelijk aanleunt bij uw antwoord.

Vertrouwelijkheid van uw gegevens

De gegevens die in het kader van uw deelname worden verzameld zijn vertrouwelijk, in overeenstemming met de Belgische Wetgeving op de bescherming van de persoonlijke levenssfeer.

Vragen?

Contacteer Anne van Driessche (uitvoerend onderzoeker)

tel: +32(0)456302963

e-mail: Anne.van.Driessche@vub.be

Deel 1: Wat uw kind belangrijk vindt in zijn of haar zorg en behandeling

Welke zorg en behandeling wil uw kind? En praat u daarover met hem of haar? Dat onderzoeken we met deze vragenlijst.

In deze vragenlijst hebben we het niet alleen over de medische behandeling tegen kanker. We bedoelen met zorg **ook** verzorging en ondersteuning die uw kind krijgt of wil krijgen. Bijvoorbeeld van u als ouder of wettelijke voogd.

1. De datum vandaag is: _____ (dag)/_____ (maand)/_____ (jaar)

2. Deze vragen gaan over praten met uw kind over wat hij of zij belangrijk vindt in de zorg en behandeling. Geef aan in hoeverre u het eens of oneens bent met de volgende uitspraken	Helemaal oneens	Oneens	Niet eens en niet oneens	Eens	Helemaal eens
i. Ik vind het belangrijk om met mijn kind te praten over wat hij of zij belangrijk vindt in de zorg en behandeling.	☐	☐	☐	☐	☐
j. Ik vind het moeilijk om te weten te komen wat mijn kind belangrijk vindt in de zorg en behandeling.	☐	☐	☐	☐	☐
k. Ik vraag mijn kind nadrukkelijk wat hij of zij belangrijk vindt in de zorg en behandeling.	☐	☐	☐	☐	☐
l. Ik ben bang dat ik mijn kind verdrietig maak als ik praat over wat hij of zij belangrijk vindt in de zorg en behandeling.	☐	☐	☐	☐	☐
m. Ik vind dat mijn kind nog niet mee kan beslissen over de zorg en behandeling.	☐	☐	☐	☐	☐
n. Als mijn kind wil praten over de zorg en behandeling, dan sta ik daarvoor open.	☐	☐	☐	☐	☐
o. Ik praat gemakkelijk met mijn kind over wat hij of zij belangrijk vindt in de zorg en behandeling.	☐	☐	☐	☐	☐

h. Indien u dat wenst, kunt u hier eventuele toelichting schrijven.

3. Hoezeer lukken deze zaken u?	Helemaal oneens	Oneens	Niet eens en niet oneens	Eens	Helemaal eens
a. Het lukt mij goed om te praten met mijn kind, als hij of zij anders denkt over de zorg of behandeling dan ik.	☐	☐	☐	☐	☐
b. Het lukt mij goed om te weten te komen wat mijn kind écht wil in de zorg of behandeling.	☐	☐	☐	☐	☐
c. Het lukt mij goed om mijn kind het gevoel te geven dat hij of zij over alles kan praten met mij.	☐	☐	☐	☐	☐
d. Het lukt mij goed om mijn kind tijdens een consultatie zelf te laten praten met een arts over wat hij of zij belangrijk vindt in de zorg en behandeling.	☐	☐	☐	☐	☐
e. Het lukt mij goed om mijn kind te stimuleren om te zeggen wat hij of zij belangrijk vindt in de zorg en behandeling.	☐	☐	☐	☐	☐
f. Het lukt mij goed om met mijn kind tot gezamenlijke besluiten te komen wat betreft de zorg en behandeling.	☐	☐	☐	☐	☐

g. Indien u dat wenst, kunt u hier eventuele toelichting schrijven.

4. Het zou mij goed lukken om een gesprek te hebben met mijn kind <u>als hij of zij begint over...</u> :	Helemaal oneens	Oneens	Niet eens en niet oneens	Eens	Helemaal eens
j. wat mijn kind belangrijk vindt in het leven	☐	☐	☐	☐	☐
k. hoe mijn kind zich voelt door de ziekte en behandeling	☐	☐	☐	☐	☐
l. waarover mijn kind piekert	☐	☐	☐	☐	☐
m. waarvoor mijn kind bang is	☐	☐	☐	☐	☐
n. waarop mijn kind hoopt	☐	☐	☐	☐	☐
o. wat mijn kind verwacht van de toekomst	☐	☐	☐	☐	☐
p. het wel of niet starten van een nieuwe behandeling, als de behandeling die mijn kind nu krijgt niet meer zou werken	☐	☐	☐	☐	☐
q. het stoppen van de behandeling, als de behandeling die mijn kind nu krijgt niet meer zou werken	☐	☐	☐	☐	☐
r. of er een kans bestaat dat mijn kind zou sterven aan de ziekte	☐	☐	☐	☐	☐

j. Indien u dat wenst, kunt u hier eventuele toelichting schrijven.

5. Als ik daar nood aan heb, zou het mij goed lukken om zelf te beginnen praten met mijn kind over....:	Helemaal oneens	Oneens	Niet eens en niet oneens	Eens	Helemaal eens
a. wat mijn kind belangrijk vindt in het leven	☐	☐	☐	☐	☐
b. hoe mijn kind zich voelt door de ziekte en behandeling	☐	☐	☐	☐	☐
c. waarover mijn kind piekert	☐	☐	☐	☐	☐
d. waarvoor mijn kind bang is	☐	☐	☐	☐	☐
e. waarop mijn kind hoopt	☐	☐	☐	☐	☐
f. wat mijn kind verwacht van de toekomst	☐	☐	☐	☐	☐
g. het wel of niet starten van een nieuwe behandeling, als de behandeling die mijn kind nu krijgt niet meer zou werken	☐	☐	☐	☐	☐
h. het stoppen van de behandeling, als de behandeling die mijn kind nu krijgt niet meer zou werken	☐	☐	☐	☐	☐
i. of er een kans bestaat dat mijn kind zou sterven aan de ziekte	☐	☐	☐	☐	☐

j. Indien u dat wenst, kunt u hier eventuele toelichting schrijven.

6. Ik heb de afgelopen 30 dagen met mijn kind gepraat over....:	Ja	Nee
a. wat mijn kind belangrijk vindt in het leven	☐	☐
b. hoe mijn kind zich voelt door de ziekte en behandeling	☐	☐
c. waarover mijn kind piekert	☐	☐
d. waarvoor mijn kind bang is	☐	☐
e. waarop mijn kind hoopt	☐	☐
f. wat mijn kind verwacht van de toekomst	☐	☐
g. het wel of niet starten van een nieuwe behandeling, als de behandeling die mijn kind nu krijgt niet meer zou werken	☐	☐
h. het stoppen van de behandeling, als de behandeling die mijn kind nu krijgt niet meer zou werken	☐	☐
i. of er een kans bestaat dat mijn kind zou sterven aan de ziekte	☐	☐

j. Indien u dat wenst, kunt u hier eventuele toelichting schrijven.

7. Ik ben van plan binnenkort te praten met mijn kind over....:	Ja	Nee
a. wat mijn kind belangrijk vindt in het leven	☐	☐
b. hoe mijn kind zich voelt door de ziekte en behandeling	☐	☐
c. waarover mijn kind piekert	☐	☐
d. waarvoor mijn kind bang is	☐	☐
e. waarop mijn kind hoopt	☐	☐
f. wat mijn kind verwacht van de toekomst	☐	☐
g. het wel of niet starten van een nieuwe behandeling, als de behandeling die mijn kind nu krijgt niet meer zou werken	☐	☐
h. het stoppen van de behandeling, als de behandeling die mijn kind nu krijgt niet meer zou werken	☐	☐
i. of er een kans bestaat dat mijn kind zou sterven aan de ziekte	☐	☐

j. Indien u dat wenst, kunt u hier eventuele toelichting schrijven.

Ga verder op de volgende pagina

Deel 2: Over uw laatste contact met een kinderoncoloog

8. Heeft u in de afgelopen 30 dagen nog een afspraak gehad in het ziekenhuis bij de kinderoncoloog?

- ☐ Ja, één afspraak
- ☐ Ja, meerdere afspraken
- ☐ Nee
- ☐ Ik weet het niet meer

Als u terugdenkt aan het laatste bezoek aan uw kinderoncoloog...

Omcirkel een cijfer aan dat voor u het beste past.

9. Hoeveel moeite is er gedaan om u te helpen de gezondheidssituatie van uw kind te begrijpen? (omcirkel)

0	1	2	3	4	5	6	7	8	9	
Helemaal geen moeite gedaan										Alle mogelijke moeite gedaan

10. Hoeveel moeite is er gedaan om te luisteren naar de dingen die voor u belangrijk zijn als het gaat om de gezondheidssituatie van uw kind? (omcirkel)

0	1	2	3	4	5	6	7	8	9	
Helemaal geen moeite gedaan										Alle mogelijke moeite gedaan

11. Hoeveel moeite is er gedaan om de dingen die voor u belangrijk zijn mee te nemen bij het kiezen van een volgende stap? (omcirkel)

0	1	2	3	4	5	6	7	8	9	
Helemaal geen moeite gedaan										Alle mogelijke moeite gedaan

Deel 3: Hoe heeft u zich de afgelopen 7 dagen gevoeld?

12. Deze vragen gaan over hoe u zich de afgelopen 7 dagen gevoeld heeft.	Nooit	Bijna nooit	Soms	Vaak	Bijna altijd
a. Ik voelde me angstig.	☐	☐	☐	☐	☐
b. Ik voelde me angstig en bezorgd.	☐	☐	☐	☐	☐
c. Ik maakte me zorgen.	☐	☐	☐	☐	☐
d. Ik vond het moeilijk om me op iets anders dan mijn angst en mijn bezorgdheid te concentreren.	☐	☐	☐	☐	☐
e. Ik voelde me zenuwachtig.	☐	☐	☐	☐	☐
f. Ik voelde me slecht op mijn gemak.	☐	☐	☐	☐	☐
g. Ik voelde me gespannen.	☐	☐	☐	☐	☐
h. Ik voelde me gelukkig.	☐	☐	☐	☐	☐
i. Ik voelde me opgelucht.	☐	☐	☐	☐	☐
j. Ik voelde me mentaal sterk.	☐	☐	☐	☐	☐

Deel 4: Demografische gegevens

13. Vul hier uw persoonlijke gegevens in:

a. Wat is uw geslacht?	☐ Man ☐ Vrouw ☐ Anders
b. Wat is het geslacht van uw kind?	☐ Man ☐ Vrouw ☐ Anders
c. Wat is uw geboortedatum?	____/____/____ (dd/mm/jjjj)
d. Wat is de geboortedatum van uw kind?	____/____/____ (dd/mm/jjjj)
e. Wat is uw hoogst behaalde diploma?	☐ geen ☐ lager onderwijs ☐ lager middelbaar ☐ hoger middelbaar ☐ graduaat (A2) ☐ bachelor (A1) ☐ master ☐ doctoraat (PhD)

f. Welke categorie beantwoordt het best aan uw huidige beroepssituatie?	☐ Voltijds werk ☐ Deeltijds werk ☐ Student ☐ Momenteel heb ik geen werk ☐ Anders: _____
g. Heeft u uw werksituatie moeten aanpassen naar aanleiding van de ziekte van uw kind?	☐ Nee ☐ Ja, namelijk: _____ _____ _____
h. Wat is uw relatie met het kind?	☐ Ik ben de biologische moeder ☐ Ik ben de biologische vader ☐ Ik ben de stiefmoeder/ plusmama ☐ Ik ben de stiefvader/ pluspapa ☐ Ik heb een relatie met de biologische moeder of vader van het kind ☐ ander/niets van bovenstaande opties
i. Wat is uw gezinssituatie? (kies wat best past)	☐ gehuwd of samenwonend ☐ gescheiden en alleenwonend ☐ weduwe/weduwnaar ☐ alleenstaande ouder – ongehuwd ☐ nieuw samengesteld gezin ☐ ander
j. Wat is uw nationaliteit?	
k. Wat is de nationaliteit van uw kind?	
l. Heeft u nog andere kinderen? Zo ja, hoeveel andere kinderen?	☐ Nee ☐ Ja, ik heb ____ andere kinderen
m. Wat zijn de geboortedata van uw andere kinderen?	_____ _____ _____
n. Bent u gelovig?	☐ Ja, voeg toe wat uw religieuze overtuiging is (optioneel): _____ ☐ Nee ☐ Ik zou deze vraag liever niet beantwoorden

Deel 5: Heeft u nog opmerkingen?

14. Schrijf het hier:



Vragen of opmerkingen? Stuur een mailtje naar
Anne.van.Driessche@vub.be of bel op +32456302963



BOOST: een studie rond vroegtijdige zorgplanning in de kinderoncologie

Vragenlijst voor kinderoncologen (T0)

Waarover gaat het onderzoek?

Deze vragenlijst kadert in een onderzoek van de **Vrije Universiteit Brussel (VUB)** en **Universiteit Gent (UGent)**, gefinancierd door het Fonds Wetenschappelijk Onderzoek (FWO) en het Kinderkankerfonds. Het doel van dit project is het evalueren van **voorafgaande of vroegtijdige zorgplanning (VZP) bij adolescenten met kanker, hun ouders en kinderoncologen**. De studie wordt uitgevoerd over een periode van 2 jaar (van 18 januari 2021 – 18 januari 2023) in de vier universitaire ziekenhuizen in Vlaanderen.

Waarom vragen we u deze vragenlijst in te vullen?

Een gezin dat deelneemt aan de studie heeft uw naam opgegeven als de kinderoncoloog met wie ze het meeste contact hebben over de zorg en behandeling van de adolescent. De data collector van het onderzoeksteam heeft u de gegevens van dit gezin per mail bezorgd. Wij zouden u willen verzoeken deze vragenlijst over de adolescent van dit gezin in te vullen, zodat we belangrijke informatie kunnen koppelen aan de vragenlijsten die het gezin heeft ingevuld. U zult later nog 2 uitnodigingen ontvangen om een soortgelijke vragenlijst over deze adolescent in te vullen (verspreid over een periode van 6 maanden).

Als u deze vragenlijst invult, dient u het volgende te weten:

- ✓ Dit project werd opgestart na goedkeuring door de ethische comités van UZ Brussel/VUB, UZ Leuven, UZ Gent en UZ Antwerpen.
- ✓ Uw deelname is geheel **vrijwillig**. Indien u deze vragenlijst invult, gaat u ermee akkoord dat de studiegegevens die voor de hier vermelde studie worden verzameld, later zullen worden verwerkt, op voorwaarde dat deze verwerking beperkt blijft tot de context van de hier vermelde studie.
- ✓ De gegevens die in het kader van uw deelname worden verzameld zijn **vertrouwelijk**, in overeenstemming met de Belgische Wetgeving op de bescherming van de persoonlijke levenssfeer.
- ✓ Uw gegevens worden **anoniem** verwerkt. De u persoonlijk toegewezen code, zal enkel door een onafhankelijke data-collector aan uw persoonlijke gegevens gelinkt kunnen worden.

Enkele instructies voor u van start gaat:

1. Het invullen van deze vragenlijst duurt **5 -10 minuten**
2. Alle vragen kunt u beantwoorden door één of meerdere van de vakjes aan te vinken ☒
3. Zou u de vragenlijst **binnen een week** willen invullen?

Vragen?

Contacteer Anne van Driessche (uitvoerend onderzoeker)

tel: +32(0)456302963

e-mail: Anne.van.Driessche@vub.be

Alvast hartelijk bedankt voor uw bereidheid om deze vragenlijst in te vullen!

Vragenlijst over de adolescent

1. Datum van vandaag:	____/____/____ (dd/mm/jjjj)
2. Wat is de hoofddiagnose van het kind op dit moment?	☐ Leukemie ☐ Hersentumor ☐ Lymfeklierkanker ☐ Neuroblastoom ☐ Retinoblastoom ☐ Levertumor ☐ Niertumor ☐ Kiemceltumor ☐ Bottumor ☐ Tumor van de weke delen ☐ Andere: _____
3. Is er sprake van een recidief?	☐ Nee ☐ Ja, eerste recidief ☐ Ja, tweede recidief of meer
4. Is er sprake van metastasering?	☐ Nee ☐ Ja (vul in), _____
5. Zijn er comorbiditeiten* bij dit kind? Zo ja, welke? *aanwezigheid van een aandoening naast de primaire, centraal staande ziekte	_____ _____ _____
6. Wanneer is het kind voor de eerste keer gediagnosticeerd met kanker?	Datum: ____/____/____ (dd/mm/jjjj)

7. Wat is het type behandeling dat het kind nu krijgt? (meerdere antwoorden mogelijk)	☐ Chemotherapie ☐ Radiotherapie ☐ Hormoontherapie ☐ Chirurgie ☐ Experimentele therapie (Farmacologische en/of non-farmacologische behandeling waarvan het nuttig effect nog dient bewezen te worden in de klinische praktijk. Specificeer: _____) ☐ Ik weet het niet ☐ Geen behandeling ☐ Andere: _____
8. Welke lijn behandeling krijgt het kind op dit moment?	☐ Eerste lijn ☐ Tweede lijn ☐ Derde lijn of meer
9. Wat is het huidige hoofddoel van de behandeling van het kind? Kies wat het meest van toepassing is.	☐ Patiënt krijgt een behandeling die in opzet curatief is. ☐ Patiënt krijgt een behandeling die in opzet levensverlengend is. ☐ Patiënt krijgt een behandeling die in opzet symptoombestrijdend is.
10. Hoe lang zorgt u al voor dit kind?	☐ 0 – 6 maanden ☐ 6 – 12 maanden ☐ 1 – 2 jaar ☐ Meer dan 2 jaar
11. Zou u de kans op overleving kunnen inschatten voor dit kind op dit moment? (in percentage)	____%

Hieronder vindt u een aantal vragen over vroegtijdige zorgplanning.

Met vroegtijdige zorgplanning (VZP) bedoelen we het communicatieproces dat kinderen in staat stelt om te bespreken wat voor hen belangrijk is en hen in staat stelt om doelen en voorkeuren te formuleren voor toekomstige zorg en behandeling, deze doelen en voorkeuren te bespreken met familie en zorgverleners en om eventuele voorkeuren vast te leggen en indien nodig te herzien. Voorbeelden van VZP-thema's zijn: beleving van de ziekte, angsten, wie wil je dat er beslissingen maakt en hoe, toekomstverwachtingen, voorkeuren voor zorg en behandeling voor nu en in de toekomst.

12. Welke thema's heeft u in de afgelopen 30 dagen besproken met dit kind?
(meerdere antwoorden mogelijk)

- ☐ Zijn/haar angsten of bezorgdheden
- ☐ Zijn/haar verwachtingen voor de toekomst
- ☐ Wat hij/zij belangrijk vindt als het om zijn of haar zorg of behandeling gaat.
- ☐ Keuzes die mogelijks gemaakt zullen moeten worden in de behandeling
- ☐ Wanneer hij/zij het stoppen van de behandeling zou overwegen
- ☐ Wanneer hij/zij het wel of niet starten van een nieuwe behandeling zou overwegen
- ☐ Met wie de behandeling verder besproken moet worden, mocht het kind wilsonbekwaam worden
- ☐ De kans dat hij/zij zou sterven.
- ☐ Andere thema's gerelateerd aan VZP: _____

- ☐ Dergelijke thema's zijn nog niet aan bod gekomen **(ga dan naar vraag 14)**
- ☐ Ik heb deze patiënt de afgelopen 30 dagen niet gesproken **(ga dan naar vraag 14)**

13. Hoe heeft u de verkregen informatie over bovenstaande thema's in vraag 12 van dit kind verwerkt en doorgegeven?
(meerdere antwoorden mogelijk)

- ☐ Ik heb deze informatie zelf bijgehouden. Ik heb deze niet gedeeld met anderen.
- ☐ Ik heb dit doorgegeven aan één of meerdere leden van het medisch team op een informele manier.
- ☐ Ik heb dit doorgegeven aan het medisch team tijdens een multidisciplinair overleg
- ☐ Ik heb deze informatie toegevoegd aan het medisch dossier
- ☐ Anders, namelijk: _____

14. Bent u van plan om de komende drie maanden bepaalde thema's te bespreken met dit kind? Zo ja, welke thema's zijn dat? (meerdere antwoorden mogelijk)

- ☐ Zijn/haar angsten of bezorgdheden
- ☐ Zijn/haar verwachtingen voor de toekomst
- ☐ Wat hij/zij belangrijk vindt als het om zijn of haar zorg of behandeling gaat.
- ☐ Keuzes die mogelijk gemaakt zullen moeten worden in de behandeling
- ☐ Wanneer hij/zij het stoppen van de behandeling zou overwegen
- ☐ Wanneer hij/zij het wel of niet starten van een nieuwe behandeling zou overwegen
- ☐ Met wie de behandeling verder besproken moet worden, mocht het kind wilsonbekwaam worden
- ☐ De kans dat hij/zij zou sterven.
- ☐ Andere thema's gerelateerd aan VZP: _____

- ☐ Ik ben niet van plan om dergelijke thema's te bespreken omdat, _____

Additional file 2. Process evaluation methods based on UK MRC guidance on process evaluations of complex interventions (Moore et al., 2015)

Dimension and subdimension (definition by Moore et al. 2015)	Outcomes and indicators (I) If no level is indicated the indicator is applicable across levels or no specific level	Data collection each outcome/indicator can be evaluated qualitatively or quantitatively using one or more data-collection methods, see corresponding letters	Timing (T0: baseline, T1: 3 months, T2: 7 months)
Implementation (<i>the structures, processes and resources through which delivery is achieved, and the quantity and quality of what is delivered</i>)			
1. How delivery is achieved (<i>the structures, processes and resources through which delivery is achieved</i>)			
1.A. Structures (how the intervention activities were implemented)	(a) description of how the intervention activities were implemented per family: I1: location of ACP conversations I2: order of activities implemented, and how those were implemented I3: who was present during the ACP conversations I4: whether and how information is transferred to paediatric oncologist I5: whether the facilitator had contact with the family in between/after ACP sessions, how (e.g. modes of communication) and about what I6: whether the facilitator used extra exercises during the ACP, how and why	(a1) To measure I1-6, facilitators will complete a <u>structured diary</u> (a2) Semi-structured individual <u>interviews</u> with facilitators	(a1) Throughout the data collection period after each facilitated ACP conversation with a patient and/or family (a2) Intermediate (every 6 months) and post data collection period
1B. Resources	(b) Time investment facilitators I1: Time spent on training I2: Time spent by facilitator on preparation of intervention activities I3: Time spent by facilitators on delivery of the intervention activities	(b) To measure I1-3, we will use specific questions in the structured diaries to keep track of time spent on preparation and delivery of key ACP activities (cf. conversations)	(b) monthly by facilitators, throughout data collection period
2. What is delivered (<i>the quantity and quality of what is delivered</i>)			
2A. Dose (<i>how much intervention/the quantity of what is delivered</i>)	(c) Amount of intervention activities delivered per family I1: number of ACP activities held per family I2: number of topics discussed and not discussed during the conversations	(c1) To measure I1-I2 we will ask facilitators to complete a <u>structured diary</u> (c2) To measure I2 we will <u>audiotape ACP conversations</u>	(c1) Throughout the data collection period after each facilitated ACP conversation with a patient and/or family (c2) Each ACP conversation held is ideally audiotaped (after

			informed consent of participants)
2B. Reach (<i>extent to which a target audience comes into contact with the intervention</i>)	(d) Number of eligible families approached by facilitator, and proportion of families included in total I1: number of adolescents involved I2: number of parents involved I3: average ratio adolescent: parent	(d) Trial monitoring	(d) Throughout the study
2C. Fidelity (<i>consistency of what is implemented with the planned intervention</i>)	(e) activities delivered as intended: I1: number of activities delivered as intended I2: order of intervention activities delivered as planned (f) content of ACP conversations delivered as intended I1: number of ACP conversation sessions in which (<i>all, half, less than half</i> - of the topics were discussed	(e) To measure I1-2 we will ask facilitators to complete a <u>structured diary</u> (f) To measure I1 we will <u>audiotape ACP conversations</u> ; we will use the pre-structured checklist based on conversation manuals to check fidelity (we aim to select 8 families who have participated in all 4 BOOST pACP conversations, from whom we will analyse all 4 conversations. We intend to include dyads from different hospitals and with adolescents from different age categories)	(e) Throughout the data collection period after each facilitated ACP conversation with a patient and/or family (f) Each ACP conversation held is ideally audiotaped (after informed consent of participants)
2D. Adaptations (<i>alterations made to an intervention in order to achieve better conceptual fit</i>)	(g) Type of adaptations made in intervention activities (as described by manual) (h) Type of adaptations made in intervention activities per hospital	(g1) Facilitators complete a <u>structured diary</u> (g2+h) Semi-structured <u>individual interviews with facilitators</u> (h) Semi-structured <u>individual interviews with paediatric oncologists (n = 8)</u>	(g1) Throughout the data collection period after each facilitated ACP conversation with a patient and/or family (g2) Intermediate (every six months) and after the data collection period. (h) After 12 months and after data collection period
2E. Quality (<i>the quality of what is delivered</i>)	(i) Perceived quality of the ACP conversations	(i) <u>Semi-structured interviews with adolescent and parent(s) separately (n=10)</u>	(i) Post-intervention maximally two months after the last ACP session
Mechanisms of impact (<i>the intermediate mechanisms through which intervention activities produce intended (or unintended) effects/how intervention activities, and participants' interactions with them, trigger change</i>)			

1. Responses and interactions <i>(how participants interact with the intervention)</i>	(j) Level of satisfaction about the intervention as a whole and the different components (k) Perceived benefit and relevance of the intervention/value placed on the intervention	(j1+k1) <u>Semi-structured interviews with adolescent and parent(s) separately (n=10)</u> (j2+k2) <u>Semi-structured individual interviews with paediatric oncologists(n=8)</u> (k3) <u>Semi-structured interviews with facilitators</u>	(j1) Post-intervention maximally two months after the last ACP session (j2) after 12 months and post data collection period (k3) every 6 months and post-intervention
2. Mediators <i>(intermediate processes which explain subsequent changes in outcomes)</i>	(l) Evaluation of <u>perceived mediators</u>: l1: the extent to which BOOST has contributed to more knowledge about ACP l2: more positive attitude on ACP l3: better self-efficacy in ACP l4: a higher intention to communicate on ACP themes l5: improved communication between ... adolescent, parent(s) and healthcare professionals	(l1) <u>Semi-structured interviews with adolescent and parent separately (n= 10)</u> (l2) <u>Semi-structured interviews with facilitators</u> (l3) <u>Semi-structured interviews with paediatric oncologists (n = 8)</u>	(l1) post-intervention (in adolescents/parents, maximally two months after the last ACP session) (l2) every 6 months and post-intervention (l3) after 12 months and post-intervention
3. Unanticipated pathways or consequences	(m) + (n) Potential unanticipated consequences of the BOOST pACP program in adolescents, parents (per family) and in oncologists, teams, hospital wards (whether the intervention led to other changes)	(m) <u>Semi-structured interviews with adolescent and parent separately (n = 10)</u> (n) <u>Semi-structured interviews with paediatric oncologists(n = 8)</u>	(m) post-intervention (in adolescents/parents, maximally two months after the last ACP conversation of the family) (n) after 12 months and post-intervention
Context <i>(factors external to the intervention which may influence its implementation, or whether its mechanisms of impact act as intended / how external factors influence the delivery and functioning of interventions)</i>			
1. Contextual moderators	(o) + (p) Contextual barriers that inhibit/facilitators that facilitated pACP implementation and/or effectiveness (eg. skills, attitudes, or organisational norms, culture (human, financial, resources)	(o1+p1) <u>Semi-structured interviews with adolescent and parent separately (n = 10)</u> (o2+p2) <u>Semi-structured interviews with facilitators</u> (o3+p3) <u>Semi-structured interviews with paediatric oncologists (n=8)</u>	(o1 ,p1) post-intervention (in adolescents/parents)-, maximally two months after the last ACP conversation of the family) (o2+p2) every 6 months and post-intervention (o3 + p3) after 12 months and post-intervention

2. Intention for maintenance <i>(extent to which the program is intended to be part of routine organisational practice and policy)</i>	(q) + (r) Intention of adolescents/parents/healthcare professionals to conduct ACP conversations (or other BOOST pACP activities) in the future	(q) Semi-structured <u>interviews with adolescent and parent</u> separately (n = 10) (r) Semi-structured <u>interviews with paediatric oncologists</u> (n=8)	(q) post-intervention (in adolescents/parents)-, maximally two months after the last ACP conversation of the family) (r) after 12 months and post-intervention
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PART II

RESULTS FROM THE BOOST pACP STUDY

Chapter 3

MULTI-CENTER RANDOMIZED CONTROLLED TRIAL ON ADVANCE CARE PLANNING FOR ADOLESCENTS WITH CANCER AND THEIR PARENTS: IMPACT ON PARENT-ADOLESCENT COMMUNICATION AS THE PRIMARY OUTCOME

This chapter is based on:

van Driessche A, Cohen J, Deliëns L, Kars MC, Willems L, De Buyser S, Verlooy J, Renard M, Eecloo K, De Vleminck A*, Beernaert K*. Randomized controlled trial on advance care planning for adolescents with cancer and their parents: impact on parent-adolescent communication [Submitted]

*Shared last author

Abstract

Objective: This study evaluates whether the **B**enefits of **O**btaining **O**wnership **S**ystematically **T**ogether in **p**ediatric **A**dvice **C**are **P**lanning (BOOST pACP) intervention improves parent-adolescent communication compared to care as usual.

Study design: In this multi-center parallel-group superiority trial, adolescent patients (10-18 years old) diagnosed with cancer and their parent(s) were randomized with a 1:1 allocation to a pACP intervention or care as usual. The primary endpoint was the adolescents' assessment of quality of parent-adolescent communication at 3 months, and the secondary was quality of parent-adolescent communication at 7 months.

Results: Forty-nine families were enrolled (28% enrollment rate) between March 2021 and March 2023. No significant differences in parent-adolescent communication were observed between the BOOST and care as usual groups at 3 months (T1) (baseline-adjusted mean difference = 1.4; 95% CI -4.1 to 6.9; $p=0.608$), effect size 0.13. Similarly, at 7 months (T2) differences were not significant (baseline-adjusted mean difference = 5.2; 95% CI -0.6 to 11.0; $p=0.077$), effect size 0.49 (and 0.67 for father-adolescent communication). No significant differences in anxiety scores of adolescents and parents were found and no adverse events were reported.

Conclusion: The BOOST pACP intervention did not significantly improve parent-adolescent communication for adolescents with cancer and their parents at 3 months after baseline. However, the results indicate it might have a clinical impact in later stages of the follow-up period. Limitations of this study are the underpowered sample size and the lack of validated questionnaires for specific ACP communication.

Introduction

Adolescents with cancer are increasingly recognized as important voices in their own healthcare. Yet, they often face obstacles in having their opinions, wishes, and values heard when health care decisions are made [1, 2], and they are not routinely asked about their experiences of living with their illness and views on future treatment and care [3]. One reason for this is that tools or guidance to support participation of adolescents in their own healthcare are scarce [3]. Advance care planning (ACP) provides potential in that respect. ACP is a process that explores the values, beliefs and wishes to inform healthcare decisions and guide future care [4]. Pediatric ACP (pACP) has the potential to improve outcomes for both adolescents and their families, such as reducing parental decisional regret and child suffering at the end of life [4] and adolescents want to and benefit from addressing difficult topics in advance [5]. In focusing on the short and long-term quality of life for the adolescent and their immediate family, ACP can contribute to comprehensive pediatric care [6].

However, the majority of evidence relates to ACP in adult patients [7]. Evaluations of pACP interventions are rare and the interventions that have been evaluated often do not include children or adolescents themselves but only their caregivers [5]. Moreover, some of the interventions that were evaluated do not go beyond aiming to increase congruence on end-of-life preferences. The study on family-centered pediatric advance care planning intervention (FACE) is the only pACP intervention RCT worldwide and has shown to improve congruence between adolescents and their families regarding end-of-life treatment for one year [8]. Such a focus does not reflect the current prognostic landscape within pediatric palliative care where advancements have led to more adolescents with previously lethal conditions surviving into adulthood and the end-of-life phase difficult to mark [9]. Giving adolescents choices in their healthcare by empowering them to actively participate in decision-making, irrespective of whether this anticipates a specific scenario of death may be a more promising route for ACP with adolescents. The IMPACT program is the first ACP program providing a holistic approach giving children a voice addressing both views on living well in the context of a life-limiting condition, as well as views on what is important to them also when their health is worsening. Qualitative evaluation showed positive results in terms of appropriateness, but evidence on effectiveness is still lacking [10]. The MAPPS program also recognizes the need for individualization of pACP discussions by offering different modules. However, children were not involved in the development phase and no evidence on effectiveness is currently available [11]. In conclusion, there is a lack of robust evaluative research for these types of interventions [3, 12].

The BOOST pACP (**B**enefits of **O**btaining **O**wnership **S**ystematically **T**ogether in **p**ediatric **a**dvance **c**are **p**lanning) intervention was developed to facilitate conversations on ACP themes between adolescents and their parents, while also lowering the threshold for discussing similar themes with their healthcare professionals, ultimately aiming to normalize and integrate ACP in routine care. Parent-adolescent communication was chosen as the primary outcome measure due to evidence showing the need for improvement in discussing illness, treatment, and quality of life when an adolescent is diagnosed with cancer, as families often try to protect each other from unpleasant emotions [13–15].

Objective

This study aims to evaluate whether the BOOST pACP intervention improves parent-adolescent communication, as assessed by adolescents with cancer using the Parent-Adolescent Communication Scale (PACS), compared to care as usual.

Methods

Trial design

We conducted a multi-center parallel-group superiority trial, comparing the BOOST pACP intervention to care as usual (control group). Adolescent patients and their parent(s) were randomized to the intervention arm or the control arm after baseline assessment. Main results of a study in which adolescents, parents and pediatric oncologists participate are presented in this article. Details on the trial procedures are described more extensively in the research protocol [16]. We applied the 2017 Consolidated Standards of Reporting Trials (CONSORT) statement to report on all relevant aspects of the trial [17].

Participants

Inclusion criteria for the adolescents were: aged between 10 – 18 years, diagnosis of cancer at least 3 months ago, aware of cancer diagnosis according to parent(s), receiving active treatment in a pediatric oncology ward (last treatment was maximally 3 months ago), fluent Dutch language understanding. Exclusion criteria for the adolescents were: participation in the feasibility test of this study, intellectual disabilities, life expectancy less than 3 months [16]. Inclusion criteria for the parents were: aware of the cancer diagnosis of their child, fluent Dutch language understanding. Exclusion criteria for parents were: participated in the feasibility test of this study and intellectual disabilities. At least one parent had to participate for the family to be included [16].

Setting

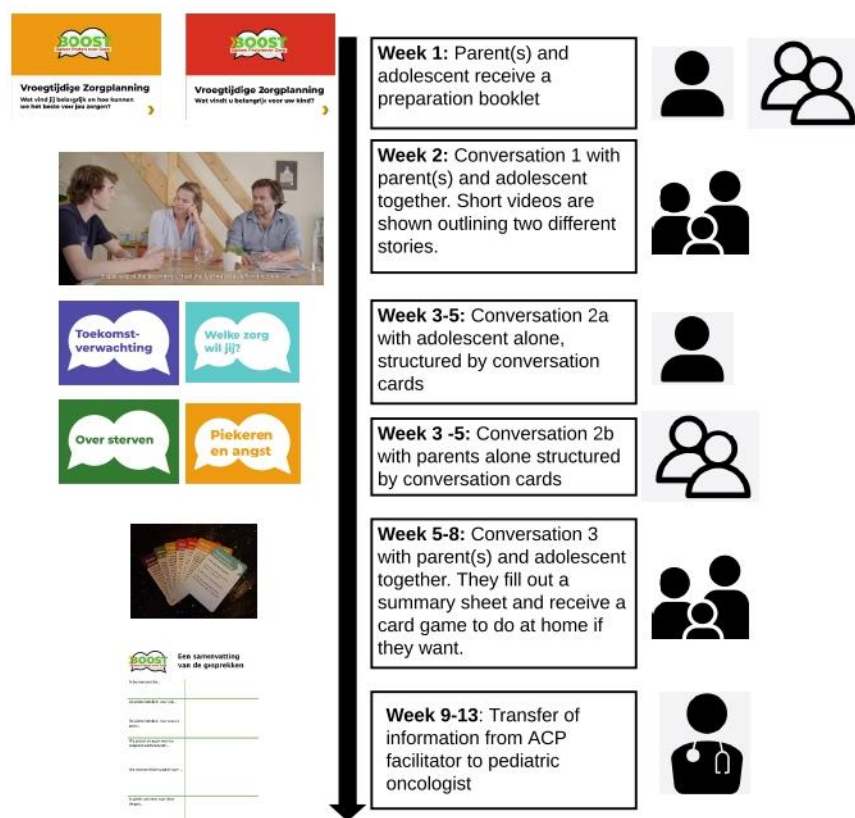
Families were recruited between March 2021 and March 2023 from 4 pediatric oncology wards in Flanders, Belgium: University Hospitals of Leuven, Ghent, Antwerp and Brussels. The University Hospital of Brussels dropped out after one year, because their pediatric oncology department was dissolved. Parents and adolescents could choose the location of the intervention sessions: either online, at home or at the hospital.

Intervention and control

All families in the BOOST group received the “BOOST pACP” intervention, alongside care as usual. This contained four ACP conversation sessions with the adolescent and/or parent(s) provided by a trained facilitator (external to the medical team), structured by interactive conversation cards covering different ACP topics based on the existing ACP conversation guide of IMPACT[10], followed by a transfer of information from the intervention facilitator to the pediatric oncologist (see **Figure 1**). All intervention components were administered within approximately three months. The development and content of the BOOST pACP intervention have been described elsewhere [18].

The control group received care as usual. Pediatric ACP is not implemented in a structured way in Belgium. ACP themes may be discussed throughout the illness trajectory in a non-standardized way, depending on system-, attitude-, parent- or clinician-related factors [18]. Families have access to psychologists upon request.

Figure 1: The BOOST pACP intervention



The images on the left shows the materials we developed in Dutch. English translation of some conversation cards of the adolescents: 1) Talking with others; 2) Hope and comfort; 3) Worries and fears; 4) Care preferences; 5) Expectations for the future; 6) About dying. For more information on the content of the materials, see the article on the development of the BOOST pACP intervention[18].

Data collection procedures and outcomes

Questionnaires were filled out at baseline measurement before randomization (T0), after 3 months (T1) and after 7 months (T2). Data collectors assisted adolescents with filling out the questionnaire at all timepoints, unless adolescents insisted on filling out the questionnaires themselves and were 15 years or older. The questionnaires were pseudonymized using individual identifier codes attributed by the data collector. More details are published elsewhere [16].

The primary endpoint was defined as parent-adolescent communication on ACP themes at 3 months (T1). This was measured in adolescents using the Parent-Adolescent Communication Scale (PACS) [19–21]. This is a validated questionnaire to measure perception of the quality of communication, which we applied to pACP themes (**Additional file 1**). Adolescents report on 20 items on openness of communication and problems in communication with each involved parent. Hence, observations on both mother-adolescent communication, as well as father-adolescent communication can be collected. The score ranges from 20 to 100, with higher scores indicating better communication.

The protocol-specified [16] secondary endpoint reported here is parent-adolescent communication at 7 months (T2) from the perspective of the adolescent using the PACS.

Anxiety was measured with the PROMIS measure, using response pattern scoring. Higher scores indicate more anxiety, and 50 is the mean of the reference population [22]. Other outcomes were measured [16], but are not reported in this article. Socio-demographic characteristics of the adolescents were retrieved from parents and pediatric oncologists.

Sample size

To detect a clinically relevant difference of 7 points (range 20 – 100) on the primary outcome (PACS) at T1 between the care as usual group and the BOOST group (assuming a pooled standard deviation of 11.4), with alpha set at 0.05 and power at 80%, and a 90% retention rate, we anticipated a required sample size of 48 in each arm, i.e. 96 in total [16].

Randomization and blinding

Block randomization was performed after at least one of the parents had completed the baseline measurement, with a 1:1 allocation ratio to either the intervention arm (BOOST group) or the care as usual arm (control group). We used a concealed envelope method and stratified the allocation by age (10-14 years old vs 15-18 years old). An independent statistician had prepared the list of group allocation and there was no way data collectors knew beforehand the result of the randomization for that particular family. Data collectors opened the envelope together with the family after the family had officially been enrolled in the trial and after having filled out the baseline measurement, so that allocation concealment was ensured. Researchers were single blinded as to which arm families belong to including data analyses. Participating families, the ACP trained facilitators and pediatric oncologists could not be blinded, as they were involved in the intervention.

Statistical analysis

Our primary analysis was based on the intention-to-treat (ITT) principle, in addition we performed several sensitivity and subgroup analyses. The ITT analysis, for which the analysis set included all observations of all adolescents who were randomized, aimed to estimate the causal effect of being allocated to the BOOST intervention, regardless of compliance to the intervention. The analysis sets for the sensitivity analyses included all observations of adolescents allocated to care as usual and all observations of those adolescents allocated to the BOOST intervention, whose parent(s) were present for at least one/ two/ three sessions. These sensitivity analyses give an estimate of the causal effect of the BOOST intervention, in the hypothetical scenarios where all parents of adolescents allocated to the intervention would have been compliant to attend at least one/ two / all three sessions.

Missing data were imputed implicitly through maximum likelihood estimation assuming data were missing at random. We performed subgroup analyses on communication with mothers and fathers separately.

Mean differences between the control group and the BOOST group in quality of communication were estimated using a linear mixed model. A random intercept for adolescent was included to account for the correlation between repeated measures within an adolescent (over time and over parent). Age category (stratification factor, 10 -14 years old vs 15 – 18 years old), parent, randomization arm, timepoint (baseline, T1, T2), and the interaction between randomization arm and timepoint were included as fixed factors. The interaction effect (with 95% CI and p value) is reported and reflects the estimated mean difference in change from baseline between the BOOST and control group. In addition, we reported the

estimated marginal mean PACS scores at each timepoint by group with 95% CI. Effect sizes were calculated as the ratio of the estimate of the interaction term to the square root of the sum of the residual and random intercept variance from a null model.

Analyses were performed using IBM SPSS statistics for Windows, Version 29.0.1.0 Armonk, NY (IBM Corp).

Registration, protocol and funding

This trial is registered with isrctn.com, number 33228289. The protocol of the BOOST trial was published in BMC Pediatrics. The project received funding from the Research Foundation-Flanders (under grant Agreement G.0194.18N) and by Kinderkankerfonds (no grant number).

Ethics

Ethics approval was obtained from the Central Ethics Committee of the Vrije Universiteit Brussel (Brussels, Belgium) and from the local ethics committees of the participating hospitals (B1432020000177) [16].

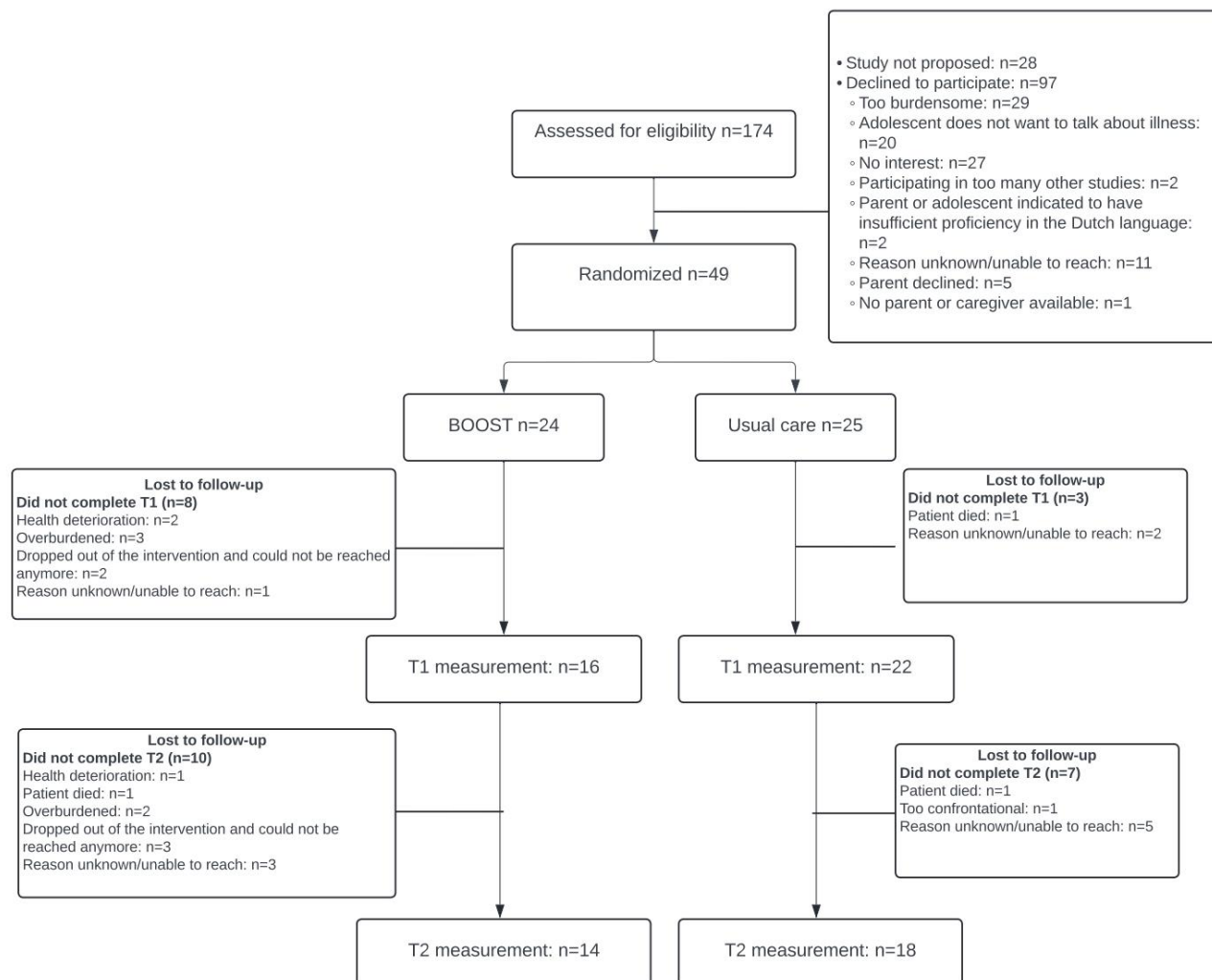
Results

Study flow and baseline characteristics

In total 174 adolescents were screened for eligibility (**Figure 2**). In total, 49 families enrolled, resulting in an enrollment rate of 28.2% (Hospital of Brussels n=1; Antwerp n=9; Leuven; n=19; Ghent n=20). Baseline characteristics for randomized adolescents are displayed in **Table 1**.

Figure 2: CONSORT flow diagram

These are the best possible estimates based on the information we have received from the hospitals. The pediatric oncology department of the University Hospital of Brussels



was dissolved in summer 2022.

