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Toward best ethical practices for including children in childhood cancer research

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Abstract

Norberg Wieslander, K. 2026. Toward best ethical practices for including children in childhood cancer research. *Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine* 2222. 79 pp. Uppsala: Acta Universitatis Upsaliensis. ISBN 978-91-513-2701-3.

This thesis is based on an empirical-ethical approach with the overall aim to explore and describe ethical aspects of including assent-aged children in childhood cancer research, and to develop empirically informed, ethically grounded guidance for research practice.

Study I was a qualitative interview study with healthcare professionals in Swedish pediatric oncology. The aim was to investigate their perspectives on ethical values, challenges, and opportunities to strengthen ethical aspects in recruitment of children with cancer to research, and their perspectives on ethical competence. Manifest inductive qualitative content analysis generated five categories: establishing relationships and trust, meeting informational needs, acknowledging vulnerability, balancing roles and interests, and ensuring ethical competence.

Study II was a qualitative interview study with members of the Swedish Ethical Review Authority. The aim was to explore their perspectives on ethical values, challenges, and opportunities to strengthen ethical aspects of participant recruitment in pediatric research, and their perspectives on ethical competence. Manifest inductive reflexive thematic analysis generated three themes: promoting participation, protecting children, and regulatory adherence.

Study III was a qualitative interview study with children, siblings, and parents who had participated in childhood cancer research. The aim was to describe how they experience children's participation in assent. Latent inductive reflexive thematic analysis generated two themes: a moral and emotional commitment to research, and relational assent: trust, loyalty, andparental constraint.

Study IV was a prescriptive normative study aimed at developing ethically grounded guidance for children's participation in assent. Using reflective equilibrium, a normative analysis was conducted based on empirical findings from Studies I–III, previous research, moral judgments, ethical principles, and relevant guidelines. The study proposed that childhood cancer research should not only respect children's autonomy but also actively promote it, acknowledging that relationships and trust can both enable and constrain autonomy.

This thesis contributes to a context-specific understanding of ethical aspects in childhood cancer research, particularly concerning autonomy and vulnerability. It highlights the need to actively support children's autonomy and participation in assent and the importance of ethical competence in navigating ethical, relational, and clinical complexities in research recruitment. Further, it provides empirically informed normative guidance for research practice.

Keywords: assent, children, pediatric research ethics, pediatric oncology, research recruitment, relational autonomy, vulnerability, ethical competence

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To Otis and Fredrik,
And to my parents

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I. Norbäck, K., Höglund, A., Godskesen, T., & Frygner-Holm, S. (2022). Ethical concerns when recruiting children with cancer for research: Swedish healthcare professionals' perceptions and experiences. *BMC Medical Ethics, 23*(1), 117. https://doi.org/10.1186/s12910-022-00875-3

II. Norberg Wieslander, K., Höglund, A., Frygner-Holm, S., & Godskesen, T. (2023). Research Ethics Committee members' ethical perspectives on Paediatric research: A qualitative interview study. *Research Ethics, 19*(4), 494–518. https://doi.org/10.1177/17470161231179663

III. Norberg Wieslander, K., Frygner Holm, S., Nilsson, S., Lövgren, M., Höglund, A. T., & Godskesen, T. Children's participation in assent to paediatric oncology research: Experiences of children, siblings and parents. *Manuscript*.

IV. Norberg Wieslander, K., Godskesen, T., Höglund, A. T., Frygner Holm, S., & Juth, N. Why children's research assent matters: Exploring three dimensions of autonomy. *Submitted.*

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Contents

Abbreviations

HCP	Healthcare professional
REC	Research ethics committee
DoH	Declaration of Helsinki
CIOMS	Council for International Organizations of Medical Sciences
CR	Critical realism
RE	Reflective equilibrium

Key concepts

Child	A person between 0-18 years, in accordance with the UN Convention on the Rights of the Child and Swedish legislation.
Parent	A person with legal rights and responsibilities for a child, such as a parent or legal guardian. In this thesis, the term "parent" is used for simplicity.
Assent	A child's affirmative and meaningful agreement to participate in research, based on appropriate information and an opportunity for the child to express a voluntary choice and to dissent. Absence of dissent is not regarded valid assent.
Assent-aged child	A child who has not reached the legal age of consent (15 years in Sweden) but is considered capable of participating in assent, often referring to school-aged children. World Health Organization (WHO) recommends assent from 7 years, but assent should be sought also for younger children who are able to provide it (1). In this thesis, we have included children from 5 years.
Parental permission	Authorization given by a parent or legal guardian for the child's participation in research.
Respect for autonomy	Principle in the biomedical ethical framework of Beauchamp and Childress (2). Refers to an individual's right to self-governance and to make voluntary, deliberated, and informed decisions free from controlling influences. In research, it is closely connected to the requirement for informed consent. Respecting autonomy is a prima facie moral obligation,

	even for those whose capacity for autonomy is not fully developed.
Relational autonomy	Autonomy and decision-making understood as a relational, social, and emotionally situated process (3-5).
Capacity	An individual's ability to understand relevant information, appreciate the information and its consequences, reason about choices, and communicate a decision in a specific context. Capacity is graded and children's autonomous capacity develops over time, as they mature. In this thesis, capacity and competence are used interchangeably (2).
Vulnerability	A reduced ability to protect one's own interests, for example due to limited capacity for autonomous decision-making or increased risk of coercion or harm (6, 7)
Ethical challenge	A situation in which competing moral values, duties, or interests create uncertainty or conflict about the right course of action (2)
Paternalism	Intentionally deciding for another person regardless of their own preferences or actions with the aim of benefiting them or preventing harm. It can involve both active and passive forms of influence and may be justified depending on the trade-off between expected benefits and the degree to which autonomy is undermined (2)

Introduction

It was the day of the end-of-school ceremony – a day that, for Swedish schoolchildren, typically signifies lilacs in bloom and the anticipation of a long summer vacation. She was finishing sixth grade, on the verge of becoming a teenager, beginning middle school in the fall. A summer camp and a family trip to the Mediterranean lay ahead.

But recently, she had not been feeling well. She was unusually tired, pale, and had skipped activities that she normally enjoyed. There was something going on with her body. It began with a routine visit to the primary care clinic, just to make sure everything was fine – surely nothing to worry about.

Then the diagnosis came. On the last day of school before summer break.

Her mother, shocked and in disbelief, said: *"I kept thinking it must be a mistake. That someone had read the results wrong. She has never been sick before."* In an instant, life was turned upside down for the family. There would be no summer camp. Instead, a new reality took over; worry, difficult examinations, and medical terms that were hard to understand and even more difficult to accept. The summer was spent in the hospital receiving rounds of aggressive treatment, and the girl lost her hair.

This is the story of one of the families I had the privilege to meet during this PhD. Each day, a family in Sweden receives the news that their child has cancer. Today, 85 percent of children with cancer survive in Sweden, and pediatric oncology is in much a success story – enabled by research collaboration, committed clinicians and researchers, and families' willingness to participate in research for the benefit of others. Yet some childhood cancers remain incurable, and survival often comes at high cost for the child, with significant adverse effects and long-term late complications from intensive treatment. Also, the psychosocial impact of a child's cancer diagnosis is profound on families. A five-year old sibling described the fear she had felt: *"Is my brother going to die? I was really hoping, so much [that he would not]… I even prayed to God, even though I knew He didn't exist."*

Childhood cancer research is essential to ensure access to safe and evidence-based treatments, nursing care, and psychosocial support for the child and family. However, when families are approached about research participation in such straining and vulnerable circumstances, this brings complex ethical questions.

The bioethical model of informed consent is founded upon the ideal of an autonomous adult decision-maker, free from pressure and coercion. Children, however, have a capacity for autonomy that is not complete but under development, and their family context is an integral part of their lives, characterized both by own agency and parental caregiving responsibilities. Therefore, parental consent supplements the child's own assent. As proxy-decision makers, parents are expected to possess sufficient capacity and emotional stability to make well-reasoned and informed research decisions in the best interests of their child. This is a demanding expectation on parents who have just received their child's cancer diagnosis. As one physician noted: "*They are drowned in information, and at the same time they are often emotionally blocked after getting the diagnosis. All of this is pouring over them. It's like an avalanche of information"*.

Historically, pediatric research ethics has focused primarily on obligations to safeguard children's wellbeing, in spite of their vulnerability. Today, the emphasis has shifted more towards children's participatory rights. The contemporary pediatric research ethics landscape therefore concerns aspects of both protection and participation, enabled through partnership between families, healthcare professionals and researchers, and research ethics review. This requires trust, communication, and sensitivity to the child's life perspective and situation and to the family's emotional landscape: worry and fear, loss of control, the desire for normality, and the need for hope, in treatments, cure, and a good life despite the diagnosis.

Unlike clinical care, which is given with the child's best interest in mind, research is conducted for future children. It intends no direct benefit for the child and may entail risks or severe side effects and long-term complications. Therefore, attentiveness to the child's voice is especially critical – both to what is said and to what remains unsaid under mutual pretense between child and parents. As one nurse said: *"I think we should be attentive, because sometimes the parents want to, but the child doesn't. Because the child doesn't have the strength or has had enough [of research]*." For such reasons, a relational and care-ethical approach is essential.

Throughout this PhD project, a quotation has persistently remained with me:

> *"Out beyond ideas of wrongdoing and right doing, there is a field. I'll meet you there."*
>
> – Jalal al-din Rumi

This should not be read as a denial or relativizing of ethical principles. On the contrary, principles form the very foundation of research ethics, with requirements for informed consent and protection of the most vulnerable, including children. Yet, research ethics is not only about rules and principles. It is also about relationships and what emerges in the triadic interaction between children, parents, and healthcare professionals – about attentiveness, empathy, and presence. Aspects that have often been neglected in this field. The human dimension cannot be lost, but should remain at core, within a framework of principles.

This thesis therefore integrates principle-based ethics with a care-ethical understanding. Using an empirical ethics approach, it contributes context-sensitive knowledge about the ethical dimensions of childhood cancer research – knowledge intended to be of clinical relevance. The aim has been to bridge the gap between theory and practice by drawing on the lived experiences of children, siblings, parents, and healthcare professionals, as well as perspectives from ethical review – with a clear normative aim, to support ethical research practice.

Background

Childhood cancer globally

Globally, around 400,000 people under the age of 19 are diagnosed with cancer every year (8, 9). In Europe childhood cancer affects about 35,000 children under the age of 15 annually, and in the Nordic countries (Sweden, Denmark, Finland, Norway and Iceland) around 1,200 children are diagnosed with cancer (10, 11). The term 'childhood cancer' encompasses a wide range of relatively rare diseases that are biologically distinct from adult cancers. Different types of cancer are prevalent in different geographic regions, but among common cancers affecting children are leukemia, central nervous system tumors, neuroblastoma, lymphoma, kidney tumors and bone tumors (12). Improved treatments have led to dramatic increases in five-year survival rates in high-income countries; in many of these countries, five-year survival rates now exceed 80%. Nevertheless, childhood cancer is life-threatening and remains a major cause of death due to disease in children aged between one and 14. Significant health inequalities persist, with less than 30% of children surviving cancer in low-income countries where treatment is often unavailable or unaffordable (12-15).

Childhood cancer in Sweden

In Sweden, approximately 350 children under 18 years are diagnosed with cancer each year. Treatment options for children diagnosed with cancer are often good in Sweden, and 85% of children survive. However, the prognosis varies greatly between diagnoses, and some forms of cancer affecting children remain incurable (11, 16). Treatment varies by diagnosis, but often includes chemotherapy, surgery or radiotherapy, along with immunotherapy or targeted therapy, and sometimes stem cell transplantation (17). There are six childhood cancer centers in Sweden, providing cancer care for children aged up to 18. They are located in Gothenburg, Linköping, Lund, Stockholm, Umeå and Uppsala. Children may receive additional care at clinics located closer to their homes. After cancer treatment ends, children typically receive follow-up care for a number of years (16, 18).

