Pediatric Oncology
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Pamela S. Hinds
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Pediatric Oncology Nursing

Defining Care Through Science

Springer

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The authors dedicate this book to the visionary scientists and clinicians whose legacies continue in the personalized care of children, adolescents, and young adults who are in treatment or in survivorship from childhood cancer and their families. We dedicate this book additionally to the children and families that have participated in research; by their participation, they have contributed to excellence in nursing care. Finally, we dedicate this book to the nurses and other health care professionals who contributed to the knowledge and ideas in this text and to those who will use this knowledge to make the cancer care and the future better for pediatric oncology patients, their families, and the nurses who care for them.

Foreword by Gregory H. Reaman and Franklin O. Smith

Pediatric Oncology Nursing: Defining Care Through Science

This exceptional text has adopted a bold and timely concept to provide a contextual framework for its entire contents. Precision medicine in oncology and specifically in pediatric oncology best defines the evolving scientific paradigm for basic discovery and translational and clinical investigation. The concept spans the evaluation of genomic perturbations implicated in the etiology of specific cancers, their potential role in treatment response and resistance, and new drug development. As well, the use of gene defects and their expression as well as other biologic variables of tumors and hosts are increasingly employed for prognostication, risk stratification, and biomarker-directed enrichment of patient subpopulations for clinical trial design and conduct.

It should come as no surprise to pediatric oncologists that pediatric oncology nurses can do the field one better by extending Precision Medicine to Precision Health. Here they address the impact of cancer on the whole child and his/her universe: physical status, emotion, physical functionality and mobility, cognitive capacity and developmental potential, quality of life, family, and community. It is also evident from the broad contents of this text that the concept of “precision” is taken seriously and is continuously informed by science. In addition to core nursing tenets for optimizing care for seriously ill children, advocating for and defining family-centered care, initiating timely consideration of palliation, distinct from end of life care, rigorous research in areas of self-management, resiliency, symptom monitoring and reporting, including self-reporting, treatment compliance, treatment decision-making, informed consent for participation in clinical research, and coping with survivorship have emerged as additional scientific focus areas for nursing research. The research strategies, study considerations, results, and potential for translation to further improvements in the care of children with cancer are poignant and offer rich insights into the probability that optimal care of the child with cancer will continue to be refined by scientific precision.

The pivotal and oftentimes unsung contributions of nursing excellence to every success in pediatric oncology to date cannot be overstated. The emerging paradigm for nursing research that is thoughtfully described in this text continues to offer real promise for children with cancer and their families.

Gregory H. Reaman
Franklin O. Smith
Washington, DC, Cincinnati, OH

Foreword by Ann O’Mara and Diane St. Germain

We are deeply humbled by Drs. Hinds’ and Linder’s invitation to write the Foreword for*Pediatric Oncology Nursing: Defining Care Through Science.* Their combined expertise in the nursing care of children and their families diagnosed with cancer guarantees a valuable text for practicing nurses and graduate students.

Incorporating the child’s voice in all aspects of care and research has been the hallmark of Drs. Hinds’ and Linder’s work. With Dr. Hinds, we see this in her successful efforts to validate the adult version of the Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) in the pediatric population. This will be a game changer in the cancer clinical trials setting. For decades, the world of oncology clinical trialists has overlooked the importance of asking patients who are enrolled on cancer clinical trials about their symptomatic toxicities. However, a new generation of clinical trialists in the adult setting addressed this gap and with National Cancer Institute (NCI) support developed and validated PRO-CTCAE. As of this writing, it is being incorporated into an increasing number of phase 1, 2, and 3 NCI supported clinical trials. With NIH support, Dr. Hinds and her team took on the challenge and successfully validated these items in the pediatric setting. Knowing Dr. Hinds’ resilience and persistence, we are very confident that we will see the same level of enthusiasm to use them in pediatric cancer clinical trials. Data from these trials will be so informative to pediatric oncology nurses and scientists as they design and implement more targeted supportive care interventions for their patients and families. Employing the same level of passion and persistence as Dr. Hinds, Dr. Linder’s work in gaining a more comprehensive understanding of the symptom experience in the adolescent and young adult (AYA) population adds incredible depth to the textbook. Recognizing the importance of a national collaboration, Dr. Linder is a member of the Consortium to Study Symptoms in Adolescents and Young Adults with Cancer (CS ^{2} AYAC), a consortium of nurse researchers in the United States with a shared interest in studying symptoms in adolescents and young adults with cancer. With funding from the St. Baldrick’s Foundation, Dr. Linder and her team developed and demonstrated feasibility of an iPad application, the Computerized

Symptom Capture Tool (C-SCAT) in the AYA setting. She has now taken this a step further by demonstrating the preliminary efficacy of C-SCAT as a resource to support symptom self-management among AYAs receiving chemotherapy. A common theme of both of these leaders is symptoms, ranging from developing valid and reliable assessment measures to developing and testing supportive care interventions. With these impressive backgrounds, who is better poised to convene experts and guide them in writing a very needed and most excellent textbook?

Pediatric Oncology Nursing: Defining Care Through Science is a timely textbook as cancer care becomes increasingly complex in the face of an ever-changing treatment landscape. Increased use of targeted agents and immunotherapy has introduced new challenges facing patients and their families including a cadre of new and often severe toxicities, genetic testing and counseling, difficult decision–making, and financial toxicity to name a few. The complexities of care require patients and their caregivers to deliver more intense self-care and management. Prolonged oral treatment has introduced challenges with adherence. The sheer volume of new agents has care providers in constant need of education, including how to educate patients and families regarding treatment options, which has become multifaceted and time consuming.

Hinds and Linder adroitly create a textbook to address these complexities, using precision health as a framework. They thoughtfully introduce the content of the book in the first chapter preparing the reader for how it is conceptualized and organized. Importantly, they underscore the critical role nurses play in the care of children and their families facing a life-threatening illness and their influence on care outcomes.

The editors have assembled an impressive array of pediatric oncology clinicians and scientists and have succeeded in presenting a highly organized compendium of topics essential to the care of children and their parents across the cancer trajectory. The book focuses on evidence-based, personalized, and total care of the child and their families. By presenting, at the end of each chapter, the latest scientific findings that are ready for translating into practice, Drs. Hinds, Linder, and their team demonstrate their commitment to the importance of evidence-based practice. Each chapter takes into account the interplay of biological, developmental, social, psychological, environmental, and cultural factors. The reader is reminded of their dynamic nature and influence on health and care outcomes. The book focuses on topics that nurses are uniquely positioned to influence such as symptom management, education, communication, decision-making, and patient-centered care. Further, they pique the reader's potential "inner" research proclivities by identifying a list of recommendations for what needs to be studied next. As champions for supportive cancer care research, we believe this approach to writing a textbook is essential to enticing the next generation of nurse scientists.

The content of the book will remain timely for years to come given the concepts shared and approaches to care. Readers of the book can be assured of increasing their fount of knowledge and will return to the book time and again for information.

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1. A Central Organizing Framework for Pediatric Oncology Nursing Science and Its Impact on Care

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Abstract

This chapter provides the meaning and the rationale for the organizing framework that guides the content of the entire text. The framework, precision health in pediatric oncology, reflects the impact of cancer on the ill child's cells, emotions, function, quality of life, developmental milestones, family health, and community. The interface of these areas of impact provides opportunities for the discovery of new knowledge essential to the care of the ill child and the child's family. The components of the precision health in pediatric oncology framework are identified and defined, and their relationships are depicted to represent how pediatric oncology nursing practice and nursing science together influence the health of the ill child and the child's family during and following the treatment of cancer.

Keywords Precision health – Pediatric oncology – Pediatric oncology nursing science – Nursing practice – Child health – Family health

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1.1 Introduction

A child (here used as an inclusive term for the neonate to the young adult) experiencing a cancer and its treatment is a profoundly unsettling and long-lasting experience for the child, the family, the ill child's community, and perhaps for the universe. That a child has a life-threatening and potentially life-ending disease is antithetical to our life beliefs and life plans, yet children can have one or more cancers in their lifetime. The response to cancer treatment varies by child and even within a child by phase of treatment. The child's response across time is at the level of a gene, a cell, a symptom, an emotion, as well as a social, family, or clinical care interaction. The child's response at these levels can be simultaneous, interactive, or at least concurrent, and always dynamic. Nursing as a discipline and nursing science in pediatric oncology are concerned and caring about the child's response at each of these levels and about the multiple points of interaction amongst these levels. Additionally, nursing and nursing science are concerned and caring about the greater collective that can influence health, including the health of the child with cancer, such as public health policy. All of these interacting or concurrent and interdependent levels can influence clinical assessments, treatment decision-making, and care outcomes.

These points of interaction, when identified, are our opportunities to seek knowledge and understanding of the child's response to the disease and the illness experience [1]. As such, they give guidance to our care of the child and the family. More explicitly, pediatric oncology nursing and nursing science are focused on the family and ill child's responses to the child's disease and treatment. This multiplicity of focus is because care given by nurses is purposefully, theoretically, and with evidence, targeted at the child, the child's family, and all levels of interactions involving one or both. The word "both" is central as the levels of interaction are most likely interdependent between the child and family.

In addition, pediatric oncology nursing and nursing science are genuinely focused on the total care environment across settings, including the home, for the child with cancer. This includes seeking knowledge to understand, and, as needed, to improve, the care provided by members of the pediatric oncology care team. The broad and deep scope of nursing practice and science within pediatric oncology is the basis for our decision to have a central organizing framework for this text and for the selection of a specific set of interrelated concepts that we have selected to frame the science in this text and its translation into nursing care. Of note, the selected concepts are not inclusive of all influences on the child and family health or on their responses to the disease and its treatments. The framework we are using for the text is precision health. This framework represents all available knowledge (and its application) that spans the ill child's biology and genetics, growth and development, behavior, sense of self, family connection, and social and treating environments [2]. Many of these elements are present in the nursing care of adults with cancer, are consonant with recently specified nursing science priorities [3], and represent the commitment in nursing science to the use of big data and precision health across well and ill groups [4]. The elements in pediatric oncology nursing, however, are uniquely and strongly influenced by the developmental state of the child and of the family.

Precision health is a framework described by the National Institutes of Health as a strategy to both generate scientific evidence and help translate that evidence into practice (https://www.ninr.nih.gov/researchandfunding/precisionmedicine; https://www.ninr.nih.gov/newsandinformation/events/precision-health). The commitment of the American Academy of Nursing to use policy to support the efforts of nurses to implement precision health in research and care is similarly conveyed in a recently issued position paper [5]. We are adopting the framework of precision health for this text because of its recognition of the uniqueness of each person and its emphasis on customizing care for patients and families based on systematically identified and analyzed information that is used to give effective care in consideration of environmental, lifestyle, and genetic factors. We are purposefully also emphasizing the concept of family within this framework given its actual or potential role biologically, emotionally, socially, spiritually, and cognitively on the ill child's response to the disease and treatment experience. Importantly, this framework requires a careful examination of the family's response to treatment as well as the child's response.

The applicability of this framework across cultures, ethnic and racial groups in diverse illness states, and age groups during childhood cancer furthers the relevance of this framework for this text. The framework can be used to guide scientific discoveries and clinical application of evidence at the level of the individual and of groups. The framework can also be used to guide prevention care and intense intervention care by nurses in pediatric oncology.

Within nursing, this precision health approach to framing scientific initiatives and evidence translation has been most prominent in symptom management, self-care management, and initiatives to integrate basic science and clinical science and the translation of these two to care [6]. Concurrently, the precision health approach is being used to frame scientific efforts for more specific groups such as critical care patients [7], underserved populations at risk of health disparities [8], family caregivers [9], and minority groups [10]. However, within the narrowing of focus, the broader concepts of precision health continue to be applied. In this text, we shall broaden the precision health frame across chapter topics. Translation of research findings cannot take place without a complete plan [11] that reflects the realities of clinical care and the setting in which this care occurs, whether the setting be the hospital, clinic, home, or community. We believe that the content in each chapter related to the research findings that are ready for translation into care will form the evidence base for such plans.