Table 1. Baseline characteristics for adolescent patients

Characteristics	Patients (adolescents)	
	Care as usual group (n=25)	BOOST group (n=24)
Age (years)		
Mean age (SD)	13.7 (2.3)	14.2 (2.4)
Age range	10 - 18	10 - 18
Gender		
Male (%)	13 (52%)	15 (62.5%)
Female (%)	12 (48%)	9 (37.5%)
Main diagnosis		
Leukemia	10 (41.7%)	10 (41.7%)
Brain tumor	3 (12.5%)	4 (16.7%)
Lymph node cancer	3 (12.5%)	5 (20.8%)
Neuroblastoma	1 (4.2%)	0 (0%)
Kidney tumor	1 (4.2%)	0 (0%)
Bone tumor	2 (8.3%)	1 (4.2%)
Tumor of the soft tissues	2 (8.3%)	1 (4.2%)
Other	2 (8.3%)	3 (12.5%)
Recurrence of cancer		
No	21 (91.3%)	19 (82.6%)
Yes. the first recurrence	1 (4.3%)	4 (17.4%)
Yes. the second recurrence or more	1 (4.3%)	0 (0%)
Metastasis		
No	19 (82.6%)	18 (75%)
Yes	4 (17.4%)	6 (25%)
Comorbidities		
No	23 (92%)	18 (75%)
Yes	2 (8%)	6 (25%)
Type of current treatment		
Chemotherapy	21 (87.5%)	19 (79.2%)
Radiotherapy	4 (16.7%)	8 (33.3%)
Hormone therapy	0 (0%)	0 (0%)
Surgery	7 (29.2%)	7 (29.2%)
Experimental therapy	1 (4.2%)	0 (0%)
No treatment	1 (4.2%)	1 (4.2%)
Other	1 (4.2%)	1 (4.2%)
Line of treatment		
First line of treatment	22 (91.7%)	20 (83.3%)
Second line of treatment	0 (0%)	3 (12.5%)
Third line of treatment or more	2 (8.3%)	1 (4.2%)
Current main goal of the treatment		
Curation	19 (86.4%)	21 (87.5%)
Life prolonging	2 (9.1%)	3 (12.5%)
Comfort care	1 (4.5%)	0 (0%)
Estimated prognosis by the oncologist		
Mean chance of survival percentage	81.6	73.9
Time between diagnosis and study enrollment		
Mean number of months (median)	12.8 (median 6.2)	19.6 (median 7.6)

Footnote Table 1: Missings care as usual group: n=1 for main diagnosis. line of treatment and time between diagnosis and study enrollment. n=2 for recurrence of cancer and metastasis. n=3 for current main goal of treatment. Missings intervention group: n=1 for recurrence of cancer. n=3 for time between diagnosis and study enrollment.

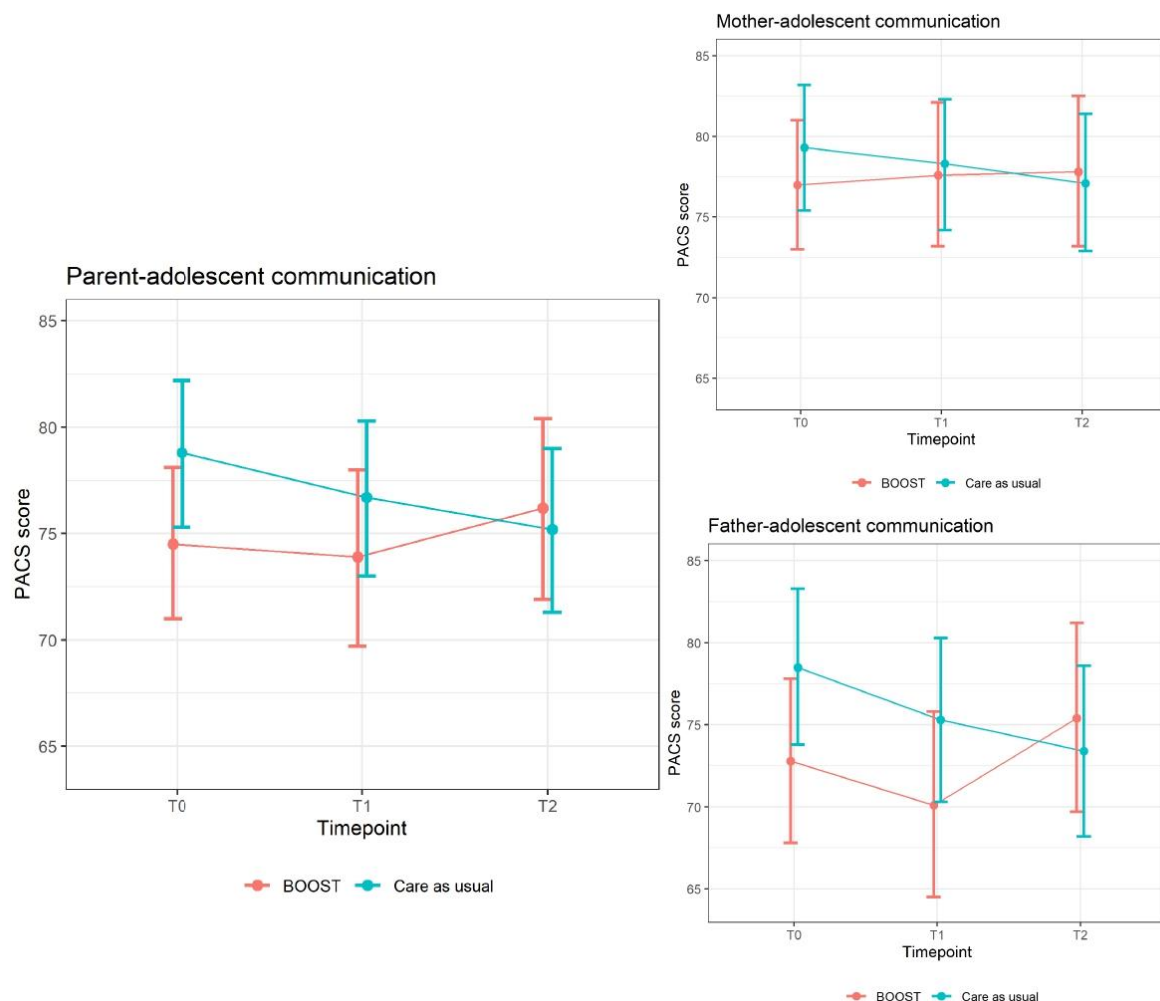
Exposure to the BOOST intervention

Of the 24 families in the BOOST group, 20 completed all sessions. One family dropped out after session 1, two after session 2 and one did not participate (due to low interest, not wanting to focus on ACP topics anymore, health deterioration or not being in active treatment anymore). The BOOST sessions were completed within 21 to 147 days ($M=58$ days; $SD=32.8$ days). In 25% of the cases, both parents were present during all sessions. In 42% of the cases, only the mother was present during all sessions, and in 8% of the cases, only the father was present during all sessions.

Endpoints

The measurement points occurred slightly later than scheduled. At T1, the mean was 118 days (4 months, $SD=23.3$, range 87 – 188 days) as opposed to 3 months, and at T2, the mean was 233 days (7.7 months, $SD=26.2$, range 193 – 337 days), as opposed to 7 months. The estimated marginal mean PACS scores with 95% CI at each timepoint by group are presented in **Table 2** and **Figure 3**.

Figure 3: PACS scores for the BOOST and care as usual groups at T0, T1 and T2



Parent-adolescent communication

Based on the ITT analysis (**Table 2**), at T1, the estimated mean change from baseline in parent-adolescent communication was 1.4 points higher (better) in the BOOST group compared to the control group (95% CI -4.1 to 6.9), although this difference was not statistically significant ($p=0.608$). At T2, the estimated mean change from baseline in parent-adolescent communication was 5.2 points higher in the BOOST group compared to the control group (95% CI -0.6 to 11.0). Results from sensitivity analyses were similar to that of the main analysis (**Additional file 2**).

Mother-adolescent communication

In the subgroup analysis using only observations of the adolescents on mother-adolescent communication, the estimated mean change from baseline was also in favor of the BOOST group (at T1: baseline-adjusted mean difference = 1.6; 95% CI -3.5 to 6.8; at T2: baseline-adjusted mean difference = 3.0; 95% CI -2.5 to 8.5).

Father-adolescent communication

In the subgroup analysis using only observations of the adolescents on father-adolescent communication, the estimated mean change from baseline was also in favor of the BOOST group (at T1: baseline-adjusted mean difference = 0.6; 95% CI -5.6 to 6.8; at T2: baseline-adjusted mean difference = 7.8; 95% CI 1.3 to 14.3).

Adverse events and safety measures

No adverse events were reported from the intervention. In adolescents, the estimated change from baseline of anxiety levels was in favor of the BOOST group at T1 (baseline-adjusted mean difference = -4.5; 95% CI -10.3 to 1.3) and at T2 (baseline-adjusted mean difference = -2.0; 95% CI -8.2 to 4.1). In parents, the estimated change from baseline of anxiety levels was in favor of the BOOST group at T1 (baseline-adjusted mean difference = -0.5; 95% CI -5.8 to 4.8) and at T2 (baseline-adjusted mean difference = -1.1; 95% CI -6.9 to 4.7) (**Additional file 3**).

Conditional power analysis

A conditional power analysis showed that if we would have continued to recruit patients until 96 patients were randomized (as initially intended), assuming that the data to be observed in the remainder of the study would follow the effect estimated from the current data (effect size 0.489), we would have had 66% power to detect a mean difference in change from baseline at T2 for PACS.

Table 2. Estimated mean scores at baseline, 3 months and 7 months and differences on parent-adolescent communication

	Baseline (T0) Mean score (95% CI)*		3 months post- baseline (T1) Mean score (95% CI)		Mean difference in change from baseline (95% CI)	P value	Effect size**	7 months post-baseline (T2) Mean score (95% CI)		Mean difference in change from baseline (95% CI)	P value	Effect size**
	BOOST intervention	Usual care	BOOST intervention	Usual care				BOOST intervention	Usual care			
Quality of parent-child communication (PACS) – reported by the adolescent												
Total score	74.5 (71.0 – 78.1)	78.8 (75.3 – 82.2)	73.9 (69.7 – 78.0)	76.7 (73.0 – 80.3)	1.4 (-4.1 – 6.9)	0.608	0.13	76.2 (71.9 – 80.4)	75.2 (71.3 – 79.0)	5.2 (-0.6 – 11.0)	0.077	0.49
Openness scale	39.9 (38.1 – 41.8)	41.9 (40.1 – 43.7)	39.0 (36.9 – 41.2)	40.8 (38.9 – 42.7)	0.3 (-2.8 – 3.3)	0.857	0.05	40.9 (38.6 – 43.2)	39.7 (37.7 – 41.7)	3.2 (0.0 – 6.4)	0.051	0.55
Problems scale***	34.6 (32.4 – 36.7)	36.8 (34.7 – 39.0)	34.7 (32.3 – 37.2)	35.9 (33.7 – 38.1)	1.1 (-1.9 – 4.2)	0.472	0.18	35.3 (32.7 – 37.8)	35.5 (33.1 – 37.8)	2.1 (-1.2 – 5.3)	0.205	0.34
Quality of mother-child communication (PACS) – reported by the adolescent												
Total score	77.0 (73.0 – 81.0)	79.3 (75.4 – 83.2)	77.6 (73.2 – 82.1)	78.3 (74.2 – 82.3)	1.6 (-3.5 – 6.8)	0.527	0.17	77.8 (73.2 – 82.5)	77.1 (72.9 – 81.4)	3.0 (-2.5 – 8.5)	0.279	0.31
Openness scale	42.2 (40.2 – 44.2)	42.4 (40.4 – 44.4)	41.4 (39.1 – 43.6)	41.8 (39.7 – 43.9)	-0.2 (-2.9 – 2.5)	0.884	-0.04	42.0 (39.7 – 44.4)	41.3 (39.1 – 43.4)	1.0 (-1.8 – 3.8)	0.487	0.20
Problems scale	34.8 (32.3 – 37.3)	36.9 (34.4 – 39.3)	36.3 (33.4 – 39.1)	36.5 (33.9 – 39.1)	1.9 (-1.6 – 5.3)	0.285	0.30	35.8 (32.8 – 38.7)	35.9 (33.1 – 38.6)	2.0 (-1.7 – 5.6)	0.294	0.32
Quality of father-child communication (PACS) – reported by the adolescent												
Total score	72.8 (67.8 – 77.8)	78.5 (73.8 – 83.3)	70.1 (64.5 – 75.8)	75.3 (70.3 – 80.3)	0.6 (-5.6 – 6.8)	0.848	0.05	75.4 (69.7 – 81.2)	73.4 (68.2 – 78.6)	7.8 (1.3 – 14.3)	0.019	0.67
Openness scale	37.8 (35.0 – 40.6)	41.7 (39.1 – 44.3)	36.9 (33.8 – 40.1)	40.1 (37.3 – 42.9)	0.7 (-2.9 – 4.3)	0.703	0.11	40.2 (36.9 – 43.4)	38.4 (35.5 – 41.3)	5.6 (1.8 – 9.4)	0.005	0.85
Problems scale	35.0 (32.3 – 37.6)	36.8 (34.3 – 39.4)	33.3 (30.1 – 36.4)	35.2 (32.5 – 37.9)	-0.1 (-4.2 – 4.0)	0.967	-0.01	35.4 (32.1 – 38.6)	35.0 (32.1 – 37.9)	2.2 (-2.0 – 6.5)	0.300	0.37

*Estimated marginal means, adjusted for the variables included in the model.

**Effect sizes were calculated as the ratio of the estimate of the interaction term to the square root of the sum of the residual and random intercept variance from the null model.

*** Items on the Problems scale were reversed in value. The total score of the PACS ranges from 20 – 100. Higher scores reflect better communication

Discussion

This multicenter trial aimed to evaluate whether the BOOST pACP intervention can improve parent-adolescent communication in adolescents with cancer, when compared to care as usual. Although our point estimates for the changes from baseline at three months and at seven months in parent-adolescent communication (as perceived by adolescents) were in favor of the BOOST pACP intervention compared to care as usual, we could not find any significant differences between the groups (despite a medium effect size at the secondary endpoint).

The FACE-TC trial by Lyon et al. demonstrated significant effects of an ACP intervention on caregiving appraisals of family members [23] and sustained families' knowledge of their adolescents' end-of-life treatment preferences [8]. The lack of significance in our trial might be explained by several reasons. First, our trial was underpowered due to lower enrollment than expected, decreasing the probability of finding statistically significant effects. Second, the PACS measures general parent-adolescent communication. Although we applied it to communication about ACP themes, it is possible that this adaptation did not capture differences effectively and may not be sensitive to detect differences in communication in that regard. Due to the lack of validated questionnaires for cancer-related parent-adolescent communication [15] or communication on pACP topics specifically, we selected the most widely used communication scale PACS [24]. Intervention-related factors may also underlie the lower impact on parent-adolescent communication. External facilitators led the BOOST sessions and did not know about the medical trajectory of the adolescent beforehand. The conversations might have been more care- and treatment-focused if conducted by someone from the medical team.

Interestingly, although we could not find a statistically significant effect on parent-adolescent communication at the second timepoint (7 months after baseline), the effect size was 0.49. This is higher than the effect size of 0.28 found in the FACE-TC intervention on positive caregiving appraisals [23] and the effect sizes of 0.10 and 0.20 on the PACS of a legacy intervention for children with advanced cancer [25]. The higher effect size at seven months rather than three months might be due to more follow-up points in the illness trajectory allowing adolescents to notice communication improvements. We found a large effect size of 0.67 for father-adolescent communication, aligning with findings from a web-based legacy intervention [25]. Baseline data showed lower scores for open communication with fathers than with mothers, providing more room for improvement. Previous studies show that parent-adolescent communication worsens over time following an adolescent's cancer diagnosis [13, 20], which is reflected in the declining scores of our usual care group. No significant differences in anxiety scores were found, for adolescents as well as for parents, suggesting that these ACP conversations do not cause distress.

To the authors' knowledge, this is the second study evaluating the effectiveness of an ACP program in adolescents with cancer through a randomized controlled trial [8, 23], and the first to include a more contemporary broader approach to ACP [10, 26]. The multi-center RCT was successfully designed and conducted, involving a diverse cohort of adolescents aged 10 to 18, with various types of cancer, across several pediatric centers in the country, enhancing the study's external validity. However, the trial also faced several methodological difficulties that might have impacted the internal validity of the study. Enrollment was lower than anticipated, as is often the case for psychosocial interventions in pediatric oncology [27],

resulting in an underpowered sample size. Lower enrollment was attributed to overburdened families, competing medical trials, the need to recruit a dyad and hectic family life [27]. Mostly adolescents with a good prognosis in the first line of treatment were recruited, possibly leading to smaller effect estimates. To limit measurement bias, experienced and well-trained data collectors assisted adolescents with filling out the questionnaires. This approach was taken for several reasons: to minimize missing data, to alleviate the potential burden caused by repetitive questions about ACP topics (such as when to start or stop treatment) that were used to assess various behavioral determinants included besides the PACS as secondary outcomes, and to provide necessary clarification on certain questions if anything was unclear. This strategy was recommended by psychologists from the involved department during the development phase of the intervention and the ethics committee. Nevertheless, this strategy risks introducing some interviewer bias and can cause possible placebo effects in the care as usual group. Enrollment may have impacted the study, as families with less open communication might have been less likely to participate, complicating efforts to reach those who would benefit most from this support.

Conclusion

In conclusion, while our findings could not demonstrate a significant improvement compared to care as usual in parent-adolescent communication shortly after participation in the BOOST pACP program, there is some indication that it might have a more pronounced clinical impact in the longer term. These findings seem to align with other literature, particularly qualitative studies, suggesting that pACP may provide a pre-initiation process necessary to establish foundations for engaging in ACP when needed [28]. Appropriate and sensitive tools for communication in pACP are required. This study lays a foundation for future meta-analyses that can further elucidate the effects of ACP in this population.

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Additional file 1. Extra information on application of the PACS to ACP themes

In the introduction of the questionnaire, it was formulated that the statements of the PACS are particularly about communication on what they find important regarding their care and treatment. It was clarified that we did not only mean the medical treatment from healthcare professionals in the hospital (such as from nurses, oncologists or psychologists), but that we also mean help or support received from other people, such as from parents, friends or family. This was emphasized verbally by the data collector throughout administering the questionnaire.

Additional file 2. Sensitivity analyses – estimated mean scores at baseline, 3 months and 7 months and differences on parent-adolescent communication

	Baseline (T0)		3 months post- baseline (T1)		Mean difference in change from baseline (95% CI)	P value	7 months post-baseline (T2)		Mean difference in change from baseline (95% CI)	P value
	Mean score (95% CI)		Mean score (95% CI)							
	BOOST intervention	Usual care	BOOST intervention	Usual care			BOOST intervention	Usual care		
Only with parents who were present during all three BOOST pACP conversation sessions										
Total PACS score	76.2 (71.8 – 80.5)	78.9 (75.6 – 82.3)	74.0 (69.4 – 78.6)	76.8 (73.3 – 80.3)	-0.08 (-5.5 – 5.3)	0.978	78.2 (73.2 – 83.2)	75.3 (71.6 – 79.0)	5.6 (-0.3 – 11.5)	0.061
With parents who were present during at least two BOOST pACP conversation sessions										
Total PACS score	76.1 (72.1 – 80.1)	79.0 (75.6 – 82.4)	75.4 (70.9 – 79.9)	76.9 (73.3 – 80.5)	1.5 (-4.2 – 7.1)	0.610	77.8 (73.0 – 82.5)	75.4 (71.6 – 79.2)	5.3 (-0.7 – 11.3)	0.082
With parents who were present during at least one BOOST pACP conversation session										
Total PACS score	76.1 (72.3 – 79.9)	79.0 (75.6 – 82.4)	75.4 (70.9 – 79.8)	76.9 (73.3 – 80.5)	1.4 (-4.2 – 7.0)	0.617	77.5 (72.9 – 82.2)	75.4 (71.6 – 79.2)	5.1 (-0.8 – 10.9)	0.089

Footnote: In the hypothetical scenario that all parents of adolescents allocated to the intervention group would have been present during the BOOST intervention sessions. The analysis sets for the above sensitivity analyses included all observations of adolescents allocated to care as usual and all observations of those adolescents allocated to the BOOST intervention, whose parent(s) were present for at least one/ two / three sessions.

Additional file 3. Estimated mean scores at baseline, T1 and T2 and differences on anxiety

	Baseline (T0)		3 months post- baseline (T1)		Mean difference in change from baseline (95% CI)*	P value	Effect size*	7 months post-baseline (T2)		Mean difference in change from baseline (95% CI)	P value	Effect size**
	Mean score (95% CI)		Mean score (95% CI)									
	BOOST intervention	Usual care	BOOST intervention	Usual care				BOOST intervention	Usual care			
PROMIS Anxiety – reported by the adolescent – TScores***												
Total score	51.7 (47.9 – 55.5)	51.1 (47.3 – 54.9)	48.8 (44.3 – 53.2)	52.7 (48.7 – 56.7)	-4.5 (-10.3 – 1.3)	0.124	-0.46	47.7 (43.0 – 52.5)	49.2 (45.0 – 53.4)	-2.0 (-8.2 – 4.1)	0.513	-0.20
PROMIS Anxiety – reported by the parents– TScores***												
Total score parents	61.2 (58.2 – 64.2)	59.9 (56.9 – 62.9)	59.3 (55.8 – 62.8)	58.6 (55.3 – 61.8)	-0.5 (-5.8 – 4.8)	0.855	-0.06	58.2 (54.1 – 62.3)	58.0 (54.7 – 61.4)	-1.1 (-6.9 – 4.7)	0.714	-0.12
Total score mothers	64.2 (60.2 – 68.2)	62.4 (58.1 – 66.6)	61.5 (56.9 – 66.0)	60.5 (56.1 – 64.8)	-0.8 (-7.7 – 6.1)	0.810	-0.08	58.8 (53.1 – 64.5)	59.5 (54.9 – 64.2)	-2.6 (-10.4 – 5.3)	0.515	-0.27
Total score fathers	56.4 (52.7 – 60.1)	57.5 (54.3 – 60.8)	55.2 (51.0 – 59.4)	55.2 (51.6 – 58.8)	1.1 (-3.6 – 5.9)	0.626	0.15	57.1 (52.8 – 61.5)	55.6 (52.0 – 59.2)	2.7 (-2.1 – 7.5)	0.270	0.37

*Estimated marginal means, adjusted for the variables included in the model

** Effect sizes were calculated as the ratio of the estimate of the interaction term to the square root of the sum of the residual and random intercept variance from the null model.

***Adolescent: T-scores can range from 33.5 to 83.3 on this measure. Parents: T-scores can range from 36.3 – 82.7 on this measure

Footnote: PROMIS Pediatric Item Bank v2.0 – Anxiety – Short Form 8a – reported by the adolescents. PROMIS Item Bank v1.0 – Anxiety – Short form 7a – reported by the parents. Response pattern scoring was used (item-level calibrations). This way is preferred because it is more accurate than the use of raw score. A score of 50 is the average for the US general population, with a SD of 10. We used the manual of the Dutch-Flemish PROMIS National Center.

Chapter 4

INFLUENCE OF PEDIATRIC ADVANCE CARE PLANNING ON THE SECONDARY OUTCOMES OF THE BOOST pACP TRIAL: DETERMINANTS OF COMMUNICATION BETWEEN PARENTS AND ADOLESCENTS WITH CANCER

This chapter is based on:

van Driessche A, Beernaert K, Deliens L, Kars MC, Wallaert S, Willems L, Morren H, Vercruysse G, Vandenbossche A, De Vleminck A*, Cohen J*. Influence of pediatric advance care planning on determinants of communication between parents and adolescents with cancer: a randomized controlled trial. [Ready to submit]

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Abstract

Purpose: This study explores the impact of a pediatric advance care planning program (BOOST pACP) on adolescents with cancer and their parents, focusing on behavioral determinants such as attitudes, self-efficacy, intention and behavior regarding the discussion of ACP topics.

Methods: A multi-center, parallel-group superiority trial was conducted with adolescent-parent dyads recruited from four pediatric oncology wards in Belgium. The intervention group received four structured ACP sessions facilitated by an external professional, while the control group received care as usual. The acquired insights were shared with their oncologist. The behavioral determinants were measured through self-developed questionnaires based on the Theory of Planned Behavior (TPB) at baseline (T0), 3 months (T1), and 7 months (T2). This secondary data analysis used exploratory factor analysis and linear mixed models to assess the impact of the intervention.

Results: Forty-nine families were enrolled and randomized to the BOOST pACP group (n=24) or care-as-usual (n=25). At T1, fathers in the intervention group had significantly lower negative attitudes towards discussing ACP topics than their counterparts in the control group; mothers in the intervention group had increased intentions to discuss end-of-life care topics; and adolescents had reduced intentions to discuss ACP topics with their oncologist. No significant differences between intervention and control were observed in self-efficacy and mothers' attitudes.

Conclusions: Our RCT suggests a limited effectiveness of a pediatric ACP intervention in changing behavioral determinants associated with ACP communication. As the study was eventually underpowered, these findings underscore the need for a better understanding of the mechanisms driving or hindering outcomes and impact of pediatric ACP and highlight the complexity of influencing ACP behaviors within the pediatric oncology setting.

Keywords: advance care planning, communication, behavioral determinants, pediatric oncology, cancer

Introduction

Advance care planning (ACP) involves discussing and reflecting on values, goals, and preferences for future treatment to ensure that individuals with serious illness are actively involved and heard throughout their illness trajectory [1]. ACP with children can be challenging. Previous research has shown that adult ACP cannot be directly applied to pediatric situations [2]. Children's capacity to make health decisions varies depending on the type of decision and context [3], adding complexity to when and how to involve them in their healthcare. Family dynamics also play a significant role [4]. Parents can experience considerable distress, especially when their child is confronted with decisions about ceasing treatment and discussions about mortality [1]. Even in cases where the prognosis is relatively positive, comparable distress may arise during or immediately after active cancer treatment [5]. These factors can complicate constructive communication between adolescents and parents about the illness [6].

While adolescents have reported preferring honest information and benefiting from pediatric advance care planning (pACP) [7], healthcare professionals report several barriers to engaging in ACP with pediatric populations [4]. Effectively stimulating pediatric ACP may particularly require a focus on strengthening parent-adolescent communication, and empowering adolescents to address ACP topics themselves, thereby also lowering the barriers for healthcare professionals. Communication and ACP can be regarded as health behaviors [8–11] that, according to the Theory of Planned Behavior (TPB), are influenced by determinants such as behavioral intention, attitude, subjective norms and self-efficacy [12]. The "Benefits of Obtaining Ownership Systematically Together in pediatric Advance Care Planning (BOOST pACP)" was developed [13] as a pACP intervention that addresses these behavioral determinants in adolescents with cancer in all stages and who face a high symptom and treatment burden with uncertainty about the long-term impact, regardless of whether a specific scenario of death is anticipated [14]. The intervention viewed ACP as an ongoing communication process, rather than being limited to conversations when there is bad news, aiming to either introduce ACP communication early or build upon existing ACP communication [13]. The intervention was tested in a randomized controlled trial [15]. Analysis of the primary endpoint, i.e. parent-adolescent communication, did not indicate significant effects. However, its influence on the different determinants of ACP communication behavior has not been explored. By understanding these processes, we may be able to better amplify the child's voice in ACP discussions and reduce the inability or resistance to engage in these conversations [16]. This study aims to explore the impact of the BOOST pACP intervention on behavioral determinants, i.e. attitudes, self-efficacy and intention regarding discussing ACP topics, as well as the actual behavior of discussing ACP topics.

Methods

Trial design

This multi-center, parallel-group superiority trial compared the BOOST pACP intervention with usual care (control group). The intervention targeted adolescent patients with cancer, their parents and their pediatric oncologist, with randomization at the dyad patient-parent level. The 2017 Consolidated Standards of Reporting Trials (CONSORT) statement was used to report on all relevant aspects of the trial [17].

Participants and setting

From March 2021 to March 2023, families were recruited from the only four pediatric oncology wards in Flanders, Belgium at the: University Hospitals of Ghent, Antwerp, Leuven and Brussels.

Adolescents were eligible for inclusion if they were between 10 and 18 years old, had been diagnosed with cancer at least 3 months prior, were aware of their cancer diagnosis (as confirmed by their parents), were currently receiving active treatment in a pediatric oncology ward (with the last treatment occurring no more than 3 months ago), and had a sufficient proficiency in Dutch. Exclusion criteria for adolescents included prior participation in the feasibility test of this study, intellectual disabilities (as estimated by the pediatric oncologist and psychologist), and a life expectancy of less than 3 months. Parents were eligible if they were aware of their child's cancer diagnosis and had a sufficient proficiency in Dutch. Exclusion criteria for parents included prior participation in the feasibility test and intellectual disabilities. For a family to be included, at least one parent had to participate.

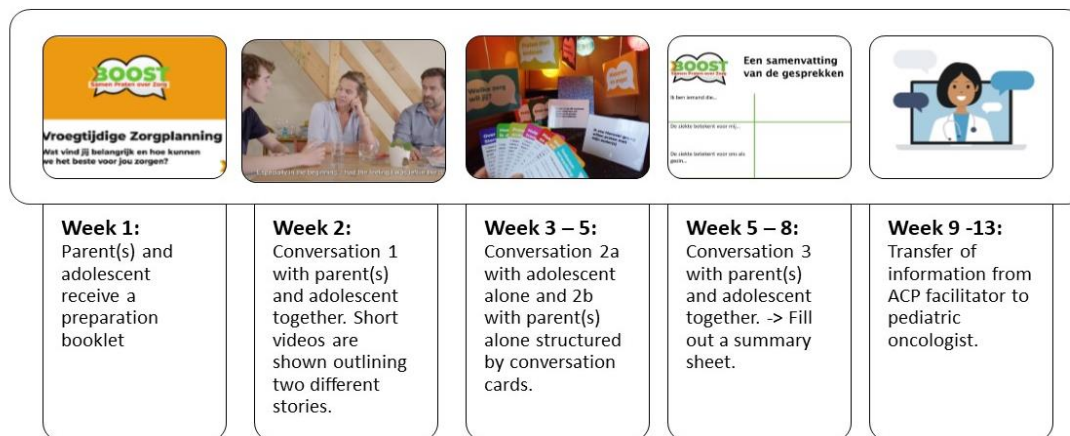
Pediatric oncologists were identified by the family and needed to have at least three months of remaining employment in the department.

Intervention and control

Families in the BOOST group received the "BOOST pACP" intervention in addition to usual care. This intervention included four ACP conversation sessions with the adolescent and/or parents, conducted by a trained facilitator external to the medical team. These sessions were structured using interactive conversation cards based on the existing IMPACT ACP conversation guide[18], and were followed by the conversation facilitator transferring information to the pediatric oncologist (**Figure 1**). All components were completed within approximately three months. The BOOST pACP intervention sessions took place at a location of the family's choice: either at home, at the hospital, or online. Pediatric oncologists were mostly informed by the facilitator about the most relevant points of the intervention sessions via (video)call. The development and content of the BOOST pACP intervention are detailed elsewhere [13].

The control group received usual care. In Belgium, adolescents in the pediatric oncology ward are treated by a variety of oncologists and nurses. Pediatric ACP is not implemented in a structured manner. There is no standardized method for documenting ACP-related information in medical records or for discussing it in multidisciplinary meetings, although this may occur in a fragmented manner by different healthcare professionals. A segment of the oncological population that requires complex care is monitored by pediatric liaison teams [19]. Discussing ACP topics is more common in this context, although it has not yet been implemented in a standardized manner.

Figure 1: The BOOST pACP intervention timeline and content



Data collection procedures and outcomes

Questionnaires were administered at baseline (T0), prior to randomization, as well as at 3 months (T1) and at 7 months (T2). Data collectors provided assistance to adolescents in completing the questionnaire, except when adolescents aged 15 years or older preferred to complete them independently. Each questionnaire was pseudonymized using individual identifier codes assigned by the data collector. Parents were given the option to fill out the questionnaire on paper or online. The family was asked to identify the oncologist they had most frequently consulted during their illness trajectory thus far. This oncologist was invited to complete the questionnaire via an online link. The individual code assigned to them was linked with the adolescent's individual code, ensuring that we could identify the family to which the oncologist's responses pertained at each time point.

Measures

There were no validated questionnaires available for the outcomes we aimed to measure. The questionnaires were self-developed based on a logic model designed for the BOOST pACP intervention, for which we applied the Theory of Planned Behavior (TPB) [13] (see **Figure 2 for the logic model**). We followed three steps in constructing the questionnaires: 1) Using the TPB, we developed items addressing key behavioral constructs to form a prototype questionnaire; 2) This prototype was then adapted for linguistic and age-appropriateness in collaboration with a specialized language center; 3) We conducted cognitive interviews for face validation with four adolescents/young adults with cancer and six parents, which informed the final adjustments that were discussed in detail within the research team. We originally aimed to test face validation with a higher number of adolescents. However, this phase took place during the summer of 2020, when strict COVID-19 regulations complicated recruitment. **Additional file 1** provides examples of adaptations made to the questionnaires.

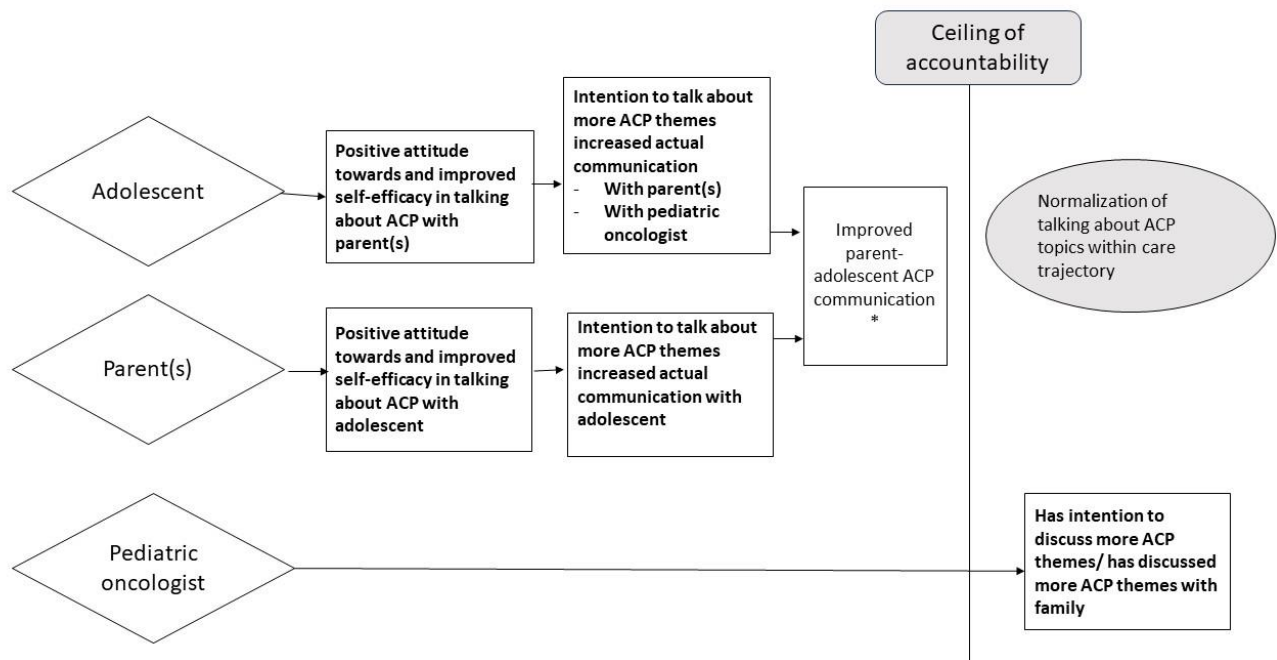
Attitude towards discussing adolescents' care and treatment preferences was assessed using eight items for adolescents and seven for parents on a Likert scale from 1 (totally disagree) to 5 (totally agree).

Self-efficacy in discussing ACP topics in the parents' questionnaire was measured in two ways, both on a Likert scale from 1 (totally disagree) to 5 (totally agree). One method included self-efficacy items on facilitating child-centered healthcare discussions. The other way aligned

with the adolescent questionnaire, and focused on nine ACP topics, such as hopes, worries, expectations and future treatment.

Behavior and intention to discuss ACP topics were measured in adolescents, parents, and pediatric oncologists using a dichotomous scale (yes/no), with the same ACP topics as those used for the self-efficacy items.

Figure 2. Logic model of the BOOST pACP intervention



Footnote: the bold texted determinants are the secondary outcomes of the trial we are reporting on in this article.

** is the primary outcome that was evaluated elsewhere (submitted article)*

Sample size

The sample size for this trial was determined based on our primary outcome measure[15] which was the Parent-Adolescent Communication Scale (PACS)[20]. We required a sample size of 48 participants in each arm, totaling 96 participants. Alpha was set at 0.05, and power at 80%.

Randomization and allocation concealment

Block randomization was performed after at least one parent completed the baseline measurement, with a 1:1 allocation ratio to either the intervention arm (BOOST group) or the control arm (care as usual). A list of group allocations was prepared by an independent statistician. A concealed envelope method was used, with allocation stratified by age (10 – 14 years old vs. 15 – 18 years old) to ensure a similar allocation of adolescents in early adolescence and middle/late adolescence in both groups [21]. Data collectors were unaware of the randomization outcome for each family and allocation concealment was ensured. Only researchers remained single-blinded to group assignments during data analysis. Due to their involvement in the intervention, families, ACP trained facilitators, and pediatric oncologists could not be blinded.

Statistical methods

Exploratory factor analysis and reliability analysis

To reduce the dimensionality, we used sum scores for the binary items (intention and behavior) and factor scores for the 5-point Likert scale items ranging from ‘totally disagree’ to ‘totally agree’ (attitude and self-efficacy). Factor scores were calculated using exploratory factor analysis (EFA) with listwise deletion for handling missing data. Maximum likelihood (ML) estimation, varimax rotation, and Kaiser normalization were used. In a first step, the number of factors and factor structure were explored. In a second step, the factor scores were calculated by performing separate factor analyses for each factor identified in the first step.

Both the EFA and factor score calculations were performed using Timepoint 1 data (baseline data). Factor selection decisions were guided by theoretical considerations following statistical exploration, taking factor scores, total variance explained and scree plots into consideration.

Linear Mixed Model Analysis

To compare the BOOST and the control group, mean differences in change between baseline and T1 (3 months) and between baseline and T2 (7 months) in sum/factor scores were compared, using linear mixed models. To account for within subject dependencies of repeated measures (over time) a random intercept per individual was added. Age category (stratification factor, 10 – 14 years old vs 15 – 18 years old), randomization arm and timepoint, as well as the interaction between time point and randomization arm were included as fixed factors. Interaction effects (with 95% CI and p-value) reflected the estimated mean difference in change from baseline between the BOOST and control group. In addition, we reported the estimated marginal mean factor scores and sum scores at each timepoint by group with 95% CI. Effect sizes were calculated as the ratio of the estimate of the interaction term and the square root of the sum of the residual and random intercept variance from a null model. No corrections for multiple comparisons were made, as the analyses were exploratory in nature. The significance level was set at $p=0.05$. Analyses were performed using IBM SPSS statistics for Windows, Version 29.0.1.0 Armonk, NY (IBM Corp).

Registration, protocol, and funding

This trial is registered with isrctn.com, number 33228289. The protocol of the BOOST pACP trial was published in BMC Pediatrics[15]. The project received funding from the Research Foundation Flanders (under grant Agreement G.0194.18N) and from Kinderkankerfonds (no grant number).

Ethics

Ethics approval was obtained from the Central Ethics Committee of the Vrije Universiteit Brussel (Brussels, Belgium) and from the local ethics committees of the participating hospitals (B1432020000177)[15].

Results

Out of the 174 adolescents who were screened for eligibility (**Figure 3**), a total of 49 families were enrolled (enrollment rate 28.2%). The mean age of the adolescents was 14 years (mode 13 years). The main diagnosis was leukemia (40.8%). The majority of included adolescents had cure as the current main goal of the treatment (87%); for 59.1% their mother was the most present parent during hospital appointments, for 29.5% both parents equally, for 6.8% their father, and in 4.5% someone else (grandfather or stepfather). **Table 1** presents the adolescents' characteristics, **Table 2** those of the parents. **Additional file 2** those of the treating pediatric oncologists.

Table 1. Baseline characteristics for adolescent patients

Characteristics	Patients (adolescents)	
	Care as usual group (n=25)	BOOST group (n=24)
Age (years)		
Mean age (SD)	13.7 (2.3)	14.2 (2.4)
Age range	10 - 18	10 - 18
Gender		
Male (%)	13 (52%)	15 (62.5%)
Female (%)	12 (48%)	9 (37.5%)
Recurrence of cancer		
No	21 (91.3%)	19 (82.6%)
Yes, the first recurrence	1 (4.3%)	4 (17.4%)
Yes, the second recurrence or more	1 (4.3%)	0 (0%)
Line of treatment		
First line of treatment	22 (91.7%)	20 (83.3%)
Second line of treatment	0 (0%)	3 (12.5%)
Third line of treatment or more	2 (8.3%)	1 (4.2%)
Current main goal of the treatment		
Cure	19 (86.4%)	21 (87.5%)
Life prolonging	2 (9.1%)	3 (12.5%)
Comfort care	1 (4.5%)	0 (0%)
Estimated prognosis by the oncologist		
Mean chance of survival percentage	81.6	73.9

Footnote: More baseline characteristics of the adolescents are described in the article on the main effectiveness. Missings care as usual group: n=1 for main diagnosis: line of treatment n=2 for recurrence of cancer n=3 for current main goal of treatment: Missings intervention group: n=1 for recurrence of cancer

Table 2. Baseline characteristics of the parents

Characteristics	Parents			
	Control group (n=24)		BOOST pACP intervention (n=24)	
	Mothers (n=20)	Fathers (n=20)	Mothers (n=23)	Fathers (n=16)
Age (years)				
Mean age (SD)	45.1 (5.1)	47.6 (5.6)	42.6 (5.4)	45.5 (7.0)
Age range	39 - 58	41 - 64	35 - 59	37 - 66
Relationship to the patient				
Biological mother/father	20 (100%)	20 (100%)	22 (95.7%)	14 (87.5%)
Stepmother/stepfather	0 (0%)	0 (0%)	1 (4.3%)	2 (12.5%)
Highest education				
High school	5 (25%)	6 (30%)	9 (39.1%)	4 (25.1%)
Graduate	2 (10%)	1 (5%)	0 (0%)	2 (12.5%)
Bachelor	5 (25%)	7 (35%)	10 (43.5%)	7 (43.8%)
Master	8 (40%)	6 (30%)	4 (17.4%)	3 (18.8%)
Current professional situation				
Fulltime job	10 (50%)	16 (80%)	11 (47.8%)	12 (75%)
Parttime job	6 (30%)	1 (5%)	6 (26.1%)	2 (12.5%)
Other	4 (20%)	3 (15%)	6 (26.1%)	2 (12.5%)
Having had to adapt their professional situation				
Yes	18 (90%)	13 (65%)	21 (91.3%)	10 (62.5%)
No	2 (10%)	7 (35%)	2 (8.7%)	6 (37.5%)
Family situation				
Married/living together	15 (75%)	17 (89.5%)	17 (73.9%)	13 (81.3%)
Divorced or living alone	2 (10%)	1 (5.3%)	2 (8.7%)	1 (6.3%)
Widow	1 (5%)	0 (0%)	0 (0%)	0 (0%)
Single parent – unmarried	0 (0%)	0 (0%)	2 (8.7%)	1 (6.3%)
Extended family	2 (10%)	0 (0%)	2 (8.7%)	1 (6.3%)
Other	0 (0%)	1 (5.3%)	0 (0%)	0 (0%)
Religious				
Yes	7 (35%)	6 (30%)	10 (43.5%)	5 (31.3%)
No	8 (40%)	13 (65%)	11 (47.8%)	11 (68.8%)
Unknown	5 (25%)	1 (5%)	2 (8.7%)	0 (0%)

Missings: control group fathers family situation n=1

Out of 24 families randomized to the BOOST pACP intervention, 20 completed all four BOOST pACP sessions (83%). In 41.7% of cases, the information from the BOOST pACP sessions was transferred to the pediatric oncologist through a (video)call with the BOOST facilitator. In 58.3%, only the summary sheet was sent by email by the BOOST facilitator.

Factor structures and reliability of behavioral determinants

Based on the results of the factor analyses and theoretical considerations the following factors were retained as operationalizations of the behavioral determinants (see **Additional file 3** for details).

- Positive attitude towards open communication with the other (adolescent: 4 items – parent: 4 items)
- Negative attitude towards open communication with the other (adolescent: 4 items – parent: 3 items)
- Self-efficacy in facilitating child-centered healthcare discussions (parent: 5 out of the 6 items)

- Self-efficacy in discussing value-and emotion-oriented ACP (6 items)
- Self-efficacy in discussing end-of-life care-oriented ACP (3 items)
- Intention to discuss value- and emotion-oriented ACP (6 items)
- Intention to discuss end-of-life care-oriented ACP (3 items)
- Actual behavior of having discussed value- and emotion-oriented ACP (6 items)
- Actual behavior of having discussed end-of-life care-oriented ACP (3 items)

Text box 1. pACP topics covered in the questionnaire categorized by factor analysis results

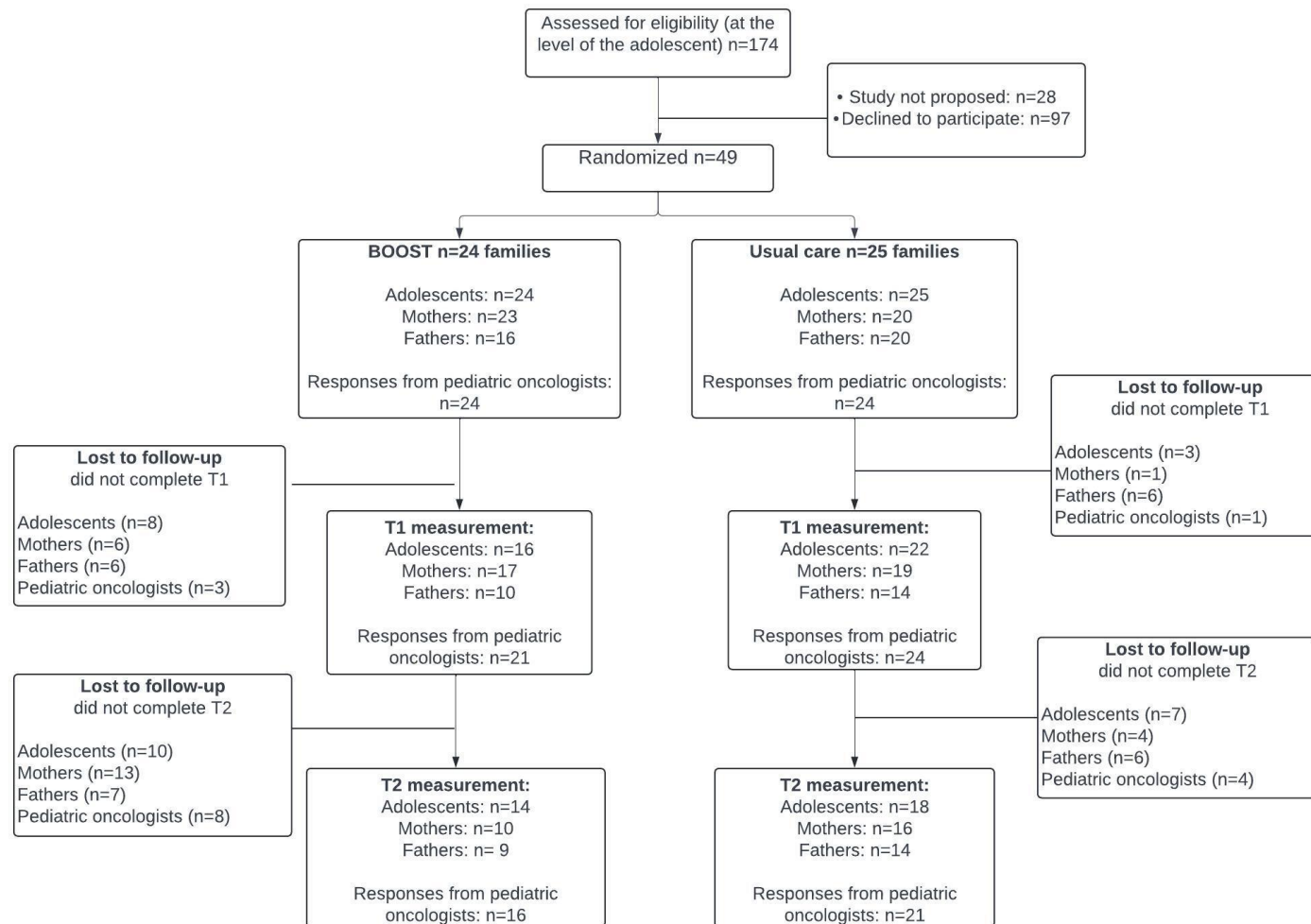
Value- and emotion-oriented ACP topics

- 1) what the adolescent finds important in life
- 2) how the adolescent feels because of the illness and treatment
- 3) what the adolescent worries about
- 4) what the adolescent is afraid for
- 5) what the adolescent hopes for
- 6) what the adolescent expects from the future

End-of-life care-oriented ACP topics

- 1) whether or not to start a new treatment if the current treatment is not effective
- 2) stopping the treatment if the current treatment is not effective
- 3) the likelihood the adolescent might die from the illness

Figure 3. CONSORT flow diagram of the BOOST pACP trial



Footnote: see main effectiveness paper for more details on reasons for loss to follow-up (article submitted). Lost to follow-up due to health deterioration or death: BOOST group: n=3 – Usual care: n=2. The most common reasons were participants indicating they are overburdened and data collectors being unable to reach them.