The impact of childhood cancer

Being diagnosed with cancer profoundly affects children's lives, with consequences in terms of their well-being, development and everyday functioning, along with long periods of dependency on healthcare services (19-22). Treatment is often lengthy and burdensome, and children remain at risk of late physical, psychological and cognitive complications long after treatment is complete (23-25). These late effects and adverse outcomes are recognized as a significant public health concern (26).

Parents also shoulder substantial burdens, including increased depression, anxiety and post-traumatic stress, and disruptions to family functioning and financial stability (27-30). Further, siblings of children with cancer often face emotional distress, such as anxiety, loneliness or guilt, and experience disruptions in normalcy and daily life due to hospital stays, altered caregiving routines, contributing to a sense of being set aside within the family and unmet needs of care and support (31-33). The profound impacts of childhood cancer on children and their families should be recognized when considering the ethical context of research participation.

Childhood cancer research

In pediatric oncology, research is often integrated with clinical care, and many children receive treatment or components of treatment while participating in multicenter or multinational research studies. Childhood cancer research includes a broad range of scientific activities aimed at improving care, including diagnostics, mapping of cancer types, genetics and precision medicine, longitudinal cohort studies, biobank and registry-based studies, epidemiological and observational research, as well as supportive and psychosocial care, which also targets the family, including parents and siblings (34-37).

Clinical trials play a central role in evaluating new pharmacological treatments and determining their safety, efficacy, optimal dosing and comparative value against standard care. These studies are critical for ensuring that new treatments not only work as intended but also pose acceptable risks, especially in vulnerable populations such as children (38). A major goal is to generate robust evidence that reduces reliance on untested 'off-label' medicines, which remains common due to the lack of pediatric-specific data in oncology (39). As survival rates increase, there is also a need for treatments that are not only effective but less toxic, to improve long-term health and quality of life (26, 40).

Clinical trials commonly use phased designs that evaluate safety and side effects (Phase I), dosage and preliminary effect (Phase II) and comparison with standard treatment (Phase III) (41). In cancer research, Phase I trials are often conducted with patients who are not responding to standard treatment, because the benefits and risks are uncertain. Clinical trial enrollment rates vary between countries, ranging from 27–86%, and are highest in younger children and in high-income countries where trials are more available (12, 42, 43).

In Swedish pediatric oncology, protocols are evaluated through international collaboration, for example via the Nordic Society of Paediatric Haematology and Oncology (44). To support clinical research, Sweden has two clinical trial units for children with cancer, located in Stockholm and Gothenburg. Through these units, Sweden participates in the international Innovative Therapies for Children with Cancer network, which enables inclusion of Swedish children in multinational clinical studies and the testing of new treatments and drugs (45). In addition, the centers run their own investigator-initiated studies. There is a clear ambition to encourage clinical research involving children, supported by the recently-established Fostering Oncology Research by Charities in Europe consortium. This initiative, of which the Swedish Childhood Cancer Fund forms a part, aims to expand childhood cancer research across Europe (46, 47).

Research ethics in pediatric oncology

As children and adults have the same rights to high quality, evidence-based care and safe treatments, there is a moral duty to involve children in childhood cancer research. Children should neither be overburdened with research, nor excluded from research based on vulnerability (6, 39). Nevertheless, involving children in research necessitates additional ethical considerations and safeguards, and a reasonable balance must be struck between protecting children and promoting their developing autonomy as research participants (48).

Recruitment and assent

The Declaration of Helsinki (DoH) outlines ethical principles for medical research, such as the requirement that all prospective participants should be adequately informed about the risks and benefits of participation, and their right to decline or withdraw from research. These are iterated in operational standards such as the ICH Guidelines for Good Clinical Practice (7, 49). Informed consent is closely connected to the ethical principle of respect for persons:

researchers are obliged to respect participants' autonomy, and also to protect participants with diminished autonomy, including children. To protect and respect children, minimal risk exposure is combined with requirements for parental permission and the child's own assent (6, 50). According to the Council for International Organizations of Medical Sciences (CIOMS) guidelines (6), assent practices involve several essential features:

- Meaningfully engaging the child in research discussions according to their capacity and providing age-appropriate information.

- Viewing assent as a process (rather than a one-off, formal event) and actively involving the child in the actual decision-making.

- Seeking the child's active agreement (not just absence of dissent), preferably in writing when possible.

- Considering not only the child or adolescent's age but also their individual circumstances, life experiences, emotional and psychological maturity, intellectual capabilities, and family situation.

No uncontested definition of assent has yet been established, and ethical guidelines and law typically do not provide specific criteria or guidance for designing assent procedures, which may result in ambiguity for pediatric researchers. Recent initiatives have sought to overcome these challenges by contributing age-specific recommendations and more specific practical guidance (51-53). It is often recommended for assent to be sought from the age of seven. However, this should not be regarded an age threshold, as all capable children should be involved in assent (1, 6). As a point of reference, Tait and Geisser have proposed that for children's assent to research participation to be meaningful:

> Children should understand the basic study-specific information, should have a developmentally appropriate awareness of their condition, and be able to appreciate, at a rudimentary level, how the information applies to their own situation. Children should be free to decide whether or not to participate in a study and articulate their choice absent of any undue influence or coercion (54).

Swedish research legislation

The legal requirements for children's participation in research vary between countries (55). In Sweden, research involving humans is regulated by the national Swedish Ethical Review Authority, under the Swedish Ethical Review

Act. The Act prescribes respect for human dignity and protection of participants from physical, psychological and integrity-related risks (56, 57). Research involving children aged under 15 requires permission from both parents or custodians. Researchers are required to obtain assent from children younger than 15 and to always respect the child's dissent, regardless of whether the parents have granted permission. Children older than 15 can provide legal consent without parental permission, if they are mature enough to understand what their participation entails. Children of all ages should be informed as far as possible about the study, and specific ethical consideration is necessary if the child is in some way dependent on the researcher (for example by virtue of being a patient), as this can make it more difficult for them to protect their rights. In clinical drug research, the parents' permission is required until the child reaches the age of 18 (58).

The United Nations Convention on the Rights of the Child, which has been incorporated into Swedish law since 2020, strengthens the legal responsibility to respect and promote children's rights in all decisions that concern them across different societal arenas, including healthcare and research. Article 12 specifies that children who are capable of expressing their own views are entitled to do so freely, and that their opinions must be taken into account in accordance with their age and maturity (59).

The legal right of children to actively participate in their own healthcare is also prescribed in the Swedish Patient Act. This obliges healthcare professionals (HCPs) to take children's own preferences regarding their healthcare into account and to give those preferences due consideration. It further requires that the child's best interests are a primary consideration in health decisions (60).

Ethical challenges in recruitment

Research involving children raises ethical challenges, not least in recruitment. As previously described, children under 15 are not authorized to provide legal consent. Further, it is harder for them to protect their rights and they may be at greater risk of harm (6, 7). Children diagnosed with cancer may be particularly vulnerable when invited to participate in research due to their medical and psychosocial circumstances, and because they are dependent on healthcare (19). Information about research can be difficult for children to understand and recall, and research indicates that children are sometimes excluded from assent or play only a minimal role, that they sometimes feel unable to dissent, and that they are sometimes unaware of their research participation (61-64). Deciding whether to take part in research can be challenging for families, as protocols can be complex and decisions often are made in situations characterized by medical urgency and distress. Limited understanding of information about the study, the impact of psychological distress, a lack of alternative treatment options, and influence from the treating physician can all complicate these decisions (65). Further, it can be difficult for parents to distinguish between standard care and research, and they may consent to enrolling their children in research based on high expectations of therapeutic benefits; this is commonly referred to as “therapeutic misconception” (66, 67).

The integration of care and research can lead to conflict between ethical values related to patients’ autonomy and best interests, and opposing research interests (68, 69). HCPs in pediatric oncology in Sweden have described ethical challenges relating to balancing care with research interests while trying to protect families from psychological distress, which sometimes resulted in HCPs acting paternalistically or authoritatively in recruitment. This meant that HCPs sometimes made decisions about research participation on behalf of families, or abstained from inviting certain families to participate based on their perceived vulnerability (69). Moreover, decisions about a child’s care and research participation are complex processes, in the sense that they involve a triad of stakeholders with interests and goals that may pull in different directions (70-72). As children’s access to participation in decision-making in the context of healthcare is largely controlled by parents and HCPs, the process is asymmetrical rather than equal in terms of power and knowledge (73-75).

Research suggests that ethical issues related to assent-aged children’s enrollment in research, and descriptions of assent procedures, are under-reported by clinical researchers (76, 77). While assent is regarded as an ethical imperative, regulations and ethical guidelines provide little guidance or criteria on adapting study information and assent procedures for children of different ages. Consequently, there is a need for clearer best practices, informed by children’s perspectives and needs, to ensure that children’s rights are safeguarded consistently in childhood cancer research – in line with the ethical values and principles outlined by law and ethical guidelines (51-53).

Theoretical and normative framework

Principles of biomedical ethics

This thesis explores ethical aspects of pediatric research recruitment with reference to several ethical perspectives. Among these are the four *Principles of Biomedical Ethics* (principle-based ethics) proposed by Beauchamp and Childress – beneficence, non-maleficence, justice and respect for autonomy (2). These four principles are mid-level ethical principles developed for biomedicine, and are reflected in ethical guidelines such as the DoH (7).

The principle of *beneficence* entails a moral obligation to benefit others by reducing or preventing harm and providing benefits. In research, beneficence can for example surmount to a duty to conduct research that has the potential to promote the health and life quality of patients. The principle of *non-maleficence* entails a duty to avoid harming others or causing detriment to their health and life quality. In research, non-maleficence corresponds to the duty to prevent harming research participants, physically, psychologically, or by violating their integrity. The principle of *justice* requires standards ensuring fair distribution of benefits, risks and costs. In research, justice implies a duty to include under-served patient groups, such as children or minorities, in research without subjecting them to disproportionate risks or burdens (2).

The principle of respect for *autonomy* entails respecting and supporting people's autonomous actions, enabling them to act according to their own self-chosen plan. Respect for autonomy consist of both negative and positive obligations, where the negative entails showing respect for others by not unduly controlling others, and the positive entails supporting others through information and choice (2).

The central concept of *capacity* is closely related to autonomy and informed consent. Beauchamp and Childress refer to capacity as the cognitive, psychological, or legal capability to engage in decision-making: "Patients or research participants are competent to make a decision if they have the capacity to understand the information provided, to make a judgment of this information in light of their values, to intend a certain outcome, and to communicate freely their wishes" (p. 116) (78). A person's capacity may vary over time, in different situations, and according to the type of decision to be made. Regardless of whether a person's capacity for autonomous decision-making is not fully developed (as is often the case with children) they should always be acknowledged, respected and supported with regard to the autonomous capacity they do have (2).

For pediatric researchers, the distinction between capacity and the legal entitlement to consent is essential. A child may understand relevant information, deliberate, and form an intentional preference, yet still lack the legal authority to decide independently of parental permission. Although laws and ethical guidelines rely on age thresholds for reasons of feasibility, individual children should not be presumed incapable solely based on age. The Nuffield Council on Bioethics suggests distinguishing between three cases to clarify children's decision-making capacity: (I) children who are unable to express views (e.g., infants or children who cannot communicate due to severe illness); (II) children who can form views and express wishes but are not yet able to make fully considered, independent decisions; and (III) children who may possess full decision-making capacity but lack legal entitlement due to being minors. These children may be fully competent, yet parental permission is still required by law. Importantly, children may move between these cases in non-linear ways depending on context, complexity, what is at stake, and their physical and psychological condition. It is recommended not to seek assent from Case I children, but to seek meaningful assent from Case II children, and to obtain consent from Case III children together with parental permission (79).