The framework for personalized health for the child with cancer in this text will include the concepts of precision health, environment, nursing practice, nursing science, family, lifestyle behaviors, and response to disease and treatment (Fig. 1.1). Our descriptions of these concepts and the sources that helped to inform these descriptions are listed below:

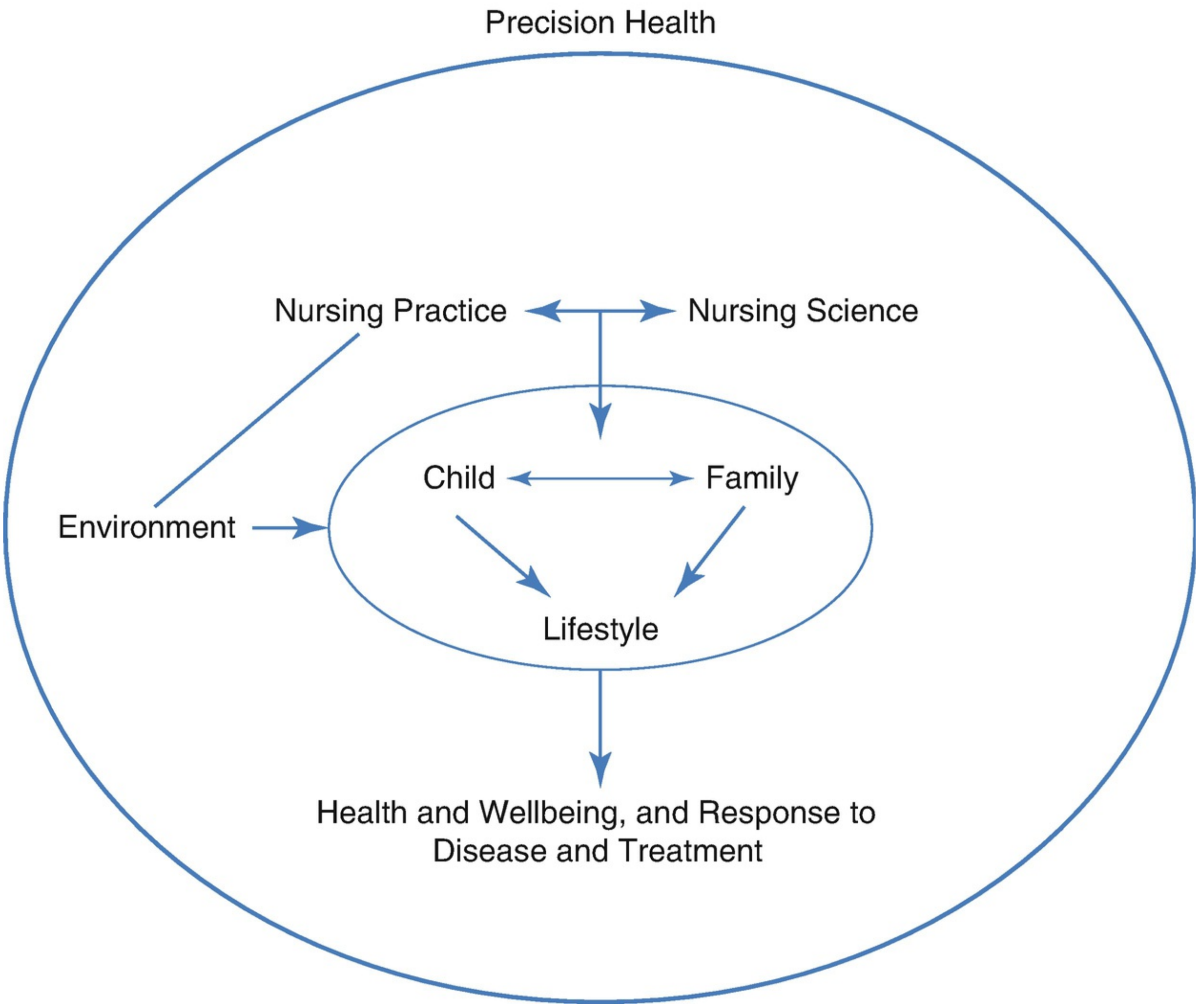

Fig. 1.1 Influence of nursing practice and nursing science on child and family health and response to disease (cancer) and its treatment within the context of precision health

Precision health: the use of all available personal (including biological, genetic, lifestyle, and values), family, and environmental information to sustain and enhance individual and family health and prevent the development of disease [4, 12] over the life span of the individual and the family [5].

Environment: a central component of nursing practice that influences health states a*nd* outcomes and includes the internal and external conditions of the individual patient, family, and nurse as well as the greater setting of health determinants including social determinants and health policy [13, 14].

Nursing practice: person-and family-centered, tailored care delivered always within the principles of respect for person, justice, and beneficence [15, 16] to promote health, prevent illness and injury, restore health, and alleviate pain and suffering directed in all aspects of a person [1, 13].

Nursing science: body of knowledge in relationship with that of other disciplines and sciences [16] intended to support the health and well-being of individuals, families, communities, and nations.

Family: individuals who are structurally, functionally, and, likely, emotionally related though may or may not have biologically relatedness as identified by these individuals but who seek to protect and promote each other's health [17, 18].

Child: the individual who is between birth and the age of majority whose development is characterized uniquely by change (biological, psychosocial, and emotional changes, among others). The process of development is influenced by life experiences, including illness [19].

Lifestyle: behaviors and a way of life at the level of an individual or family that may be modifiable to diminish the likelihood of disease [20] and improve the response to the child's disease and its treatment.

Health and well-being: global and specific positive outcomes of actions from self and others that can influence quality of life, confidence, resilience, and physical activities as well as performance even during illness [21–24].

Response to disease and treatment: evidence of illness in clinical, laboratory, and biologic variables and presence or degree of or resolution of symptoms. The response to disease and treatment is influenced by genetics, molecular targets and supportive care measures [25, 26] as well as the child and family's ability to adapt to and manage the demands of the illness experience.

Each chapter specifically addresses the concepts of this framework as they relate to the nursing science described and each chapter presents the deduced aspects of the science deemed ready for translation into practice. The strength of the derived applications is described as well.

Although this text is focused on pediatric oncology nursing science and its impact on patient care, nurses and nurse scientists appreciate the discoveries and advances in science that derive from diverse collaborations with patients, families, settings, and health care clinicians and scientists from very different disciplines, backgrounds, and experiences. Most certainly, applying research findings to clinical care is not limited to a single discipline or specialty.

Each chapter that follows has content that represents the current state of the science for its topic and with a particular effort to include an international perspective on the content. Each chapter also addresses to what extent the findings reported in the chapter are ready for translation into practice and care, and finally, what next steps are needed to be taken to continue advancing the science and evidence of the chapter's content focus. We anticipate that the content of each chapter, the list of evidence-based findings ready to be translated into practice, and the identified priorities for next steps in research will guide well the current and future efforts of pediatric oncology nurses and colleagues to protect the health of all children at any point of the cancer trajectory and of their families. This is the very reason for our work and for our specialty.

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2. Family-Centered Care in Pediatric Oncology

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Abstract

Family-centered care (FCC) is a philosophy and an approach to care that provides a pathway to engage with children and their families during their experience with cancer. Adopting a family-centered perspective in pediatric oncology requires a dynamic and evolving approach. As treatments evolve and the landscape of childhood cancer changes, so, too, do needs within the context of patient- and family-centered care. Thus, we propose family-centered precision health in pediatric oncology as a framework to guide engagement with and care of children with cancer and their families. We address what is ready to translate into clinical nursing practice with families and what elements of FCC require more robust evidence to achieve FCC conceptual maturity.

Keywords Family-centered care – Pediatric oncology – Parents – Children – Siblings – Grandparents

2.1 Introduction

Family-centered care (FCC) is a philosophy and an approach to care that provides a pathway to engage with children and their families during their experience with cancer. Specifically, FCC provides a platform to inquire about, understand, and attend to the child and family response to the cancer experience. The core components of FCC include (a) respect for family preferences; (b) flexibility and customization of care; (c) honest information sharing to promote collaborative and shared decision-making; and (d) a strength-based approach to working with families. Much of the existing FCC research focuses on how families and nurses define FCC and includes emphasis on dignity and respect, information sharing, family participation, and collaboration which are key attributes of FCC delivery as identified by the Institute for Family-Centered Care (http://www.ipfcc.org/). While we recognize that the way any one person defines family is socially constructed and contextual, we adhere to Wright and Bell's definition for family in this chapter: "The family is who they say they are. With this definition, nurses can honor individual family members' ideas about which relationships are significant to them and their experience of health and illness" [1].

Adopting a family-centered perspective in pediatric oncology requires a dynamic and evolving approach. As treatments evolve and the landscape of childhood cancer changes, so, too, do needs within the context of patient- and family-centered care. We propose family-centered precision health in pediatric oncology as a framework to guide engagement with and care of children with cancer and their families (See

Fig. 2.1). As the needs of children with cancer and their families evolve, our understanding of their needs must also evolve. Examining the care of children as beings nested within families that are nested within extended families and communities who move through time within given sociopolitical and cultural contexts is needed to address this evolution. Indeed, the child and family are each greater than the sum of their parts. A family-centered care perspective acknowledges this and incorporates a multi-pronged focus on the family or individual to improve the health of the family as a unit [2, 3]. For example, family-centered strategies that promote parent and provider interaction contribute to parents' understanding and coping with cancer treatment; when nurses engage families meaningfully and extend concern for parents, children can benefit [2, 3].

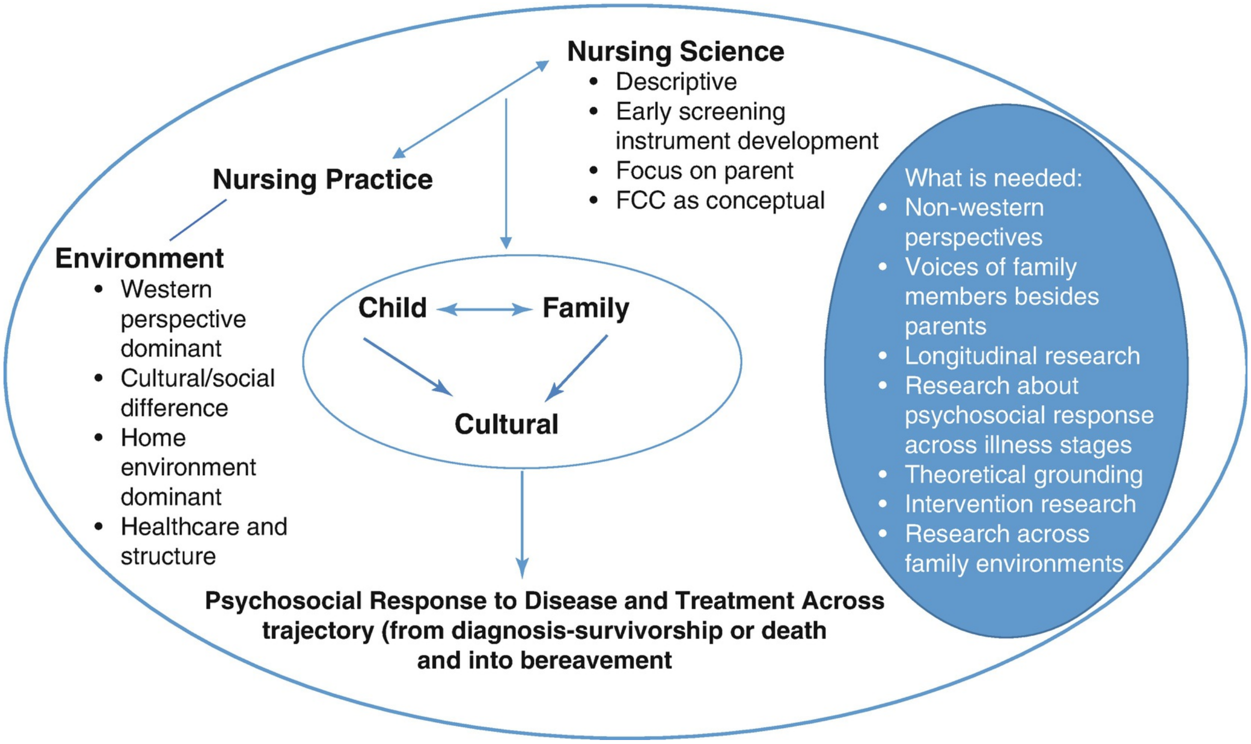

Fig. 2.1 Influence of nursing practice and nursing science on child and family health and response to disease (cancer) and its treatment within the context of precision health

Our vision for family-centered precision health in pediatric oncology incorporates the core FCC tenets of collaboration, flexibility, customization of care, respect for family difference, and aligns them with precision health's "*emphasis on customizing care for patients and families based on systematically identified and analyzed information that is used to give effective care in consideration of environmental and lifestyle factors*" (*Hinds and Linder*, Chap. 1). This alignment acknowledges the child, family, extended family, and their surrounding ecology. Precision health's emphasis on systematic identification and analysis of research evidence to provide effective care, as well as eliciting meaningful information from families to customize their care, provides an evidence-based method for FCC. The key elements of FCC and precision health are intersecting and interrelated. We view the care of children with cancer and their families through a lens of multidimensional, overlapping factors that influence the family's experience of the illness and its effects on the family as a whole and on its members as individuals.