Intervention effects on key behavioral determinants for adolescents and parents

An overview of significant baseline-corrected differences between the BOOST and control groups, and effect sizes greater than 0.50 or less than -0.50 at T1 and T2 is provided in **Table 3. Additional file 4** includes additional details on the estimated marginal means of factor scores, sum scores, and effect sizes. **Figure 4** summarizes these findings.

For the positive and negative attitudes towards discussing ACP topics, no significant differences between BOOST and control were found in the adolescents and the mothers. Fathers in the BOOST group had a significantly stronger reduction in their negative attitudes towards discussing ACP topics at T1 with the child compared to their counterparts in the control group (baseline-adjusted mean difference [MD]: -0.57; 95% CI - 1.10 to -0.03, $p=0.038$; effect size = -0.67).

For parents' self-efficacy to facilitate child-centered healthcare discussions and decision-making no significant effects of the BOOST pACP intervention were found, although a non-significant but large effect size of 0.92 was found in fathers in the BOOST group, indicating increased self-efficacy (MD: 0.67; 95% CI -0.04 to 1.38; $p=0.062$) at T1. For self-efficacy in discussing value- and emotion-oriented ACP topics and in discussing end-of-life care-oriented topics, no significant differences between the BOOST and the control group were found in adolescents (for discussion with parents), nor in the fathers and mothers (for discussion with their child). However, regarding value- and emotion-oriented ACP, a non-significant but large effect size of 0.78 was found in mothers in the BOOST group, indicating increased self-efficacy when the child initiates the conversations (MD: 0.78; 95% CI -0.15 to 1.72; $p=0.099$) at T2 and of -0.56 in fathers in the BOOST group, indicating decreased self-efficacy when they initiate the conversation themselves at T1.

The adolescents in the BOOST group were found to have a significantly reduced number of value- and emotion-oriented ACP topics they intended to discuss with the pediatric oncologist at T2 (MD: -2.1; 95% CI -3.6 to -0.6; $p=0.008$; effect size=-0.72) and a significantly reduced number of end-of-life care-oriented ACP topics they intended to discuss with the pediatric oncologist at T1 (MD: -0.6; 95% CI -1.2 to -0.1; $p=0.029$; effect size = -1.04) and at T2 (MD: -0.8; 95% CI -1.4 to -0.2; $p=0.012$; effect size=-0.97). Additionally a non-significant but large effect size of -0.64 was found in adolescents in the BOOST group in intention to discuss value- and emotion-oriented ACP topics with the pediatric oncologist at T1 (MD: -1.3; 95% CI -2.7 to 0.1; $p=0.071$). Compared to the usual care group, mothers in the BOOST group intended to discuss an increased number of end-of-life care-oriented ACP topics with their child at T1 (MD = 1.0; 95% CI 0.1 to 1.9; $p=0.037$; effect size =0.85).

Although not significant, mothers in the BOOST group intended to discuss a decreased number of value- and emotion- oriented ACP at T1 with an effect size of -0.54 (MD: -1.1; 95% CI -2.6 to 0.4; $p=0.137$). In fathers, no significant differences were identified.

In terms of actual behaviors, the number of value- and emotion- oriented ACP topics or of end-of-life care-oriented ACP topics discussed in the last month did not significantly differ between BOOST and control at T1 and T2 for adolescents, mothers and fathers. However, effect sizes were high for adolescents' behavior with their father at T1 (MD = -1.2; 95% CI -2.5 to 0.1; $p=0.075$; effect size =-0.64) and T2 (MD = -1.2; 95% CI -2.5 to 0.2; $p=0.084$; effect size =-0.64). Adolescents in the BOOST group showed a decrease in the number of value- and emotion- oriented ACP with the pediatric oncologist at T1 (MD = -0.9; 95% CI -1.9 to 0.1;

p=0.082; effect size =-0.52). An effect size of -0.57 was found for fathers regarding the number of value- and emotion- oriented ACP topics discussed with their child (MD = -0.9; 95% CI -2.1 to 0.3; p=0.133). The intention of pediatric oncologists to discuss ACP topics, as well as their actual behavior in discussing these topics with the adolescent, was also assessed. However, no significant effects were found, and the effect sizes were neither less than -0.50 nor greater than 0.50 (not included in **Table 3** and **Figure 4**).

Table 3. Simplified overview of the results on adolescents', mothers' and fathers' attitude, self-efficacy, intention and behavior of discussing ACP topics

Respondents	Adolescents						Mother		Father	
	With their mother		With their father		With the pediatric oncologist		With their child	With their child	With their child	With their child
Determinants	T1	T2	T1	T2	T1	T2	T1	T2	T1	T2
Attitude										
Positive attitude towards discussing care and treatment	/	/	/	/	NA	NA	0/-	/	/	0/-
Negative attitude towards discussing care and treatment	/	/	/	/	NA	NA	/	/	+	/
Self-efficacy										
Facilitating child-centered healthcare discussions	NA	NA	NA	NA	NA	NA	/	/	0/+	/
Self-efficacy in discussing ACP topics										
Value/emotion oriented ACP topics	/	/	/	/	NA	NA	NA	NA	NA	NA
- If initiated by the child	NA	NA	NA	NA	NA	NA	/	0/+	/	/
- If initiated by the parent him/herself	NA	NA	NA	NA	NA	NA	/	/	0/-	/
End-of-life care oriented ACP topics	/	/	/	/	NA	NA	NA	NA	NA	NA
- If initiated by the child	NA	NA	NA	NA	NA	NA	/	/	/	/
- If initiated by the parent him/herself	NA	NA	NA	NA	NA	NA	/	/	/	/
Intention to discuss										
Value- and emotion-oriented ACP topics	/	/	0/-	/	0/-	-	0/-	/	/	/
End-of-life care oriented ACP topics	/	/	/	/	-	-	+	0/+	/	/
Behavior of discussing										
Value- and emotion-oriented ACP topics	/	/	0/-	0/-	0/-	/	/	/	0/-	/
End-of-life care oriented ACP topics	/	/	/	/	/	/	/	/	/	/

Footnote: Exploratory factor analyses was utilized for the attitude and self-efficacy items to guide decisions on which items should be grouped together as a single latent construct and to identify any items that needed to be removed due to low factor loadings. For intention and behavior, sum scores for each of the ACP types were used as a dependent variable in our linear mixed model.

+ significant effect in favor of BOOST

- Significant effect in favor of control

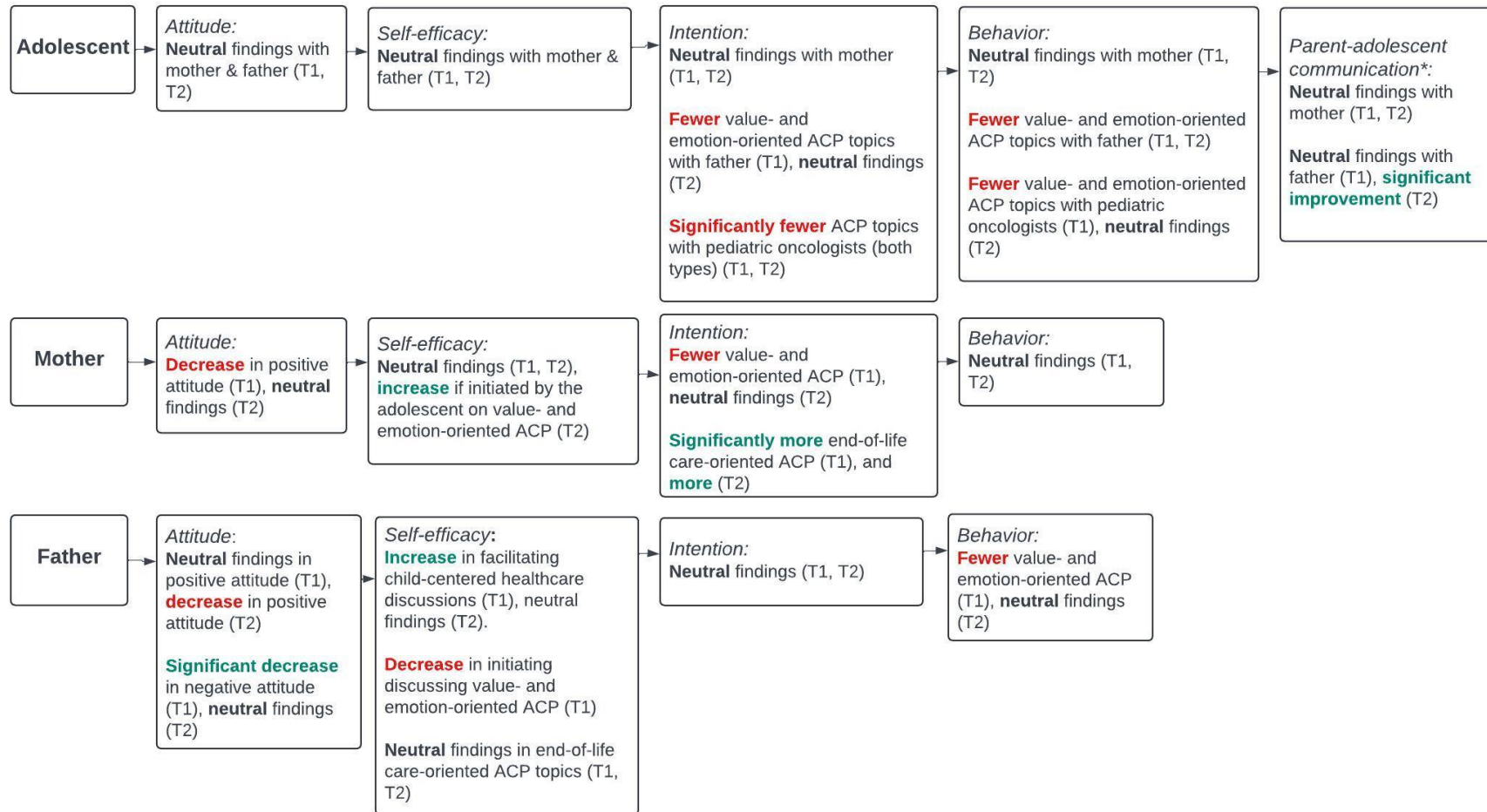
0/+ Not statistically significant, but an effect size of at least 0.50 in favor of BOOST

0/- Not statistically significant, but an effect size of at least 0.50 in favor of control

/ not statistically significant and effect sizes between -0.50 and 0.50

NA this was not studied for this target group

Figure 4: Schematic presentation of the results of the BOOST pACP trial based on the logic model



Footnote: A 'decrease' or 'increase' is indicated when the effect size is less than -0.50 or greater than 0.50, respectively. Findings between these values are labeled as 'neutral'.

Discussion

This multicenter randomized controlled trial evaluated the impact of the BOOST pACP intervention on secondary outcomes, namely on behavioral determinants (attitude, self-efficacy, intention and behavior) towards discussing ACP topics. We found that fathers in the BOOST pACP group showed a significant decrease in their negative attitudes towards discussing care and treatment with their child at the first timepoint (three months after baseline), compared to the usual care group. Additionally, mothers in the BOOST pACP group intend to discuss more end-of-life care-oriented ACP topics with their child at the first timepoint. Contrary to the expectations, the adolescents in the BOOST pACP group intend to discuss fewer ACP topics with their pediatric oncologist at both timepoints. No other significant effects were found.

The finding that adolescents in the BOOST pACP group intended to discuss fewer ACP with the pediatric oncologist was unexpected. However, this is consistent with other studies showing that adolescents tend to discuss ACP more with family members than with clinicians [22]. We had anticipated that the intervention would change adolescents' perceptions of the value of discussing ACP topics with their oncologist, which could lead to shifts in their intentions and behaviors. The pediatric oncologist was not directly involved in the BOOST pACP conversations, and adolescents in the intervention group may have felt that the ACP topics were thoroughly covered with the external facilitator. As a result, they might not have seen additional value in discussing these topics again with the oncologist, indicating the importance of having a facilitator who is directly involved in the adolescent's clinical care or maintains regular communication with the treating clinicians. The lack of effects on self-efficacy may be attributed to a lack of specific behavior change techniques, such as goal setting, action planning, or implementation intentions [23].

The BOOST pACP intervention is grounded in existing pACP principles and behavioral theories, recognizing the increasingly common view of ACP as a behavioral act [24], and aiming to enhance patient empowerment [25]. The program was based on a logic model that we developed informed by the Theory of Planned Behavior (TPB) [26], studies using behavioral models [8,25,27–30], existing literature on barriers to parent-adolescent communication [31–33] and ACP in adolescents [2,13,18]. To select outcome measures that aligned with this logic model [34,35] – and in a context where validated instruments for the central concepts identified in the logic model are lacking– we developed study specific constructs to measure the secondary outcomes related to ACP determinants. However, while we tested the face validity of these constructs with end users, we did not assess their construct validity.

Our use of behavioral models in interventions also presents challenges. While the TPB provides more flexibility, compared to the linear nature of the Transtheoretical Model [36], it remains an individual-focused theory and may not fully consider environmental influences [8]. The TPB's focus on cognitive processes leaves less room for unconscious or automatic behaviors, as well as contextual and social influences [8,37,38]. Clinical circumstances [22] may not be sufficiently addressed by an individual behavioral model, which might have limited the BOOST pACP intervention effects. For example, the intervention sessions were facilitated by individuals external to the medical team who were not involved in the adolescents' clinical

care. Also, most adolescents in the study had a primary goal of curation, and may not have found it useful to consider scenarios involving health deterioration at that moment [39].

Further research is needed to understand how adolescents with different types of cancer at various stages perceive and engage in ACP discussions. The behavior of discussing ACP topics may be influenced less by attitude and self-efficacy and more by habit, emotional states [38], and perceptions of personal relevance [39]. Qualitative research is essential to better understand how adolescents view planning for health changes and discussing these issues [39], potentially followed by a larger survey to assess factors associated with the intention to discuss ACP topics [25]. Additionally, a content analysis of the BOOST pACP conversations will further contribute to this understanding. We observed varying – and sometimes opposing – effects among fathers, mothers, and adolescents, indicating a need for further process evaluations and deeper exploration to inform the tailoring of pACP programs. It is also possible that adolescents with cancer, who generally have a high 5-year survival rate [40], might benefit more from support focused on coping with their illness, strengthening family communication and adaptation, maintaining psychosocial well-being, and living well with the illness and its potential long-term effects [41–44], with ACP integrated into this support.

Our study uniquely gathered separate perspectives from adolescents, mothers, and fathers, which is uncommon in pediatric oncology research [45]. Additionally, this is the first RCT, to our knowledge, that tests a holistic pACP intervention. Another unique aspect of this trial is the general oncology population involving adolescents younger than 14 years old, regardless of whether a specific scenario of death was anticipated. This study contributes to the important discussion on what ACP for this target group should look like and provides additional insights into the use of behavioral theories in (pediatric) ACP. The results should be interpreted cautiously due to the study's underpowered nature and the use of outcome measures that were not fully validated in this population.

The BOOST pACP intervention demonstrated limited effectiveness in changing behavioral determinants associated with ACP communication. A decrease in fathers' negative attitudes toward openly discussing care and treatment with their child was found, as well as increased mothers' intentions to discuss end-of-life care- oriented ACP. Notably, the BOOST pACP intervention decreased adolescents' intentions to discuss ACP topics with their oncologist. Self-efficacy in discussing ACP topics was not significantly affected. Our findings underscore the need for a better understanding of the mechanisms driving or hindering outcomes and impact of pediatric ACP, and suggest a complexity of influencing ACP behaviors within the pediatric oncology setting.

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Additional file 1. Socio-demographic characteristics of participants and adaptations from the face validation of the questionnaires

	Adolescents and young adults (n=4)	Parents (n=6)
Age (years)		
Age mean (range)	19 (range 16 – 23)	-
Age category		
30 - 39	-	1 (16.7%)
40 - 49	-	5 (83.3%)
Gender		
Male	2 (50%)	1 (16.7%)
Female	2 (50%)	5 (83.3%)
Time since cancer diagnosis		
<1 year ago	1 (25%)	-
>3 years ago	3 (75%)	-
Highest degree		
Secondary education	-	3 (50%)
Post-secondary education	-	3 (50%)
Marital status		
Single parent/unmarried	-	1 (16.7%)
Married or living together	-	5 (83.3%)

Adaptations	Old version	New version
Structure of the sentences in the introduction of the questionnaire. Rewriting long sentences into short sentences. (adolescent questionnaire)	<i>'You have been diagnosed with cancer. There may already have been many discussions about your care and treatment with you and your parents. For many things – both small and large aspects of your care – you might have your own preferences. By this, we mean not only medical care but also the care and support you receive from other people, to make your life with the illness a bit more bearable. How you experience your illness, what you expect from the future, what you enjoy, and what your</i>	<i>'What care and treatment for cancer do you need? There may already have been a lot of discussions about this with you and your parent. But what do you find important? And with whom do you talk about it? This part of the questionnaire is about that. We are not only talking about your medical treatment from healthcare professionals in the hospital (such as the nurse, doctor, or psychologist). By care, we also mean the help or support you receive from other people, such as your parents, friends or family.'</i>

	<i>concerns are, can change over time. As a result, your preferences for care and treatment also change.'</i>	
Adding subtitles to the questions	-	<i>'to what extent do you agree with each statement? Check the box'</i>
Specified terms that were unclear	- <i>'Pediatrician'</i>	- <i>'Pediatric oncologist'</i>
Clarifying/removing clinical jargon and ACP concepts or unclear terms and simplifying complex sentences that had to be read multiple times	- <i>'Preferences in care and treatment' and 'what kind of treatment I/my child want(s)'</i>	- <i>'What I/my child find(s) important regarding care and treatment'</i>
	- <i>'I am afraid of upsetting my child if I talk to him/her about his/her preferences for care and treatment'</i> - <i>'I take the initiative to ask my child about his/her preferences for care and treatment'</i> - <i>'I am open to talking about my preferences for care and treatment with my parents, if they want to'</i> - <i>'I have the feeling that...'</i>	- <i>'I am afraid of making my child sad if I talk about what he or she finds important in care and treatment'</i> - <i>'I explicitly ask my child what he or she considers important in care and treatment'</i> - <i>'I am okay with my parents wanting to talk about what I find important in my care and treatment'.</i> - <i>'I think that...'</i>
Specifying references to time	- <i>'The past period'</i> - <i>'The near future'</i>	- <i>'The past month'</i> - <i>'The next month'</i>
Removing or rephrasing parts or single items perceived as inappropriate (parent questionnaire)	- The Active-Emphatic Listening Scale (AELS) was included. Examples of items: - o <i>'I assure my child that I will remember what they say.'</i> - o <i>'I assure my child that I am listening by using verbal acknowledgements.'</i> - o <i>'I assure my child that I am receptive to his/her ideas.'</i>	- This questionnaire was removed due to unclarity and it was perceived as offending. They considered it normal to do all the actions that were mentioned in the questionnaire. It did not fit in the logic model perfectly either.
	- Formulation of several items: - o <i>'If I have the desire, I would be able to initiate a conversation with my child about...'</i> - o <i>'I feel comfortable when talking with my child about...'</i>	- Reformulation of several items, because parents said that, as a parent, it does not matter what your desire is or whether you feel comfortable. The word choice was badly received. - o <i>'If I feel the need, I would be able to initiate'</i> - o <i>'I easily talk with my child about...'</i>

Text boxes were added in the parents' questionnaire	- During the cognitive testing, parents elaborated on the questions. However, it was not possible to have data collectors fill out these questionnaires together with them also.	- Parents sometimes felt the need to add explanations to their answers. We therefore added: <i>"If you would like, you may write any explanations or comments here"</i> .
The list of ACP topics were shortened	- 11 items were included in the recurring list of ACP topics (self-efficacy, intention, behavior items)	- 2 items were deleted: 1) What I want and don't want concerning my care and treatment 2) Which treatment I would or would not want if my condition were to deteriorate There was little additional value in including these items, as they were not clear to our respondents. Adolescents struggled to envision the possibility of different treatment options.

Additional file 2. Baseline characteristics of the pediatric oncologists (n=19)

Age category (years) n (%)	
31-40	2 (10.5%)
41-50	6 (31.6%)
51-65	10 (52.6%)
Gender	
Female	14 (73.7%)
Male	5 (26.3%)
Number of years experience as a pediatric oncologist	
0 – 5 years	1 (5.3%)
5 -10 years	5 (26.3%)
10 – 20 years	5 (26.3%)
20 - 30 years	6 (31.6%)
More than 30 years	2 (10.5%)
Training in advance care planning	
No	17 (89.5%)
Yes	2 (10.5%)
Training in palliative care	
Yes, postgraduate or specialization	2 (10.5%)
Yes, a course of one or more days or session/seminar/ other	9 (47.4%)
Yes, in basic training	2 (10.5%)
No	9 (47.4%)
<i>Missings: age category n=1</i>	

Additional file 3. Factor scores and reliability (Cronbach's alpha) of items from the self-developed questionnaires

Table 1. Attitude and self-efficacy of the adolescents' questionnaire

Factor names and items questionnaire	Factor scores		Cronbach's alpha	
	With their mother	With their father	With their mother	With their father
<i>Positive attitude towards open communication with their parents</i>			0.709	0.728
I find it important to talk with my parent about what matters most to me in my care and treatment.	0.306	0.348		
I am okay with my parent wanting to talk about what I find important in my care and treatment.	0.434	0.374		
Think about the care you are currently receiving. I find it easy to talk with my parent about what I find important in my care and treatment.	0.802	0.761		
Think about the care you may receive in the future. I find it easy to talk with my parent about what I find important in my care and treatment.	0.789	0.864		
<i>Total variance explained</i>	38.7%	39.6%		
<i>Negative attitude towards open communication with their parents</i>			0.608	0.467
I am afraid that I will upset my parent if I talk about what I find important in my care and treatment.	0.469	0.166		
I know too little about my illness or treatment to talk with my parent about what I find important.	0.613	0.983		
I think my parent finds me too young to talk about what I find important in my care and treatment.	0.773	0.657		
I think nothing will change if I talk with my parent about what I find important in my care and treatment.	0.772	0.334		
<i>Total variance explained</i>	44.7%	38.4%		
<i>Self-efficacy in talking with my parent about value- and emotion-oriented ACP</i>			0.816	0.783
<i>If I wanted to, I would be able to talk with my parent about...</i>				
What I find important in my life	0.716	0.667		
How I feel about my illness and treatment	0.647	0.468		
What I think or worry about a lot	0.662	0.396		
What I am afraid of	0.751	0.392		
What I hope for	0.523	0.607		
What I expect from the future	0.661	0.623		
<i>Total variance explained</i>	44.1%	28.9%		
<i>Self-efficacy in talking with my parent about end-of-life care-oriented ACP</i>			0.853	0.884
<i>If I wanted to, I would be able to talk with my parent about...</i>				

The decision to start or not start a new treatment if the current treatment is not effective	0.835	0.879		
The decision to stop the treatment if the current treatment is not effective	0.956	0.897		
The likelihood that I would die	0.706	0.563		
<i>Total variance explained</i>	70.3%	63.1%		

Table 2. Attitude and self-efficacy of the parents' questionnaire

Factor names and items questionnaire of parents	Factor scores		Cronbach's alpha	
	Mother	Father	Mother	Father
<i>Positive attitude towards open communication with their child</i>			0.628	0.747
I find it important to talk with my child about what matters most to him or her in care and treatment.	0.288	0.748		
I explicitly ask my child what he or she finds important in care and treatment.	0.820	0.523		
If my child wants to talk about care and treatment, I am open to it.	0.508	0.964		
I easily discuss with my child what he or she finds important in care and treatment.	0.796	0.554		
<i>Total variance explained</i>	41.2%	51.8%		
<i>Negative attitude towards open communication with their child</i>			0.386	0.681
I find it difficult to find out what is important to my child in care and treatment.	0.524	0.744		
I'm afraid that I will upset my child if I talk about what he or she finds important in care and treatment	0.671	0.731		
I believe that my child is not yet able to participate in decisions about care and treatment.	0.399	0.762		
<i>Total variance explained</i>	29.5%	55.7%		
<i>Self-efficacy in facilitating child-centered healthcare discussions</i>			0.782	0.747
I am confident that I can talk to my child when he or she has different thoughts about care or treatment than I do.	0.529	0.553		
I am confident that I can find out what my child truly wants in his or her care or treatment.	0.665	0.825		
I am confident that I can make my child feel that he or she can talk to me about anything.	0.358	0.703		
I am confident that I can encourage my child to say what he or she finds important in care and treatment.	0.621	0.766		
I am confident that I can come to joint decisions with my child regarding care and treatment.	0.714	0.557		
<i>Total variance explained</i>	34.9%	47.5%		
<i>Self-efficacy when my child initiates a conversation about value- and emotion-oriented ACP</i>			0.899	0.919

<i>I would be able to have a conversation with my child if he or she starts talking about...</i>				
what my child finds important in life	0.720	0.827		
how my child feels because of the illness and treatment	0.743	0.870		
What my child worries about	0.707	0.830		
what my child is afraid of	0.737	0.804		
what my child hopes for	0.926	0.936		
what my child expects from the future	0.755	0.817		
<i>Total variance explained</i>	59.0%	72.0%		
<i>Self-efficacy when my child initiates a conversation about end-of-life care-oriented ACP</i>			0.873	0.857
<i>I would be able to have a conversation with my child if he or she starts talking about...</i>				
whether or not to start a new treatment if the current treatment is not effective	0.874	0.571		
stopping the treatment if the current treatment is not effective	0.972	0.976		
the likelihood that my child might die from the illness	0.801	0.796		
<i>Total variance explained</i>	78.3%	63.7%		
<i>Self-efficacy in initiating conversations with my child about value- and emotion-oriented ACP</i>			0.961	0.947
<i>If I feel the need, I would be able to start a conversation with my child about...</i>				
what my child finds important in life	0.901	0.789		
how my child feels because of the illness and treatment	0.923	0.821		
what my child worries about	0.794	0.888		
what my child is afraid of	0.894	0.914		
what my child hopes for	0.968	0.949		
what my child expects from the future	0.896	0.902		
<i>Total variance explained</i>	80.6%	77.2%		
<i>Self-efficacy in initiating conversations with my child about end-of-life care-oriented ACP</i>			0.923	0.851
<i>If I feel the need, I would be able to start a conversation with my child about...</i>				
whether or not to start a new treatment if the current treatment is not effective	0.864	0.638		
stopping the treatment if the current treatment is not effective	0.956	0.999		
the likelihood that my child might die from the illness	0.738	0.757		
<i>Total variance explained</i>	73.5%	66%		

Reliability of the items on parents' and adolescents' intention and behavior (Cronbach's alpha)

	Mother with their child	Father with their child	Adolescent with their mother	Adolescent with their father	Adolescent with the pediatric oncologist
Intention to discuss					
Value- and emotion-oriented ACP	0.919	0.835	0.851	0.786	0.817
End-of-life care-oriented ACP	0.899	0.574	0.647	0.618	0.811
Behavior of discussing					
Value- and emotion-oriented ACP	0.680	0.684	0.691	0.733	0.694
End-of-life care-oriented ACP	0.715	0.606	0.503	0.393	0.640

Additional file 4. Effects of the BOOST pACP intervention on the behavioral determinants in adolescents and parents on T1 (3 months post-baseline) and on T2 (7 months post-baseline)

For all tables below:

- The mean score refers to the estimated marginal means, adjusted for the variables included in the model.
- Effect sizes were calculated as the ratio of the interaction term to the square root of the sum of the residual and random intercept variance from the null model.
- Details of the items surveyed under each category can be found in **Additional file 3**.

The following tables present the estimated mean factor scores for various determinants measured at baseline, 3 months, and 7 months.

Value- and emotion-oriented ACP topics - what the adolescent: 1) finds important in life; 2) how he/she feels because of the illness and treatment; 3) worries about; 4) is afraid for; 5) hopes for; 6) expects from the future.

End-of-life care-oriented ACP topics: 1) whether or not to start a new treatment if the current treatment is not effective; 2) stopping the treatment if the current treatment is not effective; 3) the likelihood the adolescent might die from the illness

Adolescents discussing ACP topics with their parents

1a. Attitude of adolescents towards discussing ACP topics with their mother/father

	Baseline (T0) Mean score (95% CI)		3 months post- baseline (T1) Mean score (95% CI)		Mean difference in change from baseline (95% CI)	P value	Effect size**	7 months post-baseline (T2)		Mean difference in change from baseline (95% CI)	P value	Effect size**
	BOOST intervention Mean (SD)*	Usual care Mean (SD)*	BOOST intervention Mean (SD)*	Usual care Mean (SD)*				BOOST intervention Mean (SD) N=	Usual care Mean (SD) N=			
Attitude towards discussing ACP topics with his/her parent												
<i>With their mother</i>												
Positive attitude	0.014 (-0.354 – 0.382)	0.021 (-0.342 – 0.383)	0.103 (-0.332 – 0.537)	0.328 (-0.052 – 0.709)	-0.219 (-0.840 – 0.402)	0.484	-0.24	0.105 (-0.353 – 0.564)	0.175 (-0.237 – 0.586)	-0.062 (-0.720 – 0.595)	0.851	-0.07
Negative attitude	-0.063 (-0.358 – 0.233)	0.040 (-0.252 – 0.331)	-0.264 (-0.611 – 0.083)	-0.133 (-0.438 – 0.173)	-0.028 (-0.512 – 0.456)	0.907	-0.04	-0.517 (-0.549 – 0.108)	-0.221 (-0.549 – 0.108)	-0.193 (-0.714 – 0.328)	0.461	-0.26
<i>With their father</i>												
Positive attitude	0.036 (-0.350 – 0.421)	-0.045 (-0.413 – 0.323)	0.266 (-0.208 – 0.741)	-0.089 (-0.498 – 0.320)	0.274 (-0.425 – 0.974)	0.436	0.31	0.286 (-0.205 – 0.778)	0.393 (-0.037 – 0.824)	-0.188 (-0.911 – 0.536)	0.606	-0.22
Negative attitude	-0.068 (-0.408 – 0.271)	0.030 (-0.294 – 0.355)	-0.291 (-0.706 – 0.123)	-0.176 (-0.535 – 0.183)	-0.016 (-0.612 – 0.580)	0.956	-0.02	-0.345 (-0.773 – 0.084)	-0.336 (-0.713 – 0.040)	0.090 (-0.526 – 0.707)	0.771	0.12

1b. Self-efficacy of adolescents in discussing ACP topics with their mother/father

	Baseline (T0) Mean score (95% CI)		3 months post- baseline (T1) Mean score (95% CI)		Mean difference in change from baseline (95% CI))	P value	Effect size*	7 months post-baseline (T2)		Mean difference in change from baseline (95% CI))	P value	Effect size*
	BOOST intervention Mean (SD)*	Usual care Mean (SD)*	BOOST intervention Mean (SD)*	Usual care Mean (SD)*				BOOST intervention Mean (SD) N=	Usual care Mean (SD) N=			
Self-efficacy in discussing ACP topics with his/her parent												
<i>With his/her mother</i>												
Value- and emotion-oriented ACP	0.073 (-0.276 – 0.422)	-0.132 (-0.471 – 0.207)	0.123 (-0.303 – 0.550)	0.180 (-0.181 – 0.541)	-0.261 (-0.850 – 0.327)	0.379	-0.31	0.409 (-0.016 – 0.835)	0.069 (-0.314 – 0.451)	0.136 (-0.466 – 0.737)	0.654	0.16
End-of-life care oriented ACP	0.136 (-0.205 – 0.476)	-0.117 (-0.453 – 0.218)	0.032 (-0.397 – 0.461)	-0.038 (-0.399 – 0.323)	-0.183 (-0.802 – 0.436)	0.557	-0.22	0.314 (-0.116 – 0.743)	-0.244 (-0.628 – 0.141)	0.304 (-0.329 – 0.937)	0.341	0.36
<i>With his/her father</i>												
Value- and emotion-oriented ACP	0.117 (-0.304 – 0.537)	-0.146 (-0.529 – 0.237)	0.068 (-0.429 – 0.565)	0.137 (-0.290 – 0.563)	-0.331 (-1.082 – 0.420)	0.381	-0.37	0.311 (-0.225 – 0.847)	0.051 (-0.398 – 0.500)	-0.003 (-0.793 – 0.788)	0.995	0.00
End-of-life care oriented ACP	0.010 (-0.416 – 0.437)	-0.012 (-0.413 – 0.389)	-0.086 (-0.624 – 0.452)	-0.055 (-0.505 – 0.395)	-0.054 (-0.774 – 0.667)	0.882	-0.06	0.157 (-0.364 – 0.677)	-0.154 (-0.614 – 0.307)	0.288 (-0.431 – 1.007)	0.427	0.31

Footnote: Value- and emotion-oriented ACP topics - what the adolescent: 1) finds important in life; 2) how he/she feels because of the illness and treatment; 3) worries about; 4) is afraid for; 5) hopes for; 6) expects from the future.

End-of-life care-oriented ACP topics: 1) whether or not to start a new treatment if the current treatment is not effective; 2) stopping the treatment if the current treatment is not effective; 3) the likelihood the adolescent might die from the illness

1c. Intention of adolescents to discuss ACP topics with their mother/father and pediatric oncologist

The following tables present the estimated mean sum scores for behavior and intention, with possible scores ranging from 0 to 6 for value- and emotion-oriented ACP and scores ranging from 0 to 3 for end-of-life care-oriented ACP.

	Baseline (T0) Mean score (95% CI)		3 months post- baseline (T1) Mean score (95% CI)		Mean difference in change from baseline (95% CI)	P value	Effect size**	7 months post-baseline (T2)		Mean difference in change from baseline (95% CI)	P value	Effect size**
	BOOST intervention Mean (SD)*	Usual care Mean (SD)*	BOOST intervention Mean (SD)*	Usual care Mean (SD)*				BOOST intervention Mean (SD) N=	Usual care Mean (SD) N=			
Intention to discuss ACP topics												
<i>With their mother</i>												
Value- and emotion-oriented ACP <i>Score can range from 0 - 6</i>	3.4 (2.5 - 4.3)	3.6 (2.7 - 4.5)	3.7 (2.7 - 4.8)	3.6 (2.7 - 4.6)	0.3 (-1.1 - 1.8)	0.640	0.14	2.4 (1.3 - 3.5)	3.4 (2.4 - 4.4)	-0.7 (-2.3 - 0.8)	0.345	-0.32
End-of-life care oriented ACP <i>Score can range from 0 - 3</i>	0.3 (0.0 - 0.5)	0.3 (0.0 - 0.6)	0.5 (0.1 - 0.9)	0.6 (0.3 - 0.9)	-0.1 (-0.6 - 0.5)	0.865	-0.14	0.2 (-0.2 - 0.6)	0.1 (-0.2 - 0.5)	0.1 (-0.5 - 0.7)	0.672	0.14
<i>With their father</i>												
Value- and emotion-oriented ACP <i>Score can range from 0 - 6</i>	3.3 (2.4 - 4.2)	4.6 (2.8 - 4.4)	2.5 (1.5 - 3.6)	3.8 (2.9 - 4.7)	-1.0 (-2.5 - 0.6)	0.209	-0.50	2.3 (1.1 - 3.4)	3.4 (2.4 - 4.4)	-0.8 (-2.4 - 0.8)	0.307	-0.40

End-of-life care oriented ACP Score can range from 0 - 3	0.2 (0.0 – 0.5)	0.4 (0.2 – 0.7)	0.2 (-0.2 – 0.6)	0.4 (0.2 – 0.7)	-0.1 (-0.6 – 0.5)	0.848	-0.16	0.0 (-0.4 – 0.3)	0.1 (-0.2 – 0.4)	0.1 (-0.5 – 0.6)	0.810	0.16
<i>With the pediatric oncologist</i>												
Value- and emotion-oriented ACP Score can range from 0 - 6	2.8 (1.9 – 3.6)	1.8 (1.0 – 2.6)	2.0 (1.0 – 3.0)	2.4 (1.5 – 3.3)	-1.3 (-2.7 – 0.1)	0.071	-0.64	1.6 (0.6 – 2.7)	2.8 (1.8 – 3.7)	-2.1 (-3.6 to -0.6)	0.008	-0.72
End-of-life care oriented ACP Score can range from 0 - 3	0.7 (0.4 – 1.0)	0.1 (-0.2 – 0.4)	0.3 (-0.2 – 0.7)	0.3 (0.0 – 0.7)	-0.6 (-1.2 to -0.1)	0.029	-1.04	0.2 (-0.2 – 0.6)	0.4 (0.0 – 0.8)	-0.8 (-1.4 to -0.2)	0.012	-0.97

Footnote: Value- and emotion- oriented ACP topics - what the adolescent: 1) finds important in life; 2) how he/she feels because of the illness and treatment; 3) worries about; 4) is afraid for; 5) hopes for; 6) expects from the future.

End-of-life care-oriented ACP topics: 1) whether or not to start a new treatment if the current treatment is not effective; 2) stopping the treatment if the current treatment is not effective; 3) the likelihood the adolescent might die from the illness

1d. Behavior of adolescents discussing ACP topics with their mother/father and pediatric oncologist

	Baseline (T0)		3 months post- baseline (T1)		Mean difference in change from baseline (95% CI)	P value	Effect size**	7 months post-baseline (T2)		Mean difference in change from baseline (95% CI)	P value	Effect size**
	Mean score (95% CI)		Mean score (95% CI)									
	BOOST intervention Mean (SD)*	Usual care Mean (SD)*	BOOST intervention Mean (SD)*	Usual care Mean (SD)*				BOOST intervention Mean (SD) N=	Usual care Mean (SD) N=			
Behavior of discussing ACP topics												
<i>With their mother</i>												
Value- and emotion-oriented ACP <i>Score can range from 0 - 6</i>	4.1 (3.3 – 4.8)	3.7 (3.0 – 4.4)	4.1 (3.3 – 5.0)	4.1 (3.3 – 4.8)	-0.3 (-1.6 – 1.0)	0.639	-0.17	3.7 (2.8 – 4.6)	3.8 (3.0 – 4.6)	-0.4 (-1.8 – 0.9)	0.512	-0.22
End-of-life care oriented ACP <i>Score can range from 0 - 3</i>	0.1 (-0.1 – 0.4)	0.2 (0.0 – 0.5)	0.4 (0.1 – 0.8)	0.6 (0.3 – 0.9)	-0.1 (-0.5 – 0.4)	0.824	-0.15	0.2 (-0.1 – 0.6)	0.4 (0.1 – 0.7)	-0.1 (-0.6 – 0.4)	0.798	-0.15
<i>With their father</i>												
Value- and emotion-oriented ACP <i>Score can range from 0 - 6</i>	3.7 (2.9 – 4.5)	3.9 (3.1 – 4.7)	3.0 (2.0 – 3.9)	4.3 (3.5 – 5.2)	-1.2 (-2.5 – 0.1)	0.075	-0.64	2.8 (1.8 – 3.8)	4.2 (3.3 – 5.1)	-1.2 (-2.5 – 0.2)	0.084	-0.64
End-of-life care oriented ACP <i>Score can range from 0 - 3</i>	0.2 (-0.1 – 0.4)	0.4 (0.1 – 0.6)	0.0 (-0.3 – 0.3)	0.3 (0.1 – 0.6)	-0.1 (-0.6 – 0.4)	0.655	-0.19	0.1 (-0.2 – 0.4)	0.3 (0.1 – 0.6)	0.0 (-0.5 – 0.5)	0.991	0.0
<i>With the pediatric oncologist</i>												

Value- and emotion-oriented ACP Score can range from 0 - 6	2.2 (1.5 – 2.9)	1.8 (1.1 – 2.5)	2.1 (1.3 – 2.9)	2.6 (1.9 – 3.3)	-0.9 (-1.9 – 0.1)	0.082	-0.52	2.0 (1.2 – 2.9)	1.9 (1.2 – 2.7)	-0.2 (-1.3 – 0.8)	0.666	- 0.12
End-of-life care oriented ACP Score can range from 0 - 3	0.2 (-0.1 – 0.5)	0.3 (0.0 – 0.6)	0.3 (-0.1 – 0.6)	0.6 (0.3 – 0.9)	-0.2 (-0.8 – 0.4)	0.562	-0.28	0.3 (-0.1 – 0.7)	0.4 (0.1 – 0.8)	0.0 (-0.6 – 0.7)	0.936	0

Footnote: Value- and emotion-oriented ACP topics - what the adolescent: 1) finds important in life; 2) how he/she feels because of the illness and treatment; 3) worries about; 4) is afraid for; 5) hopes for; 6) expects from the future.

End-of-life care-oriented ACP topics: 1) whether or not to start a new treatment if the current treatment is not effective; 2) stopping the treatment if the current treatment is not effective; 3) the likelihood the adolescent might die from the illness

2. Parents discussing ACP topics with their child

2a. Attitude of parents towards discussing ACP topics with their child

	Baseline (T0) Mean score (95% CI)		3 months post- baseline (T1) Mean score (95% CI)		Mean difference in change from baseline (95% CI))	P value	Effect size*	7 months post-baseline (T2)		Mean difference in change from baseline (95% CI))	P value	Effect size**
	BOOST intervention Mean (SD)*	Usual care Mean (SD)*	BOOST intervention Mean (SD)*	Usual care Mean (SD)*				BOOST intervention Mean (SD) N=	Usual care Mean (SD) N=			
Attitude on discussing ACP topics with their child												
<i>Reported by the mother</i>												
Positive attitude	0.110 (-0.252 – 0.473)	-0.166 (-0.541 – 0.208)	-0.032 (-0.429 – 0.365)	0.175 (-0.209 – 0.558)	-0.483 (-1.009 – 0.043)	0.071	-0.58	-0.035 (-0.510 – 0.439)	0.054 (-0.350 – 0.459)	-0.366 (-0.967 – 0.234)	0.227	-0.44
Negative attitude	0.039 (-0.274 – 0.353)	-0.026 (-0.356 – 0.305)	-0.074 (-0.418 – 0.270)	-0.137 (-0.474 – 0.201)	-0.003 (-0.430 – 0.424)	0.990	0.0	0.208 (-0.196 – 0.613)	0.049 (-0.304 – 0.402)	0.094 (-0.394 – 0.582)	0.701	0.13
<i>Reported by the father</i>												
Positive attitude	0.242 (-0.136 – 0.620)	-0.178 (-0.513 – 0.158)	0.345 (-0.123 – 0.813)	0.140 (-0.255 – 0.535)	-0.215 (-0.923 – 0.494)	0.546	-0.29	0.134 (-0.359 – 0.627)	0.127 (-0.268 – 0.521)	-0.412 (-1.136 – 0.312)	0.259	-0.55
Negative attitude	0.154 (-0.277 – 0.584)	-0.138 (-0.519 – 0.243)	-0.380 (-0.866 – 0.105)	-0.104 (-0.520 – 0.311)	-0.568 (-1.102 to -0.034)	0.038	-0.67	-0.314 (-0.814 – 0.185)	-0.284 (-0.700 – 0.132)	-0.323 (-0.870 – 0.225)	0.241	-0.38

2b. Self-efficacy of parents

	Baseline (T0) Mean score (95% CI)		3 months post- baseline (T1) Mean score (95% CI)		Mean difference in change from baseline (95% CI))	P value	Effect size*	7 months post-baseline (T2)		Mean difference in change from baseline (95% CI))	P value	Effect size*
	BOOST intervention Mean (SD)*	Usual care Mean (SD)*	BOOST intervention Mean (SD)*	Usual care Mean (SD)*				BOOST intervention Mean (SD) N=	Usual care Mean (SD) N=			
Facilitating child-centered healthcare discussions												
Reported by the mother	-0.088 (-0.457 – 0.280)	0.087 (-0.301 – 0.476)	0.135 (-0.272 – 0.542)	0.518 (0.120 – 0.915)	-0.207 (-0.727 – 0.313)	0.428	-0.23	0.293 (-0.207 – 0.793)	0.030 (-0.387 – 0.447)	0.438 (-0.171 – 1.047)	0.156	0.49
Reported by the father	-0.116 (-0.482 – 0.250)	0.107 (-0.218 – 0.432)	0.514 (0.058 – 0.970)	0.064 (-0.320 – 0.449)	0.673 (-0.036 – 1.381)	0.062	0.92	0.337 (-0.144 – 0.817)	0.282 (-0.103 – 0.666)	0.278 (-0.445 – 1.002)	0.444	0.38
Discussing ACP topics if their child initiates the conversation												
<i>Reported by the mother</i>												
Value- and emotion-oriented ACP	0.024 (-0.389 – 0.437)	-0.039 (-0.492 – 0.414)	0.306 (-0.187 – 0.799)	-0.172 (-0.628 – 0.284)	0.414 (-0.402 – 1.231)	0.314	0.41	0.495 (-0.151 – 1.141)	-0.352 (-0.845 – 0.141)	0.784 (-0.151 – 1.718)	0.099	0.78
End-of-life care-oriented ACP	0.072 (-0.329 – 0.472)	-0.135 (-0.584 – 0.315)	-0.076 (-0.538 – 0.387)	-0.098 (-0.553 – 0.357)	-0.184 (-0.950 – 0.583)	0.634	-0.19	0.369 (-0.217 – 0.955)	-0.192 (-0.684 – 0.301)	0.355 (-0.513 – 1.222)	0.417	0.37
<i>Reported by the father</i>												
Value- and emotion-oriented ACP	-0.018 (-0.449 – 0.414)	0.026 (-0.366 – 0.419)	0.063 (-0.475 – 0.600)	0.021 (-0.433 – 0.474)	0.086 (-0.749 – 0.922)	0.837	0.10	0.125 (-0.441 – 0.692)	-0.012 (-0.465 – 0.442)	0.181 (-0.672 – 1.034)	0.672	0.22
End-of-life care-oriented ACP	0.066 (-0.404 – 0.535)	-0.002 (-0.430 – 0.427)	0.284 (-0.291 – 0.859)	0.109 (-0.378 – 0.595)	0.108 (-0.727 – 0.943)	0.796	0.12	0.277 (-0.327 – 0.880)	0.508 (0.021 – 0.994)	-0.298 (-1.151 – 0.555)	0.487	-0.32
Initiating the conversation on ACP topics												
<i>Reported by the mother</i>												

Value- and emotion-oriented ACP	-0.118 (-0.508 – 0.273)	0.153 (-0.275 – 0.582)	0.072 (-0.361 – 0.504)	0.162 (-0.269 – 0.592)	0.181 (-0.397 – 0.760)	0.533	0.20	-0.016 (-0.532 – 0.499)	0.051 (-0.395 – 0.498)	0.203 (-0.449 – 0.856)	0.535	0.22
End-of-life care-oriented ACP	-0.090 (-0.527 – 0.348)	0.112 (-0.358 – 0.582)	-0.152 (-0.636 – 0.332)	0.119 (-0.353 – 0.592)	-0.069 (-0.699 – 0.561)	0.827	-0.07	0.058 (-0.517 – 0.632)	0.169 (-0.339 – 0.676)	0.091 (-0.630 – 0.813)	0.801	0.09
<i>Reported by the father</i>												
Value- and emotion-oriented ACP	0.219 (-0.253 – 0.691)	-0.142 (-0.561 – 0.277)	0.131 (-0.444 – 0.705)	0.290 (-0.195 – 0.775)	-0.520 (-1.331 – 0.290)	0.204	-0.56	0.150 (-0.452 – 0.752)	-0.160 (-0.645 – 0.326)	-0.052 (-0.881 – 0.777)	0.901	-0.06
End-of-life care-oriented ACP	0.216 (-0.274 – 0.706)	-0.154 (-0.602 – 0.293)	0.397 (-0.230 – 1.025)	0.333 (-0.175 – 0.841)	-0.306 (-1.198 – 0.586)	0.494	-0.32	0.378 (-0.252 – 1.008)	0.337 (-0.171 – 0.846)	-0.330 (-1.222 – 0.562)	0.461	-0.34

Footnote: Value- and emotion-oriented ACP topics - what the adolescent: 1) finds important in life; 2) how he/she feels because of the illness and treatment; 3) worries about; 4) is afraid for; 5) hopes for; 6) expects from the future.