The four principles of biomedical ethics provide a useful framework for identifying ethical tensions in research. One such example is conflict between patients' rights to decide whether to participate in research (autonomy), and physicians' professional moral obligation to promote health through research (beneficence) (7).

Care ethics and relational autonomy

HCPs and researchers who involve children in research have a professional obligation to safeguard children's rights and integrity, and to ensure their well-being and safety. At the same time, the child must be respected as a moral agent with developing autonomy (6). During consent procedures, balancing the child's autonomy against parents' legal authority and caregiving responsibility to protect and make decisions on behalf of the child is a central ethical conflict (56, 80).

Autonomy in bioethics has traditionally been conceptualized through an individualistic account of personhood, emphasizing independence and self-determination, for example through models of informed consent and freedom from undue influence (2, 81, 82). This view has been criticized for being too narrow, on the grounds that it undervalues the significance of relationships and social context in moral conduct and reasoning (3, 83).

The care ethics tradition has been developed in response to this critique. It highlights the importance of interpersonal relationships, emotions as a source of moral insight, and trust and care as central ethical values in human life and morality. *Relational autonomy* is a key concept within care ethics, built upon the notion that decision-making is a relational, social, and emotionally situated process (3-5). Relational autonomy rests on the assumption that the involvement of trusted others does not necessarily constrain a persons' autonomy, but may also enable or support it. Consequently, care ethics emphasizes relational competencies and virtues among HCPs as essential resources for supporting the agency of their patients, within the context of specific care encounters based on dialogue and reciprocity (3, 83).

Relational accounts of autonomy have helped further the concept of autonomy by offering a complementary viewpoint that ensures the social and relational conditions for decision-making are taken into account, without negating the ethical importance of individual autonomy (2, 84). This perspective is particularly relevant in pediatric care, where children, parents, and HCPs are closely interconnected, mutually dependent, and personally invested in decisions (72).

In pediatric oncology, research decisions are taken in the family context, where especially the assent-aged child's autonomy is dependent and inseparable from the communicative, emotional, and pedagogical abilities of researchers and parents. This means that there is an inherent risk that parental dominance will restrict the child's right to freely assent or dissent, or that researchers' recruitment practices will contribute to limiting the child's involvement. Children's autonomy can therefore be both supported and constrained through relationships (85, 86). A child-centered ideal thus involves recognizing the child as socially and relationally situated within the family and care contexts, while maintaining the centrality of the child's own rights, perspectives, and agency (87). Research has identified a need for a more relationally-oriented ethical approach to pediatric research, to move beyond assent as a mere formal procedure towards a more meaningful and substantive realization of children's assent, for example in pediatric oncology (88, 89).

Vulnerability

The concept of vulnerability is central in research ethics, although there is significant variation in how it is defined and understood across ethical guidelines (90). A common assumption is that certain groups – such as children – are situated in conditions of increased vulnerability, rendering them more susceptible to potential harm during research. At the same time, their participation is ethically important and should be facilitated on grounds of justice. The potential harms at stake may be physical, psychological, privacy-related, or social in nature (6).

A frequently emphasized dimension of vulnerability concerning children relates to autonomy, and entails an increased risk of coercion, exploitation, or undue influence. The DoH underscores that individuals who lack the capacity to provide informed consent are in a particularly vulnerable position, necessitating specific ethical consideration (7). The CIOMS defines vulnerability as a relative or absolute inability to safeguard one's own interests. This may stem from individual factors – such as incomplete or temporarily impaired decision-making capacity – as well as from social and institutional conditions, including inadequate support or information, or exclusionary attitudes and practices (6).

This autonomy-related understanding of vulnerability is central to this dissertation; nevertheless, other vulnerabilities arising during the research process, beyond the consent stage, also remain important. Children and families in pediatric oncology may be particularly vulnerable, not only due to the context of cancer diagnosis and treatment (89, 91), but also because of their dependent position in relation to researchers, HCPs, and the child's dependency on parents (6).

While often assigned to children on a categorical basis, vulnerability is increasingly regarded as contextual – arising from a multitude of complex and interacting factors related both to the individual and the context (90, 92, 93). An influential conceptualization in research ethics distinguishes between *inherent, situational,* and *pathogenic* vulnerability. This taxonomy acknowledges vulnerability as an unavoidable feature of the human condition – which includes inherent susceptibility to illness, suffering, and dependence on others for care and protection – while also recognizing that situational and context-specific vulnerabilities can be identified and mitigated. A particularly ethically problematic sub-type is pathogenic vulnerability, where institutional or relational practices unintentionally exacerbate existing vulnerabilities or generate new ones, especially by undermining autonomy and limiting agency. Such vulnerabilities may disproportionately affect children in pediatric oncology, who are already vulnerable in both medical and autonomy-related terms (94).

Vulnerability can also be understood as layered rather than categorical (93). Gordon proposes a conceptualization that encompasses cognitive, medical, socioeconomic, social and cultural, deferential, and institutional vulnerability. Children in pediatric oncology may, for example, be cognitively vulnerable due to their limited capacity to exercise autonomy, medically vulnerable due to the illness and treatment, and – depending on their family's resources – socioeconomically vulnerable, particularly when research participation provides access to medical opportunities that would otherwise be unavailable. Social and cultural vulnerabilities may arise from language barriers, cultural differences, or social position. Deferential and institutional vulnerability pertain to the child and their family's dependency on the healthcare system (95).

In light of children's vulnerable position as research participants, protective measures must safeguard their rights, interests, and well-being while remaining sensitive to their needs and perspectives. Such measures may include minimizing risks in procedures that offer no direct benefit to the child, seeking parental permission, and supporting the child's ability to provide meaningful and voluntary assent (6, 7). The purpose of these safeguards is both to prevent research from creating additional vulnerabilities and to address existing vulnerabilities through empowerment (94, 96).

Parents of children with cancer may also be considered vulnerable when their child is invited to participate in research, particularly in relation to their autonomy (65). Still, the child's protection depends on parental decision-making capacity, meaning that parental vulnerabilities may amplify the child's vulnerability in research. This introduces an additional dimension of vulnerability, particularly when research involves assent-aged children (92). A relational perspective is therefore crucial to illuminate the relational dynamics of vulnerability in childhood cancer research. Wilke et al., for example, note that children's vulnerability emerges in relationships and encounters with researchers and in interactions with parents, through adult practices that enable or constrain the child's opportunities for self-determination. Thus, both vulnerability and autonomy are shaped relationally during the research process (89).

Ethical competence

Ethical competence refers to the ability to identify and manage ethical challenges in a professional context (97, 98). In health care, ethical competence is described in terms of character strength, ethical awareness, moral judgment, and a motivation to do good (97). It has also been conceptualized as perceptual sensitivity to ethical situations, knowledge, reflective capacity, and the ability to translate these into decisions, actions, and behavior (99). At the same time, ethical competence presupposes appropriate organizational conditions and a supportive ethical climate; these factors are central to the practical enactment of ethical values (100-103).

Ethical competence is closely linked to virtue ethics, since it is often conceptualized through individual abilities, skills, and personal attributes (104). Professional ethical codes also emphasize values associated with virtue ethics, such as compassion, empathy, trust, integrity, and courage. Consequently, HCPs often focus more on character than on ethical principles and formal guidelines (68, 105, 106). However, relying solely on a virtue ethics perspective and tacit knowledge may provide insufficient guidance and lead to inconsistency in ethical practice.

For this reason, Eriksson et al. proposed an integrated model comprising three interrelated components: *being, doing,* and *knowing*. Here, 'being' refers to moral character and professional virtue, while 'doing' concerns acting in accordance with rules and norms in concrete situations to meet ethical and legal requirements. 'Knowing' involves ethical awareness, self-reflection, and the ability to identify and analyze ethical problems and critically appraise guidelines (107). The model's strength lies in its recognition that ethical competence is not solely about compliance with rules, or the adoption of a virtue-based approach, but rather about an interplay between personal abilities, practical judgment, and reflexivity. Actively supporting this type of multifaceted competence is important for researchers whose work involves children, as the guidance offered by guidelines and legislation is typically limited in scope and concreteness, not least concerning assent procedures. This places great demand on the researcher's ability to translate ethical requirements into practice (107, 108). Moreover, as children are increasingly regarded as knowledgeable, rights-bearing individuals with agency, the traditional, narrow emphasis on risk minimization in pediatric research has been problematized. This shift has led to increased demands being made of researchers: not only to protect children, but also to strengthen their competence in translating children's rights into practice (48, 109).

Ethically complex decisions are common in pediatric oncology: medical benefits must be weighed against severe side-effects (100). Research participation adds another layer of ethical complexity as the child's best interests are weighed against scientific interests, and any hope of a cure must be balanced against realistic expectations of risk and benefit, as in early phase trials (110). Such situations may lead to moral stress, defined as: "a kind of stress that arises when confronted with a moral challenge, a situation in which it is difficult to resolve a moral problem and in which it is difficult to act, or feeling insufficient when you act, in accordance with your own moral values" (111). Regardless of the level of ethical competence among staff, ethical challenges and moral stress are elements of pediatric oncology care and research that cannot be completely eliminated (69, 71, 110, 112-114).

Therefore, a supportive ethical climate and initiatives that strengthen ethical competence and moral resilience are important for reducing the negative long-term consequences of moral distress for individuals, organizations, and patients (115, 116). In addition, moral stress among family members, and the need to support children and parents as they manage moral challenges, has recently begun to receive more attention as an under-researched subject (117, 118). Pediatric oncology staff in Sweden have reported a need and desire for ethical support (100, 113, 119), and lack of competence has been identified as a contributing factor to moral stress (120). The limited focus on ethical challenges related to research within existing ethical support forums, and the need for research ethics competence, have been identified as areas that should be strengthened in pediatric oncology (114).

Rationale

The participation of children in childhood cancer research is of paramount importance for the generation of evidence-based knowledge that can improve survival rates, enhance treatment safety, and support quality of life throughout the cancer trajectory, for both patients and their families. While the development of more effective and less toxic treatments remains a central objective, clinical research must also address the broader needs of children and families, which include psychosocial support.

Nevertheless, involving children in research raises complex ethical challenges. In pediatric oncology, decisions about research participation are often made under emotional strain, complicating the processes of informed parental consent and meaningful assent on the part of the child. Moreover, the integration of clinical care and research may lead to moral distress and value conflicts for HCPs, including potential role conflicts.

Assent-aged children have the right to receive age-appropriate information and to participate in decisions concerning their involvement in research. Despite a growing recognition of children's rights within healthcare, and a clear ambition to increase their involvement in research, empirical knowledge about children's experiences of assent remains scarce, especially within Swedish pediatric oncology. Strengthening children's involvement in research must therefore be accompanied by ongoing ethical reflection and a reinforced child-centered focus in research practice. This thesis aims to contribute to that development.

While substantial theoretical work and ethical discourse on children's assent exist, there is a need for a context-sensitive understanding to guide research practices in pediatric oncology. To address this, the thesis adopts an empirical-ethical approach, exploring the experiences and perspectives of HCPs, researchers, research ethics committee (REC) members, children with cancer, their siblings, and their parents. Although the primary focus is on pediatric oncology, the insights generated may hold broader relevance for child health research more generally.

Aims

Overall aim

The aim of this thesis is to explore and describe ethical aspects of including assent-aged children in childhood cancer research, and to develop empirically informed, ethically grounded guidance for research practice.

Specific aims

The specific aims of each study are outlined below.

I. To explore healthcare professionals' perspectives on ethical values, challenges, and opportunities to strengthen ethical aspects of the recruitment of children with cancer for participation in research, and to examine their perceptions of ethical competence in the context of research recruitment.

II. To explore research ethics committee members' perspectives on ethical values, challenges, and opportunities to strengthen ethical aspects in pediatric research recruitment, and to examine their perceptions of ethical competence in the context of ethical review.

III. To describe how children with cancer, their siblings, and their parents experience children's participation in assent within pediatric oncology.