2.1.1 Gaps in Providing Family-Centered Care

Gaps exist in the provision of FCC. For example, gaps occur in provision of FCC in the inpatient setting where many children with cancer receive treatment, such as inpatient wards, stem cell transplant units, and pediatric intensive care units. Baird and colleagues used interviews to learn from parents of hospitalized children that they were aware of implicit and explicit hospital rules that existed to keep order or maximize convenience for staff but caused frustration for parents [4]. For example, explicit rules forced parents to use restrooms and have their meals outside the unit, and implicit rules dictated that parents should "know the hospital routine" of shift change and not request accommodations to the schedule. Nurses are placed in a potentially uncomfortable position of both enhancing FCC while enforcing rules that parents perceive as restrictive and inhibiting FCC.

Patient- and family-centered care, as currently conceptualized, may not adequately account for the reality in which nurse and family relationships take place and evolve [4, 5]. Outdated ideas around roles of parents in the hospital setting, such as territorialism or power differential between nurses and parents, can create an adversarial environment. Such rules, when applied blindly and without a particular child and family's context, impede the provision of FCC that is intended to be tailored to the needs of child and family consistent with their needs and preferences. Indeed, when nurses practice rote application of implicit and explicit rules, they can perpetuate systemic barriers to FCC and contribute to biases that cause families to feel disenfranchised. In addition, there may also be gaps in the provision of culturally sensitive FCC across pediatric healthcare settings. For example, minority families in one US city had 30–50% lower satisfaction with inpatient pediatric care [6]. Lower ratings on cultural competence and communication throughout hospital services and sectors, despite training in cultural competence and communication in the study institution, indicate a gap in our broader conceptualization of FCC [6].

While the concept of FCC has been studied since the mid-twentieth century, it remains unclear and poorly implemented within health care today [7, 8]. The reasons for poorly implemented FCC include long-held notions of power and territorialism in pediatric inpatient settings and a limited evidence-base that is predominantly rooted in nurses' perspectives of FCC [4]. Warranted is understanding how the social determinants of health impact family life in order to promote equitable, family-centered precision health in pediatric oncology [4, 9]. The "family" and its social and community networks have not been clearly articulated as central to social determinants of health, as the role of the family is unclear and it has been considered as the context for individuals' health, such as the need of family support and the resource of education completed by the family of origin [9]. Our understanding of FCC has been relatively limited to understanding families in the clinical setting and less in the broader settings in which they live, work, and play despite the presence of pediatric cancer in their lives.

Recently, Smith conducted a concept analysis of family-centered care of hospitalized pediatric patients to describe the historical evolution of FCC, and to clarify its components and demonstrate its significance in nursing practice and research [7]. The analysis revealed that while the majority of the FCC studies focused on defining FCC and uncovering what families and nurses understand of the concept, little evidence exists about the implementation of FCC. For example, Smith found that a gap in understanding the relationship between implementation of FCC and its impact on patient and family outcomes exists. She also found that minimal intervention research exists to support a core function of FCC: promotion, maintenance, and restoration of the parental role in care of the hospitalized child. Such limitations in the literature on FCC may signal that nurses lack sufficient education on how to operationalize FCC and implement into nursing practice [7]. Similarly, previous analyses described FCC from the perspective of health care providers and families, mainly mothers. However, the perspective of the ill child is not prominent. Incorporating the voice of the ill child, adolescent, and young adult is particularly important when we consider the provision of family-centered precision health in pediatric oncology. Without the voice of the child, the impact of treatment, as well as the risks and benefits remain unknown or partially established [10]. When children, adolescents, or young adults are recognized as important members of the healthcare team, with their own lived experience, the adults who love them and are responsible for their care can make truly informed decisions on their behalf or, when appropriate, support the child's decision-making. Most importantly, the sharing of responsibilities for the child's care can raise potential conflicts between family and the healthcare team. How to address such conflicts is not clearly articulated in current conceptualizations of FCC [8]. Despite viewing FCC as a cornerstone of modern nursing practice, there are areas that need to be studied to promote the concept into its maturity. Nursing education about the elements of FCC could augment the incorporation of the FCC into current nursing practice.

One way to address gaps in delivery of FCC is to learn from families themselves. In the clinical arena, nurses need to apply the existing research in partnership with families and integrate the available personal, family, and environmental information of each particular family, and importantly, their preferences and goals. We must ask families what they feel will help promote FCC for them. In research, learning from families often requires complex study design to capture multiple sources of data about integration of families' needs and pediatric oncology nursing care. Theoretically, FCC requires a level of description and abstraction that captures the essence of FCC; how it is operationalized in practice; how it is conceptualized, defined, and measured in the context of complex chronic diseases, such as cancer.

The lack of effective interventions about the practice of FCC challenges global implementation. While we recognize multiple reasons for lack of intervention research, we suggest one may be due to complexity of FCC. Most of the research is focused on parents' ability to deliver treatment and symptom control [3, 11]. Rather than focusing on single aspects of the illness experience, studies may consider various family needs along the illness journey to provide greater perspectives in FCC continuum. We must understand how families experience, live through, and draw meaning during pediatric cancer and FCC. In addition, we must understand how current social systems/structures help to promote and advance FCC. The emphasis is typically on an individual level (be it the family or nurse), but no recognition is given to how our social systems and structures either facilitate or impede nurses in advancing FCC.

In this introduction, we have provided an overview of how FCC is described generally and whose perspectives have been privileged. We have also provided an introduction for understanding the gaps and opportunities for growth in research on FCC and its integration into pediatric oncology. Now, we describe the experiences of key psychosocial experiences for families and individual family members. Please see Fig. 2.1 for the depiction of our framework, Family-Centered Precision Health in Pediatric Oncology. This framework provides a roadmap for understanding the particular experiences and needs of individual family members and the family unit.

2.2 Key Psychosocial Experiences for Families

2.2.1 Psychosocial Impact and Family-Centered Care for Individual Family Members

"Cancer is a family disease." A beloved child, adolescent, or young adult's cancer diagnosis starts a ripple of impact across his or her family, friends, and community [2]. Families are particularly affected because of the proximity, duty of care, emotional bonds, and love that connect family members. The threat to the life of one's child, sibling, or grandchild can be experienced physically, psychologically, emotionally, existentially, and perhaps even morally.

The philosophy and approach of family-centered care acknowledges this impact, the devastation it can render, and the family strength and growth that can result [2]. It also acknowledges that what happens to one family member affects other family members and the broader community which envelopes them. This bidirectional relationship has been examined in pediatric oncology nursing research and provides a strong foundation on which to extend the envelope of care to parents, siblings, and grandparents of children with cancer [2]. FCC acknowledges that each family member will experience the illness of a loved one differently and this experience and its resulting perceptions have an impact on relationships within the family and the functioning of the family unit. We acknowledge that family-centered care is both rooted in and foundational to the care of the child with cancer.

2.2.2 Screening

Individual family members experience pediatric cancer from their unique perspective and position within the family [12]. Their perspectives and experiences are interrelated with those of other family members [2, 13, 14]. Thus, family-centered psychosocial care occurs at the intersection of individual and family. Unfortunately, dedicated service and space for sharing such experiences, perceptions, and demands among families and healthcare providers may not available across the globe. Providing such care requires effective, valid, and reliable assessment tools to help providers engage in a thorough evaluation of each family and implement FCC into pediatric oncology. Screening tools that have been developed to support FCC focus on the assessment of family psychosocial needs and quality of life [15, 16]; family use of symptoms management strategies; [11] parent and child connectedness to the treatment setting; [17] family management and perceptions of caregiver competence; [18] and family–provider connection and relationship in bereavement [19].

Additionally, screening for families who continue to struggle can be important in providing targeted FCC. Assessing experiences can be a way to engender hopefulness in parents along cancer trajectory. Understanding parental hopefulness, acceptance of diagnosis, of illness management into family life, or adaptation may be important information to guide provision of FCC. Indeed, nearly half of families in one study had not yet accepted their child's cancer diagnosis, integrated this understanding into family life, or adjusted family life to meet this new challenge. Unfortunately, parents who were not yet able to attain this level of acceptance, integration, and reorganization were also less likely to endorse feelings of hopefulness in the situation and make plans to this end. Interestingly, parents who had not yet experienced acceptance, integration, and adjustment reported higher FCC and information, either because they asked for more support, had trouble integrating the cancer diagnosis into family life because of stress, or because staff perceived such that families needed more support [20].

2.2.3 Parents

Most of the pediatric oncology nursing research in PFCC has focused on the parents of the child with cancer. In the foundational work of Hinds and colleagues [21], and research that has grown from that [22–24], parents identified what staff could do to help them achieve their internal definition of being a good parent to a seriously ill child, including: keep us informed; be attentive; provide good care; be allowed to parent child by assisting in daily care; putting child's needs first; advocating for their ill child with medical team; ensuring good quality of life (QOL). Parents in this study also described gender-based difference in describing their definitions of "being good parents" to their critically ill and injured children (most children in the sample had cancer). Fathers in couples rated making informed decisions as highest and mothers in couples rated attending to child's health and needs highest. Mothers not in couples rated ensuring informed decision-making highest. Thus, we see that targeted assessment of parents can reveal their particular strengths, opportunities, and needs in order to help them achieve their definition of being a good parent to their seriously child with cancer. A targeted assessment is consistent with our framework of family-centered precision health in pediatric oncology since it directs nurses and other healthcare to understand the way each parent defines being a good parent to their seriously ill child and how the different definitions affect the family unit.

2.2.4 Siblings

In considering PFCC, we must also acknowledge the other children who are deeply affected by pediatric cancer, the healthy siblings. While we have evidence about general screening and assessment tools from the parents' perspectives, we are lacking in-depth understanding of the needs of siblings. Non-bereaved siblings of children with cancer have described a process of “creating a tenuous balance” in which siblings notice and adapt to the multiple challenging and unexpected aspects of the family’s cancer experience [25]. Siblings are frequently on the periphery of the cancer experience and hospital care [2, 26–28]. Siblings, therefore, can observe fragility of family relationships more readily than other members and may try to initiate their own actions to maintain family functioning during the cancer experience. Despite numerous studies reinforcing that siblings of children with childhood cancer experience a different way of being within their family and a loss of a family way of life, lacking are family-based interventions that help to promote effective family functioning, coping, and resilience [28, 29]. Siblings should be recognized as important recipients in need of family-centered care [25]. Nurses and other healthcare providers can support their adjustment to the cancer experience by coaching parents on signs of maladjustment or concern or how to broker conversations about sensitive topics.

2.2.5 Grandparents

Grandparents have not received an abundance of attention in pediatric oncology nursing research in FCC, but theirs is an important perspective to understand. Grandparents serve as caregivers for both children with cancer and their healthy siblings and, for many families, provide key support in maintaining normalcy for the healthy siblings [30–32]. Grandparents can suffer, too. Their suffering has been described as “multiple and muted” [33] because they experience multiple levels and sources of distress; they experience their own distress; they witness distress in the parents (their own children); their other grandchildren; and their ill grandchild. Yet, they describe feeling “muted” in being able to share their distress and concern because, “*what suffering can be greater than that of the parents*?.” [33] Grandparents may experience elevated anxiety, depression, anger, and distress as compared to grandparents of children without cancer [34]. Grandparents also experience feelings of uncertainty and helplessness when a grandchild has cancer. Their distress, however, can interfere with their attempts to support the other family members during the cancer experience in instrumental and functional ways. Much of the literature about parents and FCC can apply to grandparents who serve in a caregiving role. Specifically, grandparents may need particular guidance regarding the healthy siblings and how to help them cope and process the illness and its impact on their parents and ill siblings. In addition, grandparents may need specific guidance and support as they support their child and grandchild and, like other caregivers, can experience strains on the physical and emotional well-being [35]. Despite viewing FCC as a cornerstone of modern nursing practice, the perspectives of grandparent and other missing family voices warrant studying in order to promote the concept into its maturity.

2.3 Psychosocial Impact and Family-Centered Care for the Family Unit

Pediatric oncology nursing research has examined the family as a unit of analysis and care. In considering the impact of FCC on the family unit, nursing research has examined the impact of relationship structure and the physical structure that can enhance or inhibit the delivery of FCC. For example, Curtis and colleagues found that spatial configurations within hospital wards, specifically single rooms or shared rooms, had significant impact on relationships and interactions among children, parents, and nurses [36]. For example, parents in shared rooms appreciated the support, social interaction, and shared sense of “looking out for one another” afforded by the shared spatial configuration [36]. This is different from families in single rooms who experienced more isolation and less interaction with their children’s nurses.