End-of-life care-oriented ACP topics: 1) whether or not to start a new treatment if the current treatment is not effective; 2) stopping the treatment if the current treatment is not effective; 3) the likelihood the adolescent might die from the illness

The following tables present the estimated mean sum scores for behavior and intention, with possible scores ranging from 0 to 6 for value- and emotion-oriented ACP and scores ranging from 0 to 3 for end-of-life care-oriented ACP.

2c. Intention of parents to discuss ACP topics with their child

	Baseline (T0) Mean score (95% CI)		3 months post- baseline (T1) Mean score (95% CI)		Mean difference in change from baseline (95% CI))	P value	Effect size*	7 months post-baseline (T2)		Mean difference in change from baseline (95% CI))	P value	Effect size**
	BOOST intervention Mean (SD)*	Usual care Mean (SD)*	BOOST intervention Mean (SD)*	Usual care Mean (SD)*				BOOST intervention Mean (SD) N=	Usual care Mean (SD) N=			
Intention to discuss ACP topics with their child soon												
<i>Reported by the mother</i>												
Value- and emotion-oriented ACP <i>Score can range from 0 - 6</i>	4.8 (3.9 – 5.6)	4.7 (3.8 – 5.6)	3.8 (2.8 – 4.8)	4.9 (3.9 – 5.827)	-1.1 (-2.6 – 0.4)	0.137	-0.54	4.4 (3.2 – 5.6)	5.0 (4.0 – 6.1)	-0.7 (-2.4 – 1.0)	0.391	-0.35
End-of-life care-oriented ACP <i>Score can range from 0 - 3</i>	0.7 (0.2 – 1.1)	1.4 (0.8 – 1.9)	0.8 (0.2 – 1.3)	0.5 (0.0 – 1.0)	1.0 (0.1 – 1.9)	0.037	0.85	0.4 (-0.3 – 1.1)	0.5 (0.0 – 1.1)	0.6 (-0.5 – 1.6)	0.279	0.50
<i>Reported by the father</i>												
Value- and emotion-oriented ACP <i>Score can range from 0 - 6</i>	4.6 (3.7 – 5.6)	5.2 (4.3 – 6.0)	4.2 (3.0 - 5.4)	4.5 (3.5 – 5.5)	0.2 (-1.4 - 1.8)	0.775	0.12	4.3 (3.0 – 5.5)	4.6 (3.6 – 5.6)	0.2 (-1.4 – 1.8)	0.809	0.10

End-of-life care-oriented ACP	0.1 (-0.2 – 0.5)	0.4 (0.1 – 0.7)	0.1 (-0.3 – 0.5)	0.3 (0.0 – 0.7)	0.2 (-0.6 – 0.6)	0.947	0.03	0.2 (-0.2 – 0.6)	0.2 (-0.1 – 0.5)	0.3 (-0.3 – 0.9)	0.346	0.47
Score can range from 0 - 3												

Footnote: Value- and emotion-oriented ACP topics - what the adolescent: 1) finds important in life; 2) how he/she feels because of the illness and treatment; 3) worries about; 4) is afraid for; 5) hopes for; 6) expects from the future.

End-of-life care-oriented ACP topics: 1) whether or not to start a new treatment if the current treatment is not effective; 2) stopping the treatment if the current treatment is not effective; 3) the likelihood the adolescent might die from the illness

2d. Behavior of parents discussing ACP topics with the adolescent

	Baseline (T0) Mean score (95% CI)		3 months post- baseline (T1) Mean score (95% CI)		Mean difference in change from baseline (95% CI)	P value	Effect size*	7 months post-baseline (T2)		Mean difference in change from baseline (95% CI)	P value	Effect size**
	BOOST intervention Mean (SD)*	Usual care Mean (SD)*	BOOST intervention Mean (SD)*	Usual care Mean (SD)*				BOOST intervention Mean (SD) N=	Usual care Mean (SD) N=			
Behavior of discussing ACP topics with their child in the past month												
<i>Reported by the mother</i>												
Value- and emotion-oriented ACP <i>Score can range from 0 - 6</i>	4.7 (4.1 – 5.3)	5.1 (4.4 – 5.7)	4.0 (3.3 – 4.7)	4.8 (4.1 – 5.5)	-0.4 (-1.5 – 0.8)	0.538	-0.24	4.9 (4.0 – 5.8)	4.7 (3.9 – 5.4)	0.6 (-0.7 – 1.9)	0.372	0.40
End-of-life care-oriented ACP <i>Score can range from 0 - 3</i>	0.3 (-0.0 – 0.6)	0.6 (0.3 - 0.9)	0.0 (-0.3 – 0.4)	0.4 (0.0 – 0.7)	-0.0 (-0.6 – 0.6)	0.989	-0.01	0.1 (-0.3 – 0.6)	0.4 (0.05– 0.8)	0.1 (-0.6 – 0.7)	0.847	0.09
<i>Reported by the father</i>												
Value- and emotion-oriented ACP <i>Score can range from 0 - 6</i>	4.7 (3.9 – 5.5)	4.9 (4.1 – 5.6)	3.6 (2.7 – 4.6)	4.7 (3.9 – 5.5)	-0.9(-2.1- 0.3)	0.133	-0.57	3.9 (2.9 – 4.9)	4.3 (3.5 – 5.1)	-0.2 (-1.5 – 1.0)	0.713	-0.14
End-of-life care-oriented ACP <i>Score can range from 0 - 3</i>	0.5 (0.2 – 0.8)	0.1 (-0.2 – 0.4)	0.3 (-0.1 – 0.7)	0.1 (-0.2 – 0.4)	-0.2 (-0.8 – 0.3)	0.440	-0.35	0.3 (-0.1 – 0.7)	0.2 (-0.1 – 0.5)	-0.3 (-0.8 – 0.3)	0.329	-0.45

PART III

OPTIMIZING COMMUNICATION AND CARE FOR CHILDREN WITH SERIOUS ILLNESSES: DEVELOPMENTAL FACTORS AND RECRUITMENT STRATEGIES

Chapter 5

CHARACTERISTICS OF CHILD DEVELOPMENT IN THE CONTEXT OF SERIOUS ILLNESS: A SCOPING REVIEW

This chapter is based on:

van Driessche A, La Rondelle L, Boelen PA, Brunetta J, Kars MC, Spuij M, Nijhof SL, Fahner JC. Characteristics of child development in the context of serious illness: a scoping review. [Submitted]

Abstract

Background: Despite evidence on the benefits for including children in their own (palliative) care, studies show that children are not sufficiently involved nor are their preferences sufficiently elicited in a developmentally appropriate manner. The aim of this scoping review is to provide an overview of characteristics of child development in the context of serious illness.

Methods: A scoping review was performed using methods from Arksey and O'Malley and the Joanna Briggs Institute. A structured literature search was conducted in four databases: Medline, Embase, Psycinfo and CINAHL. Articles were included until October 2022. Thematic analysis was performed to present domains and key factors influencing child development.

Results: We selected 24 out of 11246 articles. We found different characteristics describing the ongoing development of seriously ill children in early to middle childhood, early adolescence, and middle to late adolescence. Key themes were: psychological/emotional aspects, general cognitive aspects, social aspects, coping strategy, conceptualization of illness, conceptualization of death, and communication about their illness. Several accelerators of ongoing development were found (e.g. cortical maturation, prior medical experience, social experience with adults) and several decelerators (e.g. stress, hospital admission, avoidance of illness-related communication in the family).

Conclusion: Our review highlights essential aspects to consider when discussing illness and healthcare preferences with children at various developmental stages. However, our findings also underscore a significant gap in understanding the factors that impact the development of children with a serious illness. It is recommended to monitor development throughout the illness trajectory to gather more evidence and utilize this information to support the child's engagement in their own healthcare in a developmentally appropriate way.

Keywords: serious illness, child development, cognitive aspects, pediatric advance care planning, involvement, decision-making, childhood, adolescence, developmentally appropriate, age-appropriate

1. Background

Children suffering from serious illness want to be involved in their own medical decision making [1]. However, studies show that children are not sufficiently involved and their preferences are not being elicited as often or consistently as they could be [2]. The doctor-parent-child interaction is usually dominated by the adult [3]. Nevertheless, the advantages of involvement in conversations about their health are clear for the child patient: an improved sense of control and autonomy, improved adherence to medical treatment, and improved health status through self-determination and self-efficacy [3–5].

Integrating palliative care for children with serious illness can meaningfully benefit families by enhancing satisfaction with treatment, managing difficult symptoms, improving communication with healthcare professionals, and ensuring better care coordination [6]. Palliative care supports quality-of-life decisions, including end-of-life considerations, and can be provided alongside curative or disease-controlling treatments from the moment of diagnosis of a serious illness [7]. It is crucial to have ongoing and early discussions about the child's quality of life with the child as well as the caregivers to make well-informed decisions, a goal pursued by pediatric advance care planning (pACP) [8].

Childhood is a key period for developing skills that carry into adulthood, greatly influenced by both social and biological factors [9]. Children's ability to make health decisions is shaped by their developmental stage, experience with the illness, and attitudes of parents and healthcare professionals towards their capacity [2]. While there is no universal agreement on the age of competence for decision-making, studies have shown that age 12 is considered appropriate for involvement in medical-decision making, with the requirement of favorable environmental factors [5,10]. Therefore, the extent that children can participate in health decisions should depend on their ability and not on their calendar age [2,11]. However, establishing their ability to participate is considered difficult, as child and adolescent development is highly individual. Neurological capacity can be somewhat assessed by testing certain capacities, however, mature neurological capacity does not automatically mean that a child is competent for any medical decision [12]. Decision-making competence differs between specific decisions and situations throughout a child's development [12]. Socioeconomic status, culture, peer environment and health are sources of variance that affect neurocognitive development in children [9,13]. These factors determine the way children can, want and should participate in their own health care trajectory.

Several theoretical models, including Wallander and Varni's model of child adjustment to pediatric disorders [14] and Kazak's model of pediatric medical traumatic stress (PMTS) [15], delineate risk and protective factors for the ongoing development of children with serious illnesses. These encompass familial aspects (such as parental education and personality), medical variables (such as illness characteristics and treatment), and mediating factors (e.g., coping mechanisms, social support, communication) [16]. However, the literature lacks cohesive evidence on the appropriate way to involve children in medical decision making in a manner that suits their developmental abilities, their needs and preferences [17].

Therefore, we aim to provide an overview of characteristics and factors affecting child development in the context of serious illness. Our overview can help healthcare professionals to communicate in a developmentally appropriate way when discussing illness and health. For

instance, initiatives like pACP, emphasizing the child's perspective on current and future care goals [18], stand to benefit from these insights.

This scoping review addresses the following research questions concerning the ongoing development of children with serious illness: 1) Which prevailing theories and constructs are identified?; 2) What typical developmental characteristics are observed?; 3) What factors influence ongoing development?

2. Methods

A scoping review was performed using methods from Arksey and O'Malley [19] with further refinement from guidance by the Joanna Briggs Institute [20]. Descriptive analysis was conducted to present characteristics of child development and influencing factors. The review protocol was not registered. The PRISMA-ScR Checklist is used for reporting this scoping review [21].

2.1. Search strategy

A structured computerized literature search was conducted in four databases: Medline, Embase, Psycinfo and CINAHL. The search strategy was developed in collaboration with an information specialist and included the following domains: serious illness, child, communication, theory (**Table 1**). Serious illness encompasses health conditions that carry a high risk of mortality and either negatively impacts a person's daily function or quality of life, or excessively strains their caregiver [22]. Chronic illness entails conditions that last one year or more and require ongoing medical attention or limit activities of daily living or both [23]. In this study, we use "serious illness" to refer to serious and chronic illness. There was no restriction in publication date and we included articles published until 17 October 2022.

2.2. Study selection

Studies written in English that address what cognitive, social or emotional developmental elements are common to certain developmental stages of the child (0-18 years old) and what factors might influence this development in relation to various aspects of illness, were included. Literature reviews, conference proceedings, and complete dissertations were excluded. Articles were excluded if only biological or neurological aspects of development were described. Two reviewers independently screened all abstracts in order to select appropriate articles on Title-Abstract level first and full-text level after. Uncertainties on inclusion were resolved through discussion, including a third reviewer. The reference lists of studies we included were reviewed for additional relevant articles.

Table 1. Search string for Medline. Search date: 17 October 2022

"Catastrophic Illness"[Mesh] OR "Neoplasms"[Mesh] OR "Terminal Care"[Mesh] OR "Chronic Disease"[Mesh] OR "critical illness"[Mesh] OR "palliative care"[Mesh] OR "Catastrophic Ill"[tiab] OR "Neoplasm"[tiab] OR "Terminal"[tiab] OR "life limiting condition"[tiab] OR "life-limiting disease"[tiab] OR "life threatening ill"[tiab] OR "life limiting ill"[tiab] OR "life threatening condition"[tiab] OR "life limiting condition"[tiab] OR "serious ill"[tiab] OR "chronic disease"[tiab] OR "chronic ill"[tiab] OR "critical ill"[tiab] OR "palliative care"[tiab]
And
pediatrics[MeSH] OR child[MeSH] OR Infan*[tiab] OR minor*[tiab] OR kid[tiab] OR kids[tiab] OR child*[tiab] OR adolescen*[tiab] OR juvenil*[tiab] OR youth*[tiab] OR teen*[tiab] OR underage*[tiab] OR pediatric*[tiab] OR paediatric*[tiab] OR school*[tiab] OR teenager*[tiab] OR youngster*[tiab] OR toddler*[tiab]
And
"Communication"[Mesh] OR "social cognition"[MeSH] OR "social behavior"[MeSH] OR "exploratory behavior"[MeSH] OR "Personality Development"[MeSH] OR "psychology"[MeSH] OR "adaptation, psychological"[MeSH] OR "cognition"[tiab] OR "express"[tiab] OR "communicat*[tiab] OR "social cognition*[tiab]OR "social behavior*[tiab] OR "exploratory behavior*[tiab] OR "Personality Development"[tiab] OR "psychology*[tiab]
And
"concept formation"[MeSH] OR "Theor*[tiab] OR construct*[tiab] OR concept*[tiab]

2.3. Data extraction and synthesis

Data was extracted using multiple tables designed for data extraction, considering the defined research questions. All articles were read full text and text elements concerning typical child developmental characteristics and factors that influence child development were extracted. A descriptive analysis was performed on this data. The two researchers who performed the title and abstract screening, reviewed data independently and manually coded data using inductive analysis to identify common themes across the collected data. Findings were compared during four extensive meetings and any discrepancies were resolved through discussion. The project team reviewed the final findings.

3. Results

The study selection process is summarized in the PRISMA flow chart (**Figure 1**). A total number of 11246 unique hits were extracted from the four databases and subsequently screened for relevance. Eventually, 24 articles relevant to our research questions were selected (**Table 2**)

Figure 1: PRISMA flow diagram of the review process

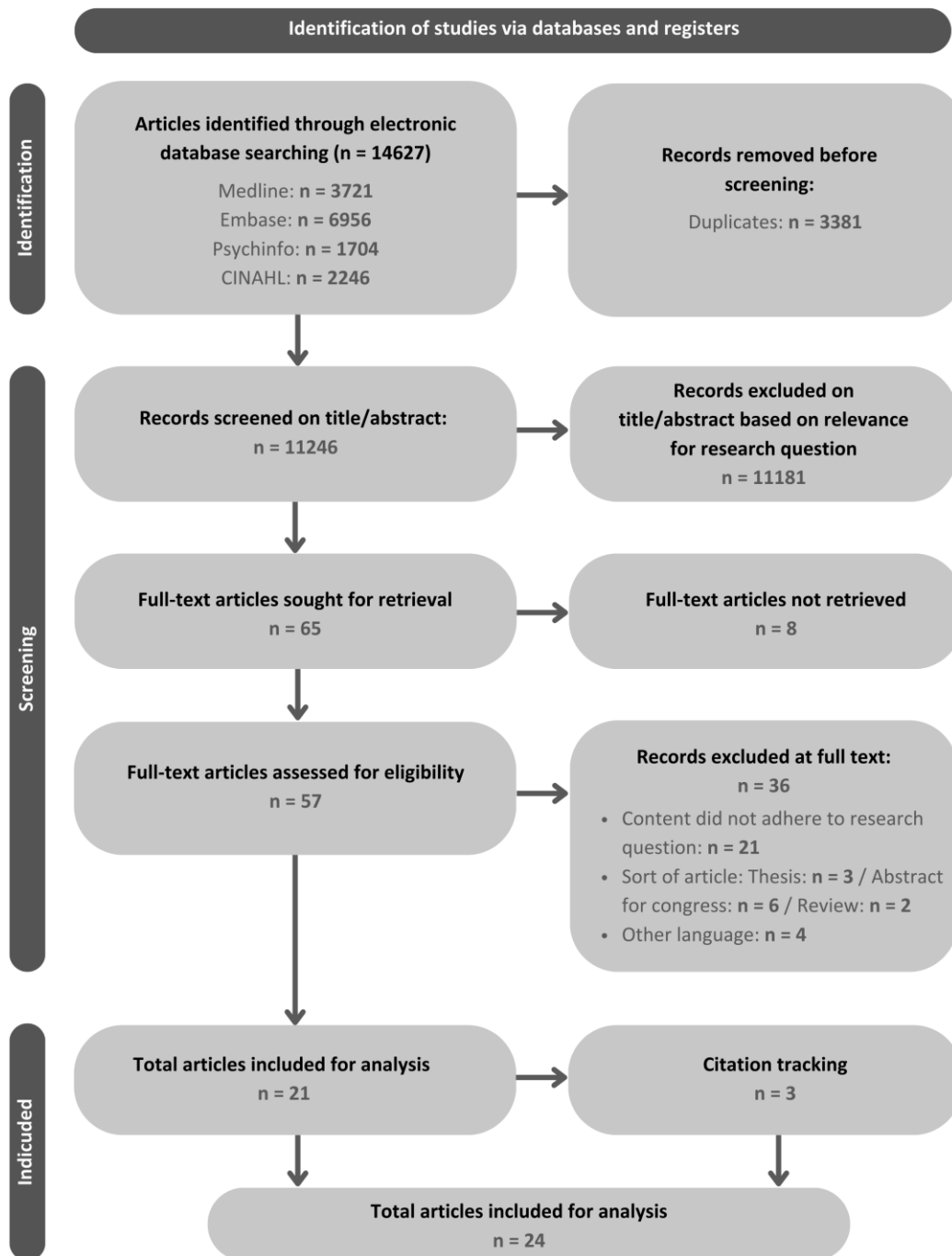


Table 2. Summary of studies included in the review

S	Author (year) Country	Aim of the study	Design	Sample and setting, n
S1	Admi (2007)[41] Israel	To determine the importance of epilepsy in the lives of the participants, to examine their view of others' perceptions of people with epilepsy, to analyze their ways of managing disease-related information, and to analyze their ways of managing medical regimens	Qualitative interview study Analyzing medical records	Adolescents and young adults with epilepsy (15-24), <i>n</i> = 14
S2	Allen (1984)[24] USA	To assess the concerns of children with insulin-dependent diabetes mellitus and how the concerns relate to their understanding of diabetes	Qualitative interview study Coding the response levels was based on the general progression from preoperational to formal operational thinking	Children with insulin-dependent diabetes mellitus, type 1 (8-17), <i>n</i> = 34
S3	Bernardo (1982)[25] USA	To integrate models of adaptation to disability and knowledge about children's cognitive development using Piagetian theory of cognitive development and Crate's stages of adaptation to chronic illness	<i>Unclear.</i>	<i>Unclear</i>
S4	Brewster (1982)[26] USA	To investigate the relationship between cognitive development and children's understanding of the cause of illness, intent of medical procedures, and role of the medical staff	Cross-sectional developmental design Standardized cognitive tasks based on Piaget's developmental theory Results were scored in ascending order of cognitive maturation	Chronically ill hospitalized children (5-12), <i>n</i> = 50
S5	Brown (1982)[27] USA	The author spells out the main struggles adolescents face due to their chronic illness. And gives recommendations by age group (10-14, 15-18 years old) how loved ones and caregivers on how to support the child	<i>Unclear. Involves 1 case study</i>	<i>Unclear</i>
S6	Cantrell (2013)[28] USA	To develop a framework based on Piaget's cognitive development theory that considers the developmental progression of illness understanding and allows reintegration of concepts	<i>Unclear.</i>	<i>Unclear</i>
S7	Clunies-Ross (1988)[38] UK	To report on the concepts of death in children with leukemia (ideas about the causes of illness)	Qualitative interview study Analyzing children's drawings using the Kinetic Family Drawing Revised Scale (KFD-R)	Children with leukemia (4-9), <i>n</i> = 21
S8	Gibson (2010)[45] UK	To explore children's and young people's views of cancer care and to present a conceptual model of communication and information sharing	Cross-sectional developmental design Three techniques were employed to offer a range of activities drawing on play and participation based on approaches: Play and puppets (4-5) Draw and write technique (6-12)	Children and adolescents with cancer at different disease stages (4-5, 6-12, 13-19), <i>n</i> = 38

			Activities day and interviews (13-19)	
S9	Hinds (1997)[29] USA	To challenge and refine existing theories of adolescent development and to contribute to the revision of current theories (Freud; Piaget; Erikson; Sullivan; Fowler; Bronfenbrenner) to better account for the unique conditions and experiences of adolescents dealing with serious health challenges	<i>Unclear. It is an editorial. Describes two cases</i>	<i>Unclear</i>
S10	Hinds (2005)[63] USA	To identify the preferences of children and adolescents with advanced cancer about their end-of life care and the factors that influenced their decisions	Qualitative interview study A descriptive decision-theoretic decision analysis model was used to analyze the data	Pediatric patients with advanced cancer (10-20), $n = 20$
S11	Kozłowska (2011)[44] AUS	To describe an individual intervention – one component of a multimodal treatment program – to help children find skills for pain management	<i>Unclear. this is an underpinning of their intervention</i>	<i>Unclear. Not clear what number of examples they tested the intervention on.</i>
S12	Campbell (1975)[39] USA	To study development of concepts of illness, to provide information on how children's views of illness evolve and change over time	Mixed-methods design Including semi-structured interviews children and mothers and questionnaires filled in by mothers	Children that were short-term patients in a pediatric hospital (6-12), $n = 264$, and their mothers
S13	Carandang (1978)[36] USA	To evaluate illness conceptualizations by children at different stages of cognitive development and to evaluate the role of sibling illness on conceptualizations about illness	Mixed-methods design Including interviews and Piagetian tasks of physical conservation	Children with a healthy sibling (6.5-15) $n = 36$, or a chronically ill sibling with diabetes (6.5-15) $n = 36$, and their mothers
S14	Claflin (1991)[37] USA	To examine how information disclosure related to the child's age and whether disclosure mediates the socioemotional distress of the illness as assumed in the protective approach	Qualitative interview study Including interviews with children and group interviews family	Children with cancer (<9, 9-14, 14>) $n = 43$, and their families
S15	Kury (1995)[42] USA	To evaluate whether previous medical experience is associated with more sophisticated conceptions of illness causality among chronically ill children	Mixed-methods design Including semi-structured interviews and intelligence subtests	Chronically ill children (4-16), $n = 64$
S16	Mouratidi (2016)[30] GR	To explore possible age differences in children's (subjective) perceptions of illness and health and to what extent these differ from adults' perceptions	Thematic content analysis design with a drawing-based method	Children from nursery and primary schools (5-11) $n = 347$, and adults ($\mu 20.6$), $n = 114$
S17	Neul (2003)[31] USA	To explore whether cognitive development level and chronological age were related to sickle-cell disease (SCD) knowledge and pain conceptualization in young children with SCD	Mixed-methods design Including a multiple-choice questionnaire, sentence completion tasks and Piagetian conservation tasks	Children with SCD (6-13), $n = 44$
S18	Poltorak (2006)[32] USA	To explore how children's understanding of death develops through various cognitive and developmental stages. The study seeks to integrate insights from both cognitive developmental and psychoanalytic perspectives to provide a comprehensive framework that can help clinicians, caregivers, and parents	<i>Unclear.</i>	<i>Unclear</i>

		approach the topic of death in a developmentally informed manner		
S19	Schmidt (2003)[43] DE	To delineate major issues involved in the study of coping with chronic conditions in childhood. The article lists and specifically discusses currently existing tests to ascertain coping strategies in children with chronic conditions	<i>Unclear. More like a critical reading to find a connection between coping and development in literature.</i>	<i>Unclear</i>
S20	Sezgin (2020)[46] USA	To understand the life journey (to independence) of adolescents with chronic diseases and their caregivers. This study proposed a new perspective to the life journey, transition stages, and personal archetypes from a patient centered approach	Qualitative design including face-to-face interviews complemented with visual materials	Chronically ill adolescents (13-18), $n = 13$, and one of their caregivers
S21	Sigelman (1993)[33] USA	To trace developmental changes in the content and organization of knowledge (theoretical perspective). To emphasize that it is useful to shift from a Piagetian perspective, with its emphasis on the complexity of thinking about disease, to theoretical perspectives that focus on developmental changes in the content and organization of knowledge	Cross-sectional descriptive survey design	152 Middle-class children ($\mu 9$, $\mu 11$, $\mu 13$), $n = 152$, and psychologists' college students ($\mu 19$), $n = 58$
S22	Thies (1999)[34] USA	To test the hypothesis 'cognitive appraisal of stress changes with cognitive development'	Mixed-methods design including structured interviews by the Stress Appraisal Protocol, rating emotions on Likert scale and the Piagetian task of causal reasoning	Chronically ill children (8-9, 11-12, 14-16), $n = 79$
S23	Werner-Lin (2018)[35] USA	To offer recommendations for parental disclosure of genetic risk to children, case examples with critical discussion of relevant topics, common child questions with sample scripted responses, and additional printed and online resources. Recommendations are based on well-established theories of child development, empirical research on family communication of hereditary cancer risk, and clinical counseling experience	<i>Unclear. More like a critical reading of well-established theories of child development and a how-to to disclosure genetic risk to children.</i>	<i>Unclear</i>
S24	Yeh (2001)[40] TW	To establish a conceptual framework for the adaptation process of Taiwanese children with cancer. Comparison with Roy's adaptation theory is discussed.	Mixed-methods design including in-depth interviews , observations, medical chart review and researchers' reflective journals review	Pediatric cancer patients with different illness trajectories ($\mu 11.4$), $n = 34$, and their caregivers

Child development theories and constructs

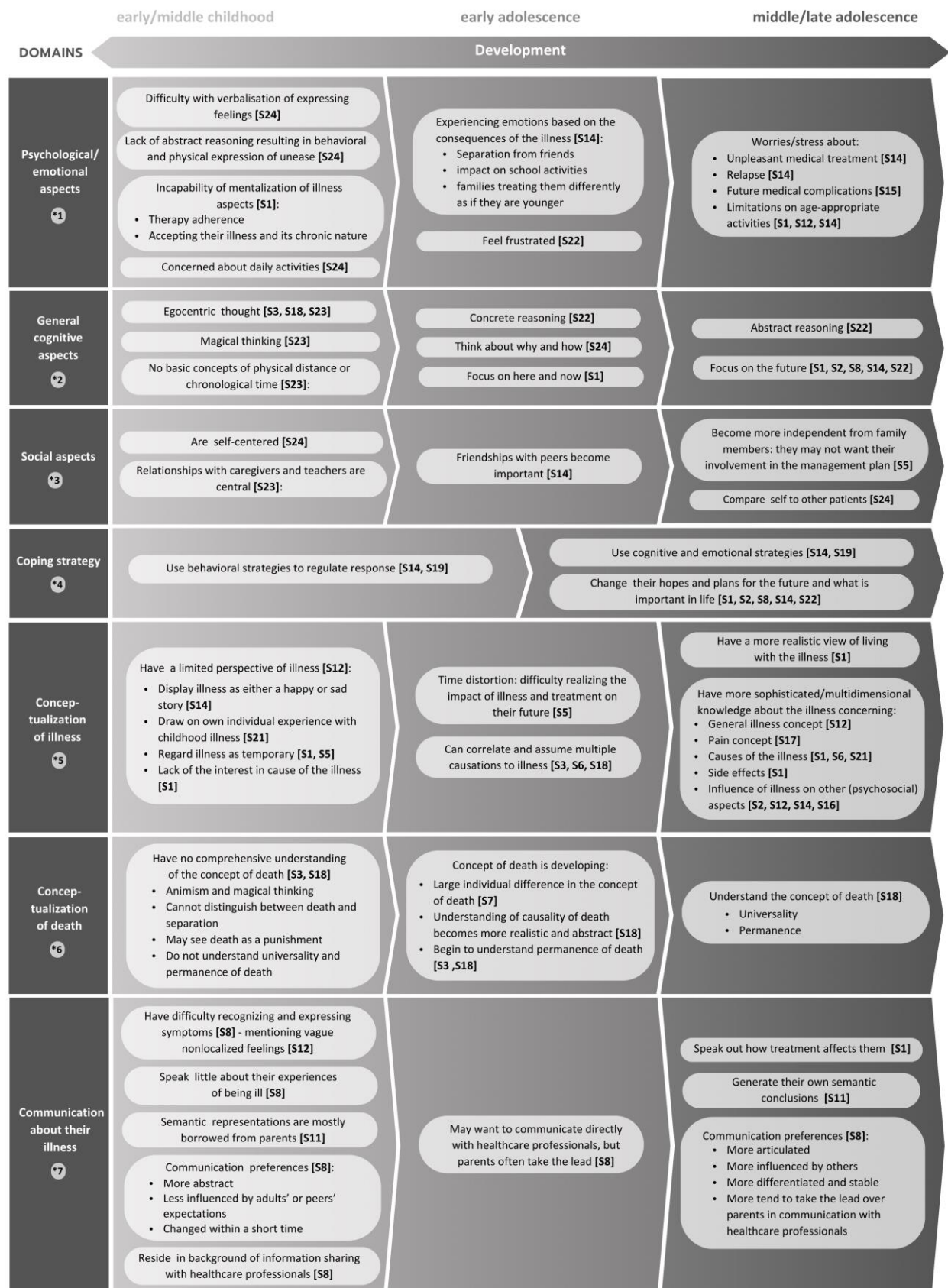
Several theories of child development were discussed in the selected studies. The most prevalent theory cited was Piaget's theory of cognitive development, which consists of four stages: 1) sensori-motor; 2) pre-operational thought; 3) concrete operations; 4) formal operations [24–35]. While some aspects of Piaget's theory were supported by authors based on their study results, such as the idea of development as a linear process with overlapping stages and the potential for progression to be hindered by various physical and social factors, other aspects were contradicted. For example, articles stated that the notions that young children have incorrect reasoning or often provide an explanation for illness based on immanent justice were not supported [36–38]. Other theories were mentioned in the introductory background section of the selected articles but were often not elaborated on (see **Additional file 1**).

Developmental characteristics throughout childhood and adolescence in the context of illness

Various characteristics of general childhood development were identified. Other factors are specific for children with an illness (**see Figure 2**). The characteristics were organized into the following domains: 1) psychological/emotional aspects; 2) general cognitive aspects; 3) social aspects; 4) coping strategy; 5) conceptualization of illness; 6) conceptualization of death; 7) communication about their illness. Definitions of the domains are given in the legend of the figure. The characteristics identified in the various domains are interrelated and are not mutually exclusive, suggesting that they could overlap across different domains.

Figure 2 illustrates characteristics throughout development from young to older, consistent with the consensus that child development is an individual process. Characteristics in early/middle childhood include: a limited perspective on illness [39], difficulties in verbally expressing their feelings about being ill [40], and concerns about daily activities they are unable to participate in due to their illness [40]. Children developing towards early adolescence engage more in concrete reasoning [34], and thinking about why and how they got ill [40]. Their focus however is still predominantly on the present 'here and now' [41], rarely fully realizing the impact of illness and treatment on their future [27]. Developing into middle/late adolescence, abstract reasoning increases and worrying about relapse, future medical complications and limitations on age-appropriate activities are reported [34,37,39,41,42]. It was highlighted that cognitive operations necessary to imagine different scenarios is a complex task for children and that the use of cognitive coping strategies in hypothetical problem situations increases with the age of the child [37,43].

Figure 2: Developmental characteristics throughout childhood and adolescence



**Footnote: Definitions on some of the defined domains[61]: 1) psychological/emotional aspects: the experiences, behaviors, traits, attitudes and emotions that characterizes that development group; 2) general cognitive aspects: skills involved in performing the tasks associated with perception, learning, memory, understanding, awareness, reasoning, judgment, intuition and language; 3) social aspects: the gradual acquisition of certain skills (e.g., language, interpersonal skills) and behavior that enable to interact with others and to function as a member of society; 4) coping strategy: an action, a series of actions, or a thought process used in meeting a stressful or unpleasant situation or in modifying one's reaction to such a situation; 5) and 6) conceptualization of illness and death: the process by which a person abstracts a common idea from one or more particular examples and learns the defining features or combination of features that are characteristic of the concepts 'illness' and 'death'; 7) communication: the transmission of information, which may be by verbal or nonverbal means.*

Factors influencing ongoing development in the context of serious illness

Evidence on accelerating and decelerating factors of ongoing child development was diffuse (see **Figure 3**). Age was reported as an obvious accelerator [39], as higher age often goes hand in hand with more knowledge on the illness [39], cortical maturation and increased cognitive abilities, which allows older children to generate own semantic conclusions [44]. Stress may serve as a decelerator through mechanisms hypothesized: 1) egocentric or magical thinking is retained serving as an important defense mechanism; 2) limited capacity to identify and differentiate body states when distressed [26,36,44]. The illness itself can either accelerate cognitive development, for example through a maturational effect [29], or it can slow development through information deficit [36,38]. Prior medical experience may relate to more specific illness concepts rather than to general conceptions of illness causality [42]. Furthermore, social experience with adults was deemed important to accelerate development by helping children learn new dialogues and integrate them into their own speech [45]. Parenting style was found to be influential. Authoritative parenting by offering a democratic climate of both high support and adapted control stimulates the child development over a passive (indulgent or uninvolved) or authoritarian parenting (providing strict control without being supported) [46]. Moreover, the way of communicating about illness in family settings impacts the child's development [38,44]. Furthermore, social experience with adults was deemed important to accelerate development by helping children learn new dialogues and integrate them into their own speech [45]. Parenting style was found to be influential. Authoritative parenting by offering a democratic climate of both high support and adapted control stimulates the child development over a passive (indulgent or uninvolved) or authoritarian parenting (providing strict control without being supported) [46]. Moreover, the way of communicating about illness in family settings impacts the child's development [38,44]. Several studies found shaping factors of child development, without specifying a unified direction of the impact (see **Figure 4**).

Figure 3: Influencing factors of child development

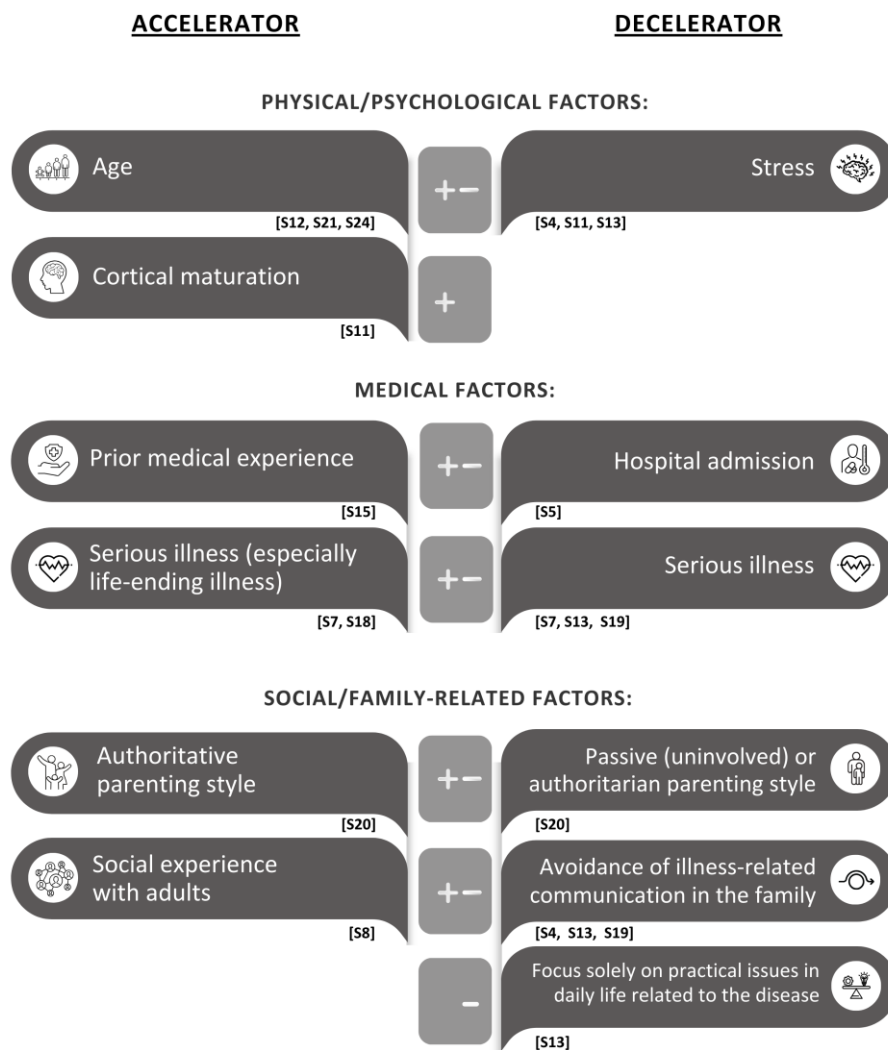
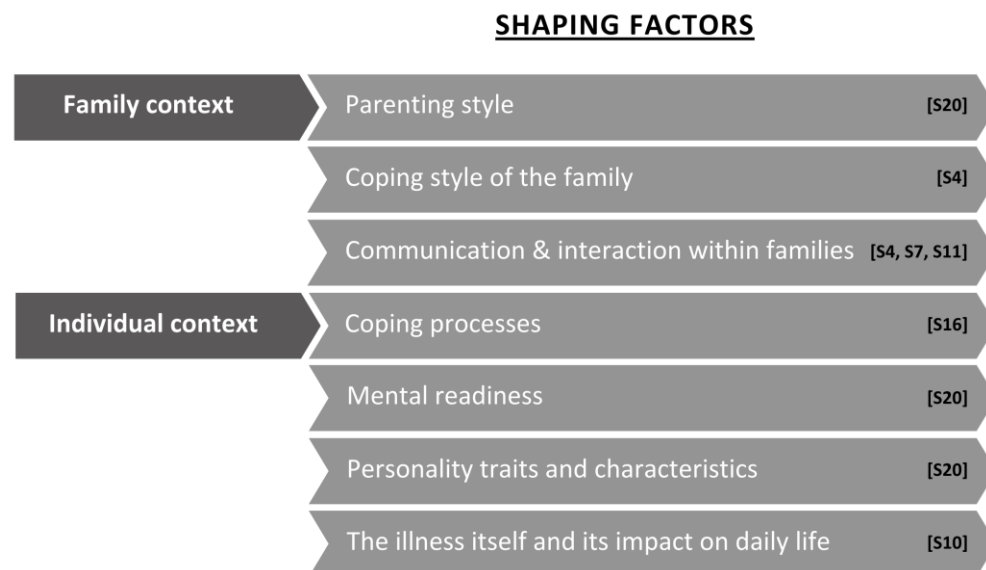


Figure 4: Shaping factors of child development



4. Discussion

Our scoping review aimed to outline current scientific literature on childhood development amidst serious illness. Recognizing children's development is vital for fostering productive collaboration among patients, families and healthcare professionals. Effective communication, a WHO standard for enhancing pediatric care, contributes to alignment with children's needs and preferences [47]. Additionally, the interplay between physiological, psychosocial, functional, and developmental factors influences children's coping abilities and overall adjustment to illness [14]. Supporting children's involvement in their own healthcare promotes feelings of being valued, increases a sense of control, and mitigates anxiety, which are essential for positive coping and adjustment outcomes [1,3].

Most classical theories of child development stem from the 1950s to the 1980s. In our study, we did not find recent comprehensive perspectives or multidimensional theories that integrate psychological, emotional, cognitive and social aspects of development, within the context of serious illness. However, research on the influence of specific risk factors on the favorable development of children, or on specific areas such as emotion regulation, attachment, decision-making and illness identity, continues to evolve and the essential relevance of the earliest years of life is increasingly recognized by researchers as well as policy makers [48]. Insights into the mechanisms through which these factors affect development in children with serious illness remains limited. This may be attributed to the complex and dynamic nature of child development, which resists rigid categorization.

Similar challenges to those encountered in pediatric palliative care research may contribute to the lack of studies in this area. Factors such as a broad range of patient diversity and small population sizes, driven by the diverse causes and durations of pediatric serious illness, as well as varying condition severity and dynamics, pose significant hurdles [49]. Additionally, the complex and interdependent relationships between children, families, and caregivers across developmental stages present conceptual and technical challenges for analysis [49]. Moreover, the lack of diversity in publications is a notable issue in the field of child development research [51]. Although Central and South America, Africa, Asia, and the Middle East collectively represent the majority of the global population, research studies predominantly originate from the USA, leading to underrepresentation from these regions [50].

While existing research underscores the necessity of involving children and adolescents in their healthcare in developmentally appropriate manners, practical tools or interventions for achieving this are lacking [18]. pACP, aimed at facilitating communication about preferences and future care goals in serious illness, could benefit from strategies tailored to children's developmental stages. In particular adolescence represents an opportune time for acquiring skills crucial for social interaction, like communication [12]. Therefore, initiating pACP at diagnosis and then continuing it could cultivate the skills necessary for active participation in their healthcare and specifying desired levels of involvement.

Children's needs, preferences and capacities to be involved in their own healthcare may vary at different stages in the healthcare trajectory [51]. Developing and implementing a tool for healthcare professionals to map changes in this for children with a serious illness may help tailoring their approach to train children to be involved in their current and future healthcare decisions. Therefore, studies to map best practices and test different ways of asking questions to children are crucial for refining communication strategies in pediatric healthcare settings. Rigid frameworks should not be strived for, as flexibility and sensitivity to each child's unique

needs and capacities are key in fostering meaningful involvement in their healthcare decisions. Existing systems in clinical practice, like the collection of generic patient reported outcomes (PROMs) through the KLIK portal, assess children's well-being across various domains over time [52–54]. Integration of assessing certain developmental aspects might offer a more comprehensive understanding of children's overall health and the mutual influences on each other, potentially providing insights into how to effectively engage the child in his or her own healthcare. Examining illness conceptualization in particular is important, and is influenced by cognitive as well as psychological, emotional and social factors and could be integrated in such systems. Beyond verbal communication, various behaviors, such as play activities, offer insight into development and can contribute to engaging children in a suitable manner, potentially preventing adverse health outcomes [55].

The aim of this scoping review was to explore literature on characteristics of and factors affecting child development in the context of serious illness, rather than constructing a comprehensive model of child development. Consequently, certain known protective and risk factors for child development, evidently also applicable to children with serious illness, were possibly not covered. Family communication and parenting style emerged as important factors in this scoping review. While some aspects of family communication are trainable, parents often encounter difficulty with coping with loss, particularly towards the end of life of the child, which may hinder their ability to fully consider the child's perspective or actively involve him in decision-making [56]. pACP programs such as IMPACT and BOOST aim to facilitate communication between parent(s), child and healthcare professionals [8,57], but could benefit from more evidence on developmentally appropriate ways to do so [18]. Other potentially family-related factors such as resilience, material resources, aberrant or suppressed play, and socio-economic status [55,58] were not encountered in this review. This omission may be attributed to the difficulty of modifying these factors in healthcare settings, thus deeming them less pertinent for inclusion in the literature that was selected for the purpose of this review.

A limitation of our scoping review is that we did not include gray literature such as policy documents and academic textbooks. Especially the part on existing child development theories thus gives limited insights. Furthermore, only English literature was included. Although we aimed for comprehensiveness by using broad search terms and using terms such as chronic and serious illness, it cannot guarantee the inclusion of all relevant literature. The studies primarily covered illnesses where development follows a typical trajectory, albeit with potential delays [59]. Conditions involving profound delays and following an atypical development trajectory, such as genetic disorders, disorders defined by one or more behavioral deficits, intellectual disability of unknown etiology and disorders resulting from environmental factors [60] were not addressed in the selected studies. In our search, we focused on characteristics of child development within the context of serious illness, as well as theories or constructs related to child development. This focus was driven by our primary interest in understanding how these factors influence children's ability to discuss their illness and their overall quality of life. We excluded articles that focused solely on biological factors, although such studies could offer valuable insights into aspects that interventions could target, such as emotion-related neural pathways for early intervention which would ultimately help children better manage their emotions [61]. While including these articles might have provided a more comprehensive overview of factors affecting child development, it was not considered feasible to report this breadth of research into one scoping review. Strengths are that we searched four databases and inclusion of studies to the next phase was discussed in detail with three researchers. As we performed a scoping review, we did not aim to rate the quality

of the included studies. However, it was notable that for some of the included studies, both the method of data collection and the population were unclear, underscoring the necessity for new high-quality studies.

Conclusion

This article provides a comprehensive overview of characteristics concerning the ongoing development of children in the context of serious illness. It sheds light on the intricate interplay of psychological, emotional, social, and cognitive factors that impact the extent and manner in which children can meaningfully participate in their healthcare decisions. Moreover, our findings revealed a significant gap in understanding the factors that influence the ongoing development of seriously ill children. These insights highlight the need for further research aimed at elucidating these factors and their implications for pediatric healthcare. Moving forward, our findings lay the groundwork for future research endeavors focused on enhancing the involvement of children and adolescents living with serious illness in healthcare in alignment with their developmental stage.

List of abbreviations

pACP Pediatric advance care planning; PRISMA-ScR Preferred Reporting Items for Systematic Reviews and Meta-Analyses – Scoping Review; CINAHL Cumulative Index to Nursing and Allied Health Literature; PROM Patient Reported Outcome Measure.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Extra information on the data analyzed during the study is available from the corresponding author upon reasonable request.

Competing interests

The authors declare no competing interests

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Authors' contributions

Conception and design of the work: JCF, AVD, LLR

Drafting the work: AVD, JCF, LLR

Critical revision for important intellectual content: AVD, JCF, LLR, JB, MCK, MS, PAB, SLN.