IV. To provide empirically informed, ethically well-grounded guidance for research practice.

Design and methodology

Ontology and epistemology

Research always rests on assumptions about the world (ontology) and about how knowledge should be acquired and regarded (epistemology). These assumptions should be reflected upon and communicated to the reader as they may shape the research process, including analytical choices and constructions. This allows the research and its findings to be situated in a wider perspective (121).

Ontologically, the thesis is grounded in *critical realism* (CR), a philosophical framework developed by Roy Bhaskar (122, 123). CR combines a realistic view of reality – that is, the view that reality objectively exists – with the perception of knowledge as interpreted and subjective; shaped by people's own interpretations, experiences, and social contexts. As such, knowledge is seen as context-bound and pluralistic, rather than universal and multifaceted. CR construes reality as existing independently of our senses, but stratified into three mutually interconnected hierarchical levels: 1) the *empirical domain* of what people experience, which may, through our engagement with those people, become the subject of our empirical investigations; 2) the *actual domain* of concrete events and practices that these experiences pertain to; and 3) the *real domain*, referring to underlying structures and mechanisms that are not directly observable but exist independent of our perceptions, and provide the conditions and constraints for the events and practices unfolding in the actual domain. Together the intersection of generative factors in the real domain, in a specific context, give rise to the events in the actual domain, which are then subjectively experienced, narrated and accounted for through the researcher's interpretative work.

CR offers a valuable philosophical framework for healthcare and nursing research (121, 124, 125). It has informed this thesis by supporting a multi-layered understanding of childhood cancer research that considers both the biological realities of illness and treatment, and the relational, institutional and social context. Its stratified ontology enables an analysis that moves beyond surface-level observations to explore the deeper mechanisms and conditions shaping research practice. At the same time, its epistemological openness allows for the interpretation of subjective experience and meaning-making central to qualitative and normative research (125, 126).

Adopting a critical realist approach in this thesis has involved working across all three interconnected ontological domains: 1) the empirical domain is engaged through participants' expressed experiences, as co-created through researcher-participant interplay; 2) the concrete research practices and experiences that these narrated experiences refer to; and 3) the generative mechanisms that are not directly observable but nonetheless shape and provide the underlying structural conditions for recruitment practice, which thereby impact parental autonomy and children's assent (121, 122).

Empirical bioethics

This thesis applies an empirical ethics approach in which qualitative research is integrated with normative analysis to develop context-sensitive and practically useful guidance (126, 127). Empirical ethics is a young and interdisciplinary field, typically combining social scientific methods – such as interviews to understand lived experiences and moral perceptions – with ethical analysis (128). Table 1 outlines normative ethics, empirical ethics and qualitative research, comparing the characteristics of each (126, 127, 129).

A central strength of this approach is that ethical knowledge becomes more relevant and grounded in the realities of practice. By engaging with concrete situations, it becomes possible to identify overlooked moral dimensions and produce context-sensitive ethical recommendations that are more applicable to practitioners' lived experiences. This not only enhances the practical utility of ethical insights, but also increases their perceived legitimacy among stakeholders, fostering stronger connections between ethical theory and real-world decision-making. In this thesis, empirical ethics is used for combined descriptive and normative purposes: to describe experiences and moral considerations related to research recruitment and identify ethically relevant contextual factors, and to develop normative guidance through the method of RE (126, 127). This involved a process of specification in which the meanings and implications of principles like autonomy and concepts like vulnerability were concretized to support ethical research practice in pediatric oncology (2). In this way, empirical ethics functions as a bridge between normative ideals and actual practice, so that theory and empirical findings mutually inform one another.

Table 1. Overview of normative ethics, empirical ethics and qualitative research

	Normative ethics	Empirical ethics	Qualitative research
Purpose	Formulate principles about right and wrong to guide moral conduct	Combine normative analysis with empirical data to make ethics context-sensitive	Provide rich, detailed descriptions of lived experiences, often without normative claims
Method	Philosophical reasoning, deduction	Empirical research combined with normative analysis	Interviews, focus groups, ethnography, observations
Focus	Universal moral rules and theories	Practical and clinical situations and practices; social, cultural and institutional contexts	Subjective perspectives, perceptions, meanings and interpretations
Source of Knowledge	Philosophical theories	Empirical data (surveys, interviews, observations) and normative theoretical frameworks	Participant accounts and observational data
Strength	Provides clear moral guidance	Makes ethics context-informed, relevant and applicable, increases legitimacy	Captures depth, nuance, and complexity of human experience and perception
Risk	Can be too abstract, detached from reality	Can become overly descriptive if not normatively well-engaged	Lacks normative guidance; cannot prescribe what ought to be done based on it
Application	Development of moral theories, concepts and principles	Description of practices, identify ethical aspects, context-sensitive guidance, reflective equilibrium	Understanding patient/participant perspectives and contexts

Qualitative research paradigm

Empirically, the qualitative work departs from principles of *naturalistic inquiry* – a research paradigm based on interpretivist principles, where reality is understood through individuals' interpretations and social constructions (130-132). Within this approach, the researcher and the participant are seen as actively influencing each other in the research process. The researcher often shifts between closeness and distance throughout the study, meaning that the relationship with participants and data is dynamic. Data analysis is not neutral; rather, the researcher is considered a co-creator of the understanding produced, making reflexivity a central part of the process. The study design is intentionally flexible to allow in-depth exploration of new ideas and themes. At its core, qualitative research seeks to understand the subjective meanings that participants attach to their experiences, recognizing the contextual and relational nature of meanings, rather than pursuing universal or objective truths.

This epistemological standpoint presupposes a conscious and deliberate approach to scientific inquiry, consistent with a qualitative research paradigm, in which the researcher is regarded as the key instrument of investigation. It acknowledges both personal experience and active engagement as fundamental to the production of knowledge through *empathic neutrality,* wherein the researcher seeks to understand participant's experiences with empathy, presence, openness, and mindful presence. Reflexivity is essential for acknowledging and critically engaging with one's own pre-understandings, ensuring transparency and integrity. Methodological strategies such as triangulation can be employed to enhance trustworthiness. This standpoint also presupposes an openness to change through a dynamic mode of inquiry, with fidelity to the particularities of each individual case and constant movement between the specific and the general in a creative synthesis of meaning. This approach is grounded in a holistic and context-sensitive perspective that values depth, complexity, and nuance in human experience (129).

Overview of studies

The thesis includes four studies, all conducted in the Swedish context. An overview of the studies is presented in Table 2.

Table 2. Overview of designs, participants, data and analysis of each study

Study	Design	Participants	Data	Analysis
I	Exploratory and descriptive qualitative design	Healthcare professionals in pediatric oncology (n=17)	Individual semi-structured interviews	Qualitative inductive manifest content analysis
II	Exploratory and descriptive qualitative design	Research ethics committee members (n=15)	Individual semi-structured interviews	Inductive manifest reflective thematic analysis
III	Descriptive qualitative design	Children with cancer (n=11), siblings (n=17) and parents (n=9)	Individual interviews	Inductive latent reflective thematic analysis
IV	Prescriptive normative theoretical study	See study I-III	Empirical results of study I-III and qualitative research combined with ethical theory	Reflective equilibrium

Study I

Setting and participants

HCPs were recruited in Sweden via childhood cancer care centers, a professional network of nurses, and university research groups. Seven physicians and ten nurses were interviewed. Of these, three reported as male, thirteen as female and one as non-binary. The majority had more than ten years' experience of recruiting participants for medical and/or psychosocial research.

Data collection and analysis

Individual semi-structured interviews were conducted from April 2021 until September 2021, via Zoom. The interviews lasted on average 46 minutes. They explored ethical values and challenges related to information provision and consent, the role of children, parents and HCPs in informed consent, and perceptions of ethical competence among HCPs. Demographic data were collected through a short questionnaire. The interview transcripts were subjected to qualitative content analysis, using an inductive approach with focus on manifest content (133, 134).

Results

The HCPs' ethical challenges and values in relation to participant recruitment primarily concerned: 1) establishing relationships and trust; 2) meeting informational needs; 3) acknowledging vulnerability; and 4) balancing roles and interests. Given the ethical complexity of recruiting children with cancer, 5) ensuring ethical competence was also raised as important, and relational values such as empathy, responsiveness, and communicative skills were emphasized.

Study II

Setting and participants

REC members were identified via lists obtained from the Swedish Ethical Review Authority. Invited members belonged to RECs reviewing medical research. Fifteen members were interviewed, of which seven reported as female and eight as male. The majority were aged 60 or older, and had more than five years' experience of ethics review.

Data collection and analysis

Individual semi-structured interviews were conducted from June 2021 until October 2021, via Zoom. The interviews lasted on average 47 minutes. They explored the ethical values and challenges encountered by REC members in research applications involving children with severe diseases, the basis underlying ethical decision-making, beliefs about which aspects of recruitment are important to parents and children, and perceived ethical responsibilities when reviewing applications involving children with severe diseases. Demographic data were collected through a short questionnaire. The interview transcripts were subjected to inductive reflexive thematic analysis (135).

Results

The REC members' ethical challenges and values revolved around: 1) promoting children's and parents' autonomy; 2) protecting children's well-being and integrity; and 3) ensuring regulatory adherence. Concerns were raised about aspects relating to the quality of information adapted for children, dependency, vulnerability, honesty, voluntariness, and potential conflicts of interests among pediatric researchers.

Study III

Setting and participants

The study combined two datasets: 1) data from a psychosocial pilot intervention, the Family Talk Intervention (FTI) (37); and 2) an extended sample of interviews with families involved in pediatric oncology on the topic of clinical research participation. Participants were recruited in Sweden via pediatric oncology centers and a national clinical trial unit, with four centers represented in the final combined sample. The study included 37 participants: 11 children diagnosed with cancer, 17 siblings, and nine parents. The children were between five and 13 years old. Fifteen reported as female and 13 as male, and the majority (64%) had been diagnosed with central nervous system tumors. Participants had experience of various types of research, including psychosocial interventions, clinical trials, and observational studies. Participants were Swedish-speaking, and the majority of parents had higher (post-secondary) education.

Data collection and analysis

Interviews were conducted during two time periods: 2018–2019 (the FTI sample) and 2024–2025 (the extended sample). Interviews with children took place at their homes (n = 26) or via video call (n = 2), and interviews with parents were conducted via video call (n = 4) or by phone (n = 5). Interviews with children lasted on average 15 minutes, and interviews with parents 35 minutes. The interviews explored the experiences of the child being invited to participate in research. Interviews with parents also explored other aspects of their experiences with recruitment, beyond the child's participation in assent. These data are not included in this thesis. Demographic data were collected via questionnaire. The interview transcripts were subjected to inductive, latent reflexive thematic analysis (135). Although this study was conducted within a relatively unexplored field, the child data were not dense enough to support a deeper exploratory analysis, and a descriptive design was adopted (136).

Results

Two overarching themes were generated: 1) a moral and emotional commitment to research; and 2) relational assent: trust, loyalty and parental constraint. Both children and parents viewed research participation as meaningful and morally important; these perspectives were often shaped by gratitude and solidarity. Children's involvement in assent varied, and was influenced by their emotional state, parental mediation, and relational dynamics, sometimes constraining the child' participation. These findings highlight the need for child-centered, continuous and dynamic assent procedures that account for children's evolving capacities and relational contexts.

Study IV

Analysis

This study used Reflective Equilibrium (RE) as a method of moral reasoning to develop well-founded normative guidance on children's assent to participation in research. As theoretical philosophical papers typically do not include a methods section, the methodological approach of Study IV is described here.