Increasing the provision of single rooms within wards is therefore likely to directly affect how family-centered care manifests in practice. Additionally, Rollins and colleagues found that children in shared rooms reported receiving support from their parents, other children, and the parents of other children, which enhanced coping [37]. On the other hand, families in single-patient rooms described enhanced intra-family (parent–child) interaction. Children and families from the shared room design seemed to prefer this more socio-petal design. Off-unit support areas, such as playrooms and lounges, and single family rooms were found in the US study site and deemed less helpful with coping. Researchers found children and families in the US hospital spent most of their time in room versus the off-unit playroom [37]. Thus, this research demonstrates physical structure of units and rooms impacts the way nurses deliver FCC and how families respond to cancer experience.

Two important gaps in pediatric oncology nursing research on family-centered care are the focus on the family as the unit of analysis or the unit of intervention. To date, it appears that intervention research is focused not on the family unit but on the individual family member. This is important because when parents perceive pediatric services to be family centered, they may experience lower caregiving burden; increased quality of life; and increased satisfaction with care [17]. Parental perceptions can benefit the children in their care, thus promoting not only the child's, but also family's best interest [38].

2.4 Cultural Difference and Family-Centered Care

The concept of family-centered care finds its true meaning in the social context where it has occurred, honoring the difference from one culture to another. FCC is a context-based concept that needs to be studied from the perspectives of diverse cultures and contexts in order to provide a comprehensive definition. Despite the fact that the concept of FCC originated in western culture, the awareness of the basic elements of FCC has been identified in both developed and emerging countries. For example, Khajeh and colleagues analyzed FCC within Iran and created a definition of the FCC concept that emphasizes addressing the entire needs of the family in hospital, including effective interaction, education, information sharing, and providing individualized care. Also it requires collaboration of health care providers and families [39]. Literature included in this concept analysis was from both English and Persian languages, thus providing a contextualized and deeper understanding of FCC that will assist with implementation [39]. However, since many nations are diverse and embrace umpteen ethnic and religious cultures, the concept and application of FCC should be adaptable enough to meet the needs of children and families across cultures, points in cancer journey, and family developmental state. This is an important element of family-centered precision healthcare. Please see Fig. 2.1 for a depiction of the impact of sociocultural factors on delivery of family-centered precision healthcare to families in pediatric oncology.

2.4.1 Culturally Sensitive Measurement of Family-Centered Care

An important step towards advancing family-centered pediatric oncology care is adapting existing family screening measures across languages and cultures, in addition to creation of culturally based and culturally relevant tools. For example, the Shields and Tanner Questionnaire explores and compares healthcare providers' and parents' perspectives of FCC in pediatric settings [40]. This questionnaire was developed in English and a cross-cultural adaptation to Brazilian Portuguese was completed to measure FCC in Brazil. The translated questionnaires into the Brazilian culture showed acceptable reliability and validity such that this questionnaire can be used in pediatric clinical practice to identify barriers in implementing FCC in these two countries [41]. However, further studies are needed with other populations and sufficient sample sizes (20 respondents peer one item) to support cross-cultural use [41]. Doing so recognizes family diversity around world; to address patient- and family-centered outcomes, we need to meet their preferred needs and outcomes rooted in cultural norms and understandings. What is valued across cultures may differ and hence, it is important to investigate clinical practice within given cultural contexts.

Provision of culturally relevant, family-centered care is challenged by the lack of descriptive and exploratory research from a global perspective. Nurses manage various challenges in eliciting and understanding families' values and beliefs; addressing language barriers; navigating cultural contrast related to gender disparities and family role allocation. These challenges can create a significant barrier to equitable family-centered care [42]. Not only do we need effective strategies to integrate FCC into systems of care worldwide, but we need to consider the way we train nurses and other healthcare providers from across cultures who care for children with cancer and their families. Learning from a variety of family members and from different cultural perspectives will provide a solid foundation for this translation.

In addition, little knowledge exists about the global implementation of FCC in pediatric oncology. Foster and colleagues show that FCC concepts, such as collaboration, are reported more frequently in studies from developed countries [43]. Our international pediatric oncology research on FCC could be advanced through the use of family theories and qualitative methods to provide a rich, contextualized understanding of what the core components of FCC mean for affected families and can provide a foundation for intervention and translational FCC research.

Finally, cross-cultural studies are important to compare multiple realities of FCC in different cultures. For example, Feeg and colleagues found, in a multi-site comparative survey in USA, Turkey, and Australia, that nations with a tradition of earlier implementation of FCC also demonstrated a stronger underlying policy supporting FCC [44]. Others countries may face lack of education or shortage of nurses more frequently, without a formal policy of family care. This demonstrates how the social determinants of health impact the uptake of FCC. Such challenges demand more efforts to integrate FCC into education programs to ensure the workforce can meet the needs of children with cancer and their families. Worldwide, the focus of care tends to still be on the child. This challenges partnership with families, a core component of FCC.

2.5 Evidence-Based Findings Derived from the Science of Family-Centered Care in Pediatric Oncology Ready for Translation to Clinical Practice

Considering the body of pediatric oncology nursing research in PFCC, we must now consider what is ready for translation into clinical practice, how such translation should be done, and with whom.

1. Through our analysis of the empirical literature, we have learned that most of the FCC research is not informed by a family theory. This may limit the ability to translate research findings into clinical practice or to develop interventions that are rooted in available evidence.
2. In addition, we found that a great deal of the pediatric oncology nursing research on PFCC is descriptive in nature. To date, the existing intervention research that promotes FCC has involved mostly pilot work and smaller samples [45, 46]. Shortening hospital

stays in pediatric oncology populations has focused attention on effective short-term psychosocial interventions. The FAM-TCI is promising as an effective short-term intervention but requires additional investigation. At this point, further research is needed before the intervention work can be deemed translatable.

3. The work that details families' and nurses' perspectives of FCC is translatable. Nurses can use the evidence, to date, to help inform their practice. As previously noted, further research that involves different populations across the globe will add to the evidence on what FCC looks like in pediatric oncology. Systematic reviews of current work that address different questions on FCC are also warranted and will help solidify the research to date.
4. Considering the conceptual and philosophical basis of FCC, we clearly need efforts to modernize the practical conceptualization of FCC so that family units and individual family members are not marginalized. This includes reflection on one's positionality as a nurse and healthcare provider; power differentials that exist in practice between parents, family members, children, and providers. It also requires assessment of, reflection upon, and addressing of implicit and explicit biases that can erode relationships versus enhancing FCC.
5. Considering the conceptual and philosophical basis of FCC, we should also consider whose perspective is privileged in existing FCC research and whose is missing. Does a FCC approach minimize the voice of the child? We assume that FCC is the right approach and never entertain adopting a person-centered approach which is the norm in adult care. Research that addresses young people's transition from a FCC approach to a person-centered approach is needed.
6. From a research perspective, while the provision of FCC is at the heart of pediatric oncology nursing practice, our pediatric oncology nursing research should investigate gaps between the conceptual ideal and actual practice. Consistent with patient and family-centered outcomes research, it may be time to re-examine with

children and families what FCC means to them and what they perceive this care should look like in practice. For example, the research described by October and team brings this to life [22]. Rather than assuming what FCC is and should include, we can pivot the conversation to learn from families about what is most important to them in “being good parents” to their seriously ill children and construct our family-centered efforts around helping them achieve this in a way that promotes child and family best interest [38].

7. From a clinical perspective, such reflective and personal questions can also shape clinical practice with families. By asking about the meaning of their parental role, what parents believe they need to do to enact this role, and their perceived barriers and facilitators, we can provide precise, targeted FCC. Since their responses may evolve over the course of a child’s illness, so too may the FCC and family-centered interventions, programs, and services we provide. This fine-tuning allows us to provide the right kind of FCC, to the right family or family member, at the right time along the family’s cancer journey.
8. Research by Curtis and Northcott describes the environmental impact of unit structure on FCC and relationships between nurses and families [36]. This is ready for translation because it should be an integral aspect of deliberations and considerations about changes in unit physical structure. Nurses’ contribution to FCC may change when structure and design of a ward changes. Consideration of how design and structure of institution/unit can influence FCC; conscientious designers try to create spaces that promote healing and this can affect social interaction and privacy; ideas can be translated, but other area of research.
9. Screening should be implemented into practice. Screening for coping and adaptation, providing care that engenders hopefulness, FCC that emphasizes family perspectives (versus lip service) can potentially provide targeted care for families who are struggling.

2.5.1 Future Research Recommendations for

Precision Family-Centered Care in Pediatric Oncology

Much of the research on FCC in pediatric oncology is not informed or guided by family theories and this limitation can affect the translation of research into practice.

1. There is a lack of methodologically diverse studies [47]. This poses a challenge to implement FCC worldwide because we have descriptive research from the perspectives of healthcare providers and parents, but are missing key perspectives (e.g., children, siblings, grandparents) [48].
2. We must incorporate research that explains the relationships between the components of FCC and child and family outcomes, as well as research that includes the family as the unit of analysis.
3. With this solid foundation of descriptive and correlational research, we can create more interventions to enhance the impact of FCC within a particular context. Such examples include important interventions to improve family-centered cultural care and family satisfaction by using the service of Limited English Proficient patient family advocate, [49] as well as Svavarsdottir's work on the adaptation of a family communication intervention will make timely contributions to improving the provision of FCC globally. Nursing intervention research has demonstrated how FCC can improve child and family outcomes [45].
4. More research is needed to capture multiple family members and cultural diversity in childhood cancer. Researchers should identify strategies to advance FCC research to inform practice and policies.
5. We must also consider research across the contexts in which families receive FCC care. For example, home care is not well developed worldwide, since it requires great structure and support for families, especially those facing end-of-life situations [50].
6. Additional voices in research that we need to hear from to enrich

FCC include immigrant families; families from diverse cultures; families headed by single parents or same sex couples; various family roles, including fathers, siblings, and grandparents; families experiencing financial or other life stressors; and families in rural or geographically isolated places where care may be hard to access.

7. Considering the challenge of translating research into clinical practice, we must consider the complexity of human relationships and the barriers and facilitators to the implementation of research evidence in clinical settings. This requires continued education programs to teach nurses about family theory undergirding family interventions; how to manage boundaries, maintain integrity and cope with moral and ethical distress; and how to access support for themselves in caring for seriously ill children and their families [51]. The challenge to support the family as the context of care involves a new perspective that requires more specific education to nurses and research initiatives that address the implementation of the right FCC to the right family at the right time.

8. Child-centered care considers the child in a more prominent role, and the family as part of the environment which may cause direct influence on the care provision. Ford and colleagues describe an ecological approach to understanding the intersection between family-centered care and child-centered care [52]. Research is needed to see how health outcomes are impacted by a child-centered approach versus a FCC approach.

9. We need more research on the ways FCC shapes and is shaped by policy. Health and social policy is a major determinant of health [53, 54]. We need more research around the feasibility of family-centered care as a consolidated policy across diverse contexts; the complexity of the psychosocial approach for multiple family members; and barriers and facilitators to its implementation across clinical, clinician, and family contexts.

10. Nursing research in pediatric oncology highlights collaborations between clinicians and families as essential to care of affected

children. The negotiated care model (NCM) can help with implementing FCC by advocating partnership between clinicians and families in planning and delivering care to hospitalized children. Such models emphasize collaboration with and engagement of key stakeholders and development of strategies for addressing challenges. Thus, we need to study various models of FCC.

11. We need more research that amplifies the voices of children, adolescents, and young adults. This is supported by the children's rights paradigm explicitly woven into the care of hospitalized children and their families. This paradigm acknowledges the growing and developing child, adolescent, or young adult within the context of his or her family; the child's impact on the family; and the priority of acting in the best interest of the child with cancer [55].
12. We need more research that marries the intersection of pediatric oncology and social determinants to elucidate structural factors that influence families' experiences of care in clinical and community settings. We also need to elucidate family variables related to the social determinants of health and family as context and determinant of care.

2.5.2 Precision and FCC: Right Care to the Right Family at the Right Time in the Right Way?

FCC is an avenue for precision health in pediatric oncology. FCC, at its essence and from its long-standing conceptual and philosophical roots, is precision healthcare for families. The core tenets of FCC, collaboration, flexibility, customization of care, respect for family difference, are aligned with precision health's "*emphasis on customizing care for patients and families based on systematically identified and analyzed information that is used to give effective care in consideration of environmental and lifestyle factors*" (*Hinds and Linder*, Chap. 1). This alignment acknowledges the child, family, extended family, and their surrounding ecology. Precision health's emphasis on systematic identification and analysis of research evidence to provide effective care, as well as eliciting meaningful information from families to customize their care, provides an evidence-based method to the concept or philosophy of FCC. Through the joining of research evidence with child and family values, within an envelope of care that sees family as partner and recipient, we can provide FCC that will promote adaptation and ameliorate suffering in pediatric oncology.