All authors have read and approved the final manuscript.

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Additional file 1. Theories on child development

Theory (reference to selected study)	Short explanation of the theory
Erikson's model of psychosocial development (S5, S9, S23)	Posits eight sequential stages of individual human development influenced by biological, psychological and social factors throughout the lifespan. Stages: stage 1 – infancy period; stage 2 – early childhood period, stage 3 – play age period, stage 4 – school age period, stage 5 – adolescence period, stage 6 – young adulthood period, stage 7 – adulthood period. Each stage is defined by two opposing psychological tendencies – one positive/syntactic and negative/dystonic [1].
Werner's orthogenetic principle (S21)	States that wherever there is development, it is characterized by increasing differentiation and hierarchic integration. 'Differentiation' refers to the process where systems or entities develop more complex structures by evolving more specialized parts or functions. 'Hierarchical integration' means that these increasingly diverse parts work together in a more coordinated and systematic way, forming an ordered hierarchy. This principle means that developmental analysis can be applied broadly to a wide range of phenomena and not just to those phenomena involving changes that occur from infant to adult [2].
Carol Gilligan's theoretical model focusing on interdependence and care in important relationships (S23)	Highlights the critical roles of interdependence and care within meaningful relationships. According to Gilligan, moral decisions are 'insistently contextual', meaning that they are best understood within the specific circumstances of each situation. She argues that individuals' moral reasoning is deeply influenced by their personal experiences, which can be comprehensively understood when they recount these experiences themselves [3,4].
Bronfenbrenner's ecological system theory (S23, S9)	States that to understand human development, one must consider the entire ecological system in which growth occurs. This system is composed of five socially organized subsystems that help support and guide human growth (ranging from microsystem such as school and family to the macrosystem, referring to institutional patterns of culture). Each of these layers has a direct or indirect impact on individual development, highlighting the importance of interactions within and between these layers [5].
Life span development psychology (Baltes) (S20)	Asserts that development is not completed at adulthood or maturity. Ontogenesis extends across the entire life course and lifelong adaptive processes are involved [6].
Attachment theory (Bowlby and Ainsworth) (S19)	Explains positive maternal-infant attachment as a dyadic relationship between the infant and mother that provides the infant with a secure base from which to explore the world. With respect to cognitive, social and behavioral domains, securely attached infants tend to have more favorable long-term outcomes, while insecurely attached infants are more likely to have adverse outcomes [7].

Dynamic-maturational model of attachment (Crittenden) (S11)	Emphasizes the interplay of genetic inheritance, maturational processes, and person-specific experiences. This model posits that these factors collectively influence the development of unique individual strategies for ensuring personal safety [8].
Freud's psychosexual theory (S9)	Highlights the impact of the sexual pleasure drive in shaping personality. The child's libido centers on behavior affecting the primary erogenous zone of his age; he cannot focus on the primary erogenous zone of the next stage without resolving the developmental conflict of the immediate one, affecting adult personality [9].
Sullivan's theory on anxiety/ interpersonal theory of psychiatry (S9)	Describes anxiety as a warning of threats to our self-esteem and self-worth. Sullivan thought anxiety could be contagious and could be transmitted directly from mother to child [10].
Fowler's theory on attempt to make meaning/ model of faith development (S9)	Explores how individuals' pursuit of purpose and meaning evolves qualitatively throughout their lives. This theory posits that both the extent and the ways in which people find purpose and meaning develop and change qualitatively over the lifespan [11].

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Chapter 6

RECRUITMENT AND RETENTION CHALLENGES AND STRATEGIES IN RANDOMIZED CONTROLLED TRIALS OF PSYCHOSOCIAL INTERVENTIONS FOR CHILDREN WITH CANCER AND THEIR PARENTS: A COLLECTIVE CASE STUDY

This chapter is based on:

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Abstract

Objective: In pediatric oncology there are few examples of successful recruitment and retention strategies in psychosocial care research. This study aims to summarize experiences, challenges, and strategies for conducting randomized controlled trials (RCTs) of psychosocial intervention studies among children with cancer and their parent(s).

Methods: We conducted a collective case study. To identify the cases, Pubmed and two trial registries were searched for ongoing and finished RCTs of psychosocial intervention studies for children with cancer and their parents. Online semi-structured expert interviews discussing recruitment and retention challenges and strategies were performed with principal investigators and research staff members of the identified cases.

Results: Nine studies were identified. Investigators and staff from seven studies participated, highlighting challenges and strategies within three major themes: eligibility, enrollment and retention. Regarding eligibility, collaborating constructively with healthcare professionals and involving them before the start of the study were essential. Being flexible, training the research staff, enabling alignment with the participants' situation, and providing consistency in contact between the research staff member and the families were important strategies for optimizing enrollment and retention. All studies followed a stepped process in recruitment.

Conclusion: Although recruitment and retention in some selected studies were successful, there is a paucity of evidence on experienced recruitment and retention challenges in pediatric psychosocial research and best practices on optimizing them. The strategies outlined in this study can help researchers optimize their protocol and trial-implementation, and contribute to better psychosocial care for children with cancer and their parents.

Key words: psychosocial studies, pediatric oncology, intervention studies, randomized controlled trials, recruitment, retention

What's Known

Performing RCTs is challenging, particularly in pediatric psychosocial research when both the child and parent are targeted. Recruitment and retention are common concerns. In pediatric oncology, there are few examples of successful recruitment and retention strategies in psychosocial care research.

What's New

Key strategies to collaborate constructively with healthcare professionals were outlined. Being flexible, training the research staff, alignment with the participant's situations and providing consistency in contact between the research staff member and the families were considered as essential strategies.

Abbreviations:

pACP – pediatric Advance Care Planning

RCT – Randomized controlled trial

SWAT - Study Within A Trial

Introduction

Randomized controlled trials (RCTs) are the optimal way to minimize bias and optimize inference when evaluating treatments, therapies, and innovation in healthcare [1]. However, performing RCTs is challenging, particularly in pediatric psychosocial research. Recruitment and retention are common concerns, in part because potential subjects may have preconceived notions about the interventions being studied (i.e., those that address mental health or communication of sensitive topics), and in part because these studies often involve substantial time commitments (i.e., for study procedures or questionnaires) [1,2]. Approximately half of these trials require extensions of time and/or budget to successfully recruit their target sample [1].

Previous studies in children with serious illnesses have explored recruitment and retention challenges [3,4]. In studies testing interventions for adolescents and young persons with chronic conditions, for example, participation may require directly identifying with their illness at a time when the subjects prefer otherwise. As a result, enrollment rates have ranged from 10 to 50% [3]. Similarly, psychosocial interventions may address topics that are sensitive to healthcare professionals and parents, raising challenges in the approach and enrollment for clinical trials [4]. Even when subjects do enroll, retaining them on these studies can be difficult due to the inherent burdens of study-participation; in a review of 40 clinical RCTs for parents and youth living with chronic illness, reported attrition rates were as high as 54% [5].

In pediatric oncology, there are few examples of successful recruitment and retention strategies in psychosocial care research [6]. Strategies such as medical director involvement in the recruitment group and information sessions for eligible families were ineffective in one study in a large children's cancer center [7]. In another study, a stepped process for recruitment was identified as an effective approach, where families were introduced to the study in a more person-centered way, spread over multiple contacts [6], and recruitment at diagnosis, face to face, and with the use of short questionnaires yielded higher participation [8]. Although having a coordinator to monitor data collection across sites as a strategy to improve response rates lacked effectiveness [9], involvement of the clinical team in the contact strategy does seem to enhance retention [10]. However, due to the inadequacies of current reporting practices, judging the impact of different recruitment and retention strategies is challenging [11]. In general, there is a clear knowledge gap with regard to effective strategies aimed at recruitment [12].

To advance the conduct of psychosocial RCTs among children, we aimed to provide a detailed description of the experienced recruitment and retention challenges, and strategies to overcome them, from psychosocial intervention studies conducted among children with cancer and their parent(s).

Methods

Design

We conducted a collective case study, selecting multiple cases to generate an in-depth, multifaceted understanding of a complex issue in its real-life context [13], and to allow us to detect patterns in recruitment and retention challenges and strategies to overcome these across the different psychosocial intervention studies. Online semi-structured expert interviews were conducted with principal investigators and research staff members of a selection of recent or

ongoing trials testing psychosocial interventions for children and/or adolescents with cancer and their parents.

Selection of cases

To identify our cases, we used an elaborate search on Pubmed (**Table 1**) and the ClinicalTrials.gov and ISRCTN.com trial registries in January 2022. Inclusion of studies was critically discussed with the core research team (ADV, KB, LD, JC, MK). Included cases (a) involved interventions that have psychosocial components (defined as any intervention that emphasizes psychological, educational, or social factors, rather than solely biological factors) [14], (b) included children/adolescents with cancer (on treatment) up until 25 years old, (c) included at least one parent in the study, (d) were either finished or ongoing studies and (e) were individually randomized controlled trials without an active comparator (**Table 2**). This search allowed us to identify the principal investigators (PI) of these studies and to collect relevant recruitment- and retention-related information, which was used to learn about the study before the interviews and was processed in our topic lists. The PIs were contacted by email and were allowed to invite a maximum of two other research staff members they thought would be able to give in-depth information on recruitment and retention challenges and strategies.

In March 2022, the corresponding authors were invited per email for an online interview of approximately one hour. If they did not respond after a maximum of three reminders, we contacted them via ResearchGate or contacted one of the other authors. Participants were offered a reimbursement of 60 euros for their time.

Table 1. Search string for Pubmed (January 2022)

"Randomized Controlled Trials as Topic"[Mesh] OR "Random Allocation"[Mesh] OR "Program Evaluation"[Mesh] OR trial*[tiab] OR test[tiab] OR effect*[tiab] OR "control group"[tiab] OR "intervention group"[tiab] OR random*[tiab] OR "test effectiveness"[tiab]
And
"Psychosocial Intervention"[Mesh] OR intervention*[tiab] OR program*[tiab] OR "psychosocial intervention"[tiab] OR "psychological intervention"[tiab] "Patient Education as Topic"[Mesh] OR "Psychotherapy" [Mesh] OR "Quality of Life" [Mesh] OR "Resilience, Psychological"[Mesh] OR "Adaptation, Psychological"[Mesh] OR "communication"[tiab] OR "Communication"[Mesh] NOT "Therapeutics"[Mesh] NOT "Medication Therapy Management"[Mesh] NOT medication*[tiab] NOT "Pharmacology"[Mesh]
And
"Child"[Mesh] OR "Adolescent"[Mesh] OR child*[tiab] OR adolescent*[tiab] OR "adolescent patient"[tiab] NOT "Cancer Survivors" [Mesh] NOT "cancer survivors"[tiab]
And
"Neoplasms"[Mesh] OR neoplasms[tiab] OR "Pediatrics"[Mesh] OR "pediatric cancer"[tiab] OR cancer[tiab] OR "pediatric oncology"[tiab]
<i>Filters used:</i> - Time period from 2011/1/1/ - 2022/1/1 - Study type: Randomized Controlled Trial - Age: Child (Birth – 18 years)

Table 2. Inclusion- and exclusion criteria for the selection of studies

Inclusion criteria	Exclusion criteria
1. Target group of the intervention is children / adolescents with cancer up until 25 years old (with at least n=5 children recruited younger than 18 years old)	1. Pharmacological studies
2. Parents are included in the study (not necessarily involved actively in the intervention itself, but involved in, for example, filling out questionnaires)	2. Studies involving medical devices
3. The intervention has psychosocial components and is being tested in an individually randomized controlled trial	3. Cluster RCTs or RCTs in which the control group receives an active comparator (such as attention control)
4. The child / adolescent and parent(s) are randomized in an intervention group and control group with care as usual	4. Studies registered before 1 January 2011
5. Studies are registered after 1 January 2011	

Data collection

The interviews took place in March and April 2022, via Zoom, using a self-developed topic list (see **Additional File 1**). Domains represented in the interviews were: 1) Actions before the study start; 2) Screening for eligibility; 3) Enrollment; 4) Attrition; 5) Encountered challenges; 6) Additional strategies to enhance recruitment; 7) Advice to other researchers.

To prepare and tailor each interview, we asked the participants to send us documents (such as information letters and protocols) they used regarding all aspects of recruitment and retention.

Analysis

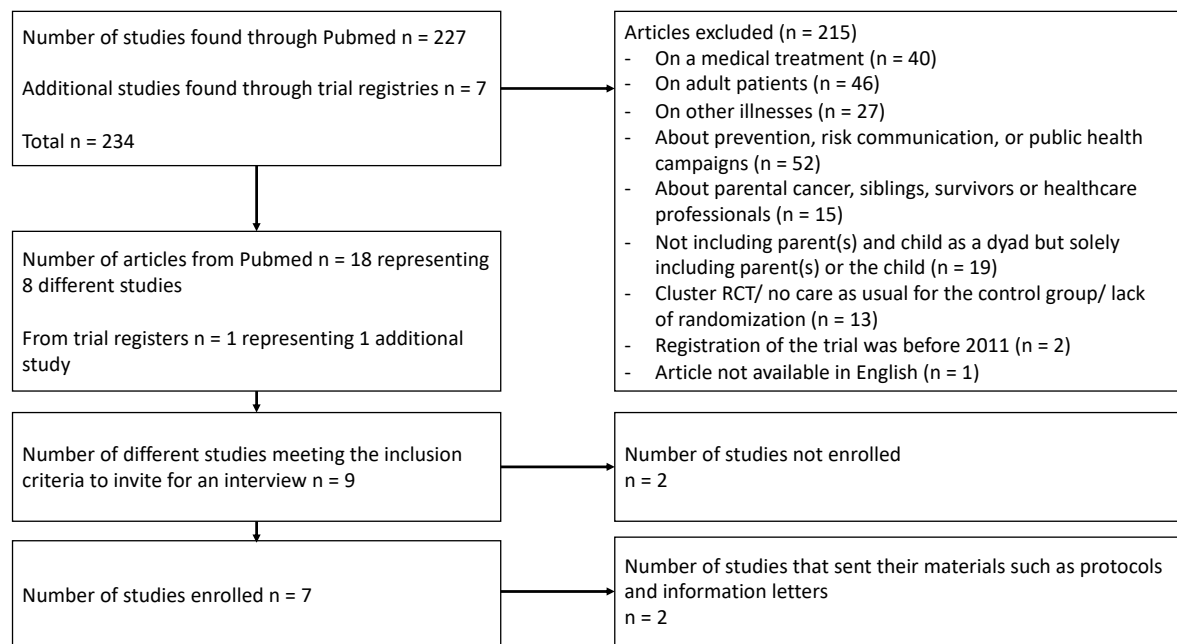
All interviews were audio recorded and transcribed verbatim. The principal author analyzed all interviews, using a combination of deductive and inductive thematic analysis [15]. Transcripts were read line by line and data were coded into an a priori framework of the seven domains of the topic list (deductive component). Data within each category was then coded in order to create sub-categories (inductive component). NVivo version 20 software assisted in data organization. Main findings were discussed with the research team to enhance reliability of interpretations.

Results

3.1. Selection of cases

In total, 234 studies were identified. Of these, nine studies met the inclusion criteria (see **Figure 1**). The authors of one study [16] declined participation in the interview and we could not reach the authors of one other study [17]. The remaining 7 studies were included (**Table 3**).

Figure 1. Flow chart of the selection process



*Studies meeting the inclusion criteria and invited for an interview: 1). PRISM [30]; 2) EPSI [31]; 3) PediQuest [32]; 4) FACE [35]; 5) Legacy [40]; 6) FAMOS [37]; 7) Cognitive Behavioural Therapy [17]; 8) Homebased Multimodal Symptom Management Program [16]; 9) BOOST pACP [39].

3.2. Results from the interviews

The interviews lasted between 59 and 83 minutes. We identified challenges related to three major themes: eligibility, enrollment and retention (discussed below) - as well as participant-suggested strategies to address these challenges (listed in **Table 4**) and general considerations for future investigation including illustrating quotes (**Table 5**).

Eligibility

We identified three challenges related to eligibility screening. First, respondents indicated that determining eligibility criteria could be challenging because they needed to balance feasibility of enrollment within a certain timeframe with the need to target experiences within specific, small populations of youth. A psychosocial intervention is often developed and tested for a specific age group with a corresponding cognitive development. This creates **a tension between broadening eligibility in view of numbers and the target group specificity in view of the intervention**. Some respondents indicated they changed certain criteria, such as the age of children or types of cancer, because they noticed interest in that group or because they saw this increased the feasibility of recruiting a sufficient number of participants within their timeframe.

Second, **gatekeeping by healthcare professionals** was often mentioned as a barrier. Respondents believe this behavior was usually well-intentioned; clinicians hoped to protect families from potential stressors associated with the study-topics. Although some respondents regarded healthcare professionals watching out for the potential risks of participating in a study as a strength because they know more about the family's illness trajectory and burden, this sometimes led to disagreement between data collectors and healthcare professionals concerning the family's eligibility. Studies depending on healthcare professionals for

introducing the study experienced additional challenges in maintaining awareness among the professionals about the study and their crucial task of checking families' eligibility and introducing the study to eligible participants.

Third, as childhood cancer qualifies as a rare disease [18], **multiple sites must often be involved to increase the pool of eligible participants**, which entailed extra challenges such as a lack of control over the approach and the procedures in the various sites. Moreover, it took a lot of time to arrange legal contracts to be able to share protected health information among the different sites, with some legal departments being extra cautious because the research involved children with cancer. In the case of the BOOST pACP study, additional legal parties had to be involved, which required extra time.

Enrollment

Seven themes related to enrollment challenges were identified. Enrollment rates varied depending on the site and research assistant. Recruitment for psychosocial studies in this target group usually takes a long time. Within the long recruitment period, **staff turnover within the research team** was inevitable, which created difficulties regarding finding new motivated and flexible members. Some respondents noticed that the enrollment rate would drop after hiring new research assistants. Finding and training suitable new staff took time and resources. New research staff members, in particular, found it often difficult to interact with families going through these difficult experiences, because they did not want to add to the family's burden. Consequently, they were extremely careful introducing the study, which sometimes negatively impacted enrollment rates.

Willingness to participate was often overestimated by the research team. Through surveys, several respondents had tried to gain insight into families' reasons for not participating in the study, but the response rate on these surveys was low. The insights obtained revealed that the families' reasons for refusing to participate were: feeling overwhelmed having to combine their family life with regular visits to the hospital; perceiving the health status of the child as not good enough; or simply not having the mental headspace to commit to something extra, regardless of the study. The children's most mentioned reason for not participating was wanting to feel normal without being preoccupied with being sick.

Respondents acknowledged that **children or adolescents with cancer and their parents are an overburdened research population**. Our respondents mentioned that there were often competing studies in the same target group during the time of recruitment. One study (FAMOS) could not include families of children between 6 – 18 years for that reason, and were thus constricted to include only a part of their original target group (0 – 18 years). Medical studies are often prioritized: for example, a child eligible for the BOOST study said she had already participated in a medical trial, preferring that over a study with psychosocial components.

According to our respondents, another factor potentially influencing enrollment rates was that **families are randomized into groups**. Families did not always understand the concept of randomization and did not fully know what they were signing up to. Some families also had a clear preference for one of the groups.

The dyadic nature of the enrollment and needing both the parent(s) and the child to be willing to participate, complicated this kind of research. Encountering both the child and one of the parents in the same room at the moment of introduction in the hospital often took several visits. Parents regularly assumed that their child did not want to participate, or they wanted to protect them from potential harm. Requiring the signatures of both caregivers took additional

time, because they were usually not present at the hospital at the same time and they had to discuss participation at home.

Finding an appropriate time to introduce the study to the family was experienced as an important part of building up contact with the families. However, this was also seen as a prominent challenge because, as many families were in the hospital to receive news or heavy treatment, it was difficult to estimate the burden at that moment.

Lastly, ***the COVID-19 pandemic*** was detrimental to many ongoing studies, because it further negatively influenced families' willingness to participate. Moreover, some respondents felt that in-person recruitment worked better (addressing families and being present in the wards), which was not possible during the lockdown periods.

Retention

Two themes in retention challenges were identified. All respondents faced ***non-response and drop-out*** in their studies. In some studies, the drop-out rate was higher in the intervention group compared to the control group. Respondents hypothesized that this could be due to the intervention taking a lot of time or not being sufficiently user-friendly. The respondents from studies in which drop-out was higher in the control group speculated that this could be caused by them being contacted and engaged less often throughout the study period or by them being less motivated because they did not receive an intervention in return.

Another challenge impacting retention was ***keeping per-protocol timelines versus required flexibility***. Once families had been enrolled, it was challenging to follow the protocol and keep to the predefined time window, especially when psychosocial interventions consisted of several intervention sessions and questionnaires. Some children were admitted to the intensive care unit (ICU) during the study period, or sessions needed to be rescheduled because parents were exhausted or had other obligations, which impacted the planning of the follow-up sessions. Therefore, the risk of families having to drop-out is increased and a certain amount of flexibility is required.

General challenges experienced by the respondents

Three overarching challenges were elaborated on during the interviews. For an indication of how many recruitment sites are required and how much time is needed to enroll the target number of participants, most respondents performed a pilot test. However, in some cases – due to different circumstances in the larger study - ***the numbers in the pilot study were vastly different from the numbers eventually enrolled in the larger scale trial***.

In addition, ***some studies had to pause enrollment because another recruitment strategy they wanted to implement was not included in their initial, IRB-approved, protocol***.

Lastly, ***ending up with enough recruitment sites willing and able to participate in the study*** was mentioned to be challenging. Therefore, one respondent recruited via social media (Facebook) instead. Although this eventually worked well after gaining expertise in creating and running an advertising campaign, the respondent argued that this is not applicable to every population and success is difficult to predict.

Table 3. Key characteristics of selected studies for which we held interviews

Selected studies	Function of the participants in the interview	Target population Country, sites and timing Timepoints of surveys	Intervention goal and content	Original target goal and time window of recruitment as defined in protocol/trial register	Actual number of participants enrolled and time window of recruitment. Extra time/sites required?	Enrollment rate ¹ and retention rate ² and extra time or sites required
1. Promoting Resilience in Stress Management (PRISM)[30]	One Principal Investigator and two research assistants.	Target population: Adolescents and young adults (13 – 25 years old) diagnosed with cancer between 1- and 10-weeks prior to enrollment OR ever diagnosed with progressive, recurrent or refractory cancers and receiving systemic chemotherapy and their parents Country, sites and timing: USA - Seattle Children's Hospital (January 2015 – October 2016) Timepoints of surveys: Baseline, and abbreviated surveys measuring only the primary endpoint at 2- and 4- months post-enrollment. A final and	Goal: To bolster resilience skills, and, in turn, to improve participant-reported quality of life, hope, and mental health outcomes. Intervention components and delivery: - Stress management skills (breathing, relaxation, mindfulness) - Goal-setting skills (creating and pursuing "SMART" [Specific, Measurable, Actionable, Realistic, Time-dependent] goals - Cognitive-restructuring / positive reframing (identifying negative self-talk, reframing experiences and perspectives to make them feel manageable) - Benefit-finding / meaning-making (identifying gratitude, purpose, meaning, identity) Delivered by trained, non-clinical college graduates in 4 scripted 30 – 50 minute, 1-on-1 sessions approximately every other week.	Original target goal: 100 Original time window of recruitment: 24 months	Actual number of participants enrolled: 99 Actual time window of recruitment: 22 months Extra time or sites required?: no	Enrollment rate: 77% Retention rate: 92% among subjects well enough to participate; 75% among all subjects, including those who died during the study.

¹ Enrollment rate: defined as the proportion of people who enrolled out of all people determined to be eligible

² Retention rate: defined as the proportion of people who enroll and who complete the study

		comprehensive survey 6-months post-enrollment.				
2. Enhanced Psychosocial Intervention (EPSI)[31]	One Principal Investigator and one project manager.	Target population: Dyads of youth (10 – 17 years old) newly diagnosed with cancer (within 4 weeks of diagnosis) and their primary caregiver and siblings Country, sites and timing: Canada -SickKids Hospital (Toronto) (Nov 2017 – April 2019) Timepoints of surveys: Near diagnosis (T1) and 12 months later (T2)	Goals: Improve children's and family coping with disease-related stressors such as pain and uncertainty, improve child mood and enhance social engagement with peers. Improve the triaging of resources and enhance the effectiveness of psychosocial intervention for children with cancer. Intervention components and delivery: 1) Information about the psychosocial risk of the family and mental health of the child 2) Sharing screening results and recommendations with the treating team and with the family 3) The Psychosocial Navigator as resource for tailoring psychosocial resources to child-family distress, linking with the clinical treating team	Original target goal: 40 dyads - one caregiver, one target child Original time window of recruitment: 16 months	Actual number of participants enrolled: 38 dyads Actual time window of recruitment: 17 months Extra time or sites required?: start of the study was delayed for 6 months due to COVID-19 pandemic	Enrollment rate: 54% Retention rate: 90%
3. PediQuest (PQ)[32] followed by the PediQuest Response Study[33,34]	One Co-Investigator and one project manager.	Target population: Children >2 years old with at least a 2-week history of progressive, recurrent, or non-responsive cancer or for whom there was a decision not to pursue cancer-directed therapy, and their parents Country, sites and timing: USA - Dana Farber Children's Cancer and Blood Disorders Center, Children's	Goal: to improve quality of life in children, adolescents, and young adults with advanced cancer, and their parents Intervention components and delivery: PediQuest Response includes an enhanced system (web-based and with an app for answering surveys and viewing reports) that is coupled with early integration of a palliative care consulting team.	Original target goal: 200 child-parent dyads (to end up with at least 136 randomized) Original time window of recruitment: 3 years	Actual number of participants enrolled: 196 (155 randomized) Actual time window of recruitment: 3.5 years Extra time or sites required?: yes	Enrollment rate: 66% Retention rate: 81%

		Hospital of Philadelphia, Seattle Children's Hospital, Texas Children's Hospital (April 2018 – July 2022) Timepoints of surveys: Weekly surveys for 16 weeks in total after randomization (after a run-in period of 2 weeks)				
4. Family-Centered pediatric advance care planning for teens with cancer (FACE-TC)[35]	One Principal Investigator, one Site Principal Investigator and one research coordinator.	Target population: Adolescents with cancer 14 – 21 years old and parents Country, sites and timing: USA - Akron Children's Hospital, Children's National Hospital, St. Jude Children's Research Hospital, University of Minnesota Masonic Children's Hospital (July 2016 - April 2019) Timepoints of surveys: Baseline and at 3-months postintervention.	Goal: to facilitate goals-of-care conversations and completion of advance directives between AYAs and their families. Intervention components and delivery: Three 60-minute sessions with a certified facilitator at weekly intervals. Session 1: the Lyon Advance Care Planning Survey administered separately to AYAs and families to prepare the dyad for session 2 conversations Session 2: the Respecting Choices Next Steps pACP-facilitated conversation Session 3: the completion of the Five Wishes advance directive A protected email with a summary of the conversations and including a copy of the statement of treatment preferences and Five Wishes were sent to the treating oncologist.	Original target goal: 130 adolescent/family dyads (total of 260 participants) Original time window of recruitment: 2 years, 3 months	Actual number of participants enrolled: 130 adolescent/family dyads Actual time window of recruitment: 2 years, 9 ½ months Extra time or sites required?: 1 year no-cost extension and additional time to complete final analysis and publications. 2 extra sites added.	Enrollment rate: 39% (benchmark was 50%) Retention rate: 84% (104 of 126 dyads) retention at the 18-month assessment
5. Legacy intervention[36]	The Principal Investigator.	Target population: Children 7-17 years old with advanced cancer and their parents (advanced cancer defined as	Goal: reduce suffering of children with cancer and caregivers by improving parent-child communication and coping strategies and adjustment outcomes	Original target goal: 170 child-parent dyads	Actual number of participants enrolled: 150 child-parent dyads	Enrollment rate: 55% Retention rate: 72%

		relapsed or refractory cancer determined by parent self-report) Country, sites and timing: USA - Advertisements were placed on Facebook over a 3-year period (2015 – 2018) Timepoints of surveys: Baseline (T1), post-intervention (T2) and an intervention process survey at study end (T3). The median time between T1 and T2 was 69 days (range 7 – 176) for children and 68 days (range 7 – 176) for parents.	Intervention components and delivery: A website guided children to create a personal digital storyboard by directing them to: a) answer legacy-making questions; b) upload photographs; c) upload video, and d) upload music, and children were asked to complete it within 2 weeks. The website generated a unique electronic link that the coordinator emailed to the child or parent.	Original time window of recruitment: 3 years	Actual time window of recruitment: 3 years Extra time or sites required?: No	
6. Family-Oriented Support intervention (FAMOS)[37]	The Principal Investigator and the project coordinator.	Target population: Families of children in the age range of 0 – 6 years diagnosed with any kind of cancer. Curative intensive treatment had to be completed within 4 months. Children with leukemia could enter when receiving maintenance chemotherapy. Country, sites and timing: Denmark - University Hospital Rigshospitalet, Aarhus	Goal: Targeting psychological symptoms in the whole family after the end of childhood cancer treatment Intervention components and delivery: Delivered face-to-face at home by 1 of 3 psychologists with experience in cognitive behavioral therapy. 3 – 7 face-to-face 1 – 1.5 hour sessions at home within 6 months of inclusion. Session 1 – How cancer has affected us as parents and as a family Session 2 – How we coped with cancer Session 3 – The family's future Session 4 – Children's session: the family before, during and after cancer	Original target goal: 300 families Original time window of recruitment: 3 years	Actual number of participants enrolled: 109 families, 204 parents Actual time window of recruitment: 3 years and 7 months Extra time or sites required?: 7 months recruitment	Enrollment rate: 63% Retention rate: No families dropped out. 79% provided 6-month and 53% provided 12-month assessment.

		University Hospital, Odense University Hospital and Aalborg University Hospital. (August 2014 – March 2018) Timepoints of surveys: Baseline, 6 months after randomization and 12 months after randomization.	Session 5 – Children's session: how to move on Booster – What have we learnt?		extension at all 4 sites	
7. Benefits of Obtaining Ownership Systematically Together in pediatric Advance Care Planning (BOOST pACP)[38,39]	³Two data collectors.	Target population: Children aged 10 – 18 years with any kind of cancer in any stage, together with at least 1 parent Country, sites and timing: Belgium - University Hospitals of Antwerp, Leuven, Brussels and Ghent (March 2021 – March 2023) Timepoints of surveys: At baseline (T0), at 3 months from baseline (T1) and at 7 months from baseline (T2).	Goal: to improve parent-adolescent communication on Advance Care Planning (ACP) themes Intervention components and delivery: The core components include: 4 ACP conversation sessions with the adolescent and/or parent(s) provided by a trained facilitator, structured by interactive conversations cards covering different ACP themes, followed by a transfer of information from the intervention facilitator to the pediatric oncologist.	Original target goal: 86 Original time window of recruitment: 2 years	Actual number of participants enrolled: 49 Actual time window of recruitment: 2 years Extra time or sites required?: no, one site dropped out, because their pediatric oncology ward closed down during the recruitment period	Enrollment rate: not available yet Retention rate: not available yet

³ The executive researcher of this project (AvD) was the interviewer.

Table 4. Main strategies for addressing recruitment and retention challenges

Eligibility
Broaden the inclusion criteria to the extent possible allowed by the intervention's goal and content. Determine eligibility criteria before the start of the study and make reliable estimates of the number of families adhering to these criteria. When determining the eligibility criteria, collaboration with healthcare professionals or national cancer registers is recommended.
Use a thorough screening process to make sure eligible families are not missed in the various steps of the study. This requires a monitoring system, informed by access to medical records and patient lists or by regular meetings with healthcare professionals.
Closely involve the recruitment sites before the start of the study to discuss appropriate ways of introducing the study to potential participants. - <i>Discuss inclusion criteria and implications</i> with healthcare professionals. - Take the time to <i>"learn who your allies are"</i> at the hospital. Who is intrinsically motivated to commit her/himself to the study tasks? - <i>Explore whether study tasks could be a formal part of the healthcare professional's tasks.</i> Not as an additional task, but replacing an existing task. - <i>Arrange a reimbursement for collaborating healthcare professionals</i> (e.g. an hourly rate or per number of approaches). - <i>Arrange research assistant/data collector access to medical records</i> (or to the hospital system, if possible) <i>or arrange a monthly timepoint</i> to obtain a list of eligible people. - <i>Discuss patient eligibility regularly, or discuss beforehand the option of following an opt-out procedure:</i> inform the primary oncologist (via email) that you will contact the eligible family about the study. Only if the oncologist disagrees, will he/she will respond (via email) asking you not to contact the family within a certain time period. - <i>Create buy-in</i> by planning implementation and sustainability activities, such as: presentations at the ward, regular visits with small presents, or disseminating newsletters on the project. - <i>Provide the different recruitment sites with materials that facilitate introducing the study.</i> Develop flyers and ask permission to leave them in places visited often by parents and children, such as waiting rooms, kitchens, and the reception desk.
If possible, apply for a special grant that provides support for the initial development of clinical trials (such as the NIH Planning Grant Program (R34)) in the USA. This money can be used for time spent on arranging contracts with the various sites you are recruiting from.
Enrollment
Provide continuous training for the research staff. When hiring (new) research staff, remember that they need to be: 1) flexible in their availability and way of working; 2) relatable to study participants or having experience in working with them; 3) motivated and passionate about the theme. Be transparent with your (potential) staff regarding the kind of study population and how they might engage with you, and the flexibility you expect. This helps prevent staff turnover.
Involve the recruitment sites and the patients/families before the start of the study to determine appropriate ways of introducing the study to potential participants.
Communicate the experiences of families who have participated to the healthcare professionals and eligible participants (e.g. via newsletters, flyers or during presentations at the wards).
Have research staff follow up closely and be present at the sites regularly.
Offer a relevant intervention for you target group and design the intervention in a flexible way by involving your target group beforehand.
Increase your study's visibility by using attractive materials (for example) and think about efficient ways to distribute them (such as patient organizations, hospital wards, local health insurance fund magazines), so that people might see information about the study beforehand.
Optimize the study's introduction by research staff: - <i>Put measures in place</i> to avoid situations (such as bad news, heavy treatment) that can make the timing of the study introduction inappropriate. Use a personalized and stepped approach (sometimes only plant the seed and follow up quickly). - <i>Be as flexible as possible in introducing the study.</i> Some families do not like to be approached in the clinic because they are eager to get out of there - they prefer to be contacted at home. - <i>Make sure the families have heard about the study</i> from healthcare professionals or via a flyer or email before your first call.

- *Explain what the goal of the intervention is*, why this is important and how this may contribute to a better quality of life and why the effectiveness of the intervention is being studied.
- Have a *basic understanding of the diagnosis* as context in approaching the family.
- Use a *short pitch* not exceeding 2 minutes.
- Use *lay language*.
- *Talk to the parent and child together and engage with the child*. Experience shows that, when you talk to them together, parents will participate if their child wants to participate. Respondents have often experienced that the child has the final say.
- *Make their participation feel important*. Mentioning that their participation can help other families in a similar situation can help.
- *Acknowledge the participants' difficult situation*, be sensitive and consider the family burden.
- *Emphasize the minimal burden in participating*, and explain how participation has been made as easy as possible.
- *Respond to reasons* for them not wanting to enroll.

Retention

Be flexible when offering moments to visit the participants, and be on top of non-response by closely monitoring - and then contact the participants as soon as possible when they have missed their measurement.

Provide consistency in contact between the research staff member and the families

Facilitate filling out surveys as much as you can. Provide electronic as well as paper versions and shorten them if possible. Prioritize having the items on your primary outcome filled out. Have a language consultant look at the items of your questionnaire to optimize understandability, especially when you have developed the items yourself.

In the USA studies, in particular, **monetary incentives** were given to the participants and, in some cases, the incentive was mentioned on the recruitment materials. However, not every respondent was convinced about the effectiveness of this. A small increase in the monetary incentive per timepoint might work best.

Provide for flexibility in the intervention process by offering a range of time to enable alignment with the participants' situation.

If your study is longitudinal and entails surveys being filled out at different timepoints, **building in a run-in period** can help preventing enrolling participants who will most likely drop-out. A run-in period means that, prior to randomizing a family, a family fills out several surveys to see whether they will be engaged in the study or not. Providing this opportunity was seen as less intimidating for families than, for example, committing to an 18-week intensive study for example.

General strategies

Perform a pilot study in the target group in advance, preferably in a situation similar to that of the larger scale study (e.g. involve more recruitment sites already).

This will give insight into expected enrollment rates, as well as contribute to establishing better monitoring systems to assess eligibility, ways of cooperating with healthcare professionals, and give the opportunity to slightly adapt the intervention if you find that some components are not working in practice as expected.

Include a plan in your protocol for changing recruitment strategies, concretizing different scenarios: e.g. if the enrollment rate is less than x%, we will use strategy number 2). Having IRB approval upfront to use these strategies, will save time.

Explore other recruitment 'sources' such as social media, making a video, using email lists from the university or hospital, involving patient organizations. Pilot test these other sources, if possible. When recruiting via Facebook, for example, an algorithm needs to be developed, monitored and adapted continuously, and so involving specialists might be worthwhile. Critically appraise whether your target group is appropriate: if the target group is quite narrow in terms of diagnosis and time since diagnosis, social media might not be suitable.

Table 5. Challenges in recruitment and retention and strategies to overcome them per major theme

Challenges and illustrating quotes (study from Table 3)	Strategies and illustrating quotes (study from Table 3)
Eligibility	
1. Balancing number oriented pragmatism with intervention specificity <i>"Especially in psychosocial studies narrow inclusion criteria can add rigor. We knew that a 12 year old and a 22 year old were vastly different in the ways they were experiencing their cancer and their development. Scientifically, you could argue that it is better to focus on a narrower group of patients because you are meeting that particular age group's needs, but at the same time you can't enroll that many people if your criteria are too narrow."</i> (1. Promoting Resilience in Stress Management (PRISM))	1. Broaden the inclusion criteria to the extent possible allowed by your intervention's goal and content. <i>"We expanded that: you no longer had to have a history of a recent recurrence and we started to say well the whole experience of a recurrent cancer can be pretty stressful because of these constant spikes of uncertainty."</i> (1. Promoting Resilience in Stress Management (PRISM))
2. Gatekeeping from healthcare professionals <i>"In 8% of the cases, the principal investigators who were healthcare professionals themselves had validated their eligibility, but the primary oncologist had told us "no". This was very variable by site, but most often individual clinicians that were problematic."</i> (3. PediQuest Response)	1. Closely involve the recruitment sites before the start of the study to discuss appropriate ways of introducing the study to potential participants <i>"It's necessary to involve people from the recruitment sites, that they are aware what the study entails, and what the tasks for them entail. That they won't be surprised because their actual tasks turned to be much more time-intensive than discussed. Concretely discuss with them who is responsible for what.. and during the recruitment period of 2 years, a lot can happen so it's important to regularly ask them if they are still up to doing those tasks."</i> (7. Benefits of Obtaining Ownership Systematically Together in pediatric Advance Care Planning) (BOOST pACP))
<i>"For some other trials currently, at some of the sites they have systems where the patient primary oncology provider required them to get it approved and we have run into issues where oncologists will arbitrarily say no, and of course it's not completely arbitrarily, but we have had a scenario in some sites where there were 50% of eligible patients and the oncologists were just like 'I think they are too distressed' or 'this kid is going to college soon'. You have to kind of figure out ways to like.. respectfully listen to those things, and try to give every family the opportunity to say no to us rather than someone else opt them out."</i> (1. Promoting Resilience in Stress Management (PRISM))	2. Use a thorough screening process to make sure eligible families are not missed in the various steps of the study. This requires a monitoring system, informed by access to medical records and patient lists or by regular meetings with healthcare professionals. <i>"...following up with the research assistants at each site twice a week, having frequent meetings, using these reports and doing these intensive processes, we were still only able to approach 60% of people that we found to be eligible. So another 40% that became ineligible.. we were waiting to approach for various reasons and changes in their disease criteria or transferred care or died or other things. So we kind of lost big chunks as part of the process. That made it really important that we started with everybody."</i> (3. PediQuest Response)
3. Having to involve multiple sites to increase the pool of eligible participants	1. Create buy-in by planning implementation and sustainability activities at recruitment sites.

<i>"In the beginning it was difficult to find people at the wards that wanted to be our main contact points during the 2 year study period. And throughout the study, we noticed the different sites sometimes slightly adjusted the way of approaching patients to make it more feasible for them. At the beginning, we wanted to keep control but that is challenging. It takes time and effort to find ways that work for everyone"</i> (7. Benefits of Obtaining Ownership Systematically Together in pediatric Advance Care Planning) (BOOST pACP))	<i>"...it depended on study site... at one site we were very reliant on oncologists going through their lists, we had one key person who had a good buy-in for this study. She made sure we had the names of people who fitted our eligibility criteria."</i> (4. Family-Centered pediatric advance care planning for teens with cancer (FACE-TC)) 2. Arrange a reimbursement for collaborating healthcare professionals (f.e. an hourly rate or per number of approaches) <i>"we kept a log of every time the contact nurses approached a patient, not necessarily if they were successful, as recruiting them, but just to approach a patient. I think for every 5, we gave them a 5 dollar Starbucks giftcard. And it was a pretty good incentive, people really liked the coffee."</i> (2. Enhanced Psychosocial Intervention (EPSI))
<i>"We have spent the first year of the trial just to get contracts and agreements that we can share protected health information with other sites and some of them took up over a year."</i> (4. Family-Centered pediatric advance care planning for teens with cancer (FACE-TC))	3. If possible, apply for a special grant that provides support for the initial development of clinical trials <i>"They have a mechanism now, called an R34, you can now have 2-3 years to just set the trial up, so we have spent the first year of the trial just to get contracts and agreements that we can share protected health information with other sites and some of them took up over a year and some of them and I ended up travelling to some sites to review and that burned up money too."</i> (4. Family-Centered pediatric advance care planning for teens with cancer (FACE-TC))
Enrollment	
1. Perceived difficulty introducing the study to families in this burdensome situation and staff turnover during a long recruitment period <i>"During the windows of staff turnover our enrollment would go down because people were either less available or less skilled at having the conversations and building rapport with the families."</i> (1. Promoting Resilience in Stress Management (PRISM))	1. Provide continuous training for the research staff. <i>"Mock exercises are really helpful. We did activities like having someone to write down what their pitch would be and then another research assistant look at what she has and finding templates and cut out content. Simplify, simplify, simplify!"</i> (3. PediQuest Response) <i>"We hold weekly research meetings, in which we do sometimes role plays. Those meetings were not just to find out in terms of numbers but also what is working, how could we improve, what other strategies could we use. These are critical in building the skills of the research staff, but also providing peer support and positive energy to keep that persistence."</i> (2. Enhanced Psychosocial Intervention (EPSI))

	2. Be transparent with your (potential) staff regarding the kind of population, how the population might engage with you and what kind of flexibility you expect. This contributes to preventing staff turnover. <i>“transparency with your staff is key, from the beginning be like this is the population, this is how they like to engage with you, here is what we expect in flexibility. The flexibility piece was major in helping us with recruitment and retention. As we mentioned earlier, there are weekends and evenings, and home visits where people felt safe. Because you might have staff members that say I cannot meet those expectations, but it might help if you tell them early on, their brain gets programmed in a way, that this is how I’m going to engage in it and interact with the participants from the study.”</i> (4. Family-Centered pediatric advance care planning for teens with cancer (FACE-TC))
2. Making realistic estimations of willingness to participate <i>“We didn’t really appreciate how stressful the actual study might be to people, even if we know what might be helpful... It’s really a factor of us overestimating people’s willingness to participate”</i> (1. Promoting Resilience in Stress Management (PRISM)) <i>“Our study was on symptoms and some people don’t want to think about the symptoms. Because if you felt nauseous, would you sit and talk about how you are nauseous? Sometimes people felt like acknowledging the symptoms and thinking about them made them feel worse.”</i> (3. PediQuest Response)	1. Involve recruitment sites and patients/families to determine appropriate ways of introducing the study to potential participants. <i>“Involving people in how should we set this up, how do you want this, and developing a sort of community between those who recruit and that they have a shared task to solve together.”</i> (6. Family-Oriented Support Intervention (FAMOS)) <i>“Ideally, we should have engagement from young people and their parents doing the design of the study. And thinking about relevant strategies for recruitment. They can tell us more on what they like or what they don’t like and what will be useful.”</i> (2. Enhanced Psychosocial Intervention (EPSI)) 2. Communicate the experiences of families who participated to the healthcare professionals and eligible participants (f.e. in newsletters, flyers or during presentations at the wards). <i>“And also, for them to hear about how it was for the families. and why are we doing this of course. It’s very important to communicate that. And I think that’s for our future studies also very important that they sort of know it’s not only about recruitment, it’s also about the family is getting better. And what do the families gain from this. I think that could be done even more, for them to be aware of that all the time. Perhaps hearing some of the families and hearing about what they have experienced in the project.”</i> (6. Family-Oriented Support Intervention (FAMOS))