As a method, RE consists of an analytical, iterative process aimed at achieving coherence between specific, considered moral judgments and general moral principles, allowing them to mutually support and refine one another. RE was introduced by John Rawls in 1971 (137) and is a well-established method for normative ethical analysis (137-142). The aim is to reach an ethically well-founded *resting point* with acceptable coherence between moral principles, rules, and particular judgments. The outcome of an RE analysis should not be regarded as a final moral verdict but as something that may be revised in light of empirical or theoretical developments (137). The aim is typically to reach a wide reflective equilibrium, drawing on a broad base of theory (and not only normative theory) and empirical evidence − including third-person perspectives (143, 144).

The analysis followed the conventional RE steps: identifying considered particular moral judgments and relevant general moral principles, and engaging in iterative analysis with mutual adjustments to achieve coherence. It incorporated ethical principles, arguments and concepts, legislation and guidelines, alongside particular moral judgments derived from empirical studies, primarily in the field of pediatric oncology. This included Studies I–III, which represented perspectives from HCPs/researchers, REC members, as well as children, parents, and siblings. A review of relevant research was conducted with an emphasis on qualitative research, which tends to yield more nuanced and considered judgments than quantitative methods (145).

The particular moral judgments identified were contrasted with the Principles of Biomedical Ethics by Beauchamp and Childress (2). These established mid-level principles have the advantage of being widely accepted across various ethical traditions – such as consequentialism and deontology – and of being flexibly adaptable to clinical contexts. In addition, arguments from care ethics (4, 5, 84, 146) were integrated, as relationship-building, trust, and emotional context have been empirically proven to be relevant in recruitment and assent processes in pediatric oncology (114, 147). Finally, the analysis incorporated international ethical guidelines and national legislation on children's assent and rights to participation. Finally, the analysis incorporated international ethical guidelines and national legislation on children's assent and right to participation in research. A large language model (ChatGPT, OpenAI) was used to assist in synthesizing and thematically organizing empirical findings (mainly participant quotes) to support the analysis, but not for generative analytical purposes.

Following consideration of the particular moral judgments identified, ethical principles, arguments and concepts, legislation, and ethical guidelines, a preliminary hypothesis was formulated to guide further analysis: *Children's meaningful assent to childhood cancer research is ethically important and children's autonomy should be promoted.* This hypothesis served to test moral arguments, primarily concerned with participation and autonomy, relational autonomy, trust, respect for persons, and paternalism. To reach coherence between particular judgments and general principles, the following conclusion was ultimately formulated: *In childhood cancer research, it is important not only to respect children's autonomy but also to promote it as a value, by actively supporting children's autonomy. Central to this view is an understanding of how relationships and trust can both enable and constrain children's autonomy.*

Results

As a result of the analysis, three dimensions of children's autonomy in pediatric assent were proposed: autonomy as a right, as a value, and as relational in nature. Autonomy as a right affirms children's entitlement to participate in decisions affecting them, including the right to dissent or opt out. Autonomy as a value emphasizes the need to actively support children's decision-making capacities through tailored communication and emotional responsiveness. Relational autonomy highlights how children's preferences and understandings are shaped within trusted relationships, where adults can scaffold or constrain autonomy. Together, these dimensions call for recruitment conducted with respect for children as persons, to avoid instrumentalization.

Ethical considerations

All studies were conducted in accordance with the Swedish Act concerning the Ethical Review of Research Involving Humans (SFS 2003:460). According to the legislation, Studies I–II did not require formal ethical approval; however, an advisory opinion was obtained from the Swedish Ethical Review Authority (Dnr 2021-00570), which resulted in no objections. Ethical approval was granted for Study III (Dnr 2018/250-31/2, Dnr 2018/1852-32, and Dnr 2023-03332-01).

The ethical requirements regarding privacy, confidentiality and informed consent outlined in the DoH were adhered to (7). All participants received written information about the research, were informed of its voluntary and confidential nature, and provided informed consent or assent. Children provided assent verbally and/or in writing, and parents gave informed consent for both themselves and their child.

Assent procedures were informed by the ethical guidelines of CIOMS and the Council of Europe, the Nuffield Council on Bioethics Report, and the guidance provided by the Swedish Ethical Review Authority (6, 79, 148, 149). Age-adapted information was provided to children in written and verbal form, with questions and dialogue encouraged. A brief child-friendly video explaining the study was also sent to the child beforehand. It was emphasized that participation was voluntary and confidential.

Data were managed in accordance with the General Data Protection Regulation (GDPR) and Uppsala University's internal policies, with strong protections for participant privacy. Measures included pseudo-anonymization, encrypted password-protected interviews conducted using Uppsala University's Zoom license to ensure enhanced security, and group-level presentation of results. Consent was obtained for audio recording, and only audio files were retained. Data were stored in encrypted digital form, in accordance with applicable information classification standards, with a separately stored code key and an encrypted backup in a locked fireproof cabinet.

Given the small and closely interconnected context of Swedish pediatric oncology, demographic, clinical, and context-relevant information was reported sparingly in the studies and with care to protect the confidentiality of HCPs and families. For example, only age ranges, rather than specific ages, are reported for HCPs, and the specific type of study in which each child participated was omitted. This also applies to members of the ethical review boards, whose professions were not reported. Interviews were pseudo-anonymized by removing names and geographical identifiers prior to analysis, and quotations were presented using pseudonyms.

Pediatric oncology is a demanding care context in which HCPs may experience moral distress (100, 113). Reflecting on personal experiences with an external researcher may feel meaningful, but can also evoke feelings of shame, guilt, or distress, and reveal organizational shortcomings. A preparedness plan was in place to recommend that participants contact an occupational safety representative or appropriate care provider if necessary, though no such need was identified.

Consideration was also given to the emotional burden placed on families, the possibility of research fatigue, families' dependence on healthcare providers, and children's dependence on their parents. Families in acute crisis were not approached, and those invited were given time and encouragement to consider participation without pressure, with information about the study being provided prior to decision-making. A routine was put in place to refer families to psychosocial support services if necessary. The voluntary nature of participation in the research was particularly emphasized for children, and their explicit assent or dissent was sought. The interviewer was attentive to signs of discomfort or reluctance. When a child preferred to be interviewed in the presence of a parent, it was clarified that it was the child's, rather than the parent's, perspective that was being sought.

Interviewing experts requires particular ethical awareness. Because experts – such as pediatric oncologists and members of ethical review boards – often hold strong institutional positions, interviewing them may involve negotiation of knowledge, and traditional hierarchical factors related to age, gender, and professional status may shape this interaction. As a researcher one must balance respect for the expert's position with the need for critical analysis – being assertive (to stay truthful to the study's aims) while also being sensitive (to acknowledge the expert's experiences and potential vulnerabilities) (150). This ethical tension was evident in several interviews in Studies I and II; when asked to reason ethically about pediatric research and review, one REC member firmly stated: *"It's actually really simple: the law, that's what we should obey."* Similarly, a pediatric oncologist repeatedly remarked: *"You won't find any new ethical values – we already have ethical values that we should follow."*

In this thesis, the majority of the interviews with children were conducted by external researchers as part of a pilot implementation of FTI. This is a setup that involves ethical tension, as it entails an external party assessing the ethical dimensions of a specific research project and its practices – even if this is not the primary aim. This introduces elements of negotiation into the analytic process, necessitating both interpretative humility regarding the unique contextual knowledge possessed by the external researchers about their data, and a shared commitment to ensuring the integrity of the findings from an ethical perspective. The researcher who had collected the FTI data critically reviewed the analytic constructions, and discussions were held to ensure a faithful and context-informed representation of the data.

From a broader perspective, the findings of this thesis may influence attitudes toward childhood cancer research in Sweden among HCPs, patients, families, and society more broadly. The focus of this thesis on ethical dimensions has drawn attention to the value-laden aspects of recruitment. This framing carries the risk of portraying childhood cancer research as more ethically complex or problematic than it may be in everyday practice. Moreover, some of the challenges identified may be practical or organizational rather than strictly ethical in nature (time constraints, for example).

General discussion

The aim of this thesis was to explore and describe ethical aspects of including assent-aged children in childhood cancer research, and to develop empirically informed, ethically grounded guidance for research practice. Table 3 presents a synthesis of each study's main conclusions, themes, and contributions, followed by a discussion of four overarching themes that cut across the studies (Figure 1).

Table 3. Overview of perspective, main conclusions, illuminated themes and contributions of each study

Perspective	Conclusions	Themes	Contributions
Healthcare professionals	Recruitment is relational, role tensions between care and research; broad ethical competence.	Trust, vulnerability, informational burden, balancing children's and parents' interests.	Clinical insights; care-ethics perspective.
Ethics committee members	Emphasis on participation, protection, compliance; lack of child-adapted information.	Formal consent requirements, honesty and transparency, holistic view of risk and vulnerability.	Ethical review perspective; principle-based ethics.
Children, siblings and parents	Assent is relational; children's vulnerability; need for dynamic, continuous, child-centered assent.	Trust, emotional and moral commitment, limited participation and parental constraints.	Children's, siblings' and parents' views; care-ethics perspective.
Normative analysis	Children's autonomy as right, value, and relational practice; meaningful participation to avoid instrumentalization.	Autonomy requires respect, support, and relational scaffolds.	Normative guidance grounded in empirical data.

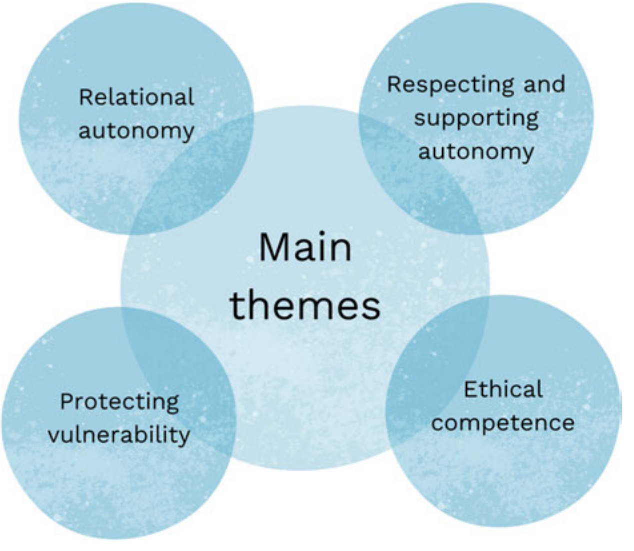

Figure 1. Main themes across the four studies

Relational autonomy

In research, children's right to participate in decisions that affect them is operationalized through assent and parental consent, typically unfolding in a triadic interaction between child, parent, and researcher. The findings of this thesis show that recruitment in pediatric oncology is deeply shaped by relationships, trust, and contextual conditions, aligning with theories of relational autonomy and care-ethics (3-5, 81, 84, 151, 152). These findings are also consistent with earlier research (85, 153).

A key insight from the four studies is that autonomy does not arise in isolation: *autonomy develops through relationships.* Children's motivations and decisions regarding research participation were often shaped by their interactions with parents (83). For children and parents, taking part in research was perceived as an act of care, a way of giving back and paying forward, and a way of feeling cared for and supported.

Autonomy was also shown to be *exercised within specific social contexts:* trust emerged as a fundamental prerequisite for recruitment, and decision-making was typically described as a collective family process rather than as a purely individual decision. Information was often mediated through parents, who acted as primary interpreters and often also decision-makers on behalf of their children.

Importantly, *autonomy could be enabled and supported.* Children depended on age-appropriate information, active involvement, dialogical communication, and emotional support, to participate meaningfully in assent procedures. Attentive and trusting relationships often served as scaffolds that bolstered children's agency.

Another essential dimension of relational autonomy is *the requirement for moral recognition***.** When children were explicitly invited to express their views, they reported feeling respected, informed, and acknowledged. Recognizing children as rights-bearing agents, rather than passive participants, was fundamental for fostering meaningful participation in assent.

Moreover, autonomy was *shaped by broader structures and institutional practices*. Recruitment to research usually took place in a clinical context characterized by high trust and commitment to research, which could unintentionally diminish critical reflection. Furthermore, the timing of recruitment – which often occurred in medically pressured situations – and the integration of research discussions with clinical care could contribute to therapeutic misconceptions and affect autonomous decision-making.