2.6 Conclusion

Whether the concept of family is considered as the center of the care or within a framework, such as precision health or child-centered care, FCC provides a unique basis to assess functioning of the family. This is an important step in advancing nursing science in pediatric oncology. FCC provides a basis for fostering and supporting the active inclusion of parents in their child's treatment and management [56]. We can bring true FCC to life, for the right child and family, at the right time, in the right way, through attention to family psychosocial care and instrumental, daily needs.

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3. Self-Management in Children, Adolescents, and Young Adults with Cancer: State of the Science

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Abstract

Children, adolescents, and young adults with cancer and their families are challenged to learn self-management strategies to cope with the medical, physical, and psychosocial aspects associated with cancer and cancer treatment. These complex behaviors include managing medications, problem-solving relief of symptoms, and engaging in health-promoting activities. This chapter reviews the literature related to self-management in children, adolescents, and young adults with cancer and provides an overview of the state of the science in this area. Using the principles of precision health, the evidence for self-management provides specific direction for tailoring approaches to the individual, family, and environment. Findings from descriptive and intervention research offer recommendations for nursing practice that can support self-management behaviors in this population. Further research is needed in multiple domains to fill the gaps in knowledge for optimal self-management and precision health outcomes.

Keywords Children – Adolescents – Young adults – Cancer – Self-management – Adherence – Precision health

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3.1 Introduction

Globally, an increasing number of young people are diagnosed with a chronic illness that requires lifelong management. In the USA, over 10,000 children (age 0–14 years) and about 70,000 adolescents and young adults (AYAs) (ages 15–39) are diagnosed with cancer each year [1]. For these young people, health and well-being are redefined as the ability to cope and adapt their behaviors to optimize their health outcomes [2]. In the context of chronic illness, the patient and family are the key role players and have agency over their decisions and behaviors, with children having an increasing ability to participate in their own self-management. Self-management of a chronic illness is defined as the process by which individuals and families use knowledge, beliefs, skills, and abilities to achieve health-related outcomes [3]. The health care team needs to use collaborative, person-centered methods to engage persons with chronic illnesses and their families in the planning, implementation, and evaluation of their care—using a comprehensive approach inclusive of medical, role, and emotional interventions to ensure optimal health-related outcomes [4]. The self-management support needs of individuals and families may vary over time and are influenced by contextual factors such as the environment, changes in the illness trajectory of the individual, and the ability to self-manage.

Multiple authors have offered theoretical approaches to self- and/or family-management used in nursing [2–8], medicine [9], and psychology. In nursing, Lorig and colleagues [4, 10] initially set the theoretical foundation for education in self-management. They based their earlier and current intervention program on self-efficacy and social cognition theories [11, 12]. Subsequent authors [3, 5, 6] built on Lorig's work and articulated more complex theoretical frameworks built on an ecological approach, considering the individual, family, and community. Each of these authors addressed self-management context, processes, and outcomes, although sometimes with differing concepts and specificity.

An ecological approach to self-management, which considers the interaction of individual, family, and environmental factors, is reflected in all theoretical frameworks of self-management and is compatible with precision health, the organizing framework for this book (see Fig. 3.1). Precision health uses various sources of information to inform targeted and personalized health care to the individual and family [13]. Cancer-specific factors, such as type of cancer, stage, and treatment, need to be considered as well as any biologic or genetic information that may be relevant to responses and outcomes. Each individual's developmental stage, learning ability, and literacy will influence his or her capacity to self-mange an illness, as well as his or her self-efficacy and self-regulation, key concepts related to self-management. The individual child or AYA also needs to be seen interacting with the family or social structure to understand the dynamics of their physical and social environment, especially related to lifestyle and social determinants [14]. When the science of self-management is integrated into nursing practice, outcomes include optimal self-management behaviors leading to improved health status, quality of life, and cost.

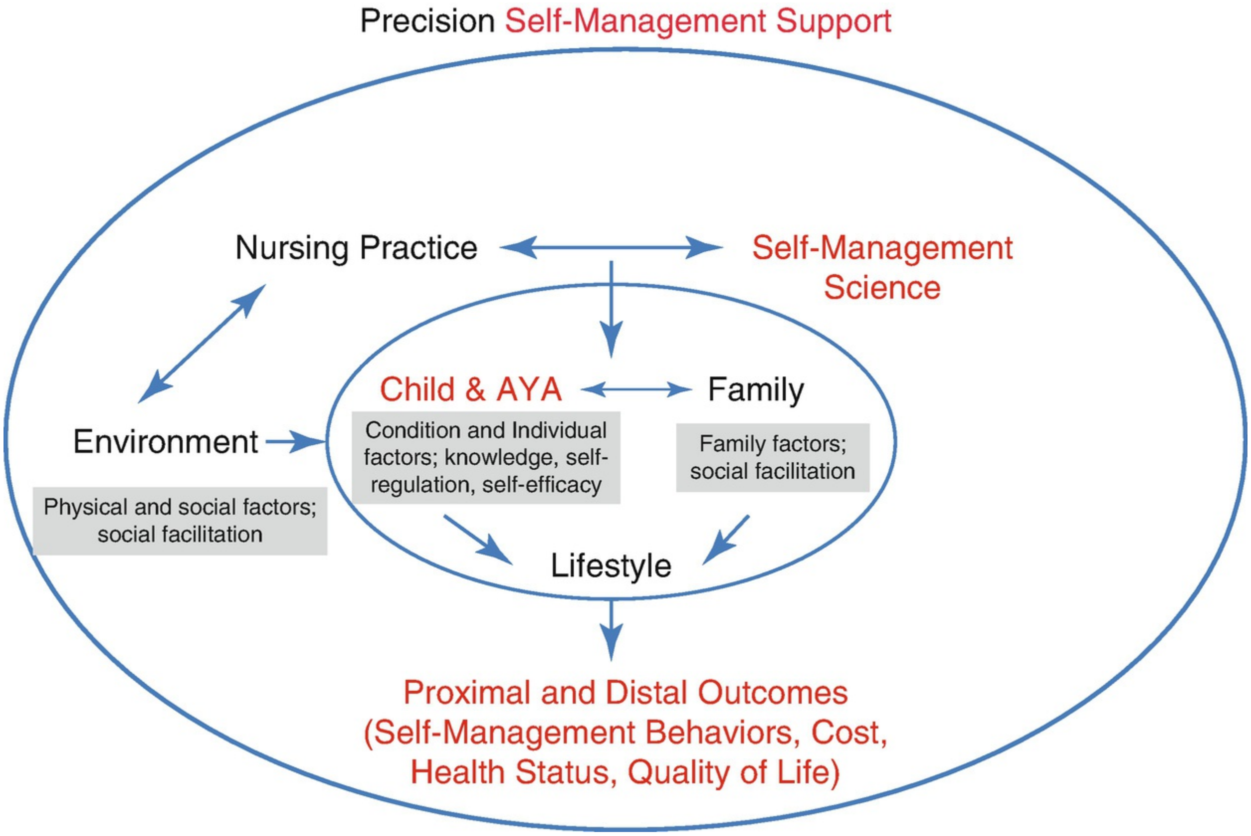

Fig. 3.1 Influence of nursing practice and self-management science on child, AYA, and family health outcomes in response to cancer and its treatment within the context of precision health

One contemporary model of self-management, the Individual and Family Self-Management Theory (IFSMT), was developed by Ryan and Sawin [3]. As detailed in Fig. 3.2, the authors of the IFSMT identified specific contextual variables of an individual or family that influence self-management (SM), the processes of developing specific SM skills and abilities, and outcomes that include the performance of SM behaviors, health status, and quality of life. They propose that the SM process occurs when individuals and family use knowledge and beliefs, self-regulation skills and abilities, and social facilitation to develop the SM outcome (e.g., SM behaviors). The performance of SM behaviors then influences the distal outcome (e.g., health status and quality of life).

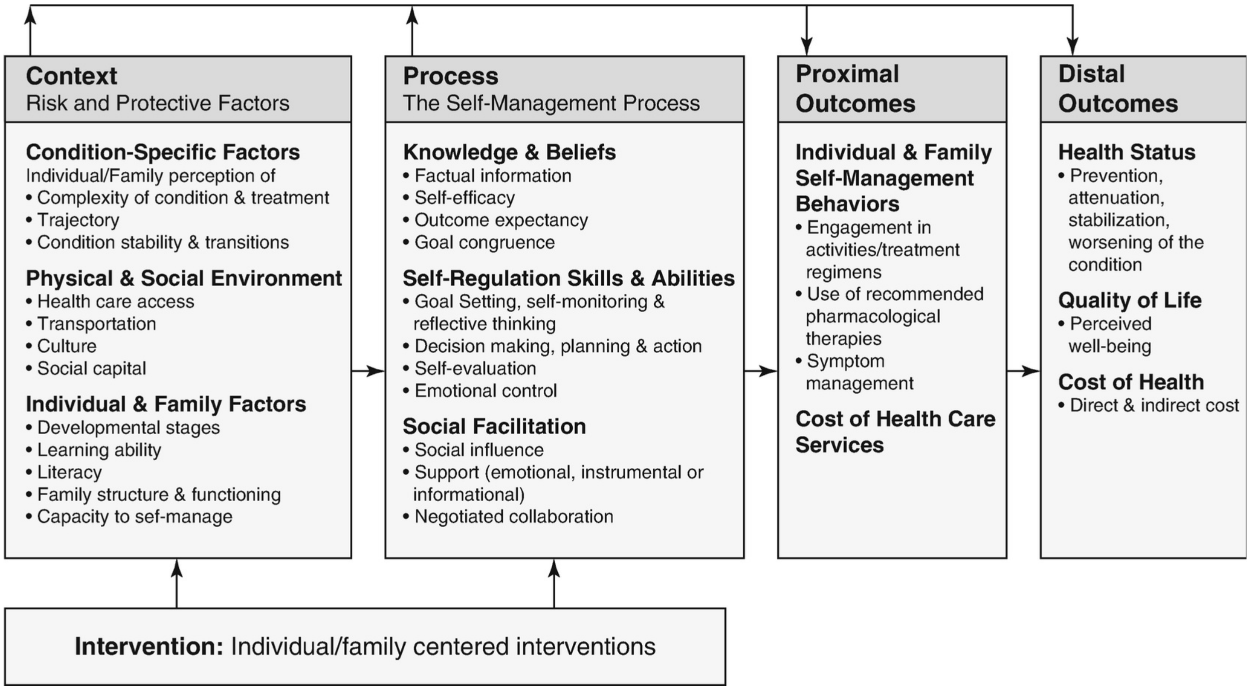

Fig. 3.2 The individual and family self-management theory
Retrieved from: http://uwm.edu/nursing/about/centers-institutes/self-management/theory/

Use of the IFSMT promotes exploration of specific factors identified in the precision health model and the interactions among the factors. Specific variables in the IFSMT context domain relate to the individual (condition, developmental stage, leaning ability) as well as the family structure and environment. The process domain likewise has three major categories, knowledge and beliefs (including self-efficacy), self-monitoring, and regulation and social facilitation that pertain to the individual, family, and environment. Both context and process can directly affect the proximal and distal outcomes; however, the schematic of the IFSMT also indicates that process variables can mediate select context variables. The proximal outcome domain includes the SM behaviors performed to manage the condition and its consequences or prevent complications and includes managing medications, other aspects of a therapeutic regime (e.g., nutrition, physical activity), or symptom management (e.g., pain, nausea, fatigue). The distal outcome domain includes health status, quality of life, and the cost of a health care condition to the individual and society (e.g., lost wages, parental burden, unrealized contributions to society). Using the IFSMT, interventions are aimed at either the context or the process, although many target the process as it has variables more amenable to change. The IFSMT organization can clarify concepts to be targeted by an intervention, variables to be measured, and the impact of the intervention on the variables and outcomes of interest.