3. Competing studies <i>“Oncology patients are in trials for almost everything that they do. They consented before about biobanking of their tissue and sperm, for their enrollment in other clinical trials. I think some of the exhaustion comes from that they do not want to hear about another clinical trial.” (4. Family-Centered pediatric advance care planning for teens with cancer (FACE-TC))</i>	-
4. The randomization aspect <i>“I do see occasions that people say no, because they say “I’ll do it if you can promise me I don’t have to do the program” or “if you can promise me that I do the program”.” (1. Promoting Resilience in Stress Management (PRISM))</i>	1. Use lay language <i>“Randomization is a very difficult concept for people to grasp. So developing easy language, easily understood for people what does randomization actually mean.” (4. Family-Centered pediatric advance care planning for teens with cancer (FACE-TC))</i>
5. The dyadic nature of enrollment <i>“Being able to reach families really is the most difficult challenge in this trial. Because it’s a study involving a child, you need the signature for consent from both parents. It takes a lot of calls and reminders to get this last signature. They often still have to discuss participation within the family, and they sometimes forget, so it takes a lot of time.” (7. Benefits of Obtaining Ownership Systematically Together in pediatric Advance Care Planning) (BOOST pACP))</i> <i>“but then also to recruit kids, you have to recruit their parents, and sometimes that’s very challenging, because sometimes you have a kid, who you think might be super excited but you have a parent that doesn’t want them to do it for some reason, so it’s hard to get everybody on board. It’s also hard: the nature of children with advanced cancer. The illness is such a rollercoaster, it’s like how the stars are aligned, if they are feeling good and schedules align or whatever to have them complete the intervention session. (5. Legacy Intervention)</i> <i>“Ideally, we wanted the nurses to talk to parents in the hospital, but some of the parents would be at home or just coming for a quick check-up. It was difficult to catch them physically.” (6. Family-Oriented Support Intervention (FAMOS))</i>	1. Close follow-up by research staff and being present at the sites regularly. <i>“Compared to a former FACE study, the recruitment was more difficult in this study. The staff this time had a lot of other things to do, although of course they were also very dedicated. But the first staff was only focused on the FACE study. They had more hands-on follow-up, or maybe they were on the ground a little bit more, in the clinic areas.” (4. Family-Centered pediatric advance care planning for teens with cancer (FACE-TC))</i> 2. Talk to the parent and child together and engage with the child. <i>“if we were able to convince the child, then it was a go. So the parent would only do it if the child wanted to do it, never did you see the opposite. So that was interesting.... the other thing is that sometimes with parents, when they are overwhelmed, assume sometimes that their child does not want to participate. So I found it was really good to be talking to them together about the study. And sometimes they would just project their own.. to the child and the child was sometimes like, yeah I have got nothing else to do, I’m here in bed anyway.” (2. Enhanced Psychosocial Intervention (EPSI))</i> 3. Offer a relevant intervention for your target group and design the intervention in a flexible way by involving your target group beforehand <i>“And I think that’s the most important part, is to offer something that is relevant to people. And I think the only way to do that is to involve the families and for you study maybe the adolescents? In both how do we sort of design and set-up that’s</i>

	most relevant to your family and also, maybe get them on board on how to do the recruitment. ...I think the fact that there was a combination of very concrete tools and then videos. And it was homebased, that was the main thing. And we were very flexible in terms of, we tried to do it on their terms. I think that were the most important things that made them feel that was comfortable for them as well.” (6. Family-Oriented Support Intervention (FAMOS))
6. Finding an appropriate time to introduce the study to the family <i>“It’s SO dependent on the family and it’s really hard to tell from a chart note or even like a conversation with the provider, because I think that different providers have different interpretations of when a family is ready or if they think they are receptive.” (1. Promoting Resilience in Stress Management (PRISM))</i>	1. Put measures in place to avoid situations that can make the timing of the study introduction inappropriate. Use a personalized and stepped approach. <i>“We do have an eligibility criteria as part of our approach checklist that asks if a family had a sort of serious conversation in the last two weeks, or if the kid is going through scans that day and might get bad news then we wouldn’t approach them that day, or if we could see through the record that last week they found out about a progression, they wouldn’t be eligible until 2 weeks after that.. and then sometimes information would come out of meeting a family, so we might come back to them one month later.. we might go and talk to them and say you know, can we tell you about this study.. and they will tell us ‘our grandpa had just died’ and we are trying to figure out the funeral next week.. and we are so overwhelmed right now.. so you could say would it be okay if I would check in with you again in a month.. in some sites we leaned more on that than in others again I would say, but that was something that we would certainly try to kind of personalize or approach each family and adopt as much as we could to make it as convenient as possible.” (3. PediQuest Response)</i> <i>“In a survey we asked teenagers when do you want to be approached and most of them said from the time of diagnosis, so it was really based on their feedback that it was okay to talk about this stuff from the time of diagnosis. And we quickly checked with the provider, is there a particular reason we shouldn’t approach today....If they were having a spinal tap, that was not the day, so sometimes we would just plant the seed, but then we came back later.” (4. Family-Centered pediatric advance care planning for teens with cancer (FACE-TC))</i>
7. Unanticipated circumstances (e.g. COVID-19 pandemic). <i>“also a key part here is the face to face contact. With COVID and so on made it much more challenging.” (4. Family-Centered pediatric advance care planning for teens with cancer (FACE-TC))</i> <i>“our visibility and presence in the hospitals would have been better if it wasn’t for the COVID pandemic. We would have been more present at the hospital wards and personal contact always helps in making things happen. The</i>	1. Increase your study’s visibility by using attractive materials (for example) and think about efficient ways to distribute them (such as patient organizations, hospital wards, local health insurance fund magazines magazines), so that people might see information about the study beforehand. <i>“Hanging flyers in the hospital ward and writing a testimonial from a family that participated in a local magazine of a patient organization and promoting this via the social media (such as LinkedIn or Facebook) of the participating hospitals helps</i>

COVID pandemic gave us a false start.” (7. Benefits of Obtaining Ownership Systematically Together in pediatric Advance Care Planning) (BOOST pACP))	increasing the visibility of your study. This won’t necessarily lead to a higher number of participants, but families may recognize the study when they are formally introduced for the first time and this might contribute to them saying “yes” to participation a bit quicker.” (7. Benefits of Obtaining Ownership Systematically Together in pediatric Advance Care Planning) (BOOST pACP))
Retention 1. Non-response and drop-out “We may have had a slightly inflated rate of drop out from our intervention arm, so maybe for some people that was almost like they hoped for the easiest study experience that took the least time and energy for them.” (3. PediQuest Response) “We followed our intervention group monthly. This was not the case for the control group, we got them a year later. We didn’t retain as many in the control group because the people we were following on a monthly basis were engaged. In the control group, we may have lost as many as 25%.” (2. Enhanced Psychosocial Intervention (EPSI)) “And I think that was part of the reason why we had attrition, especially in the control group. It was a lot of questionnaires for the parents to fill out, without sort of receiving any intervention.” (6. Family-Oriented Support Intervention (FAMOS))	1. Be flexible when offering moments to visit the participants, and be on top of non-response by close monitoring. “The people that followed-up the families were very persistent. If the family said today is not a good day, they said: “can I call you tomorrow or can I check up on you in 2 weeks, and put that in my calendar?”. In reports it is known that at some number of phone calls there is a diminishing return, they are not going to call you back after 4 or 5 phone calls, but up until that point, people were busy . So be very flexible and persistent, but not just one voicemail and then they are lost to follow-up.” (4. Family-Centered pediatric advance care planning for teens with cancer (FACE-TC)) “On every Monday and Thursday, we receive from the system whoever did not answer a survey. As the project manager, I would contact the research assistant at that site and say please follow up with so and so. The next survey is on a Tuesday so let’s call them when the next one is active, and that it might be a good time to pop by the clinic and give them the gift card. So it was a lot of monitoring to be on top of it when somebody missed a survey to reel them back in.”(3. PediQuest Response) 2. Provide consistency in contact between the research staff member and families “I think the main piece of retention that was important was engaging the research assistants to form relationships with the families.” (3. PediQuest Response) “I think that was a good strategy. That it was the same person that day that they had contact with along the way.” (6. Family-Oriented Support Intervention (FAMOS)) 3. Facilitate filling out surveys as much as you can. “But I think of course, that shortening the questionnaires as much as possible is the best strategy. And at that time, we only had paper-based questionnaires and I think

	<i>it helps today with the electronic ones as well.” (6. Family-Oriented Support Intervention (FAMOS))</i> 4. If your study is longitudinal and entails surveys being filled out at different timepoints, building in a run-in period can help preventing enrolling participants who will most likely drop-out. <i>“We have the run-in period built in that we have described as like a three survey prior to randomizing a family to kind of prove that they are going to be engaged in the study or not, and so we really invited people to test it out, which was a little less intimidating than committing to an 18-week, sometimes intensive study experience... it kinds of helps the quality of the data we are getting... one thing we have learned is that people who did not respond the first 2 surveys, were not going to respond after.. and instead, we decided to do this run-in period, and get rid of the non-responders, because they would not give you any valuable data.” (3. PediQuest Response)</i> 5. In the USA studies, in particular, monetary incentives were given to the participants and, in some cases, the incentive was mentioned on the recruitment materials. However, not every respondent was convinced about the effectiveness of this. A small increase in the monetary incentive per timepoint might work best. <i>“I think they do help decrease drop-out at certain timepoints, so that’s how we used it. My strategy now is different than what we did in this study. If I would do it over, I would have had an increasing incentive, at each data assessment point that it would increase as the study goes, I would have had a small incentive for T1, just to get them going, I would not have had an incentive with completing the intervention, because of that early attrition we would had in the beginning in the intervention group, we offered them an incentive when they completed the intervention.” (5. Legacy Intervention)</i>
2. Keeping per-protocol timelines versus required flexibility <i>“We had a window of enrollment for the study that was close to diagnosis and that made it a little tough. Because sometimes we lost kids because they went way off the window for enrollment. Sometimes, we bended the rules a little bit to keep it.” (2. Enhanced Psychosocial Intervention (EPSI))</i>	1. Provide for flexibility in the intervention process by offering a range of time to enable alignment with the participants’ situation. <i>“I know that all the psychosocial research needs to be very structured and regimented, and I think that there is also something to be said about the nature, any nature of psychosocial research, and how we need to be flexible. Flexible within the inflexibility of research too. So I think that with a lot of our interventions, when I was still working on a study, you had to be as flexible as possible, you might have to</i>

<i>"I mean we reschedule sessions constantly, because the kid has a fever and is not feeling good, the mom's exhausted.. I mean there is so much to.. so you try to be flexible, but when you're too flexible.. the range between T1 and intervention sessions sometimes is massively different from what the protocol says, because we've tried to be flexible, but for a study it kind of messes stuff up."</i> (5. Legacy Intervention)	<i>push your session out 2 weeks, because a patient is very sick in the ICU, and doing that two weeks later, is just something you have to do, to best support the patient and family, because there is patient-centered care, and not just the research too."</i> (1. Promoting Resilience in Stress Management (PRISM)) <i>"one of our research coordinators met with a family on a Saturday in the local library. Because that was convenient for them. So we were very flexible: weekends, evenings, all of those things."</i> (4. Family-Centered pediatric advance care planning for teens with cancer (FACE-TC))
General challenges	General strategies
1. The numbers in the larger scale trial could turn out vastly different from the pilot study. <i>"We enrolled 80% if I'm remembering correctly of people who we approached in our pilot study. So we felt confident, people like this are going to participate. I believe that we anticipated a 70% enrollment for this randomized trial... but in our current bigger studies that are multi-site trials, we have not been close to 70%, we're at a 60% of enrollment at our institution, but other sites are closer to 50%, and there are a couple of things there I think about a lot.. number 1 in adolescent and young adult oncology the average enrollment rates are like 30 or 40%. They are generally far less than 50%. So I think our 70% was an overly optimistic and very lucky number to pick for us on that project. I think 50 or 60% is probably more reasonable, if not ambitious. And 30 to 40% is probably more realistic."</i> (1. Promoting Resilience in Stress Management (PRISM))	1. Perform a pilot study in the target group in advance, preferably in a situation similar to that of the larger scale study (f.e. involve more recruitment sites already). <i>"Between PediQuest original and PediQuest Response, we did a pilot study regarding the next step of the intervention. And in that pilot study we also learned a lot about how to enroll and develop these kind of tracking systems."</i> (3. PediQuest Response) <i>"I think just testing the different aspects of the study beforehand is the best way to get the most knowledge."</i> (6. Family-Oriented Support Intervention (FAMOS))
2. Having to pause enrollment because another recruitment strategy was not included in the initial protocol and there was no IRB approval for that strategy. <i>"one of the sort of set-backs was that this happened during COVID, so uniquely in our study we had a big transition in the middle, pausing enrollment and changing all of the IRB procedures to allow for virtual opportunities."</i> (3. PediQuest Response)	1. Include a plan in your protocol for changing recruitment strategies, concretizing different scenarios. <i>"We're trying to do that in studies now, as much as I can and study start up, I try to anticipate challenges, and I'll try and go ahead, and have like numerous recruitment strategies written in the protocol is options to have IRB approval on for those upfront, so f.e. in hindsight in this study, I wish I would have started the protocol with three recruitment strategies: social media, recruiting from the clinic, and Research Match. And I'm gonna start with number 1 but if that doesn't go well I'm going to add number 2, and number 3 and have all of them available. So write it up in front just to have the options."</i> (5. Legacy Intervention)

3. Finding a sufficient number of recruitment sites that are able to or want to participate. <i>“To get a sample for an RCT, looking it at how many sites you would need. (laughs) That was going to be a huge, massive study. Would be 8 -10 sites and this would be very expensive. An additional challenge we were faced with, was other competing studies. Vanderbilt is a research intensive university, you know, everybody is trying to recruit from the hospitals and clinics.” (5. Legacy Intervention)</i> <i>“We shopped around a little bit for the five sites in the current study. They are not the initial ones we planned on, and one of the reasons for that are that some of the sites initiated some sort of automatic to palliative care teams for patients that met their criteria and made the patients ineligible.” (3. PediQuest Response)</i>	1. Explore other recruitment ‘sources’ such as social media, making a video, using email lists from the university or hospital, involving patient organizations. <i>“Vanderbilt has an email distribution list, so you can create kind of like a brief study description and basically sends out an email blast, but this email distribution goes to like thousands of people, so it’s Vanderbilt staff, faculty unit, and if people were eligible they could contact. And we used ResearchMatch, which is a Vanderbilt based.. it’s like a database where families can sign up to be research volunteers, so you can kind of search for certain criteria and they’ll see your description and you can kind of contact them in that way.” (5. Legacy Intervention)</i>
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Discussion

This collective case study gives an overview of the most commonly experienced recruitment and retention challenges, plus strategies to overcome them, while conducting RCTs of psychosocial intervention studies for children with cancer and their parents, sub-divided into three themes: eligibility, enrollment and retention. Although many studies were found on this target group, they mostly used different designs, such as pretest-posttest designs without a control group, cluster RCTs, or used an attention control group. Other studies we found stated that they did not randomize due to ethical and practical considerations. The limited number of studies meeting our inclusion criteria, may indicate that conducting individually randomized controlled trials without an active comparator in this field and target group is rare, possibly because it is very challenging.

All of the respondents followed a stepped process for recruitment, using a personalized approach, with several visits per family. Bradford et al. (2021) [6] estimated it takes an average of 98 min for an experienced research member to screen, approach and recruit one participant in a pediatric oncology setting, emphasizing the importance of training all research staff (involved in referral, data collection, and intervention) [19]. This training could entail ways to perform systematic screening of patient lists, thoughtful messaging to make the study relevant, and how to deal with flexible protocols to accommodate patients' needs [20]. Furthermore, communication with families in the pediatric oncology setting - and striking the balance between respectfully recognizing their burden without being too careful introducing the study - should be part of the training. As participants, including children and adolescents, reported benefits including the opportunity to talk, be altruistic, reflect, have a safe space, gain understanding or perspective, and express emotions [21], potential advantages of these kinds of studies may be presented to eligible families also. More transparency on the content of these trainings from trials in this setting would be of added value for researchers to use as a reference.

One of the overarching recommendations from our respondents was to perform a pilot study prior to the larger scale trial. Testing feasibility and acceptability by conducting a pilot study is widely accepted as a great value, if not a necessity, for RCTs [22] as they can "*inform decisions about whether further testing of an intervention is warranted*". Being aware of which features of the intervention and sample in the pilot study are not scalable or generalizable to the next stage of testing in a larger effectiveness trial - might optimize trial implementation [23]. Context and implementation are critical to the extent of an intervention's effect, especially in complex interventions [24]. Therefore, different approaches regarding effectiveness research have been suggested to improve our understanding of generalizability, stressing the need for process evaluations to understand an intervention's mechanisms of action [25]. Once identified, then larger trials, with integral process evaluations can be conducted [25]. Especially missing data (due to drop out, attrition or item or questionnaire non-response) can introduce problems of selection bias, particularly if they are influenced by what arm study participants are allocated to, affecting generalizability [26]. As recruitment and retention rates of a large-scale trial can differ from the pilot study, an additional strategy in the development phase of an intervention is pre-emptively generating strategies to address potential recruitment and retention difficulties via focus groups and interviews with the target group [27].

In general, there is little evidence that helps researchers to make well-informed decisions about how to do their trials [28]. Performing a Study Within A Trial (SWAT) - which is a self-contained research study that has been embedded within a host trial with the aim of evaluating or exploring alternative ways of delivering or organizing a particular trial process - might contribute to more evidence-based decisions within trials. However, especially in trials testing psychosocial interventions for children with cancer and their parents this might be challenging because undertaking SWATs includes challenges such as increased complexity and management burden, which are more profound in pediatric populations due to a perceived increased patient vulnerability or risk [29].

A strength of this study is the high participation rate from the researchers (75%) we approached, showing that recruitment and retention are experienced as challenging and recognized as important. Moreover, our search strategy to select cases limited the risk of missing relevant trials. Including the PI as well as other research staff in the interviews allowed us to gain an in-depth understanding of the recruitment and retention challenges and strategies.

A limitation of this study is that the overall number of included studies was low, so drawing conclusions must be done with caution. Additionally, we included studies that were registered from 2011 onwards, leading to an increased risk of recall bias for some studies. However, we noticed that, in most interviews, the respondents complemented each other when not remembering something, and some respondents could compare experiences from the selected case to follow-up trial studies of the intervention they were undertaking now, enriching the information. Another limitation is that we based our selection of cases on a search string in English, possibly missing relevant studies reported on in other languages. A final limitation is that the analysis was done by one researcher, although main findings were discussed with the core research team to enhance reliability of interpretations.

Conclusion

We identified a paucity of evidence on experienced recruitment and retention challenges and best practices on optimizing them. Respondents indicated that even after years of experience of conducting studies in this field, it is difficult to know in advance what strategies will have desired effects. Effectiveness of 'new' strategies is challenging to map because they are often used in combination with other strategies and in pediatric studies, the number of eligible participants is generally low and effectiveness cannot be directly attributed to the use of only that particular strategy or to other factors such as more eligible participants in that particular period for example. Additionally, what may have worked in a former variant of the study might not necessarily work in a different variant of the study due to contextual factors. However, some studies had high enrollment and retention rates and managed to overcome challenges successfully, which indicates that suitable recruitment and retention is possible. The close follow-up of families and maintaining regular contact with the key persons at the recruitment sites while continuing a flexible attitude to the extent possible was emphasized most often. The strategies outlined in this study can help researchers to optimize their protocol and implementation of the trial and contribute to better psychosocial care for children with cancer and their parents.

Statements and Declarations

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Competing Interests: The authors have no conflicts of interest to disclose.

Ethics approval:

The project this study is part of was approved by the Medical Ethics Committee of the University Hospital of Brussels in Flanders, Belgium (B1432020000177). The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments and in compliance with our institutional guidelines.

Consent to participate:

Informed consent was obtained from all individual participants included in the study.

Consent to publish:

All respondents provided informed consent for publication of the study characteristics and use of quotes.

Author Contributions:

All authors contributed to the study conception and design. Anne van Driessche performed the interviews and analysis, drafted the initial manuscript, and adapted the manuscript. Prof Kim Beernaert, Prof Joachim Cohen, Prof Luc Deliens, Dr Marijke C. Kars and Prof Aline De Vleminck critically reviewed and revised the manuscript. Dr Maureen E. Lyon, Dr Maru Barrera, Dr Veronica Dussel, Dr Pernille Bidstrup, Dr Abby R. Rosenberg and Dr Terrah F. Akard participated in the study as a respondent sharing expertise on the topic of interest, and critically reviewed and revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Additional file 1. Basic topic list for the interviews with the principal investigators and research staff

Introduction
- Introduce myself, and shortly explain the motivation for this interview and study & former and next steps. -Everybody agree with information that is said is being processed in the article
Introduction question
- How long have you been involved in the study and what was your role?
1. ACTIONS BEFORE STUDY START
1. Recruitment sites a. How did you decide upon the required number of recruitment sites? And how did you decide which recruitment sites you wanted to include. b. What changes did you make in the number or kinds of recruitment sites? c. What implementation activities did you plan to do in these sites to make them cooperate? How did you successfully recruit in these sites? Were there any differences you noticed in recruiting in the different sites? (different strategies f.e.)
2. Different roles in the study & recruitment strategy a. How did you determine the division of tasks in the study (such as screening of eligibility, proposing the study etc)? Could you describe in more detail who would do what? b. Did you make any changes in the division of tasks, the order of these tasks or the recruitment strategy? What kind of changes? Do you have insights in reasons why you made these changes? c. What are the most important factors to consider when determining the division of tasks or recruitment strategy?
2. SCREENING FOR ELIGIBILITY
1. Inclusion/exclusion criteria a. In what way did increasing the pool of eligible participants influence the decisions on your inclusion/exclusion criteria? b. What changes did you make in these criteria, throughout the study duration? c. How did you screen for eligibility? (if not discussed in division of tasks)
2. Resources/technologies that help map the recruitment and enrollment a. How did you track eligibility? What strategies, resources or technologies did you use to map eligibility and communication between the different stakeholders who play an important role?
3. ENROLLMENT
a. How did you estimate the enrollment rate before the start of the study? What were your strategies to maximize the enrollment rate? b. What changes did you implement to optimize the enrollment rate compared to what was mentioned in the protocol? c. What were most common reasons for families to refuse participation to the study? What did you change because of these reasons?
4. ATTRITION
a. What was your estimation in terms of attrition rates? How did you estimate this? b. What strategies to prevent attrition did you determine in the protocol before start of the study? c. What changes in your strategies or added additional strategies did you implement to prevent attrition as much as possible during the data collection period?
5. ENCOUNTERED CHALLENGES
a. What would you say are the most important challenges you encountered during recruitment? b. In what way do you think having to recruit the dyad: patient as well as one caregiver/parent complicates recruitment? c. How did you experience recruiting children/making the study attractive for children/minors specifically? In what way was it more difficult to recruit children and why? How did you tackle this? d. In what way do you think the fact that this is a study on a complex psychosocial intervention, complicates recruitment? e. In what way do you think individual randomization / randomization at patient/dyad level (either receiving the intervention or not and not knowing beforehand) & not offering an active control complicated recruitment? f. In what way did external circumstances make recruitment difficult? (f.e. pandemic, reorganization in the hospital, other studies). And how did you cope/adapt?
6. ADDITIONAL STRATEGIES TO ENHANCE RECRUITMENT

a. We have discussed strategies regarding eligibility, enrollment and attrition. What additional strategies did you determine during the study period that we have not discussed yet? Did you change a strategy that you determined in the protocol, tailored to the challenges you encountered?

7. ADVICE TO OTHER RESEARCHERS

- a. What would you have done differently in hindsight in order to optimize recruitment in your study?
 - b. What were your most important resources to prepare your recruitment strategy?
 - c. What would have supported you most when preparing a recruitment strategy (f.e. particular resources)?
 - d. If we were to develop a useful resource for optimizing recruitment and retention for these kinds of psychosocial intervention studies in this particular target group (children with cancer and parents), what would be your main suggestion/take home message?
-

Finalizing the interview

1. Do you have anything to add? Or are there any questions?

Thank you so much for your time. Don't hesitate to contact us if you have any further additions or questions.

GENERAL DISCUSSION AND RECOMMENDATIONS

General discussion and conclusion

Introduction

Pediatric advance care planning (pACP) aims to integrate the expertise of the child and family with that of the medical team, in order to establish shared care goals and effectively communicate these to all caregivers involved in the child's care[1]. The first objective of this dissertation was to develop a pACP intervention for adolescents with cancer and to outline the protocol for a randomized controlled trial (RCT) designed to evaluate the pACP intervention. The second objective was to assess the effectiveness of the pACP intervention for adolescents with cancer aged 10 to 18 years and their parents. The third objective was to offer guidance for future interventions by exploring how to tailor approaches to optimize communication and care for children with serious illnesses, as well as to enhance the feasibility and quality of RCTs in pediatric populations. This aim was addressed through a study that provided an overview of characteristics and factors affecting child development in the context of serious illness, and an international study examining recruitment challenges and strategies in RCTs of psychosocial interventions for children with cancer and their parents.

In this discussion section, the main findings of this thesis will be summarized. This will be followed by considerations regarding the methods used across the studies, and a discussion of the primary results in the context of current research on pACP, along with an interpretation of these findings. The discussion will conclude with several recommendations and implications for practice, policy, and future research.

Summary of main findings

In this section, the results of the previous chapters are summarized in two separate themes, following the two objectives of this dissertation.

The first objective was to develop a pACP intervention for adolescents with cancer and to outline the protocol for a randomized controlled trial (RCT) designed to evaluate the pACP intervention.

Content of the BOOST pACP intervention

To develop a pACP intervention, a comprehensive iterative phased approach was followed, informed by the supplementary guidance for the development of complex interventions by Bleijenberg et al. (2018) [2], as described in **Chapter 1**. Semi-structured interviews were combined with a review of the literature and qualitative feedback sessions with relevant stakeholders. We studied barriers and facilitators for pACP in pediatric oncology and identified existing tools and interventions. Interviews with healthcare professionals revealed that the challenges were largely system-, attitude- or parent-related. It was emphasized that ACP is complex, and relies on more than just healthcare professionals' behavior; it also involves broader patterns related to the family's dynamics.

Through a scoping review including grey literature, the intervention 'IMPACT' was identified as a suitable foundation for our intervention, as it promoted open conversation on a comprehensive set of holistic advance care planning (ACP) themes among clinicians, parents, and the child. This intervention was developed by Dr. J. C. Fahner and Dr. M. C. Kars from

the Netherlands. At that time, in October 2019, there was no published evidence available yet, but the acceptability of the content had been recently evaluated through a qualitative pilot study. Both developers provided feedback on how to adapt IMPACT materials to our RCT context and the specific target group - adolescents with cancer aged 10 – 18 years. This was necessary because the target group of IMPACT was children with life-limiting conditions and their families, and clinicians were trained instead of external facilitators. IMPACT can be used early in the illness trajectory and focuses on defining shared goals of care and treatment, rather than completing an advance directive (AD), aligning with the holistic approach that BOOST pACP aimed to achieve.

We developed a logic model with input from key stakeholders (i.e. international experts and researchers n=11, psychologists n=8, core research team n=6, Pediatric Palliative Care Research Network (PPCRN)) to define desired outcomes and specify the pathways through which the pACP intervention would achieve these outcomes. The resulting BOOST pACP intervention views ACP as a broad concept to be initiated early in the illness trajectory, applicable to adolescents with cancer at any stage and with any expected outcome.

The final BOOST pACP intervention consists of ten components: 1) facilitator selection and training, including a manual; 2) preparation booklets for the adolescent and parents; 3) short videos with testimonials; 4 – 7) facilitated ACP conversation sessions; 8) a summary sheet; 9) conversation cards that can be used as a game of quartet; 10) transfer of information from facilitator to the pediatric oncologist. The BOOST pACP intervention was deemed suitable and feasible.

The BOOST pACP intervention is innovative in several ways:

- 1) It targets adolescents aged 10 – 18, including a younger age group of 10 – 13. The only other pACP intervention researched in an RCT targets adolescents and young adults aged 14 – 21.
- 2) It is the first pACP intervention encompassing broad topics tested in an RCT.
- 3) It primarily aims to improve parent-adolescent communication and focuses on empowering adolescents to discuss their current and future care and treatment.

Protocol of the BOOST pACP trial

To evaluate the effectiveness of the developed BOOST pACP intervention, we designed a randomized controlled trial. The design, methods, and procedures for the trial are outlined in **Chapter 2**. The goal was to evaluate the effectiveness and gain insights into the mechanisms of impact, contextual and implementation aspects of the BOOST pACP intervention. We opted for a multi-center, parallel-group, RCT with an embedded mixed-methods process evaluation, comparing the BOOST pACP intervention to standard care. Adolescent patients and their parent(s) were randomized with a 1:1 allocation ratio to the intervention arm or the control arm after baseline assessment. Recruitment was anticipated in four participating university hospitals in Belgium. Families in the intervention group had the option of having the ACP conversations at home, in the hospital, or online.

Inclusion criteria of the adolescents were: aged between 10 – 18 years, diagnosed with any type of cancer at any stage, currently receiving (active) oncology treatment, and with a life expectancy of more than 3 months. The control group received care as usual. The primary endpoint is parent-adolescent communication from the perspective of the adolescent at 3 months (T1), measured using the Parent-Adolescent Communication Scale (PACS). Secondary endpoints include parent-adolescent communication at 7 months (T2), adolescents' and parents' attitudes towards and self-efficacy in discussing ACP, adolescents'

intention and actual communication on ACP topics with parent(s) and parents' intention and actual communication on ACP topics with the adolescent, and parents' and adolescents' anxiety (PROMIS Anxiety). Data collectors assisted adolescents with completing the questionnaire at all timepoints, unless the adolescents insisted on completing them independently and were 15 years or older.

The second objective was to assess the effectiveness of the pACP intervention for adolescents with cancer aged 10 to 18 years and their parents.

Impact of BOOST pACP intervention on parent-adolescent communication

The RCT indicated neutral findings for the BOOST pACP intervention compared with standard care on the primary endpoint, parent-adolescent communication from the adolescents' perspective three months after baseline, measured with the Parent-Adolescent Communication Scale (PACS) (**Chapter 3**). Forty-nine adolescents with cancer (aged 10 – 18 years) and their parent(s) participated in the BOOST pACP trial (BOOST pACP group n=24, control group n=25). No significant differences between the groups were observed for the PACS (ranging from 20 – 100 and consisting of two subscales: the Openness Scale and Problems scale) at T1: baseline-adjusted mean difference [MD]: 1.4; 95% CI -4.1 to 6.9; p=0.608 and T2 (MD: 5.2; 95% CI -0.6 to 11.0; p=0.077). The effect size at three months (T1) was 0.13, and 0.49 at seven months (T2). For father-child communication specifically, the effect size was 0.67 at seven months (T2), and 0.85 on the Openness scale. The BOOST conversations do not induce distress in either parents or adolescents.

The findings do not provide conclusive evidence of the intervention's effectiveness. However, the effect sizes at seven months (T2) suggest potential for a longer-term impact. The small sample size due to recruitment challenges warrants caution in interpretation.

Influence of the BOOST pACP intervention on behavioral determinants of parent-adolescent communication

In our RCT we also explored the impact of the BOOST pACP intervention on behavioral determinants, such as attitudes, self-efficacy and intention regarding discussing ACP topics, as well as actual behavior of discussing these topics (**Chapter 4**). Statistically significant differences favoring the BOOST group over standard care were found in several areas:

- 1) a decrease in fathers' negative attitude towards discussing care and treatment with their child at three months (T1).
- 2) an increase in the number of end-of-life care oriented ACP topics mothers intended to discuss with their child at three months (T1).

However, we also observed statistically significant differences favoring the usual care group over the BOOST group, specifically a decrease in the number of value- and emotion- oriented ACP topics, as well as end-of-life care- oriented ACP topics, that adolescents in the BOOST group intended to discuss with their pediatric oncologists at both three months (T1) and seven months (T2). No other significant effects were observed.

The third objective was to offer guidance for future interventions by exploring how to tailor approaches to optimize care and communication for children with serious illnesses, as well as to enhance the feasibility and quality of RCTs in pediatric populations.

Key developmental factors in children facing serious illness: implications for pediatric advance care planning

Our scoping review identified 24 out of 11246 articles that discussed key factors shaping child development in the context of serious illness (**Chapter 5**). Piaget's theory of cognitive development emerged as the most prevalent theory on child development. These factors were categorized into several themes: psychological/emotional aspects, general cognitive aspects, social aspects, coping strategy, conceptualization of illness, conceptualization of death, and communication about their illness.

We found several accelerators of child development in the context of serious illness, such as cortical maturation, prior medical experience, and social experience with adults. Conversely, we identified decelerators like stress, hospital admission, and avoidance of illness-related communication within the family. However, there is a lack of detailed insights into how these factors specifically influence the development of children with serious illnesses. While some factors may be immutable, others could potentially be modified, such as the communication patterns within a family.

This scoping review highlights the complex interaction of psychological, emotional, social, and cognitive factors that influence children's ability to participate meaningfully in their healthcare decisions. It provides insights into how these developmental aspects – along with the child's conceptualization of illness and death – relate to their communication about their illness. These findings have important implications for pACP, underscoring the importance of a tailored approach that considers the child's developmental stage. The identified factors can be key considerations in shaping the content and methods of pACP in a more developmentally appropriate way.

Recruitment challenges and strategies in RCTs of psychosocial interventions for children with cancer and their parents

Due to the complexity and challenges we experienced ourselves in recruiting adolescents and parents in the BOOST pACP trial, we decided to more systematically explore the recruitment and retention challenges in RCTs of psychosocial interventions for children and adolescents with cancer and their parent(s), by conducting an international collective case study. This involved semi-structured interviews with principal investigators and research staff from recent or ongoing trials in this field (**Chapter 6**). The study uncovered the difficulties faced and strategies used in these complex RCTs.

Our findings indicate that successful recruitment typically involved a multi-step, personalized approach, including multiple visits per family. This approach, while effective, is time-intensive and underscores the importance of thorough training for research staff. Pilot studies with process evaluations, closely mirroring the conditions of larger trials, are crucial for understanding context and mechanisms of action.

The need for greater transparency and publication of best practices was emphasized by respondents. Even experienced researchers find it challenging to predict which strategies will be effective in advance. Interviews further highlighted that maintaining close follow-up with families, regular contact with key recruitment personnel at the hospitals, and a flexible attitude to adapt to the families' challenging circumstances are crucial for success.

Given that our BOOST pACP trial is only the second pACP trial conducted to date, these insights can help refine protocols and trial implementations for pACP trials and other psychosocial interventions, ultimately aiming to improve care for children with cancer and their families.

Methodological considerations, strengths, and limitations

This dissertation presented multiple studies that used various methods. **Chapters 1 and 2** focus on the development of the BOOST pACP trial and its intervention. **Chapters 3 and 4** present quantitative data from the multicenter BOOST pACP trial, detailing primary and secondary outcomes. **Chapter 5** reviews factors influencing the development of children with serious illness, while **Chapter 6** explores recruitment and retention challenges through a collective case study with online semi-structured interviews. The strengths and limitations of each study are discussed in detail in this section.

Development of the pACP intervention and trial (Chapters 1 and 2)

The BOOST pACP intervention was developed through several iterative steps: 1) interviews with 11 healthcare professionals from the pediatric oncology ward; 2) literature search to identify existing components relevant to pACP; 3) development of a logic model and parallel 3) intervention design, via iterative discussions among our core research team (n=6), feedback on the first version of core components by an international advisory group (n=11), psychologists (n=8), the Pediatric Palliative Care Research Network (PPCRN); 5a) semi-structured interviews with adolescents with cancer (n=4), parents (n=6) and healthcare professionals (n=9) to assess acceptability; 5b) testing the core components with 3 families, followed by semi-structured interviews.

Components from IMPACT were adapted to fit our target group and (trial) context, as endorsed by the updated Medical Research Council guidance [3]. However, we did not use participatory methods in the initial design phase, which may be a limitation as more direct involvement from adolescents might have led to different components. Although there is limited evidence base for participatory approaches in research [4,5], patient involvement can be beneficial in terms of formulation of more relevant research questions, more patient-tailored recruitment strategies, and higher impact of research findings for care practices [6]. However, IMPACT was rigorously developed with input from children with life-limiting conditions and evaluated qualitatively [7].

Additionally, we experienced recruitment challenges to test the intervention's acceptability. We included two young adults who had cancer in adolescence, and were thus not directly our target group. While their feedback was valuable, as they had the ability to consider what they would have liked to address in their care and treatment trajectory in hindsight and how this should be formulated, more input from current adolescents would have been beneficial. The use of a logic model to outline the intervention's pathways to achieving desired outcomes, and the inclusion of the Theory of Planned Behavior (TPB) in our model, strengthened the development process. Behavioral theories, such as TPB, are known to enhance the effectiveness of interventions[8].

A notable strength of our development process was involving the two psychologists, who were to act as BOOST facilitators, early on. Their early engagement fostered ownership and

familiarity with the intervention, positively influencing their motivation and implementation fidelity. This was especially important as the recruitment period was two years, and it was important for the stability of intervention delivery that these psychologists remained throughout the entire period, given their extensive training.

A limitation of both the development study and the BOOST trial, is that eligibility is limited to Dutch-speaking participants due to the intervention's focus on communication. This lack of cultural diversity limits the generalizability of our findings. These families may have a high need to understand each other and the healthcare professionals better, especially concerning ACP topics, which could increase their vulnerability to adverse outcomes due to communication barriers[9]. Alternative options, such as including professional interpreters, were not feasible within the scope of our trial.

Conducting the BOOST pACP trial (Chapters 3 and 4)

We conducted a multi-center parallel-group superiority trial, comparing the BOOST pACP intervention to care as usual. Adolescent patients and their parent(s) were randomized to the intervention or control arm after baseline assessment. Families were recruited between March 2021 and March 2023 across four pediatric oncology wards in Belgium. Questionnaires were administered at baseline measurement (T0), after 3 months (T1) and after 7 months (T2).

The experimental design to evaluate the effectiveness of the intervention is a strength, given its rarity in the field of pediatric oncology communication and ACP[10,11]. The trial included a diverse cohort of adolescents in terms of age and cancer type from different pediatric centers in the country, strengthening the study's external validity. However, the study primarily included adolescents with cure as treatment goal and a relatively good prognosis, with few participants having advanced cancer where the treatment goal was life-prolonging or comfort care.

Additionally, there is a risk of ascertainment bias, as enrolling families with poorer parent-adolescent communication can be challenging. These families may be less motivated to participate, potentially affecting the representativeness of our sample and the generalizability of our findings [12]. Initial contact with the study was made through a psychologist at the pediatric oncology ward, but families who are less likely to engage with a psychologist may also be less inclined to participate. Psychologists might unintentionally have avoided introducing the study to families with limited contact or poor prognosis, anticipating that these families may view the study as a burden. To mitigate this, we held regular three-monthly meetings and closely monitored adherence to inclusion criteria to ensure that all eligible families were informed about the study. The underrepresentation of families with poor parent-adolescent communication or poor prognosis may lead to an underestimation of the intervention's effects. Additionally, we observed higher non-response rates among adolescents and mothers in the intervention group compared to the usual care group, particularly at the first timepoint. This may be due to the substantial time and effort required from families in the intervention group over the three-month period, which could lead to reduced motivation to complete subsequent questionnaires compared to those in the control group.

Although we aimed to mitigate challenges regarding internal validity through the design of our study, the most important limitation is the trial being underpowered. Our enrollment rate of

28.2% was lower than other RCTs of psychosocial interventions for similar populations (ranging from 39% to 77%)[13]. This low rate likely stems from overestimating participants' willingness to engage, as adolescents with cancer may wish to avoid additional study burdens and parents may lack the mental space for another study. Despite various mitigation strategies, such as involving recruitment sites early, increasing study visibility, and sharing experiences from former participants, recruitment challenges remained [13].

The lack of validated questionnaires for cancer-related parent-adolescent communication or pACP communication is another limitation. We adapted the Parent-Adolescent Communication Scale [14] to the ACP context. In addition, the items measuring attitude, self-efficacy, intention and behavior regarding discussions of pACP topics were self-developed using the Theory of Planned Behavior (TPB) to assess the secondary outcomes of the BOOST pACP intervention. Although these questionnaires underwent face validation, we did not fully assess their construct validity as recommended by the Standards for Educational and Psychological Testing [15]. Only the first, substantive phase was completed, using theoretical underpinnings from the TBP[16] and other literature [17–20] as references. The structural phase, involving quantitative analyses to examine the psychometric properties of the measures, was not conducted before using the questionnaires. Additionally, the external phase, which gathers evidence on how the construct relates to other constructs or predicts criteria[15], was also not conducted prior to using these questionnaires in our RCT. This limitation was due to the time constraints of our study. Rigorous subjective measures are rare in pediatrics for patients with a serious illness [10,21], leaving us with few options. We aligned our outcome measures with the goals outlined in the logic model, which is critical to ensure that the study accurately measures the intended effects of the intervention. Aligning outcome measures with intervention goals helps to avoid the common problem of selecting measures that do not fully capture the intervention's objectives [22].

Exploratory factor analysis was used to evaluate determinants such as attitude and self-efficacy, and sum scores were used for intention and behavior. Although this approach strengthened the examination of the logic model, Cronbach's alpha values did not always meet the 0.7 threshold, suggesting potential issues with unidimensionality. We provided detailed information on the items of our secondary outcomes in our article to allow readers to consider the relationships between different items (face equivalence) [23].

To ensure understanding, experienced data collectors assisted adolescents with completing the questionnaire, limiting measurement bias but introducing the risk of interviewer bias [24]. This approach was necessary for younger participants but could have impacted results through placebo effects in the control group.

Other strengths of our trial include the separate collection of perspectives from mothers, fathers, and adolescents which is uncommon in pediatric oncology research [25]. Additionally, our longitudinal design allowed us to track changes in communication processes over time. Given the inherent challenges in measuring communication – such as variations in communication patterns and the need for sensitive and specific measurement tools [26,27] – longitudinal data collection is crucial for capturing these dynamics comprehensively.

A key consideration is whether questionnaires are the most appropriate method for researching communication, particularly for adolescents. Some limitations have to be

considered related to measurement via questionnaires. Measurement bias may have influenced our findings, as it is unclear whether respondents accurately categorized topics they discussed as falling under the ACP themes we defined and whether they recalled these discussions accurately. The reporting between the two study groups might have differed [28]; specifically, we instructed the BOOST group to consider communication on ACP topics beyond the BOOST conversations themselves. This distinction could have been challenging for adolescents and possibly parents to remember, potentially leading to confusion about whether discussions occurred during the BOOST sessions or at other times. This limitation is related to the Theory of Planned Behavior (TPB), which emphasizes cognitive processes and may not fully account for unconscious or automatic behaviors [19,29,30]. Additionally, we observed a midpoint response style among adolescents using our five-point Likert scale, which could have skewed results by centralizing responses and reducing variability [24]. Although the most common quantitative methods to measure communication are patient self-report and observational coding of recordings of conversations [31], the latter was not possible, given our goal to improve illness-, care- and treatment- related parent-adolescent communication – which can occur at home also. Qualitative interviews at certain follow-up timepoints could have provided additional insights but were not feasible within the RCT framework. The adolescents' own perspectives on and active involvement in their psychosocial situation are often under-utilized [27]. This underscores the innovation of our focus on parent-adolescent communication from the adolescent's viewpoint – both in terms of intervention components and measurement methods – which can be considered an important strength of our approach.

Scoping review on characteristics of child development in the context of serious illness (Chapter 5)

We conducted a scoping review to provide an overview of factors affecting child development amidst serious illness. A scoping review was the most appropriate approach for our objectives, as it aimed to provide an overview of the existing evidence on this topic in an exploratory manner, rather than generating evidence to inform practice, which is typically the focus of a systematic review [32,33]. In line with the scoping review methodology, we did not assess the risk of bias for the included studies. However, we observed that some studies lacked clarity in their data collection methods and participants populations. In this regard, a systematic review might offer more specific recommendations on the types of research needed to address the identified gaps. Nevertheless, for this exploratory question, a scoping review was the most appropriate methodology, as it does not focus on clinical effectiveness and the PICO (Population, Intervention, Comparator, Outcomes) framework is not applicable [34].

Methods from Arksey and O'Malley [35], with further refinement from guidance by the Joanna Briggs Institute [36] were used. Our search strategy, developed with an information specialist, involved querying four databases and was validated through detailed discussion with three researchers, enhancing the study's validity and reliability. A common challenge of scoping reviews is the heterogeneity of the data, which often necessitates ongoing reflection and discussion among researchers, which we also encountered [37]. We did not include grey literature, and only articles in English were included.

Although including serious illness in general, the literature mostly covered illness groups where development follows a typical trajectory. Other illnesses, involving profound delays, behavioral deficits, mental retardation were not addressed in the selected studies. The

findings from this scoping review can therefore not be applied to all serious illnesses in general, where profound delays in development are prevalent.

Collective case study to evaluate recruitment and retention challenges and strategies in RCTs in the pediatric oncology population (Chapter 6)

To gain a comprehensive understanding of the challenges and strategies in recruiting and retaining participants for psychosocial interventions in pediatric oncology, we conducted a collective case study [38]. This study involved online semi-structured expert interviews with principal investigators and research staff members of a selection of recent or ongoing trials testing psychosocial interventions for children and/or adolescents with cancer and their parents.

Case study research has sometimes been criticized for lacking scientific rigor [38], however, our detailed search strategy to identify relevant studies and minimizing the risk of missing trials that met our inclusion criteria, addressed this pitfall. We focused on studies published from 2011 onwards, which, while risking recall bias, provided relevant follow-up data as many of these studies were designed to build on or compare with previous practices. The exclusion of non-English studies might have resulted in missing relevant trials. Furthermore, analysis was conducted by a single researcher, though key findings were reviewed in detail with the core research team to enhance the reliability of interpretations. Although incorporating our own study as a case may have reduced critical distance, we maintained methodological consistency by interviewing our team's data collectors using the same topic list as in the other cases. Knowing the data collectors personally and having collaborated with them closely for over a year may still have influenced my focus during the interviews and reporting. Nevertheless, including the BOOST pACP study provided substantial added value by offering essential insights that would otherwise be scarce in this context, given the limited number of cases available in this context. Our study specifically included trials including both children and adolescents and at least one parent, within the oncology setting, considering its unique challenges. While including studies from other settings such as chronic or other serious illnesses might have offered additional insights, the specificity of our selected studies provided in-depth perspectives that were previously lacking in the literature. Nevertheless, many of the strategies could be applicable to other target groups.

Interpretation and discussion of the main findings of this dissertation

Comparing the results with other trials in a similar target population

The primary outcome of the BOOST pACP trial was parent-adolescent communication from the perspective of the adolescent, measured by the Parent-Adolescent Communication Scale (PACS) [39]. We chose this outcome because ACP is relational, enacted less as an individual directive and more as a family-centered and social process, especially in the pediatric setting [40].

We found no significant effect on our primary outcomes. The effect size for overall parent-adolescent communication was 0.13 at 3 months post-baseline (T1) (0.17 for mother-adolescent communication and 0.05 for father-adolescent communication). At 7 months post-baseline (T2), the effect size was 0.49 (0.31 for mother-adolescent communication and 0.67 for father-adolescent communication). Effect sizes provide a description of the size of observed effects that is independent of the possibly misleading influences of sample size, thus

can allow the comparison of effects across studies [41]. However, there has been discussion on how to interpret effect sizes. Cohen's classic classification of effect sizes into small ($d=0.2$), medium ($d=0.5$) and large ($d \geq 0.8$) has been criticized, especially in the field of psychological research. For studies with small sample sizes, such as the BOOST pACP trial, interpreting effect sizes can be challenging due to their wide confidence intervals. While caution is needed when interpreting these effect sizes because of the small sample size, it is important to consider the potential for small effects to accumulate over time or across individuals, even if the effect size appears modest [42]. This consideration is particularly relevant for research on individual differences, such as communication abilities [42], as explored in the BOOST pACP study. Another consideration is that the BOOST pACP trial could have produced overestimated effect sizes, because of the small sample [42], analyzing results of 16 adolescents in the intervention group and 22 adolescents in the control group at the first timepoint and 14 adolescents in the intervention group and 18 adolescents in the control group at the second timepoint.

Since parent-adolescent communication has not been previously studied as an outcome of a pACP intervention, comparisons are difficult. Therefore, I will examine outcomes on parent-adolescent communication using the PACS, as other instruments on parent-adolescent communication measure quite different aspects [14], from other interventions in pediatric oncology. I will also consider the various outcomes from the only other pACP trial conducted with adolescents with cancer.

One of the interventions in a comparable context studying effect on parent-adolescent communication is a web-based legacy-making program [25]. The target group was children (ages 7 – 17) with advanced cancer (relapsed or refractory). Legacy making involves actions or behaviors aimed at being remembered. In this study, it included creating a personal digital storyboard by directing them to answer legacy-making questions, and upload photographs, videos and music. Legacy-making showed trends for improving the quality of communication (measured by the PACS) between children and their parents across time, especially for father-child communication. However, no statistically significant findings were reported at the follow-up point of almost 70 days after baseline. An effect size of 0.20 was found for child-reported overall communication with their father, and 0.10 for overall communication with their mother. Although these effect sizes are smaller compared to the BOOST pACP intervention, the sample size in the legacy intervention was larger, analyzing results of 32 children in the intervention group and 57 children in the control group receiving care as usual [25].

Another study using the PACS as an outcome measure in adolescents and young adults (AYA) aged 11 to 24 years old who underwent high-risk cancer treatment evaluated the effectiveness of a therapeutic music video (TMV) [43]. The study measured family environment, including family cohesion, adaptability, communication (using the PACS), and family strengths. Although parent-adolescent communication was a component of the broader "family environment" variable and specific effects on communication alone were not reported, the intervention significantly improved the overall family environment at 100 days post-transplant (second timepoint), with an effect size of 0.66. This analysis included 40 AYAs in the intervention group and 40 in the control group. No significant effects were observed at the first timepoint, which was directly after the sixth session of the intervention. In parallel, the effectiveness of a nurse-delivered "self-care and communication intervention" for parents of these AYAs was assessed. This intervention comprised three one-hour sessions: one focused

on self-care and two on enhancing parent-AYA communication [44]. However, no significant improvements in parent-adolescent communication were found from the parents' perspective, with effect sizes of -0.03 fourteen days post-intervention and 0.04 ninety days post-intervention. This analysis included 37 parents in the attention control group and 30 in the intervention group. Interviews with parents revealed that insufficient time to practice and apply the new skills led to reverting to old habits [44]. Thus, parent-adolescent communication, as measured by the PACS, has not been extensively studied as an outcome of other interventions in a similar setting either and results suggest that it is not an easy variable to influence.