Importantly, *autonomy could be constrained by relationships.* Power asymmetries between adults and children, parental dominance, and families' dependence on healthcare could limit children's role and involvement. In some cases, children reported feeling subtly influenced by their parents. Assent was also sometimes granted based more on their trust or expectations of their parents, or a striving for alignment with their parents, than understanding of the research.

One of the strengths of adopting a relational perspective on autonomy is that it helps make visible the power asymmetries and conflicts of interest between children and parents, as well as in relation to HCPs and researchers. Equally important is the increased emphasis it places on how autonomy can be relationally supported through mutual dialogue, in order to enhance children's capacity and participation – while respecting family roles and bonds.

In conclusion, the concept of relational autonomy offers a valuable perspective for understanding recruitment in childhood cancer research, because it highlights the relational, contextual, and institutional conditions that shape children's opportunities to meaningfully engage in assent.

Respecting and supporting autonomy

Across all studies, autonomy emerged as an important value that was challenging to realize in practice. In Study I, HCPs aimed to meet families' informational needs and emphasized children's participatory rights. Nevertheless, Studies I and III show that children's participation varied and was sometimes limited – due to personal preferences or contextual constraints – and that parents' autonomy as proxy decision-makers was also constrained at times; this is consistent with previous research (63-65, 85). Types of autonomy-related barriers identified in this thesis include:

- **Relational barriers:** Parental dominance, gatekeeping, or overriding of children's preferences.
- **Emotional barriers:** Crisis, fear, emotional overload, parental distress, and children's psychological burdens.
- **Informational barriers:** Overwhelming amounts of information, multiple concurrent studies, lack of child-adapted materials.
- **Structural barriers:** Systematic deficits in child-directed information and lack of criteria to assess child-friendly communication, absence of translated materials, legalistic language.

Given these challenges and barriers, researchers may need to actively support the autonomy of both parents and children. This involves providing tailored information as well as relational, emotional, and practical support throughout the recruitment process. Such an approach aligns with the understanding of autonomy not only as a value, but as 'scaffolded' through supportive relationships and adapted communication (2, 84, 154). It also aligns with the recommendations of established ethical guidelines for meaningful child participation and research assent (6, 149). In parallel, supporting autonomy is closely linked to the ethical imperative of protecting vulnerable research participants, particularly in emotionally charged and high-stakes contexts such as childhood cancer research.

Protecting vulnerability

This thesis contributes to the understanding of how vulnerability manifests in childhood cancer research recruitment. Vulnerability was found to be contextual, which aligns with the established dimensions of vulnerability as *inherent,* *situational*, and *pathogenic* (92-94). Vulnerability was also found to be multifaceted, involving cognitive, communicative, institutional, deferential, economic, social, and medical aspects (90, 95).

Forms of vulnerability that are *inherent* are unavoidable in the human condition. They relate to vulnerability to illness and suffering, children's developmental dependency, and the relational dependence and strong emotional bonds between children and their parents. Families at the diagnosis or relapse stage are profoundly and inevitably vulnerable and, in this context, children's assent is closely intertwined with family dynamics, raising complex ethical considerations.

Situational vulnerabilities are shaped by the situation, timing and context of recruitment. Moments of fear, shock, and informational overload can impair families' capacity for informed decision-making. In such circumstances, trust in clinicians or researchers may be substituted for reflective evaluation or research participation.

A third dimension is *pathogenic vulnerability,* referring to institutional or relational practices that unintentionally exacerbate existing forms of vulnerability. For example, obtaining consent during emotionally intense periods, failing to sufficiently address therapeutic misconceptions, or engaging in strategic recruitment and communication based on professional interests can all contribute to this type of vulnerability. Additionally, when psychological or privacy-related risks are overshadowed by immediate medical concerns, this may lead to insufficient safeguards and the lack of a holistic perspective on risk.

Overall, vulnerability in childhood cancer research is contextual and dynamic. Researchers should aim to identify and mitigate avoidable vulnerabilities, for example by strengthening families' decision-making capacity. Because vulnerability can disempower and reduce agency, and increase dependence, supporting autonomy as a guiding value remains a key protective measure in research (94).

Ethical competence

Ethical competence is the ability to identify and manage ethical challenges (97, 98) and is grounded in knowledge, skills, personal qualities, and organizational support (101). Findings from this thesis show that ethical competence in pediatric research recruitment is closely tied to researchers' sensitivity to relational dynamics, timing, and children's evolving capacities, highlighting the need for reflexivity and context-aware judgment. These findings align with the tripartite model of ethical competence: being, doing, and knowing (107). It is evident that ethical competence requires a balance between aspects of being, doing, and knowing to address the ethical, relational and clinical complexities of research recruitment, by both supporting autonomy and protecting vulnerability.

- **Being:** Professional virtues such as sensitivity, empathy, responsiveness, and a child-centered and relational orientation toward children and families.

- **Doing:** Acting in accordance with rules, principles, and law, possessing clinical and scientific competence, pedagogical skills, translating children's rights into assent practice.

- **Knowing:** Ethical knowledge and critical reflection, continuous research ethics development and forums for dialogue and self-reflection.

In relation to ethical review, REC members focused primarily on legal adherence (doing), but they also emphasized virtues of impartiality, conscientiousness, perspective-taking and collaborative orientation (being). They also highlighted the value of formal ethical knowledge, educational initiatives and ethical reflection (knowing). Studies III and IV did not explore ethical competence directly but highlighted knowledge of children's moral and participatory rights, and the need for navigating assent as a relational, dynamic process.

Conclusions and clinical implications

The thesis shows that many aspects of childhood cancer research in Sweden are ethically robust: families demonstrate a high level of trust in research, and HCPs show a clear commitment to advancing research while advocating for the best interests of their patients, and demonstrate high ethical awareness. They express a strong child-centered perspective and a family-centered approach. At the same time, children's participation and support for children need to be strengthened to enable more consistent and meaningful assent.

Childhood cancer research may benefit from increased relational awareness. This involves recognizing the importance of trust and responsive relationships in children's assent, as well as identifying and addressing power asymmetries between children, parents, and professionals. Clinicians need to remain alert to situations where trust is substituted for reflective understanding and take into account how family circumstances, decision-making burdens, and emotional stress affect children's autonomy and need for protection. A balance between family-centered and child-centered approaches is necessary, as is helping children express their views without being overshadowed by their parents. Moreover, children's dissent must be acknowledged and respected, even when it conflicts with parental wishes.

It is essential to actively support autonomy in research practice. This requires recognizing the child's moral status and rights, as well as integrating guidelines that emphasize dynamic and child-centered participation based on rights-based frameworks within research practice, especially as views on children's competence and status as rights-holders vary. It is crucial to provide adapted information to children, and there may be a need to follow up on assent over time, particularly when the child initially lacked the opportunity to participate meaningfully. As proposed by Sinclair: "*it is necessary to move beyond one-off or isolated participation and consider how participation becomes embedded as an integral part of our relationship with children*" (155).

Research is, and will remain, an important part of clinical practice. Competence in research ethics is therefore vital for Swedish pediatric oncology – as

HCPs and members of ethics review boards have expressed. Such competence is multifaceted and grounded in principle-based ethical reasoning, as well as care ethics and virtue ethics. Knowledge of the rights of children participating in research, and of autonomy and vulnerability, is central to competence in research ethics. Forums for ethical dialogue and reflection, coupled with interactive educational initiatives, should be implemented to promote research ethics at both individual and organizational levels.

Future directions

The findings of this thesis point to several areas in need of further investigation. Additional research is needed to deepen our understanding of children's perspectives on information, assent, and participation. Future studies should investigate how children's experiences and preferences can be systematically integrated into assent process, both during protocol development and recruitment.

This thesis proposed that autonomy should be supported as a value in assent. For assent-aged children, flexible, interactive and dialogue-based methods may facilitate meaningful involvement; and these approaches should be empirically evaluated with regards to effectiveness in autonomy promotion.

Relational autonomy merits further development as an analytical concept in pediatric research. Future empirical studies with observational design should investigate how parents and HCPs function as scaffolds for children's autonomy, and under which conditions relational dynamics may instead constrain children's self-determination. Normative research should further address how conflicts between parents and children can be managed in ways that respect parent's caregiving responsibilities and rights, without introducing unwarranted paternalism towards the child.

In the normative analysis, the focus was primarily on autonomy. More in-depth work is needed to understand the various forms of vulnerability experienced by children and parents in recruitment to childhood cancer research, and to identify practical strategies to mitigate these. An associated issue concerns fairness: children and parents who did not speak Swedish were excluded from Study III, highlighting the need for research that includes families using interpreters and families with more diverse socioeconomic backgrounds.

The thesis also points to the potential of dynamic, process-oriented models of assent, recognizing that children may become capable of more meaningful participation at later stages of illness. Future studies should design and evaluate such models – such as flexible or stepwise assent procedures, decision-support tools, and age-adapted information strategies, ideally pilot-tested or co-created with children – and examine their effectiveness in promoting autonomy. Organizational strategies to reduce information and decision burden on families should also be explored.

Given the central role of parents in assent, future research should examine models that engage parents as ethical partners in supporting children's rights and autonomy, including decision-support interventions for parents making research-related decisions on behalf of their children.

Finally, both HCPs and REC members expressed a need to strengthen research ethics competence. Future research may therefore focus on developing and evaluating educational initiatives building on principle-based, care-ethical, and virtue-ethical frameworks, with particular attention to facilitating children's rights and autonomy, and addressing both child and parent vulnerability in practice.

Methodological discussion

Empirical ethics

This thesis uses an empirical ethics approach, combining empirical investigations with normative analysis to generate context-sensitive ethical knowledge. The core strength of this thesis lies in its empirically grounded, theoretically plural, and contextually rich understanding of pediatric research recruitment, an understanding which is anchored in children's rights and relational ethics. The methodological strength of the thesis lies primarily in its attempt to bridge gaps between practice and theory in order to generate knowledge that can inform and support the ethical conduct of childhood cancer research. Another strength is the inclusion of the lived moral practices of all actors involved, which allows an understanding of the processes they are engaged in, and their relationships, attitudes, and values (126, 127).

This thesis aims to deepen and contextualize our understanding of ethical aspects of recruitment for childhood cancer research. Its iterative and cumulative design allows insights from earlier studies to inform later studies, enhancing the overall coherence and credibility of the thesis. Interviews with clinicians and REC members (Studies I–II) highlighted aspects of autonomy and beneficence, a finding which guided the exploration of experiences related to children's participation in assent in Study III. These accumulated empirical insights subsequently informed the normative analytic focus of Study IV, and the articulation of a contextualized three-dimensional understanding of autonomy.

To strengthen the overall credibility and transparency of the empirical ethics approach taken in this thesis, the work was guided by standards of practice for empirical ethics. This involved: (1) clinically relevant questions, combined with a clear normative research aim; (2) clear ontological, epistemological, and theoretical positioning; (3) rigorous empirical and theoretical analytical methods, with reflection in light of established quality markers for each method and research paradigm; (4) familiarity and immersion in the empirical realities of the research field; and (5) guidance and support from senior researchers with robust expertise in empirical research and bioethics (128).

A broad analytical scope was adopted for the whole thesis, focusing on general ethical values and challenges, without limiting its scope to specific study types or clinical circumstances. I regard this a strength, as core ethical principles – respect for children's emerging autonomy through assent and protection of children through parental permission – apply equally across pediatric oncology in general. Nevertheless, different study designs pose distinct ethical concerns (for example, the risks involved in a phase I drug trial differ from those of a play therapy intervention). Contextually important aspects should always be considered in ethical deliberation about specific cases.