3.1.1 What This Chapter Adds

In the last 10 years, six syntheses of the literature have addressed components of SM in children and AYAs with cancer. However, each review focuses on only a segment of self-management. For example, Herts et al. [15] found self-efficacy for disease management was related to health-promoting SM behaviors (a proximal outcome in the IFSMT) and negatively to mental health problems (distal outcomes in IFSMT) and recommended investigation of the role of self-efficacy in other SM behaviors. Goh et al. [16] and Kondryn et al. [17] investigated factors related to SM behavior and identified 17 factors that were summarized in five categories: patient/caregiver, therapy related, condition, health system, and SES factors (all context variables in the IFSMT). Kondryn et al. [17] found emotional functioning (depression and self-esteem), patient beliefs (illness severity and vulnerability), and family environment (patient support and parent–child concordance) related to SM behavior (context and process factors in the IFSMT). They recommended the need to target not only the patient but also health care providers in developing strategies to foster SM behavior but found only one intervention that included health care providers. Another review [18] focused on assessment of medication self-management but included only two pediatric studies in their sample. The most recent reviews focused on support needs of adolescents post-cancer treatment [19] and the effectiveness of technology [20]. The first found relationships were the critical factor in SM and well-being, and the second investigated five studies for the impact of technology-based interventions on empowerment variables (self-efficacy, cancer knowledge, locus of control, well-being, and quality of live) and found no consensus. At 3 months post-intervention, two interventions had impact on locus of control and one on self-efficacy and cancer knowledge, but none affected well-being or quality of life (QOL). Two reviews [17, 18] identified issues in measurement of SM behaviors, and most studies had small samples.

The body of evidence about the components of SM in children and AYAs with cancer is growing, but this evidence has not been synthesized around any conceptual framework or addressed SM in children and AYAs with cancer holistically. This chapter will use the specific variables of the IFSMT to synthesize what is known about the context in which SM takes place for children and AYAs with cancer; the process of SM used by children and AYAs with cancer and their families; the SM behaviors implemented; and the relationship of context, process, and SM behaviors on health outcomes. Theoretical studies that address SM in children and AYAs with cancer and the measurement issues identified in the literature are also included.

3.1.2 Adherence, Self-Management, and Medications

The body of literature about adherence with different definitions and functions in theoretical frameworks is substantial. The most frequently addressed adherence-related behaviors are medication adherence and, less frequently, other therapeutic activities, such as exercise (see Chaps. 6 and 9). Most studies focus on the behavior of taking the medication or conducting the therapeutic activities and operationalize adherence as the percentage of time the individual takes the medication or performs the therapeutic activity as prescribed. The World Health Organization (WHO) defines adherence as the extent to which a person's behavior—taking medication, following a diet, and/or executing lifestyle changes—corresponds with recommendations from a health care provider [21]. The WHO adherence model addresses five interacting dimensions that affect adherence, including health care team/health system-related system factors, socioeconomic-related factors, condition-related factors, therapy-related factors, and patient-related factors.

In contrast, Bailey et al. [22] in their approach to "rethinking adherence" argue that the single act of taking the medication is too simplistic. They propose the use of the term "medication self-management behavior" (MSMB), which they define as "the extent to which a patient takes medication as prescribed, including not only the correct dose, frequency and spacing, but also the continued, safe use over time." These authors delineate a model of medication self-management made up of six behaviors that must be performed to effectively manage a medication regimen. The assumptions of their model are that the medication is prescribed and the person (or family) is responsible for self-administering and that an individual's health literacy plays a role in each behavior in the model. Specifically, the individual and/or family needs to: (1) fill the prescription; (2) report the name of the medication, identify it, and summarize how it is to be taken; (3) implement a medication plan, which includes the organization of the medication use around daily routines; (4) take the medication; (5) take appropriate action, based on vigilant monitoring for side effects and symptoms associated with the medication, to prevent an adverse drug event occurs; and (6) sustain safe and appropriate medication-taking behaviors during the course of treatment prescribed. This conceptualization of MSMB is congruent with the proximal outcomes defined in the IFSMT.

A concept analysis of taking medications in pediatric oncology, although called "adherence," outlined variables relevant to a precision approach to MSMB [23]. Landier defined MSBM as the "active self-care behavior of taking (or having the responsibility for administering) daily oral chemotherapy, in collaboration with and according to the instructions of the healthcare provider over a defined, prolonged treatment period." Key individual and family components, specifically related to taking oral chemotherapy, included persistence, collaboration, mindfulness, cognitive capacity, flexibility, active participation, and identification of key participants. Antecedents included a diagnosis of leukemia, patient, family, and heath care system factors. Outcomes, or consequences, were improved health status, defined as both improved disease status and mental health.

The authors of this chapter, like Bailey et al. [22], recommend the term "MSMB" when the individual or family is responsible for taking a prescribed medication. Bailey et al. recommend, when feasible, that the measurement of MSMB include all of the elements above. This chapter includes all studies that address one or more components of medication self-management using the Bailey et al. definition, whether they are labeled medication self-management or adherence. However, the authors will use the term medication self-management behavior (MSMB) rather than adherence.

3.2 Methods

A two-part literature search was conducted in August 2018 and updated in March 2019. The search used the terms (self-management OR self-care OR self-efficacy OR adherence) AND (cancer). The March 2019 also included a search that included AND (survivor∗). Databases searched included PubMed, CINAHL, PsychInfo, Web of Science, the Cochrane Library, and Google Scholar.

The following inclusion criteria were applied: (1) focused on children, adolescents, or young adults (age 0–39 years); 2) an empirical study; (3) focused on cancer-related self-management; (4) published in a scientific journal; and (5) written in English. Articles were excluded if: (1) the focus was on a disease other than cancer; (2) the sample had unknown diagnoses and/or diagnosis that included only a small percentage with cancer; (3) the focus of the study was on providers' behaviors; (4) the publication was an abstract or dissertation; and (5) the study did not involve human subjects. Individual authors screened all retrieved abstracts and then the authorship team discussed each abstract. Additional articles were identified through reference lists and reviewed for inclusion. The authors read relevant full-text articles and confirmed 42 articles for inclusion in the review.

The authors extracted data from the 42 articles and organized the data in a table alphabetically according to the first author of the study (Table 3.1). Six studies were categorized as conceptual and/or instrument development. The other studies were organized by the SM behavior addressed. Because a large number of studies addressed MSMB (including those labeled as adherence), the team decided to consider evidence on MSMB as a second category ($n = 11$). The remaining studies ($n = 24$) that addressed general SM behaviors or symptom SM behaviors were placed into a third category and were further divided by study design: (1) descriptive and (2) intervention. For the final two categories, study findings were further synthesized by the IFSMT domain that was the focus of the study (context factors, process factors, proximal outcomes, and distal outcomes).

Table 3.1 Evidence from studies included in the systematic review

First author	Purpose/conceptual	Design	Sample setting	Varial

(year) Country	framework	intervention description		
Aldiss et al. (2010) [62] UK	To evaluate preliminary efficacy of ASyMS©—a mobile phone advanced symptom management system for young people with cancer *Medical Research Council framework for developing complex interventions*	RCT (pilot of developed intervention). Manuscript also included phases of intervention development *Intervention* ASyMS© collects information on six symptoms (diarrhea, mucositis, vomiting, tiredness, constipation, and pain) and fever. Based on participant's data, self-management advice is given. Red alert to participant identified need to contact HCP in 30 min	*N* **=** 3 (2 intervention; 1 control) *Age*: 13–15 *Dx* Non-Hodgkin's lymphoma and osteosarcoma *Tx status***:** On chemotherapy *Setting***:** Inpatient—One cancer unit (note only three of expected ten subjects participated)	• Pe cance • Li • St invent • Pe questi • Sy
Amaral (2016) [40] Brazil	To verify the effects of an intervention providing cancer information to children on adherence[a] (SMB) vs competing behaviors during procedure *No conceptual framework reported*	Quasi-experimental *Intervention*: three group sessions based on the book "I'm ill, what now?" Used 24 cards containing information,	*N* = 2 *Age* #1 = 9; #2 = 4 *Dx*: ALL and had competing behaviors during the invasive medical procedure in at least three consecutive treatments *Tx status***:** On	• Ob behav • C videot behav • *P* that d tend t perfor medic

	but problem-based learning inferred	recreational activities, and other exercises for expressing feelings about the illness and its treatment	chemotherapy (IM) *Tx setting*: Ambulatory	• *Co* Respo or pre the in proce
Bagnasco et al. (2016) [41] Italy	To test if the Barrow's Cards improves adherence (MSMB) to immunosuppressive therapy self-management following hematopoietic stem-cell transplantation in adolescents with blood cancer and reduce costs *No conceptual framework reported*	Quasi-experimental (no control group) *Intervention* Pilot problem-based learning intervention using 15 cards designed to teach participants to manage a specific problem. AYA chose from a list of potential SMBs. Feedback given on whether SMB was correct or incorrect for the situation	*N* = 17 *Age*: Adolescent *Dx*: Those with blood cancer following hematopoietic stem-cell transplantation *Tx status*: On treatment *Setting*: Inpatient unit	• Ac used t effecti
Berdan et al. (2014) [51] USA	To assess adherence[a] (SMB) of childhood cancer survivors in comparison to cancer-free adults of comparable age and sex (or "controls") to the 2012 American Cancer Society (ACS) guidelines on	Descriptive, cross-sectional case-control	*N* = 431 childhood cancer survivors 18.5 ± 8.1 years from dx and 361 controls *Age*: 18–59 years *Dx*: With a malignancy before age 21 *Treatment status*: Off treatment	• Sc assess four c guidel scorin • Sc exactl guidel study

	nutrition and physical activity *No conceptual framework reported*		*Setting*: Outpatient; four health care institutions	
Berg (2013) [47] USA	To describe the relationship between late effects, life activities and self-management strategies *No conceptual framework reported*	Descriptive correlational	*N* **=** 42 *Age***:** At least 25; 2 years post-cancer intervention *Dx***:** Survivors with cancer *Tx status***:** Off treatment *Setting*: Outpatient	• La fatigu memo • Su living activit partic
Bhatia et al. (2012) [33] USA	To identify determinants of adherence[b] (MSMB) and impact of adherence[b] (MSMB) on relapse, overall, and by ethnicity. *No conceptual framework reported*	Descriptive longitudinal	***N* =** 327 (158 non-Hispanic, 169 Hispanic) *Age*: 0–21 years; median age at study = 6 years *Dx*: ALL *Tx status*: On maintenance oral MP *Setting*: Outpatient	• Se • M days c the nu prescr report

Erickson (2018) [57] USA	Examined the effects of a heuristic symptom assessment tool on AYAs' self-efficacy for symptom management, AYAs' self-regulation abilities related to their symptoms, and communication with their providers about symptoms *Individual and Family Self-management Theory* *(Ryan and Sawin)*	Quasi-experimental single-group, pre-post analysis *Intervention***:** Computerized Symptom Capture Tool (C-SCAT) guides AYA to create an image of symptom/cluster experienced in last 24 h. The AYA identifies temporal and causal relationships. AYA names their symptom cluster. Final image is generated in a form that can be shared with HCP.	*N* **=** 88 AYAs *Age*: 15–29; *M* = 20.9 *Dx*: Various, 32% ALL. Some diagnosed with cancer years earlier. *Tx status*: On myelosuppressive chemotherapy *Setting*: Outpatient Five academic medical centers	• C captu SCAT) • P mana • Sa comm • Sh *regul* behav after
Foster (2014) [54]	Relations among optimism, perceived	Descriptive, cross-sectional	*N* **=** 56 adolescent survivors	• D • O

USA	health vulnerability, and academic, self-regulatory, and social self-efficacy in adolescent survivors of childhood cancer *Social cognitive theory*		*Age*: 11–20 (M = 16.19) *Dx*: Varied *Tx status*: Completed cancer treatment (range: 1 month—18.5 years) *Setting*: a pediatric hematology/oncology outpatient clinic	• Pe vulner • Ac Social
Gilliam (2011) [58] USA	To evaluate efficacy of a web-based token system to increase adherence[a] (SMB) in an exercise intervention in children and adolescents with cancer *Components of behavior and social cognitive theory*	Quasi-experimental *Intervention*: six mentored 1 h sessions that included problem-solving and exercises focused on endurance, strength, and flexibility. Tokens were earned for completion of activities for redemption at online marketplace	N = 12 *Age*: 6-18 years (M = 12.75) *Dx:* ALL or brain tumor *Tx status*: 1 year post-treatment *Setting*: Home	• Pe sessio • Ae • 15 • Th using dynan • Fu • Sit lateral • Qu generi