The only other pACP intervention studied in an RCT is the Family-Centered Advance Care Planning Intervention (FACE-TC) of Lyon et al. and different outcome measures were used to evaluate its effectiveness. This intervention is different in content, existing of three sessions: 1) A survey to set stage for end-of-life care conversation; 2) ACP Respecting Choices interview, with a goal to facilitate conversations and shared decision-making, providing an opportunity to express fears, values, spiritual and other beliefs and goals with regard to death and dying. This includes the Statement of Treatment Preferences that describes clinical situations common to cancer and related treatment choices; 3) Filling out of the Five Wishes, a legal document including medical, personal, emotional, and spiritual needs [45]. FACE-TC was proven to be feasible, acceptable and safe [46]. Subsequent studies evaluating results of around 80 parent-adolescent dyads in the intervention group and 40 dyads in the control group with pACP information showed that FACE-TC achieved higher overall congruence on end-of-life care preferences in four cancer-specific situations [47], sustained families' knowledge of their adolescents' end-of-life treatment preferences for one year [48], and families' positive caregiving appraisals and satisfaction [49]. Mostly, odds ratios were reported. Effect sizes at 3 months were 0.28 on caregiver strain (not significant) and 0.28 on caregiver distress (not significant), 0.17 on positive caregiving appraisals (significant), and 0.03 on family well-being (not significant). However, parent-adolescent communication was not assessed.

Potential explanations of the lack of significant findings in the BOOST pACP trial

The BOOST pACP trial's finding that the intervention did not demonstrate a significant effect on the primary endpoint – parent-adolescent communication measured by the Parent-Adolescent Communication Scale (PACS) – at the first follow-up point (3 months post-baseline) warrants further reflection. The lack of a statistically significant effect may be attributed to the underpowered sample size, which necessitates cautious interpretation of our findings. Other potential explanations for the lack of significant findings on the PACS at the first follow-up point as well as on some behavioral determinants are discussed below.

1. The measurement instrument may not have been appropriate

The measurement instrument on the behavioral determinants, grounded in the Theory of Planned Behavior (TPB), might not fully capture the qualitative nuances of ACP, such as the depth and quality of communication. Additionally, it may have lacked the sensitivity needed to detect subtle but critical shifts in behavioral determinants essential for ACP. The lack of a significant finding on parent-adolescent communication could be due to already good communication at baseline on the value- and emotion oriented ACP topics, and a lack of relevance of end-of-life care oriented ACP topics. Insights from our mixed-methods process evaluation will provide further context and understanding of the mechanisms of outcome and

implementation. This process evaluation included semi-structured interviews with adolescents with cancer, parents, healthcare professionals, and conversation facilitators, as well as audiotapes of the BOOST conversations and structured diaries maintained by the facilitators [50].

A legacy-making study [51] found no significant results on the PACS either, although qualitative data from parents suggested otherwise. Specifically, 72% of parents reported that the intervention improved parent-child communication, and 86% noted enhanced expression of feelings by their child [25]. The authors suggested that this discrepancy could be due to the PACS's limitations in detecting effects such as expression of feelings, or because the intervention influenced other areas of parent-child interaction, such as parenting, adaptability, or cohesion. This insight might also be relevant to the BOOST pACP intervention.

2. The application of behavioral change models to advance care planning interventions involves some limitations

After a thorough development process for the BOOST pACP intervention, we selected the Theory of Planned Behavior (TPB) as the foundation. Behavioral theories, such as the TPB, are recognized for their ability to improve intervention effectiveness [8]. Additionally, based on existing literature on barriers to parent-adolescent communication [52–54] and ACP in adolescents [7,55], the TPB appeared to be a fitting choice for our trial. However, our theories on behavioral change may not have held up adequately, or the targeted determinants might not have been sufficiently addressed. Several factors could have contributed to this:

- Limitations of the Theory of Planned Behavior (TPB): Our intervention was based on the TPB, which conceptualizes ACP behavior as an individual action. However, other influential processes – such as unconscious, circumstantial, or environmental factors[29] – may play a significant role in influencing the behavior of discussing ACP topics, processes that the TPB does not account for and that we have therefore not been able to capture. These factors include various aspects of the physical and social environments that influence behavior [56]. For instance, in our context, these could be movies watched by adolescents or parents, conversations with others, stories about similar situations, social media, or observing other families in the pediatric oncology ward. Such elements can stimulate thoughts and discussions about ACP topics or, conversely inhibit communication. Our process evaluation may provide further insights into how our logic model and the TPB framework could be adjusted to better account for these factors.
- Motivation and behavior change: Theory-based behavioral interventions are often criticized for targeting only those who are already motivated to change [57,58]. During our recruitment period, it was evident that some participants lacked motivation, as shown by their reluctance to engage in potentially sensitive discussions and the significant time commitments required for study procedures. Factors such as the abundance of proposed studies to participate in, existing satisfaction with current communication, and doubts about the relevance of improving communication contributed to their lack of motivation [13]. Effective strategies for behavior change in unmotivated individuals are relatively scarce. Improving intervention effectiveness for unmotivated participants should begin with analyzing the underlying reasons for their lack of motivation [58],

something that might have been insufficiently addressed in the BOOST pACP intervention. Factors such as low self-efficacy, poor outcome expectations, and low value beliefs – which relate to not finding the behavior worthwhile – may have contributed to this. The BOOST pACP trial results did not show effects on self-efficacy of discussing ACP topics with each other (parents and adolescents). Incorporating motivational interviewing and more effectively addressing self-efficacy through specific behavior change techniques (BCT) like goal setting, action planning, or implementation intentions could enhance the intervention's impact [58].

However, the evidence on the effectiveness of specific BCTs is limited, because BCTs often interact with one another, either enhancing or reducing their overall effectiveness, and their impact can vary depending on how they are implemented [59]. Assessing the effectiveness of a particular BCT or combination of BCTs for a specific behavior requires synthesizing information from diverse sources to develop a subjective confidence estimate – a process that demands significant effort and resources [59]. The Human Behavior Change Project is currently gathering evidence to predict the outcomes of interventions in new contexts with machine learning algorithms and Behavior Change Intervention Ontology (BCIO). However, their work has primarily focused on evaluating interventions related to smoking cessation and physical activity [60]. Insights into the effectiveness of communication interventions specifically, are still a long way off.

- Automated non-conscious behaviors: If individuals are not really motivated or are hesitant on the added value of the behavior, they are unlikely to change because they are not inclined to invest effort in overriding highly automated, non-conscious, cue-driven behaviors [58]. Therefore, structuring the environment to make undesired behaviors more difficult is essential. One of the goals of the BOOST pACP intervention was to create favorable circumstances and a safe space for discussing ACP topics. However, this approach might not have been sufficient to ensure the sustainability of these behaviors, which is necessary to increase intention and actual ACP behavior with both parents and pediatric oncologist. Although our results showed that mothers intended to discuss more end-of-life care-oriented ACP topics with their child, this effect was not observed for fathers and not for adolescents to discuss ACP topics with either of their parents. Sustained behavior change may require additional strategies, such as planning, volitional strategies, self-monitoring, and self-reinforcement [58].

A general limitation of using behavior models is that they can oversimplify complex human behaviors and interactions, reducing them to basic determinants that may not fully capture the nuanced nature of ACP discussions, which involve deep personal values, emotions, and intricate family dynamics [61]. These models often emphasize individual choice and responsibility, potentially overlooking broader systemic, environmental, or policy-related factors that also shape behaviors. However, we found the TPB to be an appropriate framework for our study because we wanted adolescents and parents to realize that ACP communication is manageable (self-efficacy), often well-received by the other (social norms), and relevant (attitude). Moreover, positive outcomes have generally been observed in ACP studies that focus on process outcomes (e.g. knowledge, readiness) and action outcomes (e.g. communication, documentation) [62], emphasizing the potential of ACP interventions on such outcomes. Furthermore, there is growing argument that the field of communication research

including ACP research could benefit from a more integrated use of behavioral change models in the design and implementation of interventions [63], because this may lead to evidence on how to reduce the delay and avoidance in the current practice of ACP [64]. Some studies on adult ACP [65] and non-ACP [66] have shown that increased patient participation can, in turn, also enhance ACP communication by healthcare professionals.

3. *The timeframe of the BOOST pACP study might have been too short*

Although immediate effects were limited, the BOOST pACP intervention showed more promise in the longer term. At the 7-month follow-up, an effect size of 0.49 was observed for parent-adolescent communication and 0.67 for father-adolescent communication, which was significant. This indicates that while the short-term impact was minimal, there may be delayed benefits as the families continue to integrate the communication strategies introduced by the intervention and more opportunities occurred to discuss ACP topics when required. ACP interventions have been measuring congruence in end-of-life care preferences between caregivers and patients and found a significant improvement. However, the effect of ACP on this outcome declined over time, in both adult studies[67] and pediatric ACP studies [48]. Finding an increase over time, as seen in the BOOST pACP study, rather than a decrease in parent-adolescent communication may indicate that it takes time for new attitudes and learned skills to be integrated into communication. Follow-ups would be necessary to maintain these new methods, as communication often reverts to old patterns [68].

4. *The broader adolescent cancer population may not be ideally suited for this type of ACP*

The BOOST pACP intervention addresses topics that are applicable to any adolescent with a serious illness, including worries and fears, whether they can talk to people about this, and expectations for the future. The BOOST pACP intervention was based on the holistic IMPACT [7] model and designed for implementation shortly after diagnosis. The content of the FACE-TC intervention, with its strong emphasis on end-of-life care decisions, is fundamentally different. The target group of the FACE-TC intervention is adolescents aged 14 to 21 years old with cancer. In the study population of FACE-TC, 21.4% were on active treatment, while 78.6% were not on active treatment but considered in remission [49]. They were recruited via tertiary pediatric hospitals, implicating that for these adolescents, advanced, specialized, or multidisciplinary care is needed. Thus, the study population of the FACE-TC intervention was vastly different from the BOOST pACP study population, with 91% in the first line of treatment and 87% with cure as the main goal of the treatment who were recruited via university hospitals where all pediatric oncology cases are represented (with favorable prognosis as well as unfavorable prognosis).

The BOOST pACP intervention highlighted the value of adopting a **holistic** approach to ACP, which encompasses discussing fears, hopes, future perspectives, and communication about the illness, beyond just focusing on “*what if*” scenarios related to health deterioration. While ACP’s ultimate goal is to align care with the adolescent’s values and preferences, it may not always be necessary or beneficial to introduce topics like “*what if the treatment is not effective*” or “*what if a complication occurs*” early in the treatment process for adolescents with a good prognosis and an uncomplicated treatment trajectory. Such questions could potentially shut down open dialogue about other concerns relevant to the adolescent’s current experience, which might have influenced our results.

Our scoping review revealed that early adolescents tend to focus primarily on the present, while concerns about the future and potential relapse become more prominent in middle to late adolescence. The BOOST pACP conversations showed that it is feasible to involve adolescents as young as 10 years old in comprehensive ACP discussions without increasing their anxiety. However, advancements in cancer treatment, which have resulted in longer survival rates and more unpredictable disease trajectories, have made the timing of these conversations more complex. Establishing standardized criteria for initiating ACP discussions is challenging, as the appropriate timing varies significantly among individuals. Since clinicians often overestimate prognosis compared to the actual disease trajectory [69], relying solely on their assessment for the timing of ACP discussions is inadequate.

Therefore, ACP should be **flexible and regular**, allowing for natural progression towards more serious discussions **tailored to the development** of the adolescent and as the situation warrants. There is no standardized tool to 'measure' an adolescent's development and relevance for such conversations, which might not be advisable, since development and preferences are highly individual. Further research is needed to explore how to effectively engage younger children in ACP or some kind of 'preparatory' ACP, ensuring that the process is beneficial and supportive rather than overwhelming or perceived as useless or not applicable to their situation. Children learn about, practice and develop communication and decision-making skills through participation, which sets the stage for increased participation over time [70], and would benefit from developing trusted relationships prior to initiating ACP [71].

Children younger than 10 years old may also benefit from discussions on several BOOST topics, though additional exercises in person-centered future planning might be necessary to explore specific issues more deeply and build rapport. The "My Choices" program exemplifies how younger children and their parents can be included in thinking about their current and future care, including a separate booklet that was specifically designed for children aged 6 to 10 years old [72]. However, this approach has not been extensively tested with this subgroup of young children. Researchers from the Netherlands have examined whether and how pACP interventions include age-appropriate elements for children [1]. They are expanding this work by interviewing children aged 4 to 18 with a chronic medical condition or life-limiting illness to study how they communicate about pACP topics and how they value these topics, providing further insights in this area.

The holistic approach of the BOOST pACP intervention makes it fairly adaptable to other populations as well. Only the videos shown during the first ACP conversation are specifically tailored to adolescent cancer patients and their families. The '*what if*' scenario topics, however, might be more relevant to families with a child facing a complex chronic condition, characterized by a heterogenous diagnosis, high healthcare utilization, reliance on medical technology, and a significant risk of morbidity and mortality [73].

Recommendations for practice, policy and research

Our findings highlight the potential to enhance ACP practices and research for adolescents with cancer and their parents. In this section, several recommendations are formulated to better support adolescents with cancer and their parents in three domains: practice, policy and future research.

Recommendations for practice

Address the importance of parent-adolescent communication

Focusing on parent-adolescent communication within ACP may be highly appropriate, given its consistently demonstrated importance. Communication is a crucial aspect of parent-child relationships [69], influencing child adjustment over time [25], as well as family cohesion and adaptability [74]. It also provides emotional and instrumental support for children, which is associated with low levels of internalizing and externalizing problems in their adolescence [74]. Discussions about cancer can include strong affective components, abstract concepts and complex information, due to which parents find it difficult to engage in illness-related communication with their child [69]. Communication challenges can negatively impact the resilience and quality of life for both the adolescent and parents [75]. However, this aspect does not typically receive standardized attention throughout the adolescent's treatment trajectory. Few communication interventions are available, apart from those focused on treatment or care planning decisions [44]. While it is valid to question whether it is the responsibility of healthcare professionals to promote such communication – and it may be a sensitive issue due to its overlap with parenting and the potential perception by parents of interference – there is a clear need to raise awareness of the preventive role that open communication within the family can play.

Integrate holistic and flexible pACP in the treatment trajectory

While there is at this time insufficient evidence to recommend the full implementation of the BOOST pACP trial in pediatric oncology wards in Belgium, I suggest integrating certain principles throughout the treatment trajectory, based on our results and available literature. These components could provide added value for all adolescents with cancer, regardless of prognosis, by promoting better integration of ACP into the care trajectory.

In the Netherlands, so-called case managers are more commonly found within the pediatric palliative care pathway. These case managers address all domains of care, coordinate with the child and parents, serve as main point of contact, organize care discussions, liaise with the general practitioner, and conduct ACP conversations [76]. However, these case managers are specifically focused on children and families with palliative care needs due to the high complexity involved, making it unfeasible to include the general pediatric oncology population in their remit [76]. Inclusion of a family-identified trusted provider in ACP discussions was suggested by clinicians to minimize mixed messaging about recommendations for their child from different healthcare professionals and to engage families in communication [77]. Therefore, strategies for a more effective integration of ACP early in the illness trajectory are:

1. Training and designating “care planners” to each family

Any healthcare professional in pediatric oncology, such as psychologists, nurses, social workers, pediatric oncologists, could be trained as “care planners”. Each child and their family would be assigned a care planner, allowing for regular contact and the opportunity to build rapport – an important element in effective ACP [55,78]. A key ‘lesson learned’ during our study is that the way questions are posed influences the information gathered, underscoring the need for training in specific communication skills (e.g., asking open-ended questions, avoiding mixed messages, and probing assumptions) [52,79]. Simple approaches such as “*could you tell me a bit more?*” and mirroring the individual repeating the exact words, followed by a silence triggers them to elaborate.

2. Adopting a holistic and flexible care planning approach:

To reflect the holistic nature of ACP and acknowledge that not all adolescents may feel the need to discuss their preferences about potential health deterioration at any given time, the care planner should adapt their role based on the family’s specific needs. An approach tailored to the development of the child is recommended, as indicated by our scoping review. Several key areas where adolescents and their families may benefit from support, which could be addressed by care planners, include:

- Facilitate family communication by providing support for effective within-family communication and raising awareness of its importance [80,81]
- Assess and strengthen family resilience [82], by fostering coping strategies and problem-solving skills [83].
- Bridge the gap between the hospital environment and daily life by connecting families with other support systems, such as peer support, school, and navigating the healthcare landscape [84]
- Discuss current and future care and treatment options, with a focus on anticipating potential disease progression (ACP) [7]. This includes balancing the pursuit of optimal treatment with the need to avoid overtreatment, which may result in additional complications in the future [85].
- Communicate relevant information to the treating oncologist and other relevant healthcare professionals, potentially fostering more patient-centered communication in the long term [66]. Training care planners as champions or frontrunners can further promote the integration of ACP among other healthcare team members [86].

Adolescents with cancer often face a range of challenges, including side effects from the disease and its treatment, a changed self and social life, and concerns about academic achievement [87]. Previous research has shown that anxiety and depression levels tend to increase over time for children with non-advanced cancer [69]. Therefore, integrating ACP into the broader goal of providing high-quality psychosocial care for adolescents with cancer, regardless of prognosis, is crucial. The development and implementation of this approach should be co-created with adolescents, their families, and healthcare professionals. Co-creation helps to clearly define the specific goals, content, materials, delivery methods, and frequency of interactions with the care planner [6].

Recommendations for policy

Reduce barriers to father involvement in caregiving

The BOOST pACP study highlights the potential for significant improvements in father-adolescent communication over the longer term (seven months post-baseline). A systematic review found that targeted strategies to increase social support for fathers both inside and outside their families are needed, along with accessible educational interventions regarding caregiving, disease progression, and daily management [88].

Our study underscores the importance of engaging fathers more actively in their child's care. In the BOOST pACP trial, nearly 60% of the adolescents reported their mother to be the most present caregiver in the hospital, while approximately 30% reported that both parents were equally present. Only around 10% identified their father, or a grandparent/ stepparent, as the most present caregiver in the hospital. Even in families where mother-adolescent communication is perceived as positive, the quality of father-adolescent communication remains crucial. Research shows that increased father involvement in caring for a child with chronic conditions is associated with better family functioning, improved treatment adherence, enhanced psychological adjustment for the child, and overall better health outcomes [89].

However, systemic barriers often prevent fathers from being more involved. These include inflexible work hours, and limited access to sufficient time off [89] while in many cases there are also other children in the family parents have to raise and care for. In Belgium, while provisions such as 'zorgverlof' allow parents to temporarily interrupt their careers with a replacement income [90], it is often financially unfeasible for both parents to take extended leave, resulting in fathers typically returning to work.

Given these findings, policy measures should prioritize reducing the barriers that limit fathers' participation in caregiving, ensuring that they have the opportunity to be more involved if they wish to do so. This could include promoting more flexible working conditions, enhancing access to family leave policies for both parents, and encouraging workplaces to support a more balanced distribution of caregiving responsibilities. By facilitating fathers' involvement, there is significant potential to improve outcomes for both the child and the family as a whole.

Provide time and resources for healthcare professionals to facilitate early and holistic implementation of pACP

To facilitate early and holistic implementation of pACP, it is crucial to allocate adequate time and resources for healthcare professionals. In Flanders, there are two pediatric liaison teams – Kites, connected to the University Hospital of Leuven, and Koester, connected to the University Hospital of Ghent. Children and adolescents under the age of 18 with severe chronic conditions are eligible for their care. The most common disease profile represented at Kites and Koester consisted of (hemato-)oncological diagnoses [91]. These teams provide, among other responsibilities, palliative and end-of-life care in the child's home environment whenever possible, ensure continuity of care and maintain the link between the hospital team, the family, and primary and secondary care providers [92]. Although ACP topics are addressed by the healthcare professionals in the pediatric liaison teams, this is not done in a systematic manner. The variation in age and pathologies of the children they encounter presents a significant challenge.

There are currently no resources consistently available for children who are not immediately at the end of life [92]. A better allocation of resources could improve the continuity and earlier integration of ACP, aligning with the goals of the BOOST pACP intervention. The Belgian Pediatric Palliative Care (BPPC) guidelines and recommendations challenge the current organization of pACP [92]. Although the BBPC handbook highlights important considerations, it lacks concrete ways to allocate resources and integrate holistic ACP early in the disease trajectory.

To facilitate the integration of ACP, it is essential to emphasize ACP's importance early in the disease trajectory within relevant training programs for healthcare professionals. During the development study of the BOOST pACP intervention, it became clear that barriers for healthcare professionals to engage in ACP conversations are due to a complex interplay of system-related, attitude-related, and parent-related factors [40]. Key barriers identified include a lack of time during standard consultations, uncertainty about the timing of discussions, insufficient training, and a lack of structure to involve other team members [40].

System-related factors that could enhance ACP practices include additional training and standardized documentation. A multidisciplinary team with improved communication would foster better relationships among professionals, which would, in turn, positively impact the families [77,93]. Developing a formal training program would enable trained facilitators, or 'care planners' as I proposed earlier, to provide feedback to other healthcare professionals, increase their confidence in assessing prognostic awareness, elicit patient and family goals and values, and incorporate these into their recommendations [77]. Besides the proposed 'care planners', a standardized approach supported by education, guidelines and clinical tools such as the BOOST pACP intervention is required, to further enhance integration efforts [64]. Financial incentives and accreditation points earned for participating in such training could motivate healthcare professionals.

Build awareness and empowerment in adolescents with serious illnesses in ACP through coordinated communication efforts

Environment and policy influences can either facilitate or hinder behavior change and its sustainability [94]. To further empower adolescents with a serious illness and equip them with the tools to understand a holistic approach to ACP, public health organizations, together with patient groups and hospitals should collaborate to create and distribute clear, consistent messages about what ACP entails, its added value, and how it can be approached in an accessible and straightforward manner [95]. Embedding pACP within a broader health promotion strategy can address key factors like awareness, attitudes, self-efficacy, intentions and behaviors. Platforms such as YouTube can effectively trigger interest and provide information on palliative care, while podcasts shared on social media can reach wide audiences [95]. Although these findings are specific to palliative care, they likely apply to ACP as well, highlighting the potential of these platforms for broader dissemination and education. However, caution must be taken to avoid the spread of misinformation [95].

Establish guidelines on providing incentives for families to participate in psychosocial research

The collective case study on recruitment and retention challenges in psychosocial studies among families with a child with cancer shows that offering monetary incentives is a common practice in the USA [13]. These incentives are used to compensate participants for their time

and effort and are typically communicated in recruitment materials to eligible families before they decide to participate.

In Belgium, however, the use of monetary incentives is less common. Ethical committees are concerned that such incentives might pressure families into participating when they otherwise might not want to. A meta-analysis found that even small monetary incentives can significantly increase consent rates and participant responses [96]. However, it also highlights the need for further research to determine the effectiveness of financial incentives in different types of RCTs and different target groups. In studies involving children, literature suggests that financial incentives can be appropriate if necessary precautions are taken [97]. Therefore, guidelines on providing incentives for families to participate in (psychosocial) research should be developed, and funding agencies should also be able to provide support for these incentives.

Recommendations for future research

Identify who benefits most from pACP discussions

Our results indicated no significant improvement in parent-adolescent communication and some behavioral determinants, in a population with mostly adolescents in the first line of treatment and few adolescents having advanced cancer. A critical unanswered question in our research is when it becomes truly valuable for adolescents to discuss hypothetical scenarios, such as potential health deterioration or the possibility of treatment failure. It is likely that ACP conversations with adolescents facing advanced cancer and/or an uncertain prognosis and their parents differ in content from those with adolescents who have a better prognosis. To better understand who benefits from what kinds of pACP strategies, future research should focus on the following:

1. Comparing the content of ACP conversations, to investigate how different factors, such as estimated prognosis, line of treatment, and the presence of metastases, affect the content and effectiveness of ACP discussions.

2. Conducting qualitative interviews, which could provide deeper insights into the mechanisms at play in ACP discussions, such as their impact on adolescents' psychological and emotional status and the specific benefits derived from these conversations. Understanding these mechanisms at play remains challenging, as reflected by the challenge of identifying appropriate outcome measures for ACP [98]. Additionally, involving healthcare professionals is essential to determine what type of information would best support them in delivering high-quality care that aligns with family's needs and wishes [99].

3. Applying a SMART design. A Sequential Multiple Assignment Randomized Trial (SMART) could be used to systematically explore which intervention strategies work best for different families and at what times. A SMART is a multi-stage experimental study that allows for multiple randomizations of participants based on their response or nonresponse to prior interventions at critical decision points [94]. The exact content of different interventions could be informed by the aforementioned methods. An example of what a SMART could entail: an initial randomization could assign families to either hypothetical scenario discussions or general informational sessions on ACP principles. If the initial intervention does not engage the families, a second stage could randomize them again to receive a tailored strategy, such as personalized counseling tailored to address specific concerns or challenges including the BOOST videos as an entry point for further communication, or written materials such as the BOOST preparation booklets and card game that families can review at their own pace, to

further support their understanding of ACP. Outcomes could include improved communication, self-efficacy in initiating ACP conversations, satisfaction with the ACP process, and overall understanding of ACP. The impact on other potentially relevant, more distal outcomes, such as resilience and coping of the child, should also be explored. However, there is currently a lack of extensively validated pediatric measures for these outcomes [100,101]. By developing an adaptive intervention for pACP, a tailored approach can be created and subsequently tested in a confirmatory randomized trial [102]. This process would contribute to identifying the most effective intervention pathways for various participant subgroups. Complete reporting of SMART designs is crucial [103], and adequate time for implementation is necessary, as they require substantial resources.

Include a focus on non-native-speaking families

During the review of BOOST pACP eligibility data and in our quarterly follow-up meetings with key hospital contacts, it became clear that a significant number of patients in the oncology wards were ineligible due to insufficient Dutch language proficiency. In our increasingly diverse society, there is an urgent need to provide better support for families who do not speak the native language. These families often face significant communication challenges due to language barriers and, at times, cultural differences. This can lead to ineffective communication both within the family – as some children do speak the native language, as well as with healthcare professionals. For some, a lack of understanding of the system and the perceived insensitivity of the system to their cultural and religious attitudes and values may further hinder access to appropriate care [104]. In research studies like the BOOST pACP trial, it is often practically challenging to include these families, as it necessitates different recruiting and delivery strategies, such as the involvement of professional interpreters or intercultural mediators. Additionally, the variability within this group of families can require considerable adjustments to the intervention materials. Nevertheless, this is a group that could potentially benefit the most from such programs, and they represent an increasingly significant portion of the population [105]. Therefore, future research should prioritize developing and testing communication interventions specifically tailored to meet the needs of non-native-speaking families.

Integrate developmental stages in the design of pACP interventions and standardize monitoring of child development

Many interventions, whether focused on ACP or other areas, highlight the need to incorporate age-appropriate or developmentally appropriate methods for involving children. However, specific details on how and why these interventions are tailored to different developmental stages are often lacking [1]. In the BOOST pACP intervention, we also faced challenges in addressing the varying stages of adolescent development. We included exercises rooted in person-centered healthcare planning [72] for adolescents who needed more support in initiating conversations and building rapport, assuming this approach would be more applicable to younger participants. Additionally, our conversation facilitators were trained to engage with children of all ages. These were the only measures taken to address developmental stages to some extent. Involving children at various developmental stages in creating ACP interventions tailored to their needs will enhance further understanding of what works best for different individuals [6].

Our scoping review also confirmed a lack of insights into factors influencing child development, which could be valuable for ensuring a more tailored approach. Some factors that may

negatively affect development could be modifiable. To gain a better understanding of child development, particularly in the context of certain illnesses, standardized monitoring could be highly valuable. The KLIK platform in the Netherlands presents a promising medium for such monitoring [106,107]. Long-term research could explore the development of children with serious or chronic illnesses, potentially detecting associations with various conditions or socio-demographic and disease-related factors. These insights could help in developing interventions aimed at supporting optimal development during a child's illness trajectory and inform the timing and approach of ACP conversations with them.

Customize recruitment and retention strategies for studies involving pediatric populations, and evaluate which strategies are most effective for improving these outcomes

The BOOST pACP trial was unfortunately underpowered, which limited its ability to detect significant differences. Recruitment challenges are common in RCTs testing psychosocial interventions and even more so in children; as our collective case study showed, these challenges are not easily resolved. While various strategies were suggested and implemented, respondents acknowledged that these alone do not guarantee successful recruitment and retention, due to different contextual circumstances [13].

For trials involving a high number of parent-adolescent dyads, I recommend dedicating at least one year to thoroughly prepare and tailor the recruitment strategy. Key activities that could enhance recruitment success include:

- 1) Engaging the target group early: conduct focus groups or small surveys with the target population to understand their preferred methods for introducing the study and potential barriers.
- 2) Extensive training of data collectors: recruiting children requires unique approaches, so it is crucial to provide comprehensive training to data collectors to ensure they are equipped with the right techniques.
- 3) Piloting the study: conduct a pilot study that closely mirrors the conditions of the larger trial. This step can be particularly challenging in a population with low numbers, but it is essential to ensure the feasibility and refine the methodology for the subsequent large-scale trial.

Including this preparatory year in your funding application is essential to account for these efforts. Additionally, gaining more insights into effective recruitment and retention strategies for this target group is necessary. Implementing SWATs (Studies Within A Trial) assessing recruitment strategies can be a valuable approach to generate this data. The recruitment strategy most tested is information given to participants [108] by for example user testing of information sheets [109]. However, within the pediatric population, it would be particularly useful to test the impact of consistent contact between research staff and families, as well as a more flexible approach taking adolescent's health and treatment into account— strategies highlighted in our collective case study [13]. Researchers should carefully weigh the additional burden that SWATs place on participants against the potential benefits gained. Conducting and publishing SWATs is advisable only when the participant burden is minimal and the potential insights gained justify the added complexity [110].

Perform mixed-methods meta-analyses on pACP

The logic model used in the BOOST pACP study did not yield all the expected results, but it did produce some positive outcomes. The BOOST pACP trial was, to our knowledge, only the

second pACP trial worldwide. However, qualitative as well as quantitative reports on pACP are increasing [1]. pACP interventions involve various actors and diverse ACP behaviors [40,111]. The relationship between an intervention and its outcomes can be complex, with many influencing factors. To address this, a growing array of synthesis methods is available to evaluate complex interventions [112]. Future reviews would benefit from mixed-method approaches that integrate quantitative, mixed-method, and qualitative evidence on pACP into a single review. Publishing trials with non-significant results is therefore essential, as these studies contribute to meta-analyses and provide a complete picture of the evidence and gaps in pACP research [113].

Conclusion

This dissertation has provided greater insights into the determinants on which a pACP intervention for adolescents with cancer and their parent(s) appears to have an effect. Possible reasons for not achieving all anticipated outcomes have been thoroughly discussed, along with potential avenues for further progress in the field of pACP. This thesis also addressed the opportunities and challenges of using a behavioral model, such as the TPB, as the foundation for our intervention. Additionally, it discusses the challenges associated with conducting quantitative research in this field. Although not included in this thesis, our process evaluation will offer additional insights into how the BOOST pACP intervention may have impacted communication or the lack of it and the underlying reasons for this. Furthermore, this thesis addresses the challenges associated with conducting RCTs involving parent-child dyads, including both the development of interventions that adequately consider child development and the need for sufficient recruitment to achieve robust results.

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SUMMARIES

ENGLISH SUMMARY

English summary

General introduction

Childhood cancer differs from adult cancer in terms of types and treatment considerations. While survival rates have improved significantly due to advancements in understanding the disease, diagnostic methods, drug development, and surgical and radiotherapy techniques, long-term survivors still face an increased risk of treatment-related complications and late mortality.

To ensure that children are actively involved in decisions about their care and treatment, even when the disease progresses, pediatric advance care planning (pACP) initiatives are becoming increasingly important. These initiatives are valuable tools that help children express their wishes and preferences regarding care and treatment, which is crucial for their quality of life. pACP is a continuous process that facilitates discussions about various potential outcomes of disease progression. It should be individualized, taking into account the child's specific concerns and needs. Effective communication within the family plays an important role in this process, as it promotes better adaptation to the illness and strengthens family cohesion, ultimately enhancing the child's quality of life. Difficulties in communication, such as parents and children trying to protect each other from challenging or uncomfortable conversations about treatment and prognosis, can have negative psychological consequences for both the parents and the child. This may occur even when the prognosis is relatively favorable.

While several pACP programs exist, many primarily focus on specifying end-of-life care preferences, such as the family-centered pediatric advance care planning (FACE) program, or on training healthcare professionals, with less emphasis on actively engaging adolescents and parents. For the BOOST pACP intervention, we chose to use the Implementing Pediatric Advance Care Planning Toolkit (IMPACT) as a foundation, as it offers a more holistic approach that can be effectively integrated early in the treatment trajectory of childhood cancer. However, there is a lack of evidence from randomized controlled trials (RCTs) on the effectiveness of such holistic pACP programs, highlighting the need for an RCT to evaluate the BOOST pACP (**B**enefits of **O**btaining **O**wnership **S**ystematically **T**ogether in **p**ediatric **A**dvance **C**are **P**lanning) intervention.

The BOOST pACP intervention was designed using the Theory of Planned Behavior (TPB). Although the TPB is commonly used in health promotion research, to our knowledge, it has not yet been applied to the development and evaluation of a pACP intervention. In addition to this gap, this dissertation addresses several other pertinent gaps in the knowledge of pACP for adolescents with cancer and their parents. To better align communication about illness and health with the developmental levels of children, which would benefit pACP initiatives, we have compiled an overview of characteristic factors within different developmental stages of children, as well as factors influencing child development in the context of serious illness. Given the significant challenges we faced in recruiting adolescents for our BOOST pACP trial, we also explored recruitment and retention strategies used in other RCTs of psychosocial studies within the pediatric oncology setting.

Study objectives and research questions

The first objective of this dissertation is to develop a pACP intervention for adolescents with cancer and their parents and to describe the protocol of a randomized controlled trial on the evaluation of this intervention. The following specific research questions will be answered:

1. What are the potential intervention components and current barriers and facilitators for ACP in the context of pediatric oncology?
2. What is the pathway through which the pACP intervention is likely to achieve change, including the selection of proximal and distal outcomes and the required intervention components?
3. How acceptable and feasible are the intervention components and materials for adolescents with cancer, their parents, and healthcare professionals?
4. What is the design, methodology, and procedure for conducting the trial?

The second objective is to test the effectiveness of the BOOST pACP intervention in a multicenter randomized controlled trial (RCT), addressing the following research questions:

5. What is the effect of the BOOST pACP intervention compared to care as usual on parent-adolescent communication?
6. What is the effect of the BOOST pACP intervention compared to care as usual on parents' and adolescents' attitudes towards and self-efficacy in discussing ACP topics with each other?
7. What is the effect of the developed intervention compared to care as usual on the behavior and intention of parents, adolescents and pediatric oncologists to discuss ACP topics with each other?

The third objective is to provide insights for future interventions on how to further develop tailored interventions aimed at optimizing communication and care for children with various serious illnesses and how to improve the feasibility and quality of RCTs in pediatric populations. Two separate studies addressed the following research questions:

8. Which prevailing theories and constructs concerning the ongoing development of children with serious illness are identified?
9. What typical developmental aspects are observed in children with serious illness and what factors influence ongoing development?
10. What are the experienced recruitment and retention challenges, and strategies to overcome them, from psychosocial intervention studies conducted among children with cancer and their parent(s)?

Methods

To address the research questions of this dissertation, various data collection methods were used. We first described the development process of the pACP intervention and designed a research protocol detailing the trial (**Chapters 1 and 2**). A randomized controlled trial was conducted across four Belgian university hospitals to assess the effects of the BOOST pACP intervention on primary (parent-adolescent communication) and secondary outcomes (attitude, self-efficacy, behavior, and intention) (**Chapter 3 and 4**). Additionally, we explored factors influencing child development in serious illness (**Chapter 5**) and summarized the experiences, challenges, and strategies for conducting RCTs in psychosocial interventions for

children with cancer and their parents (**Chapter 6**). The methods for each study are briefly described in the following paragraphs.

Study 1: Development of the BOOST pACP intervention (research questions 1-4)

A comprehensive iterative approach was used to develop and test the pACP intervention, existing of five steps:

1. Interviews with pediatric oncologists (n=4), psychologists (n=2), and nurses (n=5) working in pediatric oncology on using ACP and experienced challenges.
2. A literature search to identify existing components from academic and grey literature.
3. Development of a logic model using the Theory of Planned Behavior (TPB) through iterative discussions with the core research team (n=6).
4. Identification of core components and collection of feedback from an international advisory group (n=11), psychologists (n=8), members of the Pediatric Palliative Care Research Network (PPCRN), and researchers (n=2) to create intervention prototypes.
5. Interviews with adolescents with cancer (n=4), parents (n=6), and healthcare professionals (n=9) to evaluate acceptability and testing the feasibility with 3 families.

Study 2: Conducting the BOOST trial (research questions 5 – 7)

We conducted a multi-center, parallel-group superiority trial across four Belgian university hospitals, comparing the BOOST pACP intervention to usual care. Trained external facilitators conducted pACP conversations with families in various settings. Patient recruitment took place from March 2021 to March 2023. Outcomes were assessed at baseline, 3 months, and 7 months, focusing on adolescents, parents, and pediatric oncologists. The primary outcome was parent-adolescent communication from the perspective of the adolescent, evaluated using the Parent-Adolescent Communication Scale (PACS). Secondary outcomes included anxiety levels, attitudes, self-efficacy, behavior and the intention to discuss ACP topics, measured through a self-developed questionnaire based on the Theory of Planned Behavior (TPB). Our primary analysis adhered to the intention-to-treat principle, and data analysis was performed using linear mixed models. Secondary analysis involved exploratory factor analysis and sum scores.

Study 3: Characteristics of child development in the context of serious illness (research questions 8-9)

A scoping review was conducted following Arksey and O'Malley's methods and the Joanna Briggs Institute's guidelines. A structured search in Medline, Embase, Psycinfo, and CINAHL used keywords like serious illness, child, communication, and theory, including articles up to October 2022. Thematic analysis identified key elements of child development and influencing factors.

Study 4: Experienced recruitment and retention challenges and strategies (research question 10)

We conducted a collective case study involving online semi-structured interviews with principal investigators and research staff from recent or ongoing trials of psychosocial interventions for children/adolescents with cancer and their parents (n=7). The cases were identified through

PubMed and trial registries. The interviews, each lasting about 60 minutes, were held in March and April 2022 and focused on the challenges and strategies experienced during eligibility screening, enrollment, and retention. The interviews were analyzed using both deductive and inductive thematic analysis.

Main findings of this dissertation

Development of the BOOST pACP intervention (Chapter 1)

During the iterative development of the BOOST pACP intervention, adolescent (ex)patients, parents, healthcare professionals, and pACP experts were actively involved. Challenges highlighted by healthcare professionals were mainly system-, attitude-, or parent-related, showing that ACP is complex and influenced by more than just healthcare professionals' behavior. Our literature review identified the Implementing Pediatric Advance Care Planning Toolkit (IMPACT) as most aligned with our findings. Using the Theory of Planned Behavior (TPB) to develop a logic model, we identified the primary aim of BOOST pACP as improving parent-adolescent communication on ACP topics. Secondary goals include increasing self-efficacy, positive attitudes, intention, and behavior towards engaging in these discussions. The final intervention included these components: facilitator training, preparation booklets, testimonial videos, four structured conversations, a summary sheet, conversation cards and information transfer to the pediatric oncologist. The BOOST pACP intervention was found suitable for adolescents aged 10 to 18 years by pACP experts, healthcare professionals, adolescent (ex) patients and parents. Based on their feedback, components were changed, deleted, and added, and formulation of topics and associated questions were amended to enhance acceptability. The BOOST pACP intervention was found to be feasible.

The protocol for a randomized controlled trial on the evaluation of the BOOST pACP intervention (Chapter 2)

To evaluate the effectiveness of the BOOST pACP intervention, we have set up a multi-center parallel-group randomized controlled superiority trial with embedded mixed-methods process evaluation in Flanders, Belgium. All families were randomized with an allocation 1:1 to receive care as usual or the multicomponent BOOST pACP intervention. Inclusion criteria of the adolescents were: aged between 10 – 18 years, diagnosed with any type of cancer at any stage, currently receiving (active) oncology treatment, and with a life expectancy of more than 3 months. The primary endpoint was improved parent-adolescent communication from the perspective of the adolescent (measured by the Parent-Adolescent Communication Scale). Secondary endpoints were adolescents' and parents' attitudes, self-efficacy, intention and behavior regarding discussing ACP topics with each other and with the pediatric oncologist (self-developed items). Adolescents' and parents' anxiety in the past week was included as safety measure (PROMIS Anxiety). Clinical information was retrieved from the pediatric oncologist. Outcomes were measured at baseline (T0), 3 months after baseline, shortly after the BOOST pACP intervention has been completed, and 7 months after baseline (T2).

Effectiveness of the BOOST pACP intervention on the primary outcome (Chapter 3)

We enrolled 49 families into the BOOST pACP trial. Families were randomized to the BOOST pACP intervention (n=24) or the control group who received care as usual (n=25).

Parent-adolescent communication from the perspective of the adolescent did not show a significant difference between the BOOST pACP group and control group at 3 months (T1) (baseline-adjusted mean difference [MD]: 1.4; 95% CI -4.1 to 6.9; $p=0.608$), with an effect size of 0.13. At 7 months (T2), the estimated mean change from baseline was 5.2 points higher in the BOOST group compared to the control group (95% CI -0.6 to 11.0; $p=0.077$), with an effect size of 0.49.

In the two subgroup analyses, which only included observations of adolescents regarding communication with their mothers and fathers, the results were as follows: for mother-adolescent communication, the baseline-adjusted mean difference was 1.6 at T1 (95% CI -3.5 to 6.8; $p=0.527$), with an effect size of 0.17 and 3.0 at T2 (95% CI -2.5 to 8.5; $p=0.279$) with an effect size of 0.31. For father-adolescent communication, the baseline-adjusted mean difference was 0.6 at T1 (95% CI -5.6 to 6.8; $p=0.848$) with an effect size of 0.05 and 7.8 at T2 (95% CI 1.3 to 14.3; $p=0.019$) with an effect size of 0.67. In both cases, the estimated mean changes favored the BOOST group.

No adverse events were reported from the intervention. In adolescents, anxiety levels favored the BOOST group at T1 (MD: -4.5; 95% CI: -10.3 to 1.3) and T2 (MD: -2.0; 95% CI: -8.2 to 4.1). In parents, anxiety levels also favored the BOOST group at T1 (MD: -0.5; 95% CI: -5.8 to 4.8) and T2 (MD: -1.1; 95% CI: -6.9 to 4.7).

A conditional power analysis showed that if we would have continued to recruit patients until 96 patients were randomized (as initially intended), assuming that the data to be observed in the remainder of the study would follow the effect estimated from the current data (effect size 0.489), we would have had 66% power to detect a mean difference in change from baseline at T2 for parent-adolescent communication.

Effectiveness of the BOOST pACP intervention on the secondary outcomes (Chapter 4)

The BOOST pACP intervention showed limited effectiveness in altering behavioral determinants related to ACP communication. At 3 months (T1), there was a significant decrease in fathers' negative attitudes towards discussing care and treatment with their child (baseline-adjusted mean difference [MD]: -0.57; 95% CI -1.10 to -0.03, $p=0.038$; effect size = -0.67), and an increase in mothers' intentions to discuss end-of-life care-oriented ACP (MD: 1.0; 95% CI 0.1 to 1.9; $p=0.037$; effect size = 0.85). Adolescents in the BOOST group reported a significant reduction in the number of value- and emotion-oriented ACP topics they intended to discuss with their pediatric oncologist at 7 months (T2) (MD: -2.1; 95% CI -3.6 to -0.6; $p=0.008$; effect size = -0.72). There was also a significant reduction in the number of end-of-life care-oriented ACP topics they intended to discuss with their pediatric oncologist at both T1 (MD: -0.6; 95% CI -1.2 to -0.1; $p=0.029$; effect size = -1.04) and at T2 (MD: -0.8; 95% CI -1.4 to -0.2; $p=0.012$; effect size = -0.97). There were no significant effects on self-efficacy in discussing ACP topics for either adolescents or parents.

Characteristics of child development in the context of serious illness: a scoping review (Chapter 5)

Out of 11,246 articles, 24 were selected for review. Piaget's theory of cognitive development emerged as the most prevalent theory on child development. The review identified various

factors typical of the development of seriously ill children across different age groups: early to middle childhood, early adolescence, and middle to late adolescence. Key themes included: 1) psychological/emotional aspects (e.g., worries about relapse in adolescence); 2) cognitive aspects (e.g., a focus on the present in early adolescence); 3) social aspects (e.g., self-centeredness in early to middle childhood); 4) coping strategies (e.g., a shift from behavioral to cognitive and emotional strategies as children age); 5) conceptualization of illness (e.g., time distortion in early adolescence); 6) understanding of death (e.g., grasping the universality of death in adolescence); and 7) communication about illness (e.g., difficulty in recognizing and expressing symptoms in younger children). The review also identified factors that accelerate development (e.g., cortical maturation, prior medical experience, social interactions with adults) and factors that decelerate it (e.g., stress, hospital admissions, avoidance of illness-related communication in families).

Recruitment and retention challenges and strategies in randomized controlled trials of psychosocial interventions for children with cancer and their parents (Chapter 6)

Nine studies were identified by our literature search, with investigators and staff from seven of these studies participating in interviews. Challenges and strategies across three major themes were addressed: eligibility, enrollment, and retention. Key challenges included the need to involve multiple sites to increase the pool of eligible participants, high staff turnover within research teams, overestimating participants' willingness to engage due to the high burden on this population, the dyadic nature of enrollment, and balancing adherence to protocol timelines with the need for flexibility. Strategies for addressing eligibility challenges included collaborating closely with healthcare professionals and involving them early in the study planning. To optimize enrollment and retention, important strategies were being flexible, training research staff, aligning with participants' situations, and maintaining consistent contact between research staff and families. General strategies highlighted the importance of conducting a pilot study with the target group beforehand, having a plan in place for adjusting recruitment strategies, considering different scenarios, and exploring alternative recruitment sources beyond hospitals, such as social media. All studies followed a stepped process in recruitment, indicating that several visits were done to include a family.

Interpretation and discussion of findings

This dissertation has gathered insights on the development and evaluation of the BOOST pACP intervention and provided guidance for future interventions aimed at optimizing care and communication for children with serious illnesses. Additionally, from a methodological perspective, it has explored recruitment challenges and strategies, drawing on expertise from multiple RCTs of psychosocial interventions in the pediatric oncology setting.

Comparing the results with other trials in a similar target population

The results on effectiveness of the BOOST pACP intervention on parent-adolescent communication should be interpreted cautiously due to the study's underpowered nature. Parent-adolescent communication has not been previously assessed as an outcome of a pACP intervention, making direct comparisons with other interventions challenging. The effect size of the BOOST pACP intervention on overall parent-adolescent communication was 0.13 at 3 months (T1) and 0.49 at 7 months (T2). At T2 0.31 for mother-adolescent communication and 0.67 on father-adolescent communication specifically. This is higher compared to the effect sizes of a web-based legacy-making intervention for children with advanced cancer (ages 7 – 17): 0.10 for mother-child communication and 0.20 for father-child communication (not significant), although they included a higher number of participants. The effect size on 'family environment' of a therapeutic music video on adolescents and young adults (AYA) (ages 11 – 24) who underwent high-risk cancer treatment was 0.66 at their second timepoint, and was statistically significant. Parent-adolescent communication was only part of this latent variable though. For the parallel intervention for parents, no statistically significant findings were found on parent-adolescent communication, with low effect sizes. Thus, parent-adolescent communication, as measured by the PACS, has not been extensively studied as an outcome of other interventions in a similar setting either and results suggest that it is not an easy variable to influence. The only other pACP trial analyzing the effectiveness of FACE-TC analyzed different outcomes. They found the following statistically significant outcomes: higher overall congruence on end-of-life care preferences in four cancer-specific situations, sustained families' knowledge of their adolescents' end-of-life treatment preferences for one year, and families' positive caregiving appraisals (effect size 0.17) and satisfaction. They did not find statistically significant outcomes on caregiver strain, caregiver distress or family well-being.