Theoretical and normative frameworks

The thesis integrates principle-based ethics and care ethics. Principle-based ethics provided a structured framework for identifying core values and ethical conflicts (such as autonomy vs. beneficence), while care ethics provided a relational and practice-oriented understanding through foregrounding emotional, relational, and contextual aspects of research practice. Measures were taken to apply these different frameworks reflectively, and in a context-sensitive manner: first and foremost, through the inclusion of key stakeholders with lived experience in the critical normative analysis, in accordance with empirical ethics.

Through this empirical-normative integration, the concept of relational autonomy became central: children's self-determination is shaped, enabled and constrained through relational interactions. This use of pluralistic yet coherent theoretical frameworks allowed empirical analysis of the data to inform, question, and refine theoretical normative assumptions, in line with the logic of RE. This thesis is also underpinned by a children's rights perspective, primarily the principles of the Convention on the Rights of the Child, which emphasize respect for children's autonomy, protection, and participation; these principles shaped its conceptualization, design and analysis.

Qualitative methodology

The empirical studies used qualitative interviews to access the subjective experiences and perspectives of HCPs and families involved in pediatric oncology. Individual semi-structured interviews with HCPs (Studies I–II) provide insight into ethical and clinical reasoning and practices governing research conduct, while the interviews with children and parents (Study III) illuminate how decisions about research participation are made within families.

A notable strength is the triangulation of perspectives throughout this thesis, across clinical, regulatory, and familial contexts (see Figure 2). This broadens and deepens the analytical scope of the thesis, enhancing its overall credibility.

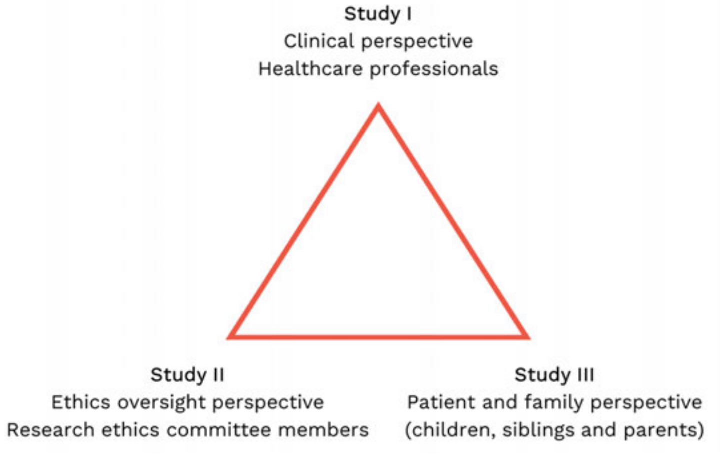

Figure 2. Perspectives triangulated in this thesis

In line with conventional qualitative interview methodology, methodological rigor and ethical sensitivity was striven for in all interviews. A good interview requires the interviewer to be knowledgeable about the topic and to maintain a balance between structure and flexibility – guiding the conversation while remaining responsive to what participants themselves find meaningful. Establishing rapport and trust was considered important, as were as principles of clarity, empathic presence and sensitivity; this was put into practice by actively listening and using efficient probing and reflective questions to gradually deepen understanding of the participants' narratives (135, 156).

The interviews with professionals in Study I and II were particularly valuable to this thesis, given its aim to understand practical experience of the recruitment of participants for pediatric research, and the decision-making and subjective reasoning processes involved. They yielded insights into procedural knowledge (routines and practices) and subjective reasoning (values and principles). However, interviewing professionals comes with specific challenges:

their knowledge is tacit, and both targeted questions and a solid pre-understanding of the expert's professional context, including regulations, policies, and routines, is required to draw it out. Further, professionals often resort to normative statements, for example by referring to institutional or legal obligations rather than their underlying personal reflections. This requires the adoption of an active approach on the part of the interviewer, through prompts that stimulate critical, deeper reflection. Moreover, experts are not neutral informants; they represent personal and institutional and professional norms and interests, and this must be critically considered in the analysis (150).

In Study III, most of the data from interviews with children had been previously collected by external researchers outside our research group as part of a family-based psychosocial pilot intervention. Notably, it is ethically and scientifically commendable – and uncommon – for researchers involving children in research to evaluate their assent procedures to identify areas of improvement (76, 77). Using these data in this thesis offered both advantages and limitations. Because the interviews were tied to a concrete intervention study in which the children themselves had actively participated over a period of time, the responses appeared spontaneous and unfiltered. However, the interviews explored assent only briefly, and were not originally designed for ethical analysis. This resulted in relatively shallow data. Therefore, transparency regarding the context, scope and limitations of the analysis, coupled with interpretive humility, was central.

Interviewing children has its own specific challenges, as children's narratives and ability to express themselves are shaped by their linguistic and cognitive capacities, but also relationally dependent and sometimes constrained (157, 158). In the extended sample, age-adapted information on research was developed using a readability index (www.lix.se), interview questions were refined by two researchers with clinical experience of pediatric care, and interview questions were adapted to the child being interviewed. Children chose whether to be interviewed alone or with a parent, and when a parent was present, they were told that the child's perspective was being sought rather than theirs. Moreover, discussing research, an abstract topic, with children can be challenging (86). Children may struggle specifically with abstract topics, recall of past events, or emotionally charged themes. As a result, their narratives can be brief, fragmented, and anchored in the immediacy of the present (159). Therefore, interpretive humility was striven for and efforts were made to remain as close as possible to the children's own formulations at the sub-theme level, while engaging in more latent and abstract interpretation at the overarching thematic level. The researcher who had collected the FTI data critically reviewed analytic constructions in light of her contextual knowledge, and suggested revisions where appropriate. Nevertheless, the retrospective and cross-sectional design, resulting in sometimes significant elapsed time between the child's assent and subsequent interviewing, should be acknowledged, given the risk of recall bias and retrospective reconstruction problems – especially given that research recruitment in this context often occurs during life situations marked by distress and uncertainty.

Methodological triangulation could have enriched our contextual understanding of children's participation in assent, for example by complementing the subjective accounts with observations which illuminate communicative practices and behaviors (160, 161). Similarly, alternative child-centered methods, such as arts-based methods, could have provided the advantage of supporting children's expression (145, 162). However, the interpretative complexity of art-based methods and the normative aims of this thesis, best achieved by analysis of interview data, made an entirely interview-based approach better suited for this thesis (145).

Trustworthiness

Study I was guided by Graneheim and Lundman's measures to achieve trustworthy qualitative content analysis (133) and Studies I and II were carried out according to the Consolidated Criteria for Reporting Qualitative Research (COREQ) (163). Study III was instead guided by the later Reflexive Thematic Analysis Reporting Guidelines (RTARG), which were developed specifically for reflexive thematic analysis (164).

The trustworthiness of this thesis is enhanced by its adherence to the conventional principles introduced by Lincoln and Guba (131, 132), further developed by Shenton (165). In addition, measures were taken to ensure alignment between aims, design, analytic choices, and reflexivity.

Credibility concerns whether the findings provide a truthful and accurate representation of the studied phenomena and the participants' lived experiences. It can be strengthened through transparent documentation of methods, familiarity with the field, diverse sampling, triangulation, iterative analysis, and reflexive collaboration (165). In this thesis, structured qualitative analytic approaches that suited each study's aim were used. A diversity of perspectives and research experiences was sought to broaden analytic scope, for example through site triangulation and strategic sampling (160, 161). Sampling was guided by the concept of *information power*: considering each study's aim, sample specificity, theoretical grounding, interview quality, and analytic approach. Data were gathered until the dataset was deemed sufficient to support credible and meaningful analysis and representation, following principles of comprehensiveness and data adequacy (166, 167). Nevertheless, the recruitment challenges encountered in Study III resulted in a final sample composition in which a majority of the children were interviewed in conjunction with psychosocial research. This should be considered in relation to credibility, as limited variation in participant experiences may reduce a study's ability to capture the full complexity of a phenomenon.

Across the three studies, qualitative analyses were conducted with varying interpretative depth, reflecting the thesis's iterative progression. Studies I-II used manifest orientations to data to ensure descriptive accuracy, while Study III combined manifest descriptions with a more latent, reflexive thematic approach, also interpreting the underlying emotional and relational patterns in children's and parents' narratives (134).). To support credibility, the analytical processes involved collaborative analytic work among different constellations of co-authors for each of the different studies, supporting reflexive practice. All studies underwent collegial scrutiny through higher ethics seminars, conference presentations, and professional seminars with clinicians. The absence of member checking or other systematic validation strategies, however, constitutes a limitation in terms of credibility.

Transferability refers to the extent to which findings are applicable to other contexts and populations beyond the one studied. While the reader is the ultimate judge of transferability, the researcher bears responsibility for facilitating this assessment, for example through detailed descriptions of participants, data collection methods, analytical procedures, and study contexts (165). In Studies I-III, transferability was supported by supplying necessary context and through 'thick' descriptions of the legal and ethical frameworks, recruitment settings, and sample compositions. Certain relevant details, however, had to be omitted to minimize the risk of participants being identified (168). The reader should bear in mind that the results of all four studies are bound to the Swedish cancer care and research context. The Swedish context is characterized by high childhood cancer survival rates, strong institutional support for research, and high levels of trust and willingness to participate in research among families. These conditions differ markedly from many low- and middle-income settings, where survival and enrollment rates are substantially lower. Cultural norms and legislation regarding children's roles in decision-making also vary across countries. Further, the focus was on assent-aged children, under 15 in accordance with Swedish consent legislation, and the majority of children in Study III were interviewed in conjunction with their participation in family-oriented psychosocial research. It should also be noted that the two datasets used in Study III were collected at different time points (2018–2019 and 2024–2025), and attitudes, conditions, and practices for clinical research may have evolved between these time points.

Dependability concerns the transparency and consistency of analytical processes and reporting. It can be strengthened through documentation of the analytical steps taken, triangulation, collaborative coding and theme development, and reflexivity – measures that support assessment of whether analytical constructions are well-founded (165). In this thesis, dependability was promoted through transparency concerning methodological choices, analytical procedures, and limitations. The analytical progression from manifest analysis in Studies I–II, to a more latent approach in Study III, culminating in the normative analysis in Study IV, also strengthens the dependability of the thesis as a whole. However, higher levels of abstraction and interpretation make proving analytic credibility more demanding (169). Therefore, supervisors and co-authors with diverse backgrounds contributed to conceptualization, design, coding, thematization, and presentation of the empirical studies, increasing their analytic richness.

Confirmability refers to whether findings genuinely reflect the data rather than the researchers' personal preconceptions (Shenton, 2004). In qualitative research, the aim is not to eliminate the researcher's theoretical or subjective standpoint – as this constitutes an important analytical resource – but rather to account for it transparently through reflexive practice (129, 135). Confirmability was established by detailing the composition of the research team and further strengthened through data triangulation and the integrative empirical–ethical approach. Further, extensive use of participant quotes supported confirmability. Importantly, this counterbalances the fact that a cross-sectional design with an absence of systematic validation (such as member checking or deviant case analysis) increases analytic reliance on the research team's internal pre-understandings, while limiting the opportunities to gradually correct or refine them (129, 170).

Normative method

The normative analysis in Study IV was guided by the method of RE (137-139, 141, 142). Diverse moral perspectives, empirical findings, theoretical frameworks, and legal considerations were integrated to reach a robust and wide equilibrium (144). Well-considered, rather than spontaneous, judgments sought through critical and collaborative reasoning among scholars with various theoretical and clinical backgrounds in psychology, pediatric physiotherapy, nursing, care ethics, and principle-based ethics. This interdisciplinary dialogue and iterative revision enhanced the relevance of judgments and the overall justificatory strength of the analysis (171).

To ensure comprehensiveness and credibility, the analysis was preceded by a thorough review of primarily qualitative empirical studies, encompassing 'third-person' experiences and the moral perspectives of key stakeholders (143). These studies were critically assessed for relevance, and original participant quotations were thematically coded, synthesized, and collaboratively scrutinized and discussed in the light of moral principles, among all co-authors. In the empirical interviews, normatively formulated interview questions were included to elicit participants' moral reasoning – prompting reflection on how practices ought to be, and what they considered right, good, reasonable, or ethically justifiable (128).