Hullmann et al. (2015) [31] USA	Medical and psychosocial associates of nonadherence[c] (problems with MSMB) in adolescents with cancer *Pediatric Self-management Model (Modi et al.)*	Descriptive correlational	*N* = 103 adolescents with cancer and a parent/ guardian. *Age*: 13–19; *M* = 15.77 (1.77) *Dx*: Various, solid tumor (41%) *Tx status*: On treatment for at least 1 month *Setting*: In and outpatient	• Pa • In factor MSMB
Jibb (2017a) [59] USA	To refine the mHealth Pain Squad+ real-time pain self-management app for adolescents with cancer and evaluate usability (defined as being easy to use, easy to understand) *Expanded Health Belief Model; Model of Self-Care in Chronic Illness; and Seto's model used to conceptualize how the app intervention improves outcomes*	User-centered design approach, with iterative cycles of usability testing to refine the prototype Three iterative usability-testing cycles. Adolescents used the app while "thinking aloud" about issues encountered. *Intervention*: Pain assessment and algorithm-informed self-management advice depending on their reported pain.	*N* = 16 *Age*: 12 and 18 *Dx*: At least 3 months from diagnosis with self-reported pain *Tx status*: Undergoing cancer treatment and having self-reported pain *Setting*: Outpatient	• Re difficu • Se about • C identi app u ease o efficie
Jibb (2017b) [60]	Test the efficacy of a real-time pain	Quasi-experimental (a	*N* = 40 *Age*: 12–18	• Ba • Fe

USA	management mHealth Pain Squad+ smartphone app in a multi-center pilot *Conceptual framework (see Jibb 2017 above)*	one-group baseline/post study design) *Intervention* (see above) Adolescents used the app at least twice daily for 28 days. A nurse received alerts in response to sustained pain and contacted adolescents to assist in pain care	*Dx*: Adolescents with cancer who have pain *Tx status*: Undergoing cancer treatment and having self-reported pain *Setting*: Outpatient	
Kato et al. (2008) [44] USA, Canada, and Australia	To determine the effectiveness of a video-game intervention for improving adherence[b] (MSMB) and other behavioral outcomes for adolescents and young adults with malignancies including acute leukemia, lymphoma, and soft-tissue sarcoma *Theories of game-based learning; principles from the self-regulation model of health and illness, social cognitive*	Experimental—RCT *Intervention*: Playing the cancer-targeted video-game intervention over and above any general effect of playing a video game	*N* = 371 (164 intervention; 140 control analyzed) *Age*: 13–29 *Dx*: Various, ALL (38.9%) *Tx status*: On treatment *Setting*: Outpatient; 34 Academic medical centers and community practices	Measu • Ca • Kr • St • Qu • Pi device measu

	theory, and learning theory			
Kaul (2017) [35] USA	To investigate cost-related medication nonadherence[b] (problems with MSMB) among survivors of adolescent and young adult cancer and a comparison group in the USA *No conceptual framework reported*	Descriptive, cross-sectional	*N* = 953 survivors with cancer; 39 comparison group *Age*: 15–39 *Dx*: Cancer *Tx status*: On treatment *Setting*: Outpatient	• 2 Healt • In skippi less m filling mone
Kleinke and Classen (2018) [29] Germany	Analyze oral medication use; compare by cohort; determine factors correlated with adherence[b] (MSMB) *No conceptual*	Descriptive correlational (comparing AYAs with older patients)	*N* = 121 (88 AYA; 33 older) with cancer (33% response rate) *Age:* 18–39 AYA 47–76 older *Dx*: Mixed	• U Kondr medic (adhe items • H depre

	framework reported		*Tx status*: Mixed. All AYA in registry invited. Random sample of 100 older patients invited *Setting*: Outpatient	• Ill menta • Fa • Ne relatic
Kock et al. (2015) [66] Germany	Design, implement, and evaluate a mobile app to increase medication taking—behavior in aftercare program. Childhood cancer and late effects take lifelong self-management. This app was developed to assist in this self-management *No conceptual*	Quasi-experimental pilot with user feedback Intervention app provides information about the patient's individual aftercare plan and supports appointment	*N* **=** 13 adolescents 9 relatives *Age*: 15–17; relatives age 40–54 *Dx*: Osteosarcoma *Tx status*: Aftercare *Setting*: Outpatients in two university hospitals (patients at home)	• Ea with 1 147 p princi evalua

	framework reported	management as well as a reminding functionality		
Kondryn (2009) [28] UK	To assess reliability of a new scale measuring low-risk non-adherence^c behaviors (problems with SMB), correlate scale scores with high-risk non-adherence^c behaviors (problems with SMB), correlate non-adherence^c behaviors (problems with MSMB) and patient attitudes about stopping treatment *No conceptual framework reported*	Descriptive, psychometric	*N* = 33 *Age*: 16–24 years; mean age = 20.1 years *Dx*: Mixed solid tumors *Tx status*: Unknown; 1 year since diagnosis *Setting*: Inpatient, outpatient, and home	• Lc probl define the co • At were patien about
Landier et al. (2011) [24] USA	To develop a model to explain the process of adherence (MSMB) to oral chemotherapy in children and adolescents with ALL *No conceptual framework reported but grounded theory developed*	Descriptive, qualitative, grounded theory	*N* = 17 children; 21 caregivers *Age*: 21 years or younger at diagnosis; median = 16 years *Dx*: ALL *Tx status*: Completed *Setting*: Outpatient or home	NA

Lee et al. (2019) [53] USA	To examine the level and predictors of knowledge of late effects risks from childhood cancer treatment in AYA survivors *Developmental model proposed by Reed-Knight et al.*	Descriptive, cross-sectional	***N* =** 73 AYAs; 67 parents of these AYA survivors *Age*: 14–21, M age = 17.16, SD = 2.23 *Dx:* Various, leukemia (40%) *Tx status*: >2 years off treatment *Setting*: Outpatient	• Su • Re transi • Br • De
Linder et al. (2017) [45] USA	To describe the symptom SM strategies reported by AYAs with cancer	Descriptive cross-sectional	*N* = 72 *Age*: 15—29 years *Dx*: Mixed cancers	• Ca (meas MSAS • St

	receiving chemo using a heuristic app *No conceptual framework reported*		*Tx status*: On treatment *Setting*: Inpatient and outpatient	manag
Linder 2018 [42] USA	To describe how school-age children with cancer perceive and represent their symptoms through drawing *Grounded in developmental science*	Descriptive, qualitative, using “draw and tell” interviews	*N* = 27 *Age*: 6-12 years; mean age = 9.1 years *Dx*: Mixed cancers *Tx status*: On treatment *Setting:* Inpatient and outpatient	• Dr days v well a feeling • Pa promp behav
Linder 2018 [46]	Evaluated oral medication	Quasi-experimental	*N* = 23 receiving at least one cancer-	• M by ele

USA	adherence[b] (MSMB) in AYAs with cancer during trial of smartphone reminder app *No conceptual framework reported*	(single group longitudinal) *Intervention*: Delivery of med reminder via app for 8 weeks, completion of weekly survey	related med for at least 1 month and expected to continue for 3 months 22 receiving med for supportive care and 9 for cancer-directed medication *Age*: 15–29 *Tx status*: 14 off treatment for cancer (drug aimed at symptoms); 9 on active treatment with cancer-related drug *Setting*: Outpatient	for 4 8 wee • Su percei reaso • 80 adequ from l interv
McGrady et al. (2014) [36] USA	Investigating adherence[a] patterns (MSMB) in AYAs undergoing SCT *No conceptual framework reported*	Descriptive, prospective observational	*N* = 6 who had undergone SCT *Age*: 12–18 *Dx*: Had SCT; multiple cancer dx *Tx status*: On oral chemotherapy *Setting*: Outpatient	• De • El medic via M

McGrady (2016) [26] USA	To investigate the mechanisms that drive the daily adherence[a] decision-making process among AYAs with cancer *No conceptual framework reported but grounded theory developed*	Descriptive qualitative-grounded theory	*N* **=** 12 AYAs *Age*: 15–39; *M* = 19.91 (4.86) *Dx*: Various, majority leukemia *Tx status***:** On treatment (oral chemotherapy or antibiotic prophylactic medication) *Setting*: Outpatient	• De infor • In • Ca
McGrady (2018) [30] USA	To develop and pilot test a discrete choice experiment (DCE) to assess the specific factors likely to motivate a given AYA with cancer to adhere[a] to medications (have positive MSMB) included in treatment protocols *Criteria established* *By the International Society for Pharmacoeconomics*	Descriptive, instrument development	*N***:** Phase 1 = 12, phase 2 = 20 AYAs with cancer *Age*: 15–24 years Phase 1 mean age = 19.91 Phase 2 mean age = 18.66 *Dx*: Various, majority leukemia *Tx status*: On treatment (oral chemotherapy and/or prophylactic medication)	• Qu • Ra • Ex interv

	and Outcomes Research		*Setting*: Children's hospital	
Miller et al. (2017) [55] US	To identify correlates of healthcare self-efficacy (HCSE) in a sample of Hispanic and non-Hispanic survivors of childhood cancer *No conceptual framework reported*	Descriptive, correlational	*N* = 193 *Age*: 15–25 years; diagnosed between 5 and 18 years *Dx*: Mixed cancers *Tx status*: Completed at least 2 years ago *Setting*: Outpatient	• He three Stanfo Resea Diseas • He life: Pe versio • Pc Post-t invent • Cl since • In rating
Moody 2015 [56] UK	To explore the self-management support needs of teenage and young adult cancer survivors and consider whether those needs can be met through a web-based self-management resource *No conceptual framework reported*	Descriptive, mixed methods *Intervention*: Model and characteristics of potential web-based self-management intervention developed to meet the needs of AYAs	*N* = 7 from focus group; *n* = 24 from survey *Age:* 17–26 *Dx*: Cancer survivor *Tx status*: 2 years off treatment *Setting*: Outpatient	• Or group teenag cancer • In surviv • Te (*n* = 8 and sc (*n* = 1
Morrison (2018a) [25] USA	Facilitators and barriers to self-management for AYAs following a SCT	Descriptive, qualitative-grounded theory	*N* = 30 (17 AYAs and 13 of their caregivers) *Age*: Average age of	• In

	No conceptual framework reported but grounded theory developed		SCT = 18.5 years (13–22.3 years) and 20 was the average age at interview (14.3–25.3 years) *Dx*: Oncology diagnosis (58.8%) *Tx status*: On treatment *Setting*: In or outpatient; Midwest pediatric hospital	
Morrison (2018b) [27] USA	To describe how AYAs manage their care regimen post-SCT and to explore	Descriptive, qualitative-grounded theory	*N* **=** 17 AYAs (13–25 years old at transplant) and 13 caregivers (dyads)	Indivi

	self-management facilitators, barriers, processes, and behaviors within individual, family, community, and healthcare system domains. *No conceptual framework reported but the authors use Modi et al definition of self-management and developed grounded theory*		*Dx*: Oncology diagnosis (58.8%) *Tx status*: On treatment *Setting*: In or outpatient; Midwest pediatric hospital	
Nandakumar et al. (2018) [48] Australia and New Zealand	To describe the attitudes and experiences of pediatric cancer survivors and their parents about transitioning from pediatric care to adult-oriented or community-based care *No conceptual framework reported*	Descriptive, qualitative	*N* = 33 and 15 parents *Age*: Diagnosed with cancer when younger than 16 years; current mean age = 26 years *Dx*: Mixed cancer *Tx status*: Off treatment at least 5 years *Setting*: Outpatient	• In questi prima cance transi

Pai (2008) [37] USA	Examined the relation between self-reported adherence[b] (MSMB) and bioassay indicators among adolescents with ALL *No conceptual framework reported*	Descriptive, correlational	*N* **=** 51 taking prescribed 6-mercaptopurine (6MP) *Age***:** 17–26 (survey) M = 21 *Dx*: ALL *Tx status*: On treatment *Setting*: Outpatient	• M 6MP n • Se oral m • In includ open-
Rodgers et al. (2013) [64] USA	Examined the acceptability and usability of the EAT! Program among adolescents and assessed the competency of the participants using the program after hospital discharge through the first 100 days after SCT *No conceptual framework reported*	Quasi-experimental (feasibility), repeated-measures design *Intervention*: EAT! app, a mobile phone application developed to assist adolescents with self-management of common eating-related issues during SCT recovery	*N* = 16 *Age*: Adolescents *Dx*: Cancer with HSCT *Tx status*: On treatment *Setting*: Post-hospital discharge through 100 days after HSCT	• Ve Likert accept the ap • A monit applic • C measu time a demo