Potential explanations of the lack of significant findings in the BOOST pACP trial

The BOOST pACP trial did not show a significant effect on the primary endpoint—parent-adolescent communication measured by the Parent-Adolescent Communication Scale (PACS) at 3 months post-baseline. While there were some significant findings regarding attitude and intention, other anticipated outcomes were not observed. Although the underpowered sample size may be a fundamental reason, it is necessary to explore other possible contributing factors.

1. The measurement instrument may not have been appropriate

The measurement instrument on the behavioral determinants, grounded in the Theory of Planned Behavior (TPB), might not fully capture the qualitative nuances of ACP, such as the depth and quality of communication. Additionally, it may have lacked the sensitivity needed to detect subtle but critical shifts in behavioral determinants essential for ACP.

2. *The application of behavioral change models to advance care planning interventions involves some limitations*

- Limitations of the Theory of Planned Behavior (TPB): Our intervention was based on the TPB, which conceptualizes ACP behavior as an individual action. However, other influential processes – such as unconscious, circumstantial, or environmental factors – may play a significant role in influencing the behavior of discussing ACP topics, processes that the TPB does not account for and that we have therefore not been able to capture.
- Motivation and behavior change: Theory-based behavioral interventions are often criticized for targeting only those who are already motivated to change. The BOOST pACP intervention may have lacked sufficient use of techniques like motivational interviewing and specific behavior change techniques (BCTs) such as goal setting, action planning, or implementation intentions, which could have more effectively addressed self-efficacy.
- Automatic, non-conscious behaviors: these are difficult to change without strong motivation or clear perceived benefits, making it essential to structure the environment to discourage undesired behaviors. While the BOOST pACP intervention aimed to create a safe space for discussing ACP topics, additional strategies like planning, self-monitoring, and self-reinforcement may be necessary to achieve sustained behavior change.

A general limitation of using behavior models is that they can oversimplify complex human behaviors and interactions, reducing them to basic determinants that may not fully capture the nuanced nature of ACP discussions, which involve deep personal values, emotions, and intricate family dynamics. However, research has emphasized the relevance for using behavioral change models in ACP research. In our context, the TPB appeared to be a suitable foundation for our objective of enhancing ACP communication between parents and adolescents.

3. *The timeframe of the BOOST pACP study might have been too short*

Although immediate effects were limited, the BOOST pACP intervention showed more promise in the longer term (effect size of 0.49). Finding an increase over time, as seen in the BOOST pACP study, rather than a decrease in parent-adolescent communication may indicate that it takes time for new attitudes and learned skills to be integrated into communication.

4. *The broader adolescent cancer population may not be ideally suited for this type of ACP*

The goal of ACP is to align care with an adolescent's values and preferences. For adolescents with cancer, with a good prognosis and straightforward treatment, discussing scenarios like “*what if the treatment fails*” may not be immediately necessary or beneficial. In contrast, these topics may be more pertinent for families dealing with complex chronic conditions, characterized by a heterogeneous diagnosis, high healthcare utilization, reliance on medical technology, and a significant risk of morbidity and mortality. Advances in cancer treatment have led to longer survival rates and more unpredictable disease trajectories, complicating the timing of these conversations. Since the appropriate timing for ACP discussions varies among

individuals and is also dependent a child's individual development, establishing standardized criteria is challenging. Therefore, ACP should be **flexible and regular**, allowing for natural progression towards more serious discussions **tailored to the development** of the adolescent and as the situation warrants.

Recommendations

To better support adolescents with cancer and their parents in terms of pACP and communication, several recommendation are proposed in three domains: practice, policy and future research.

Recommendations for practice

- Address the importance of parent-adolescent communication
- Integrate holistic and flexible pACP in the treatment trajectory via:
 - Training and designating “care planners” to each family
 - Adopting a holistic and flexible care planning approach by integrating ACP into the overarching goal of delivering high-quality psychosocial care. Different roles the care planner can take on:
 - Facilitate family communication
 - Assess and strengthen family resilience
 - Bridge the gap between the hospital and daily life by facilitating connections with other support systems and helping to navigate the healthcare landscape
 - Discuss current and future care and treatment, with a focus on potential disease progression (ACP)
 - Communicate relevant information to the treating healthcare professionals

Recommendations for policy

- Reduce barriers to father involvement in caregiving of their ill child
- Provide time and resources for healthcare professionals to facilitate early and holistic implementation of pACP
- Build awareness and empowerment in adolescents with serious illnesses in ACP through coordinated communication efforts
- Establish guidelines on providing incentives for families to participate in psychosocial research

Recommendations for future research

- Identify who benefits most from pACP discussions by:
 - Comparing the content of ACP conversations in relation to factors such as estimated prognosis, line of treatment, and the presence of metastases
 - Conducting qualitative interviews to understand how ACP discussions impact the adolescents' psychological and emotional status and how they benefit
 - Applying a SMART (Sequential Multiple Assignment Randomized Trial) to develop adaptive interventions by empirically testing which strategies are most effective under different strategies
- Include a focus on non-native-speaking families
- Integrate developmental stages in the design of pACP interventions and standardize monitoring of child development

- Customize recruitment and retention strategies for studies involving pediatric populations, and evaluate which strategies are most effective for improving these outcomes by:
 - Engaging the target group early
 - Extensive training of data collectors
 - Piloting the study
 - Implementing SWATs (Studies Within A Trial)
- Perform mixed-methods meta-analyses on pACP

NEDERLANDSE SAMENVATTING

Algemene inleiding

Kinderkanker verschilt van kanker bij volwassenen wat betreft soorten en behandeling. Hoewel de overlevingskansen aanzienlijk zijn verbeterd door vooruitgang in het begrip van de ziekte, diagnostische methoden, ontwikkelingen in medicatie en chirurgische en radiotherapeutische technieken, lopen kinderen die kanker overleven nog steeds een verhoogd risico op complicaties die door de behandeling zijn veroorzaakt en ook op sterfte op langere termijn.

Om te zorgen dat kinderen actief betrokken worden bij beslissingen over hun zorg en behandeling, ook wanneer de ziekte vordert, worden pediatrische advance care planning (pACP)-initiatieven steeds belangrijker. Deze initiatieven zijn waardevolle instrumenten die kinderen helpen hun wensen en voorkeuren rond zorg en behandeling kenbaar te maken, wat belangrijk is voor hun kwaliteit van leven. pACP is een doorlopend proces dat het gesprek over verschillende mogelijke uitkomsten van ziekteprogressie vergemakkelijkt. Het moet op het individu gericht zijn, waarbij rekening wordt gehouden met de persoonlijke zorgen en behoeften van het kind. Goede communicatie binnen het gezin speelt hierbij een cruciale rol, omdat het helpt bij het bevorderen van een betere aanpassing aan de ziekte en het versterken van de gezinscohesie met als gevolg betere kwaliteit van leven van het kind. Moeilijkheden in de communicatie, bijvoorbeeld omdat ouders en kind elkaar willen beschermen tegen moeilijke of ongemakkelijke gesprekken over behandeling en prognose, kunnen negatieve psychologische gevolgen hebben voor zowel de ouders als het kind. Dit kan zelfs het geval zijn als de prognose relatief gunstig is.

Hoewel er verschillende pACP programma's bestaan, richten ze zich voornamelijk ofwel op het specificeren van voorkeuren voor zorg aan het einde van het leven - zoals het Family-Centered Pediatric Advance Care Planning (FACE)-programma-, ofwel op het trainen van zorgverleners. Er wordt doorgaans minder aandacht besteed aan het actief betrekken van de adolescenten en ouders. Voor de BOOST pACP-interventie die in deze dissertatie centraal staat, kozen we ervoor om de Implementing Pediatric Advance Care Planning Toolkit (IMPACT) als basis te gebruiken, omdat deze een meer holistische benadering biedt die vroeg in het behandeltraject van een ziekte effectief kan worden geïntegreerd. Er is echter een gebrek aan bewijs uit gerandomiseerde gecontroleerde onderzoeken (RCT's) over de effectiviteit van dergelijke holistische pACP-programma's. Dit onderstreept de noodzaak van een RCT om de BOOST pACP (**B**enefits of **O**btaining **O**wnership **S**ystematically **T**ogether in **p**ediatric **A**dvance **C**are **P**lanning)-interventie te evalueren.

De BOOST pACP-interventie werd ontworpen met behulp van de Theory of Planned Behavior (TPB). Hoewel de TPB vaak wordt gebruikt in onderzoek rond gezondheidsbevordering, is deze voor zover wij weten nog niet toegepast op de ontwikkeling en evaluatie van een pACP-interventie. Daarnaast richt deze dissertatie zich ook op verschillende andere relevante lacunes in de kennis over pACP voor adolescenten met kanker en hun ouders. Om de communicatie over ziekte en gezondheid beter af te stemmen op de ontwikkelingsniveaus van kinderen, zoals pACP nastreeft, hebben we een overzicht opgesteld van kenmerkende factoren binnen verschillende ontwikkelingsfasen van kinderen, evenals van factoren die de ontwikkeling in de context van ernstige ziekte kunnen beïnvloeden. Bij het includeren van gezinnen in onze BOOST pACP-studie, hebben we zekere uitdagingen ondervonden. Naar aanleiding daarvan hebben we de strategieën voor het rekruteren en retentie van gezinnen in andere RCT's van psychosociale studies binnen de pediatrische oncologie verkend.

Doelstellingen en onderzoeksvragen

Deze dissertatie heeft drie doelstellingen. Het primaire doel van deze dissertatie is om een pediatrische advance care planning (pACP) interventie voor adolescenten met kanker en hun ouders te ontwikkelen en het protocol voor een gerandomiseerde gecontroleerde trial (RCT) te beschrijven ter evaluatie van deze interventie. De specifieke onderzoeksvragen die zullen worden behandeld zijn:

1. Wat zijn de potentiële componenten van de interventie en de huidige barrières en bevorderende factoren voor ACP in de context van pediatrische oncologie?
2. Op welke manieren zou de pACP-interventie verandering teweeg moeten brengen? Wat zijn de proximale en distale uitkomsten en de noodzakelijke interventiecomponenten?
3. Hoe acceptabel en haalbaar zijn de interventiecomponenten en -materialen voor adolescenten met kanker, hun ouders en zorgverleners?
4. Wat is het design, de methodologie en het protocol voor het uitvoeren van de trial?

De tweede doelstelling is om de effectiviteit van de BOOST pACP-interventie te testen door middel van multicenter gerandomiseerde gecontroleerde trial (RCT), met de volgende onderzoeksvragen:

5. Wat is het effect van de BOOST pACP-interventie vergeleken met gebruikelijke zorg op de communicatie tussen ouders en adolescenten?
6. Wat is het effect van de BOOST pACP-interventie vergeleken met gebruikelijke zorg op de houding en zelfeffectiviteit van ouders en adolescenten bij het bespreken van pACP-onderwerpen met elkaar?
7. Wat is het effect van de BOOST pACP-interventie vergeleken met gebruikelijke zorg op het gedrag en de intenties van ouders, adolescenten en kinderoncologen met betrekking tot het bespreken van pACP-onderwerpen?

De derde doelstelling is om inzichten te verschaffen voor toekomstige interventies over hoe communicatie en zorg voor kinderen met ernstige ziekten te optimaliseren, en om de haalbaarheid en kwaliteit van RCT's in pediatrische populaties te verbeteren. Dit doel wordt nagestreefd door middel van twee afzonderlijke studies, die de volgende onderzoeksvragen beantwoorden:

8. Welke theorieën en constructen met betrekking tot de ontwikkeling van kinderen met ernstige ziekten worden aangehaald?
9. Welke typische ontwikkelingsaspecten worden waargenomen bij kinderen met ernstige ziekten en welke factoren beïnvloeden hun ontwikkeling?
10. Wat zijn de uitdagingen die ervaren worden rond rekrutering en retentie, en wat zijn de strategieën om daarmee om te gaan in psychosociale interventiestudies met kinderen met kanker en hun ouders?

Methoden

Om de onderzoeksvragen van deze dissertatie te beantwoorden, werden verschillende datacollectie-methoden gebruikt. Eerst werd het ontwikkelingsproces van de pACP-interventie beschreven en werd een protocol van de trial uiteengezet (**Hoofdstukken 1 en 2**). Er werd een RCT uitgevoerd in vier Belgische universitaire ziekenhuizen om de effecten van de BOOST pACP-interventie op primaire (ouder-kind communicatie) en secundaire uitkomsten (houding, zelfeffectiviteit, intentie, en gedrag) te beoordelen (**Hoofdstukken 3 en**

4). Daarnaast verkenden we typische kenmerken van de ontwikkeling van kinderen en factoren die de ontwikkeling beïnvloeden in de context van ernstige ziekte (**Hoofdstuk 5**), en verzamelden we de uitdagingen en strategieën rond rekrutering en retentie in RCT's van psychosociale interventies voor kinderen met kanker en hun ouders (**Hoofdstuk 6**). De methoden voor deze studies worden kort beschreven in de volgende alinea's.

Studie 1: Ontwikkeling van de BOOST pACP interventie (onderzoeksvragen 1 – 4)

Een uitgebreide iteratieve aanpak werd gebruikt om de pACP-interventie te ontwikkelen en te testen, bestaande uit vijf stappen:

1. Interviews met kinderoncologen (n=4), psychologen (n=2) en verpleegkundigen (n=5) die werken in de kinderoncologie, over het gebruik van ACP en de ervaring uitdagingen.
2. Een literatuuronderzoek om bestaande componenten uit academische en grijze literatuur te identificeren.
3. Ontwikkeling van een logisch model met behulp van de Theory of Planned Behavior (TPB) door middel van iteratieve discussies met het kernonderzoeksteam (n=6).
4. Identificatie van kerncomponenten en verzameling van feedback van een internationale adviesgroep (n=11), psychologen (n=8), leden van het Pediatric Palliative Care Research Network (PPCRN) en onderzoekers (n=2) om prototypes van de interventie te ontwikkelen.
5. Interviews met adolescenten met kanker (n=4), ouders (n=6) en zorgverleners (n=9) om de acceptatie te evalueren. De haalbaarheid van de kerncomponenten werd getest bij 3 gezinnen.

Studie 2: Uitvoering van de BOOST trial (onderzoeksvragen 5 – 7)

We voerden een multicenter, parallel-groep superioriteitstrial uit in vier Belgische universitaire ziekenhuizen, waarbij de BOOST pACP-interventie werd vergeleken met gebruikelijke zorg. Getrainde externe facilitators voerden pACP-gesprekken met gezinnen. De rekrutering van patiënten vond plaats van maart 2021 tot maart 2023. Adolescenten, ouders en kinderoncologen vulden vragenlijsten in bij aanvang, na 3 maanden en na 7 maanden. De primaire uitkomst was de communicatie tussen ouders en adolescenten (vanuit het perspectief van de adolescent), geëvalueerd met de Parent-Adolescent Communication Scale (PACS). Secundaire uitkomsten zijn: angst niveaus (gemeten met de PROMIS Anxiety), en attitudes, zelfeffectiviteit, intentie en gedrag om ACP-onderwerpen te bespreken, gemeten met een zelfontwikkelde vragenlijst gebaseerd op de Theory of Planned Behavior (TPB). Onze primaire analyse volgde het intention-to-treat-principe, en lineaire gemengde modellen werden uitgevoerd om de effectiviteit van de BOOST pACP-interventie te testen. Secundaire analyse omvatte verkennende factoranalyse en som-scores.

Studie 3: kenmerkende factoren van verschillende ontwikkelingsfasen van kinderen en factoren die de ontwikkeling van kinderen met een ernstige ziekte kunnen beïnvloeden (onderzoeksvragen 8 – 9)

We voerden een scoping review uit volgens de methoden van Arksey en O'Malley en de richtlijnen van het Joanna Briggs Institute. Een gestructureerde zoekopdracht in Medline, Embase, Psychinfo en CINAHL met zoektermen zoals 'ernstige ziekte', 'kind', 'communicatie' en 'theorie' werd gebruikt, en omvatte artikelen tot oktober 2022. Met thematische analyse

identificeerden we belangrijke elementen van de ontwikkeling van kinderen en beïnvloedende factoren.

Studie 4: Ervaringen met rekruterings- en retentie-uitdagingen en strategieën (onderzoeksvraag 10)

We voerden een 'collective case study' uit, waarbij online semigestructureerde interviews werden gehouden met hoofdonderzoekers en data collectoren van recente of lopende trials van psychosociale interventies voor kinderen / adolescenten met kanker en hun ouders (n=7). De trials (cases) werden geïdentificeerd via PubMed en trial registers. De interviews van ongeveer een uur lang, vonden plaats in maart en april 2022 en richtten zich op de uitdagingen en strategieën die werden ervaren tijdens de 'eligibility screening', rekrutering en retentie. De interviews werden geanalyseerd via zowel deductieve als inductieve thematische analyse.

Belangrijkste bevindingen van dit proefschrift

Ontwikkeling van de BOOST pACP-interventie (Hoofdstuk 1)

Tijdens de iteratieve ontwikkeling van de BOOST pACP-interventie werden adolescente (ex)patiënten, ouders, zorgprofessionals en pACP-experts actief betrokken. De uitdagingen die zorgverleners ervaren waren voornamelijk systeem-, houding- of ouder-gerelateerd, wat laat zien dat ACP complex is en door meer dan alleen het gedrag van zorgverleners wordt beïnvloed. Via onze literatuurstudie, identificeerden we de Implementing Pediatric Advance Care Planning (IMPACT) als het meest overeenkomend met onze bevindingen en gedachtegoed over wat pACP moest nastreven. We maakten gebruik van de Theory of Planned Behavior (TPB) om een logisch model te ontwikkelen, en identificeerden als primaire doel van de BOOST pACP-interventie: het verbeteren van de communicatie tussen ouders en adolescenten over ACP-onderwerpen. Secundaire doelen zijn onder meer het vergroten van de zelfeffectiviteit, positieve houdingen, intentie en gedrag ten aanzien van het aangaan van ACP gesprekken. De uiteindelijke interventie bestaat uit de volgende componenten: training van gespreksondersteuners, voorbereidingsboekjes, videos met getuigenissen van gezinnen, vier gestructureerde gesprekken, een samenvattingsformulier, gesprekskaarten en informatieoverdracht aan de kinderoncoloog. De BOOST pACP-interventie werd geschikt bevonden voor adolescenten van 10 tot en met 18 jaar door pACP-experts, zorgprofessionals, adolescente (ex)patiënten en ouders. Op basis van hun feedback werd de inhoud en vormgeving van componenten aangepast, en werden formuleringen van onderwerpen en bijbehorende vragen gewijzigd om de acceptatie te verbeteren. De BOOST pACP-interventie werd haalbaar bevonden.

Het protocol voor een gerandomiseerde gecontroleerde studie om de BOOST pACP-interventie te evalueren (Hoofdstuk 2)

Om de effectiviteit van de BOOST pACP-interventie te evalueren, hebben we een multi-center gerandomiseerde gecontroleerde superioriteitsstudie opgezet met ingebedde mixed-methods procesevaluatie in Vlaanderen, België. Alle gezinnen werden gerandomiseerd met een allocatie van 1:1 om ofwel gebruikelijke zorg te ontvangen, of de multicomponent BOOST pACP-interventie. Inclusiecriteria voor de adolescenten waren: leeftijd tussen de 10 en 18

jaar, diagnose van welke vorm van kanker dan ook in elk stadium, momenteel in (actieve) oncologische behandeling, en een levensverwachting van meer dan 3 maanden. De primaire uitkomstmaat was verbeterde communicatie tussen ouder en adolescent vanuit het perspectief van de adolescent (gemeten met de Parent-Adolescent Communication Scale). Secundaire uitkomstmaten waren de houding, zelfeffectiviteit, de intentie en het gedrag van adolescenten en ouders met betrekking tot het bespreken van ACP-onderwerpen met elkaar en de kinderoncoloog (zelfontwikkelde items). Angst van adolescenten en ouders werd opgenomen als 'safety measure', om te monitoren of de BOOST pACP-interventie schadelijke effecten zou hebben (PROMIS Anxiety). Klinische informatie werd verkregen van de kinderoncoloog. Uitkomsten werden gemeten bij aanvang van het onderzoek (T0), 3 maanden na aanvang (kort nadat de BOOST pACP-interventie was doorlopen), en 7 maanden na aanvang (T2).

Effectiviteit van de BOOST pACP-interventie op de primaire uitkomst (Hoofdstuk 3)

49 gezinnen namen deel aan de BOOST pACP-studie. De gezinnen werden gerandomiseerd naar de BOOST pACP-interventie (n=24) of de controlegroep die gebruikelijke zorg ontving (n=25).

De communicatie tussen ouder en adolescent vanuit het perspectief van de adolescent vertoonde na 3 maanden (T1) geen significant verschil tussen de BOOST pACP-groep en de controlegroep (baseline-gecorrigeerd gemiddeld verschil [MD]: 1.4; 95% CI -4.1 tot 6.9; p=0.608), met een effectgrootte van 0.13. Dit niet-significante verschil bleef bestaan na 7 maanden (T2), met een geschatte gemiddelde verandering ten opzichte van de baseline 5.2 punten hoger in de BOOST-groep (95% CI -0.6 tot 11.0; p=0.077), met een effectgrootte van 0.49.

In de twee subgroep analyses, die alleen observaties van adolescenten met betrekking tot communicatie met hun moeders en vaders omvatten, waren de resultaten als volgt: voor moeder-adolescent communicatie was het baseline-gecorrigeerde gemiddelde verschil 1.6 op T1 (95% CI -3.5 tot 6.8; p=0.527), met een effect grootte van 0.17, en 3.0 op T2 (95% CI -2.5 tot 8.5; p=0.279) met een effectgrootte van 0.31. Voor vader-adolescent communicatie was het baseline-gecorrigeerde gemiddelde verschil 0.6 op T1 (95% CI -5.6 tot 6.8; p=0.848) met een effectgrootte van 0.05, en een significant verschil van 7.8 op T2 (95% CI 1.3 tot 14.3; p=0.019) met een effectgrootte van 0.67. In zowel moeder- als vader-adolescent communicatie, waren de geschatte gemiddelde veranderingen gunstiger voor de BOOST groep.

Er werden geen ongewenste voorvallen gemeld als gevolg van de interventie. Bij adolescenten waren de angstniveaus gunstiger voor de BOOST-groep op T1 (MD: -4.5; 95% CI: -10.3 tot 1.3) en T2 (MD: -2.0; 95% CI: -8.2 tot 4.1). Bij ouders waren de angstniveaus ook gunstiger voor de BOOST-groep op T1 (MD: -0.5; 95% CI: -5.8 tot 4.8) en T2 (MD: -1.1; 95% CI: -6.9 tot 4.7).

Een conditionele power-analyse liet zien dat als we zouden doorgaan met het rekruteren van patiënten totdat 96 patiënten werden gerandomiseerd (zoals aanvankelijk bedoeld), met de veronderstelling dat de te observeren gegevens in de rest van de studie het effect zouden volgen dat werd geschat op basis van de huidige gegevens (effectgrootte 0.489), we 66%

power zouden hebben gehad om een gemiddeld verschil in verandering ten opzichte van de baseline op T2 in ouder-adolescent communicatie te detecteren.

Effectiviteit van de BOOST pACP-interventie op de secundaire uitkomsten (Hoofdstuk 4)

De BOOST pACP-interventie toonde beperkte effectiviteit in het veranderen van gedragsdeterminanten met betrekking tot ACP-communicatie. Na 3 maanden (T1) was er een significante afname in de negatieve houding van vaders ten aanzien van het bespreken van zorg en behandeling met hun kind (baseline-gecorrigeerd gemiddeld verschil [MD]: -0,57; 95% CI -1,10 tot -0,03; $p=0.038$; effectgrootte = -0.67). Daarnaast was er een toename in de intentie van moeders om gesprekken over levenseindezorg-gerichte ACP te voeren (MD: 1.0; 95% CI 0.1 tot 1.9; $p=0.037$; effectgrootte = 0.85).

Adolescenten in de BOOST-groep rapporteerden een significante vermindering in het aantal waarde- en emotiegerichte ACP-onderwerpen die ze van plan waren te bespreken met hun kinderoncoloog na 7 maanden (T2) (MD: -2.1; 95% CI -3.6 tot -0.6; $p=0.008$; effectgrootte=-0.72). Er was ook een significante afname in het aantal levenseindezorg-gerichte ACP-onderwerpen die zij van plan waren te bespreken met hun kinderoncoloog, zowel op T1 (MD: -0.6; 95% CI -1.2 tot -0.1; $p=0.029$; effectgrootte = -1.04) als op T2 (MD: -0.8; 95% CI -1.4 tot -0.2; $p=0.012$; effectgrootte=-0.97). Er werden geen significante effecten gevonden op zelfeffectiviteit in het bespreken van ACP-onderwerpen voor zowel adolescenten als ouders.

Kenmerkende factoren van verschillende ontwikkelingsfasen van kinderen en factoren die de ontwikkeling van kinderen met een ernstige ziekte kunnen beïnvloeden: een scoping review (Hoofdstuk 5)

Van de 11246 artikelen werden er 24 geselecteerd voor de review. Piaget's theorie van cognitieve ontwikkeling kwam naar voren als de meest voorkomende theorie over de ontwikkeling van kinderen. De review identificeerde verschillende factoren die kenmerkend zijn voor de ontwikkeling van ernstig ziekte kinderen in verschillende leeftijdsgroepen: vroege tot middelbare kindertijd, vroege adolescentie en midden tot late adolescentie. Belangrijke thema's omvatten: 1) psychologische/emotionele aspecten (zoals zorgen over herval van de ziekte tijdens adolescentie fase); 2) cognitieve aspecten (zoals een focus op het heden in de vroege adolescentie); 2) sociale aspecten (zoals egocentrisme in de vroege kindertijd); 4) coping strategieën (zoals een verschuiving van gedragsmatige naar cognitieve en emotionele strategieën naarmate kinderen ouder worden); 5) conceptualisatie van ziekte (zoals weinig besef van de lange-termijn consequenties van de ziekte in de vroege adolescentie); 6) begrip van de dood (zoals het begrip van de universaliteit van de dood in de adolescentie); en 7) communicatie over ziekte (zoals moeite met het herkennen en uiten van symptomen bij jongere kinderen). De review identificeerde ook factoren die de ontwikkeling versnellen (zoals corticale rijping, eerdere medische ervaring, sociale interacties met volwassenen) en factoren die deze vertragen (zoals stress, ziekenhuisopnames, vermijding van ziekte gerelateerde communicatie binnen gezinnen).

Rekruterings- en retentie-uitdagingen en -strategieën in gerandomiseerde gecontroleerde trials van psychosociale interventies voor kinderen met kanker en hun ouders (Hoofdstuk 6)

We identificeerden negen studies door middel van onze literatuurstudie, waarvan de onderzoekers en data-collectoren van zeven studies deelnamen aan interviews. Uitdagingen

en strategieën werden besproken aan de hand van drie belangrijke thema's: 'eligibility', deelname en retentie. Belangrijke uitdagingen waren onder andere de noodzaak om meerdere ziekenhuizen te betrekken om het aantal potentiële deelnemers te vergroten, het hoge verloop van personeel binnen onderzoeksteams, het overschatten van de bereidheid van hoog belaste gezinnen om deel te nemen, de benodigde dyadische aard van de deelname en het balanceren van naleving van protocolschema's met de benodigde flexibiliteit naar de gezinnen toe. Strategieën voor het aanpakken van de uitdagingen rond 'eligibility' omvatten nauwere samenwerking met zorgverleners en hen vroeg bij de studieplanning betrekken. Om de deelname en retentie te optimaliseren, waren belangrijke strategieën: flexibiliteit toelaten, training van data-collectoren, afstemming op de situatie van deelnemers en het onderhouden van consistent contact tussen data-collectoren en gezinnen. Algemene strategieën benadrukten het belang van het uitvoeren van een pilotstudie met de doelgroep vooraf, het hebben van een concreet plan voor het aanpassen van rekruteringsstrategieën, het overwegen van verschillende scenario's en het verkennen van alternatieve rekruteringsbronnen buiten ziekenhuizen, zoals sociale media. Alle studies volgden een stapsgewijs proces bij de werving, wat aangeeft dat meerdere bezoeken nodig waren om tot deelname van een gezin te komen.

Interpretatie en discussie van bevindingen

Het proefschrift heeft inzichten verzameld over de ontwikkeling en evaluatie van de BOOST pACP- interventie en heeft aandachtspunten gegeven voor toekomstige interventies gericht op het optimaliseren van communicatie en zorg voor kinderen met ernstige ziekten. Daarnaast zijn er vanuit een methodologisch perspectief uitdagingen en strategieën met betrekking tot rekrutering en retentie onderzocht, waarbij gebruik is gemaakt van expertise uit meerdere RCT's van psychosociale interventies in de pediatrische oncologie.

Vergelijking van de resultaten met andere onderzoeken in een vergelijkbare doelgroep

De resultaten over de effectiviteit van de BOOST pACP-interventie op de communicatie tussen ouder en adolescent moeten voorzichtig worden geïnterpreteerd vanwege de beperkte steekproefgrootte en power van de studie. Communicatie tussen ouder en adolescent is niet eerder beoordeeld als een uitkomst van een pACP-interventie, wat directe vergelijkingen met andere interventies bemoeilijkt. De effectgrootte van de BOOST pACP-interventie op de algehele communicatie tussen ouder en adolescent was 0.13 na 3 maanden (T1) en 0.49 na 7 maanden (T2). Voor de communicatie tussen moeder en adolescent specifiek was dit 0.31 op T2, en voor de communicatie tussen vader en adolescent was dit 0.67. Dit is hoger in vergelijking met de effectgroottes van een 'legacy-making' interventie voor kinderen met vergevorderde kanker (leeftijden 7 – 17): 0.10 voor moeder-kind communicatie en 0.20 voor vader-kind communicatie (niet significant), hoewel zij een groter aantal deelnemers includeerden. De effectgrootte op 'familieomgeving' van een therapeutische muziekvideo voor adolescenten en jongvolwassenen (AYA) (leeftijden 11 – 24) die een hoog-risico kankerbehandeling ondergingen, was 0.66 op hun tweede meetmoment en was statistisch significant. Communicatie tussen ouder en adolescent was echter slechts een deel van deze latente variabele. Voor de parallelle interventie voor ouders werden geen statistisch significante bevindingen gevonden op communicatie tussen ouder en adolescent, met lage effectgroottes. Communicatie tussen ouder en adolescent, gemeten met de PACS, is niet uitgebreid bestudeerd als een uitkomst van andere interventies in een vergelijkbare setting en de resultaten suggereren dat het geen gemakkelijke variabele is om te beïnvloeden. De enige

andere RCT van een pACP-studie is de FACE-TC studie. Echter werden in die studie andere uitkomsten geanalyseerd. De volgende statistisch significante uitkomsten werden gevonden: een hogere algehele overeenstemming over voorkeuren voor zorg aan het einde van het leven in vier kanker-specifieke situaties, meer behoud van kennis bij gezinnen over de voorkeuren van hun adolescenten voor behandeling aan het einde van het leven gedurende een jaar, en meer positieve waarderingen voor zorgverlening van de ouders (effectgrootte 0.17) en tevredenheid. Ze vonden geen statistisch significante uitkomsten op belasting van de ouder, stress bij de ouder of welzijn van het gezin.

Mogelijke verklaringen voor het ontbreken van significante bevindingen in de BOOST pACP-trial

De BOOST pACP-trial liet geen significant effect zien op de primaire uitkomstmaat—ouder-adolescent communicatie gemeten met de Parent-Adolescent Communication Scale (PACS) 3 maanden na de start. Hoewel er enkele significante bevindingen waren met betrekking tot houding en intentie, werden andere verwachte uitkomsten niet waargenomen. Hoewel de beperkte steekproefomvang een fundamentele reden kan zijn, is het noodzakelijk om andere mogelijke bijdragende factoren te verkennen.

1. Het meetinstrument was mogelijk niet geschikt

Het meetinstrument voor de gedragsdeterminanten, gebaseerd op de Theory of Planned Behavior (TPB), vangt mogelijk niet volledig de kwalitatieve nuances van ACP op, zoals de diepgang en kwaliteit van de communicatie. Bovendien kan het de gevoeligheid hebben gemist die nodig is om subtiele maar cruciale veranderingen in gedragsdeterminanten te detecteren die essentieel zijn voor ACP.

2. De toepassing van gedragsveranderingsmodellen op ACP interventies kent enkele beperkingen

- Beperkingen van de Theory of Planned Behavior (TPB): Onze interventie was gebaseerd op de TPB, die ACP-gedrag conceptualiseert als een individuele actie. Er kunnen echter ook andere invloedrijke processen zijn, zoals onbewuste, toevallige of omgevingsfactoren, die een belangrijke rol spelen bij het beïnvloeden van het gedrag rondom het bespreken van ACP-onderwerpen. Deze processen worden in de TPB niet meegenomen en konden we wellicht daarom niet vastleggen.
- Motivatie en gedragsverandering: Theorie-gebaseerde gedragsinterventies worden vaak bekritiseerd omdat ze alleen gericht zijn op degenen die al gemotiveerd zijn om te veranderen. De BOOST pACP-interventie maakte mogelijk onvoldoende gebruik van technieken zoals motiverende gespreksvoering en specifieke gedragsveranderingstechnieken zoals doelen stellen, actieplanning of implementatie-intenties, die effectiever zelfeffectiviteit hadden kunnen adresseren.
- Automatische, onbewuste gedragingen: Deze zijn moeilijk te veranderen zonder sterke motivatie of duidelijk waargenomen voordelen, waardoor het essentieel is om de omgeving zo te structureren dat ongewenst gedrag wordt ontmoedigd. Hoewel de BOOST pACP-interventie erop gericht was een veilige ruimte te creëren voor het bespreken van ACP-onderwerpen, kunnen extra strategieën zoals planning, zelfmonitoring en zelfversterking nodig zijn om duurzame gedragsverandering te bereiken.

Een algemene beperking van het gebruik van gedragsmodellen is dat ze complexe menselijke gedragingen en interacties simplificeren, waardoor deze worden gereduceerd tot basisdeterminanten die mogelijk niet volledig de genuanceerde aard van ACP-gesprekken vastleggen, waarbij diepe persoonlijke waarden, emoties en complexe familiedynamieken een rol spelen. Onderzoek heeft echter het belang benadrukt van het gebruik van gedragsveranderingsmodellen in ACP-onderzoek. In onze context leek de TPB een geschikte basis te zijn voor ons doel om de communicatie over ACP tussen ouders en adolescenten te verbeteren.

3. De tijdsperiode van de BOOST pACP-studie was mogelijk te kort

Hoewel de directe effecten beperkt waren, liet de BOOST pACP-interventie op de langere termijn meer potentie zien (effectgrootte van 0.49). Het feit dat er in de BOOST pACP-studie een toename in plaats van een afname van de communicatie tussen ouders en adolescenten werd waargenomen, kan erop wijzen dat het tijd kost om nieuwe attitudes en aangeleerde vaardigheden te integreren in de communicatie.

4. De bredere populatie van adolescenten met kanker is mogelijk niet ideaal voor dit type ACP

Het doel van ACP is om de zorg af te stemmen op de waarden en voorkeuren van de adolescent. Voor adolescenten met kanker die een goede prognose hebben en een eenvoudig behandeltraject volgen, kan het bespreken van scenario's zoals "*wat als de behandeling niet werkt*" niet direct noodzakelijk of nuttig zijn. Daarentegen kunnen deze onderwerpen relevanter zijn voor gezinnen die te maken hebben met complexe chronische aandoeningen, gekenmerkt door een heterogene diagnose, hoog zorggebruik, afhankelijkheid van medische technologie en een aanzienlijk risico op morbiditeit en mortaliteit. Door de vooruitgang in kankerbehandelingen zijn de overlevingspercentages gestegen en is het ziekteverloop onvoorspelbaarder geworden, wat de timing van deze gesprekken bemoeilijkt. Omdat het juiste moment voor ACP-gesprekken verschilt per individu en ook afhankelijk is van de individuele ontwikkeling van het kind, is het moeilijk om gestandaardiseerde criteria vast te stellen. Daarom moet ACP **flexibel** en **regelmatig** zijn, zodat er een natuurlijke overgang naar serieuzere gesprekken kan plaatsvinden die zijn afgestemd op de ontwikkeling van de adolescent wanneer de situatie zich voordoet.

Aanbevelingen

Om adolescenten met kanker en hun ouders beter te ondersteunen op het gebied van pACP en communicatie, worden de volgende aanbevelingen geformuleerd in drie domeinen: praktijk, beleid en toekomstig onderzoek.

Aanbevelingen voor de praktijk

- Benadruk het belang van ouder-adolescent communicatie.
- Integreer holistische en flexibele pACP in het behandeltraject door:
 - o Het trainen en toewijzen van 'zorgplanners' aan elk gezin.
 - o Het aannemen van een holistische en flexibele aanpak door ACP op te nemen in het overkoepelende doel van het bieden van hoogwaardige psychosociale zorg. Verschillende rollen die de zorgplanner kan vervullen:

- Faciliteren van gezinscommunicatie.
- Beoordelen en versterken van de gezinsveerkracht.
- Het overbruggen van de kloof tussen het ziekenhuis en het dagelijks leven door verbindingen te leggen met andere ondersteuningssystemen en door het helpen navigeren in het zorglandschap.
- Bespreken van huidige en toekomstige zorg en behandeling, met een focus op mogelijke ziekteprogressie (ACP).
- Communiceren van relevante informatie aan de behandelende zorgverleners.

Aanbevelingen voor het beleid

- Verminder barrières voor de betrokkenheid van vaders bij het zorg dragen voor hun zieke kind.
- Zorg voor tijd en middelen voor zorgverleners om vroege en holistische implementatie van pACP te faciliteren.
- Bouw bewustzijn en empowerment op bij adolescenten met ernstige ziekten in ACP door gecoördineerde communicatie.
- Stel richtlijnen op voor het bieden van incentives aan gezinnen om deel te nemen aan psychosociaal onderzoek.

Aanbevelingen voor toekomstig onderzoek

- Identificeer wie het meest profiteert van pACP-gesprekken door:
 - De inhoud van ACP-gesprekken met adolescenten te vergelijken in relatie tot factoren zoals de geschatte prognose, het behandelplan en de aanwezigheid van metastasen.
 - Kwalitatieve interviews uit te voeren om te begrijpen hoe ACP-gesprekken de psychologische en emotionele toestand van adolescenten beïnvloeden en hoe zij hier baat bij hebben.
 - Een SMART (Sequential Multiple Assignment Randomized Trial) toe te passen om adaptieve interventies te ontwikkelen door empirisch te testen welke strategieën het meest effectief zijn onder verschillende omstandigheden.
 - Incluseren van gezinnen die de moedertaal niet of onvoldoende spreken.
 - Integreer ontwikkelingsstadia in het ontwerp van pACP-interventies en standaardiseer de monitoring van de ontwikkeling van kinderen.
 - Pas rekrutering- en retentie strategieën aan voor studies met pediatrische populaties, en evalueer welke strategieën het meest effectief zijn voor het verbeteren van deze uitkomsten door:
 - De doelgroep vroegtijdig te betrekken
 - Uitgebreide training van data collectoren
 - Het uitvoeren van een pilotstudie
 - Het implementeren van SWATs (Studies Within A Trial)
 - Voer mixed-methods meta-analyses uit op pACP.

APPENDICES



Vroegtijdige Zorgplanning

Wat vind jij belangrijk en hoe kunnen we het beste voor jou zorgen?



Waarom krijg je deze gesprekken?

We nodigen je uit voor een paar gesprekken. Je krijgt deze gesprekken omdat je in behandeling bent voor een ernstige ziekte. Ook al voel je je misschien niet echt ziek. Jij wil dingen blijven doen die je leuk vindt. En daarom willen we samen zoeken naar de zorg die bij jou het beste past.



Praten over later

Vraag jij je wel eens af hoe jouw toekomst eruitziet? Wat je plannen zijn na genezing? Of maak je je wel eens zorgen of de behandeling wel zou werken? Heb je al eens nagedacht over wat de gevolgen kunnen zijn van de behandeling? Praat je hier wel eens over?

Als we dit soort dingen weten, kunnen we daar rekening mee houden. De vragen in dit boekje zijn bedoeld om over na te denken.

Je hoeft je antwoord niet op te schrijven, maar dat mag natuurlijk wel als je dat wilt.



Over jou

Wat zijn je interesses? Wat doe je graag?

Wat of wie is er belangrijk voor jou?



Over jou

Hoe ziet je situatie er nu uit? Hoe is jouw situatie veranderd?
Welke dingen mis je nu? En wat wil je voor de toekomst?



Over je ziekte

Wat wil je nog weten over je ziekte? Heb je genoeg informatie?

Zijn er dingen over je ziekte die je wel of juist niet wilt weten?



Over je ziekte

Wat vind je het meest vervelend aan de behandeling?
Wat valt er nog mee?

Zijn er voor jou ook aangename momenten of ervaringen tijdens je ziekte?



Over je ziekte

Zijn er dingen waar je heel erg tegenop ziet?

Maak je je wel eens zorgen over de behandeling?



Over hoe wij je kunnen helpen

Hoe kunnen jouw ouders jou het beste helpen? Zijn er dingen waar je ouders rekening mee zouden kunnen houden?

Hoe kunnen ze jou in het ziekenhuis het beste helpen? Zijn er dingen waar de zorgverleners in het ziekenhuis rekening mee kan houden?



Over hoe wij je kunnen helpen

Zijn er voor jou nog andere mensen die je kunnen helpen?
Hoe kunnen zij jou het beste helpen?





Vroegtijdige Zorgplanning

Wat vindt u belangrijk voor uw kind?



Waarom krijgt u deze gesprekken?

Uw kind wordt behandeld voor een ernstige ziekte. Daarom nodigen we u uit voor een paar gesprekken. We horen graag wat u belangrijk vindt voor uw kind. Niet alleen voor dit moment. Ook als de behandeling goed verloopt en uw kind zich goed zal blijven ontwikkelen. Maar ook als de behandeling niet het gewenste effect heeft. Wat is belangrijk voor de zorg van uw kind in die omstandigheden?

Zijn er dingen waarover u zich zorgen maakt? Dan kunt u hier ook over spreken. Hoe ziet u de situatie voor uw kind? Wat is belangrijk voor uw kind?

In dit boekje vindt u vragen die u kunt gebruiken om alvast na te denken over onderwerpen die in het gesprek kunnen terugkomen.



Over uw kind

Waar wordt uw kind vrolijk van?

Wat is belangrijk voor uw kind?



Over uw kind

Waar heeft uw kind het moeilijk mee?



Over de ziekte van uw kind

Wat wil ik nog meer weten over de ziekte van mijn kind?

Wil ik meer weten over de toekomst?



Over de ziekte van uw kind

Waar wil ik op voorbereid zijn, mocht de behandeling niet de gewenste positieve resultaten bieden?



Wensen voor uw kind

Wat wil ik voor mijn kind?



Wensen voor uw kind

Waar maak ik me zorgen over?

Wat voor ouder wil ik zijn voor mijn kind?



Zorg en behandeling

Wat vind ik belangrijk in de zorg en behandeling van mijn kind? Wat vindt mijn kind belangrijk in zijn of haar zorg en behandeling?

Wat moeten zorgverleners weten over mijn kind dat belangrijk kan zijn voor de zorg en behandeling?



Zorg en behandeling

Mocht de behandeling niet goed werken, wat wil ik dan wel en niet voor mijn kind?



Appendix 3. BOOST pACP intervention materials – conversation cards for the adolescents







Appendix 4. BOOST pACP intervention materials – conversation cards for the parents









Een samenvatting van de gesprekken

Ik ben iemand die...

De ziekte betekent voor mij...

De ziekte betekent voor ons als gezin...

We praten als gezin over de volgende onderwerpen...

We moeten blijven praten over ...

Ik pieker wel eens over deze dingen...

Dit vind ik belangrijk, als het over mijn zorg en behandeling gaat...	
Mijn verwachtingen voor de toekomst zijn...	
Bij achteruitgang van mijn gezondheid is het belangrijk dat...	
Deze gedachten komen wel eens in mij op over sterven...	
Ik zou graag een gesprek met mijn dokter hebben.	☐ Ja, graag ☐ Nee, op dit moment heb ik daar geen nood aan.
Zorgverleners mogen deze informatie ook krijgen	☐ Ja ☐ Nee

Wat ik verder nog kwijt wil

CURRICULUM VITAE AND LIST OF PUBLICATIONS

Curriculum vitae

Anne van Driessche is a researcher with a Master's degree in Health Education and Promotion, as well as a second Master's in Global Health. Before starting her doctorate, she worked as a researcher at the Municipal Health Service Zeeland and Julius Center for Health Sciences and Primary Care (UMC Utrecht). In September 2018, she began her PhD at the End-of-Life Care Research Group, focusing on the development and evaluation of a pediatric advance care planning intervention for adolescents with cancer. This project is a collaboration between the Vrije Universiteit Brussel and Ghent University and is supported by a grant from the Research Foundation Flanders and Kinderkankerfonds.



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Ontwikkeling van een vroegtijdige zorgplanning interventie bij adolescenten met kanker. Nederlands-Vlaamse Wetenschapsdagen Palliatieve Zorg, Antwerpen, November 2019. [Poster](#).

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Developing a pediatric advance care planning intervention for adolescents with cancer, ACP-I Conference, Rotterdam, March 2019. [Poster](#).

Testing the effectiveness of a family-centered pediatric advance care planning intervention: study protocol for a randomized controlled trial. ACP-I Conference, Rotterdam, March 2019. [Poster](#).

Other media and press

A blog published in Raakpunt (magazine Kinderkankerfonds) *“Ik denk dat ik nu meer durf te zeggen. Ook over dingen die wat minder zijn.”*, September 2022

Study in the spotlight – Newsletter of the Pediatric Psycho-Oncology Professionals/Providers International (POPPI), issue 8, March 2022

A blog titled: *“Anne van Driessche: “Betere communicatie moet leiden tot zorg op maat voor jonge kankerpatienten”* – in the context of World Cancer Day, published February 2022 at the VUB Today website

A video developed on the BOOST project in the context of Childhood Cancer Awareness Month, September 2021

Gastcollege

Praten met ernstig zieke kinderen, als deel van Postgraduaat Psychosociale aspecten en geestelijke gezondheid voor het kind, Thomas More Hogeschool Turnhout, on 12 May 2023 en 15 March 2024.

Grants or awards received

Audience award best poster, *Recruitment and retention in palliative care trials: challenges and strategies*. 7th Public Health Palliative Care International Conference, Brugge, September 2022

Best short video 2022 at the 5th Maruzza International Congress on Pediatric Palliative Care (May 2022) from the Fondazione Charlemagne

Best abstract. Evaluating attitude, self-efficacy, behavior, and intention to engage in advance care planning communication in pediatric oncology: development and face validation of a new measurement instrument. 17th European Association for Palliative Care Congress 2021

Research stay abroad

Center of Expertise Palliative Care Utrecht – Julius Center of Health and Primary Care, UMC Utrecht
– FWO travel grant short stay abroad, October 2022