This empirical foundation supported the iterative movement between specific moral judgments identified empirically, and ethical principles (such as autonomy) – a movement which is characteristic of the process of RE. Concepts with ambiguous meaning or limited analytical utility, such as dignity, were deliberately excluded to preserve clarity, simplicity, and explanatory strength. It should be noted that specific background theories from outside the moral domain were not formally included as input in the analysis (141).

Generative AI

Generative AI (GenAI) tools based on large language models (LLMs) were used to support work on this thesis. To uphold academic integrity, including the values of reliability, honesty, respect and accountability, it is essential for authors to be transparent about GenAI usage (172). A declaration of when and how GenAI was used in this thesis follows.

GenAI was not used for the conceptualization or design of the study, or for the formulation of research questions, nor for literature searches; instead, traditional academic databases such as PubMed, Scopus, and PhilPapers were used for these purposes. Transcription was conducted by a professional, procured transcription service to prevent data leakage and safeguard participant confidentiality. GenAI (Copilot and ChatGPT) was however used to provide suggestions on improving language use, condensing text, and translating sections of the manuscripts for Study III-IV. All AI-generated text was critically reviewed and edited by the author to ensure fidelity to the intended meaning and original references. Despite these precautions, the "black box" nature of GenAI carries an inherent risk of subtly shaping the researcher's interpretative process, warranting continuous reflexive awareness (172).

In Study III, GenAI tools were used to assist the linguistic refining of codes, subthemes, and theme labels produced by a human analyst. No raw data in the form of transcripts or quotes were uploaded to the AI. All outputs were reviewed against the original data to ensure interpretative accuracy, given the known risks of hallucinations, fabricated quotations, and limited transparency in AI-generated text (173). When applied rigorously, GenAI can enhance reflexive thematic analysis by improving efficiency, documenting analytic input, and reducing reliance on researchers' preconceived frameworks. Nonetheless, challenges remain, including limited contextual and cultural understanding, insensitivity to subtle nuances, and data protection concerns (174). Accordingly, GenAI is best regarded as a complementary analytic tool – supporting triangulation rather than generating content independently (175). In Study IV, GenAI was used to synthesize, summarize, and thematically organize human-generated coding of empirical literature; all outputs were critically reviewed. Finally, in writing this thesis, GenAI was used for linguistic refinements.

Researcher reflexivity

The credibility of research is closely tied to the researcher's pre-understandings – that is, their theoretical orientation, prior experiences, and underlying assumptions (129, 164). This necessitates a reflexive account, which is presented here.

Throughout the work with this thesis, I have continuously reflected on my contribution to the field of childhood cancer research. The strong reliance on care ethics throughout this thesis was shaped not only by empirical data, but also informed by my own psychological lens. As an analyst I have been shaped by perspectives from the fields of cognitive, social, and developmental psychology, which together formed my pre-understanding of how individuals perceive and construe meaning, act within relational contexts, and develop their cognitive capacities. As part of my own learning, I have critically examined and re-examined my position through scholarly dialogue with academics and clinicians, via interdisciplinary collegial feedback in seminars and reflective discussion with supervisors. These interactions have challenged, nuanced, and widened my assumptions and interpretations about what matters, ethically, in the recruitment of children to childhood cancer research.

I have also reflected on my own positioning in the field of pediatric oncology. Clinicians' lived moral concerns are often more emotionally and relationally multifaceted than traditional bioethical frameworks may capture (176). Practitioner-driven studies therefore provide invaluable insights (113, 177). Yet belonging to a field can make it difficult to critically question its implicit assumptions, especially regarding research which is highly regarded in both clinical practice and wider society. With my position outside the clinical context, and grounding in psychology and behavioral science, I hope to contribute some complementary viewpoints.

In working on this thesis, I have adopted a critical realist approach which has meant engaging with this topic through three interconnected but stratified levels of understanding: 1) the empirical domain (participants' expressed experiences, as co-created with me), 2) the actual events and concrete research practices to which these experiences refer, and 3) the generative mechanisms that are not directly observable but nonetheless shape and provide the underlying structural conditions for research practice (121, 122). This movement beyond the descriptive empirical, which also illuminated underlying structural conditions, has been essential to fulfill the normative aims of this thesis (126) and identify areas that could be ethically strengthened (122).

Sammanfattning på svenska

Varje år insjuknar cirka 350 barn i Sverige i cancer. Tack vare stora medicinska framsteg överlever idag omkring 85 %, men barncancer är fortfarande livshotande och utgör den vanligaste dödsorsaken till följd av sjukdom hos barn i åldern 1–14 år. Prognosen varierar mellan olika diagnoser, och vissa former är ännu obotliga.

I barncancervården är forskning nära integrerad med den kliniska vården, och en stor andel barn deltar i studier. Den här avhandlingen handlar om de etiska frågor som uppstår när barn som också är patienter tillfrågas om att delta i forskning. Syftet har varit att öka kunskapen om etiska aspekter, såsom etiska värden, utmaningar och förbättringspotential inom barncancerforskning och att bidra med vägledning.

Forskningen är avgörande för att utveckla behandlingar, diagnostik, omvårdnad och psykosocialt stöd till barnet och familjen. Barn har samma rätt som vuxna till säker och evidensbaserad vård. Men många läkemedel som används i barncancervården är inte vetenskapligt utvärderade för barn och det är etiskt angeläget att forskning på barn prioriteras.

Samtidigt innebär forskning inom barncancervården etiska utmaningar. Beslut om forskning behöver ofta fattas under medicinsk brådska, när familjerna är känslomässigt överväldigade och överbelastade med information. Barns beslutsförmåga är inte fullt utvecklad och enligt svensk lag kan barn under 15 år inte själva samtycka till forskning och de är i beroendeställning till sina föräldrar. Barn i cancervården är också i egenskap av patienter beroende av vården, vilket kan göra dem sårbara. Att vård och forskning bedrivs parallellt kan göra det svårt för familjer att skilja forskning från vanlig vård och också skapa etiska värdekonflikter för vårdpersonal. Därför krävs särskild etisk hänsyn för att skydda dem och respektera deras autonomi.

För barn som ännu inte kan samtycka juridiskt men som har förmågan att ge sitt medgivande till forskning, fyller medgivandeprocessen en viktig legal och etisk funktion: den visar respekt för barnets egna rättigheter och person, i linje med Barnkonventionen och svensk forskningslagstiftning. Medgivande rekommenderas ofta från 7 år men även de yngre barn som har förmågan ska ge sitt medgivande. I praktiken innebär medgivande att barnet involveras i beslutsprocessen på ett sätt som är lämpligt och meningsfullt utifrån barnets mognad, genom anpassad information, och möjlighet att tacka nej till forskning. Men studier visar samtidigt att barn i cancervården ibland inte förstår vad forskningsdeltagandet innebär och ibland deltar utan att ha gett sitt medgivande. Kunskapen om etiska frågor inom svensk barncancerforskning är begränsad, särskilt vad gäller barnens egna erfarenheter och delaktighet vid medgivande.

Den här avhandlingen fördjupar därför kunskapen om de etiska frågor som aktualiseras när barn inom barncancervården tillfrågas om forskning, med fokus på barn mellan 5–14 år – den ålder då medgivande är aktuellt. Alla studier har gjorts i svensk kontext och avhandlingen har använt en empirisk-etisk metodik, där tre kvalitativa intervjustudier kombinerats med en normativ etisk analys. Den tar avstamp i erfarenheter hos de som på olika sätt berörs av forskningen: barn, syskon, föräldrar och vårdpersonal och ledamöter inom etikprövningen.

Först gjordes två kvalitativa intervjustudier med vårdpersonal inom svensk barncancervård (Studie I) och med ledamöter på Etikprövningsmyndigheten (Studie II) för att undersöka deras perspektiv på etiska värden, utmaningar och förbättringspotential, och deras syn på etisk kompetens vid rekrytering respektive etikprövning. Därefter gjordes en intervjustudie med barn, syskon och föräldrar som deltagit i forskning för att beskriva hur de upplevt barnets delaktighet vid forskningsmedgivande (Studie III). Slutligen gjordes en normativ teoretisk analys (Studie IV) baserat på Studie I-III och tidigare forskning, för att ta fram etiskt och empiriskt förankrad vägledning för forskningsrekrytering, med fokus på barnets medgivande.

Resultaten visade att etiska frågor i barncancerforskning är mångfacetterade och påverkar alla inblandade: barn, föräldrar och vårdpersonal. Studie I visade att vårdpersonal särskilt betonar vikten av förtroendefulla relationer, att tillgodose informationsbehov, uppmärksamhet på sårbarhet, och att balansera motstridiga roller och intressen, till exempel mellan barn och föräldrar och mellan vård och forskning. Behovet av forskningsetisk kompetens lyftes också, där empati, lyhördhet, kommunikativa färdigheter och ett barncentrerat förhållningssätt sågs som centralt.

Studie II belyste hur ledamöter framförallt fokuserar på att främja autonomi och delaktighet, att skydda barn från risker och att följa lagar och regler i etikprövning. Samtidigt lyftes behovet av att balansera juridiska krav med etiska värden så att etikprövningen inte blir ensidigt juridiskt styrd och därmed tränger undan andra viktiga etiska avväganden. De såg opartiskhet, noggrannhet, perspektivtagande och samarbetsförmåga som viktigt i etisk bedömning och lyfte utbildningsinsatser som viktiga för etisk kompetens.

I Studie III framkom att barn, syskon och föräldrar inom barncancervården har ett starkt moraliskt och emotionellt engagemang i forskning, som bygger på solidaritet, tacksamhet och tillit: något som ibland underminerar förståelse och kritisk reflektion. Barnets delaktighet i medgivande formas i stor utsträckning av relationen till föräldrar där tillit, lojalitet och föräldrars förväntningar och beteenden ibland begränsar barnets delaktighet och autonomi.

I studie IV föreslogs det att det inom barncancerforskning är viktigt att inte bara respektera barns autonomi utan att också se autonomi som ett värde att främja framförallt genom relationellt, emotionellt och praktiskt stöd. Centralt för det är förståelsen att relationer och tillit både kan möjliggöra och begränsa barns autonomi.

Sammanfattningsvis visar denna avhandling att mycket i svensk barncancerforskning är etiskt robust. Vårdpersonal uttrycker ett tydligt barn- och familjecentrerat förhållningssätt, och familjer har ett stort förtroende för forskningen. Samtidigt behöver barns delaktighet och autonomi stärkas för att säkerställa ett mer konsekvent och meningsfullt medgivande. Det är viktigt för att respektera barn som personer med egna rättigheter och undvika att de instrumentaliseras i forskningen.

Tillsammans med barnanpassad information och ömsesidig dialog är relationell medvetenhet centralt för att synliggöra hur relationer och kontext formar barns handlingsutrymme och möjlighet att ge medgivande på meningsfulla sätt. Medgivande bör ses som en dynamisk process som kan behöva följas upp över tid, särskilt när barnet mått för dåligt för att inledningsvis delta i beslutsprocessen. Att aktivt stödja barns autonomi är nära kopplat till att skydda deras sårbarhet.

Sammantaget pekar avhandlingen mot vikten av forskningsetisk kompetens inom svensk barnonkologi. Sådan kompetens bygger på att följa etiska principer, som till exempel respekt för autonomi, men att också ta fasta på omsorgsetiska förhållningssätt och värden som tillit och empati. Den förutsätter också kunskap om barns rättigheter, autonomi och sårbarhet. Forskningsetisk kompetens inom barncancervården kan stärkas genom forum för etisk dialog, reflektion och interaktiva utbildningsinsatser, både på individ- och organisationsnivå.

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