Rohan (2015) [32] USA	Describe (1) patterns of medication adherence[b] (MSMB) in early maintenance phase therapy for ALL and LBL and (2) the relationships between adherence[b] (MSMB) measures and demographic variables (baseline data in 15-month study) *No conceptual framework reported*	Descriptive, correlational Secondary analysis of data from RCT. RCT efficiency reported in Kato et al., (2008), and Pai and Drotar (2009)	*N* **=** 139 adolescents (and their caregivers) *Age*: 7–19 *Dx*: ALL or LBL *Tx status*: On treatment *Setting*: Outpatient in six geographically different centers Note: TPMT, an enzyme that metabolizes 6 MP in active metabolites, is a genetic trait inherited from both biological parents. The genotype was collected for all who signed consent for genetic testing (*n* = 125)	• Pe measu Medic systen obser • Le metab were r blood • 31 from t identi metab
Rohan (2017) [39] USA	Describe the prospective relationship between pharmacological and behavioral measures of 6-mercaptopurine (6 MP) MSMB in a multisite cohort of pediatric patients diagnosed with cancer (15 month follow-up data of Rohan 2016) *No conceptual framework reported*	Descriptive correlational, longitudinal	*N* **=** 139 children, AYAs and their primary caregiver *Age*: 7–19 (children) *Dx***:** ALL and LBL *Tx status***:** On daily dose of 6MP and second cycle of maintenance phase of therapy *Setting*: Outpatient multisite (6) cohort	• M metab self-re 2015 • 31 from t identi metab
Stinson et al. (2012) [52] Canada	To document the SM needs of adolescents with cancer	Descriptive qualitative, individual and	*N* **=** 29 adolescents, 30 parents, 22 healthcare providers	• N

	No conceptual framework reported	focus group interviews	*Age***:** 12-18 years (AYA) *Dx*: Mixed cancers *Tx status***:** On treatment or within 2 years of completion *Setting***:** Inpatient and outpatient	
Stinson et al. (2013) [64] Canada	To explore the usability of an Internet-based SM program for adolescents with cancer and their parents ("Teens Taking Charge: Managing Cancer Online") *No conceptual framework reported*	Quasi-experimental; feasibility of new intervention *Intervention*: The program consists of 12 interactive modules with cancer-specific content, SM strategies, and social support	*N* = 22 adolescents and 15 parents *Age*: 12–18 years; mean = 15.2 years *Dx*: Mixed cancers *Tx status*: On treatment or within 2 years of completion *Setting*: Not reported	• Pa about conte efficie naviga
Stinson et al. (2015) [65] Canada	To evaluate construct validity and reliability of a phone app ("Pain Squad") to assess pain in children and adolescents with cancer. *No conceptual framework reported*	Descriptive, psychometric	*N* **=** 92 in study 1, 14 in study 2 *Age*: 8–18 years *Dx*: Mixed cancers *Tx status*: On treatment *Setting*: Inpatient and outpatient	• Re • Pe (gene • Pe • Pa short-

Syed et al. (2016) [49] Canada	To identify factors associated with SM skills in teens who have survived childhood cancer *Pediatric SM model (Modi)*	Descriptive, cross-sectional	*N* **=** 184 *Age***:** 15–19 years who were diagnosed at mean age of 6.6 years *Dx*: Mixed cancers *Tx status***:** Off treatment *Setting*: Outpatient	• SM manag (SMSs
Williamson et al. (2017) [61] USA	To characterize how YA cancer survivors and parents of CCSs use an electronic personal health record (ePHR) (SurvivorLink) and if use is associated with recommended survivor care *No conceptual framework reported*	Descriptive (retrospective chart review) of a EHR intervention *Intervention* Cancer SurvivorLink™, a patient-controlled ePHR designed for survivors of pediatric cancers. Registered users upload important health documents which are	*N* = 624 *Age*: 2–21 years; mean age of 13.8 years *Dx*: Mixed cancers *Tx status*: At least 2 years off treatment *Setting*: Outpatient	• Re Surviv use, d for do

		available to providers, regardless of where the providers practice and independent of institutional or practice specific electronic medical records systems		
Wu et al. (2015) [50] USA	To identify barriers to and facilitators of exercise and healthy eating among AYA cancer survivors Intervention mapping framework *Socio-ecological framework; social cognitive theory*	Descriptive qualitative	$N = 25$ survivors; 19 supporters *Age*: 18–39 ($M = 27.6$) *Dx*: Diagnosed with cancer anytime in their lives *Tx status*: Completed active therapy *Setting*: Clinics at a NCI-designated cancer center	• Fo
Wu (2018a) [34] USA	To explore the feasibility and acceptability of a medication reminder app (Dosecast) to promote adherence[b] (MSMB) to oral meds *No conceptual*	Quasi-experimental (feasibility)	$N = 23$ ***Age*:** 15–29 years; mean age = 19.7 years ***Dx*:** Mixed cancers ***Tx status*:** On treatment	• Fe Dosec data c self-re

	framework reported		*Setting*: Outpatient	
Wu (2018b) [43] USA	To describe adherence^{b} (MSMB) to 6MP and MTX in a national sample of pediatric patients with ALL by using medication refill records *No conceptual framework reported*	Descriptive	*N* = 900 *Age*: 0–21 years, mean age = 12.7 years *Dx*: ALL *Tx status*: On treatment *Setting*: Outpatient Data abstracted from medication claims included in the Medical Outcomes Research for Effectiveness and Economics (MORE^{2}) Registry	• M the m ratio, the nu medic maint • Ra report

N number, *Dx* diagnosis, *Tx status* treatment status, *SM* self-management, *MSMB* medication self-management behavior, *SMB* self-management behavior, *HCP* health care provider, *AYA* adolescent and young adult, *RCT* randomized controlled trial, *ALL* acute lymphoblastic leukemia, *SCT* stem cell transplant, *MP* mercaptopurine, *MTX* methotrexate, *LBL* large B-cell lymphoma, *NCI* National Cancer Institute, *CHIP* Children's Insurance Program. All results are significant at $p = 0.05$.
Evidence Level I = RCT study, II = Quasi-experimental studies,
III = Descriptive studies. Quality Ratings Quantitative Studies.
HIGH = consistent, generalizable, sufficient sample size for study design, adequate control definitive conclusion, GOOD = reasonably consistent results, sufficient sample size for study design, some control, fairly definitive conclusions, reasonably consistent recommendations;
LOW = little evidence with inconsistent results, insufficient sample size for study design, conclusions cannot be drawn. Qualitative studies: HIGH/GOOD. Discusses efforts to enhance or evaluate the quality of the data and the overall inquiry in sufficient detail; describes specific techniques used to enhance the quality of the inquiry. Evidence of some or all of the following: Transparency, diligence, verification, self-reflection, participant-driven inquiry, insightful interpretation. LOW, studies contribute little to the overall review of findings and have few if any of the qualities listed in high/good (John Hopkins Nursing Evidence-Based Practice) adapted from Polit and Beck 2017. www.york.ac.uk/crd/SysRev/!SS!/WebHelp/6-4-ASSESSMENT-OF-QUALITATIVE-RESEARCH.htm

[a] Adherence is conceptualized as a self-management behavior (SMB)

[b] Medication adherence conceptualized as Medication self-management behavior (MSMB)

[c] Nonadherence is conceptualized as problems with MSMB

3.3 Results

3.3.1 Theoretical or Measurement Studies

Of the six articles in this section, four were reports of grounded theory studies and two were instrument development. Grounded theory studies generate an inductive theory about a substantive area. Each of the reviewed studies added theoretical specificity to context, process, or outcome self-management concepts. Each of the author groups interviewed a sample of AYAs to learn more about process factors specific to living with cancer. Seventeen adolescents were interviewed in each investigation with Landier [24], and Morrison [25] also included parents and caregivers.

Landier and colleagues [24] explored the process of SM for Hispanic and Caucasian children and AYAs with acute lymphoblastic leukemia (ALL) from the perspective of the AYA and parent. They identified a core theme of "Doing Our Part"—the child, AYA, or parent taking responsibility for assuring that medications are taken as prescribed. Three important phases were identified in this process: (1) recognizing the threat, (2) taking control, and (3) managing the duration. Particularly important in the first theme was the mediating factor of "making the connection" and recognizing the relationship between taking the medication and control of the leukemia. Children and AYAs who did not make the connection had less consistent medication management behaviors. Key in the second theme was figuring out what works and establishing routines. Managing for the duration included seeking normalcy, integrating a positive outlook into daily life, and feeling supported. These authors also identified contextual factors of family structure, climate, and socioeconomic status as key factors in medication self-management.

In contrast, McGrady et al. [26] focused on the process concept of "decision-making" among youth with cancer managing a medication regime that included either chemotherapy or prophylactic antibiotic medication. Decision-making (DM) was characterized as a complex multi-dimensional process with four themes and multiple subthemes that generated a model of the mechanisms related to decision-making regarding medication use in AYAs with cancer. The first main theme captured the interaction between medication characteristics and the goals or values of AYAs. AYAs were motivated to take their medication if it prevented short-term consequences or achieved short-term reward, if they saw the medication as a way to achieve a long-term goal, or if it prevented them from experiencing negative emotions. They were less inclined to take their medication if taking it yielded side effects or disrupted their normal activities. The second theme captured the AYA's knowledge—specifically, knowledge about the reason for the medications and subsequently what the consequences would be if they missed or skipped a dose. The third theme delineated the skills in problem-solving and habit formation strategies that helped the AYA to take their medication as prescribed over time. One example of the "habit formation strategy" was linking medication taking with established habits, like brushing teeth. The final theme expanded understanding of the external factors on decision-making, especially the "social support" identified in the IFSMT. AYAs identified instrumental support or physical assistance (i.e., refilling pill box, setting out medications) or emotional support (i.e., verbal reminders) from others that made them more likely to decide to take their medication.

Morrison and colleagues [25, 27] completed a grounded theory study aimed at understanding the processes AYAs use to develop self-management behaviors (SMB) and explored facilitators and barriers in four ecological spheres: individual, family, community, and society. The major finding of this study was that the process of managing their mental and emotional responses as a result of treatment was indistinguishable from managing a prescribed care regime. This component (managing emotional response) is a key aspect of the process of SM in the IFSMT. In addition, the study identified other process factors facilitating SM—specifically, information, positive attitude, social support, motivation, and organizational skills. Context variables identified as limiting SMB were isolation and single parenting. Morrison et al. [27] also found that implementing SMB was made easier by developing routines. Isolation, monotony, and managing symptoms were the biggest obstacles for these AYAs' SM behaviors.

Finally, two articles in this section reported on the development of new instruments specific to SM of AYAs with cancer. Kondryn and colleagues [28] developed a ten-item instrument aimed at measuring SM behaviors. They intended to design a measure that captured the treatment challenges, AYAs' ability to follow treatment recommendations, and a number of other health-promoting behaviors. The ten items reflected difficulties with SMB. The authors indicate that the scale can differentiate those at "low risk" or "high risk" for taking the prescribed medications consistently over time. Although the authors report internal reliability ($\alpha = 0.73$) and the ability of the scale to differentiate between known groups (those who report fever and those who do not), the psychometric evidence was limited with no factor analysis or other assessment of validity and no assessment of stability (test–retest reliability). However, the items were translated into German, and six SMBs were retained [29]. The authors also report an "attitude scale" but provide no evidence of its reliability or validity. Researchers and clinicians are advised to defer use of these instruments until further psychometric analysis is conducted.

In contrast, McGrady et al. [30] sought to develop a novel assessment (discrete choice experiment, or DCE), which identified factors likely to motivate a given AYA with cancer to take medications included in treatment. Cognitive interviews, including a concurrent "thinkaloud" strategy, were used to explore comprehension and address content validity. The DCE was modified with input from AYAs with cancer. The final DCE included nine choice sets (e.g., impact on daily activities, physician-reported efficacy, impact on long-term goals, parent/significant other support encouragement). AYAs supported its content validity by saying the DCE was understandable and relevant. Twenty AYAs with a variety of cancer diagnoses took part in the pilot testing. The assessment took an average of 5.83 min to complete, which participants identified as acceptable. This innovative assessment appears to capture different salient factors that motivate individual AYAs to take their oral medications. Although the current report was preliminary and the iPad-delivered assessment is currently undergoing testing in a large-scale study, this instrument holds promise to assist in precision healthcare. It can identify for the AYA and the health care provider specific motivational factors likely to assist individual AYAs in taking medications consistently across time.

In summary, the grounded theory studies used qualitative methods to identify salient concepts for AYAs with cancer and organized them to generate emerging theoretical models of the SM process specific to AYAs with cancer. The specificity of these phases of engaging in SM, the specific attitudes and beliefs facilitating SM, the function of social support, the importance of establishing routines, and the theoretical depiction of decision-making in AYAs with cancer provide nurses with in-depth understanding and specific strategies to facilitate AYAs' SM behaviors. However, these studies often addressed a limited population (e.g., those with stem cell transplant or those with ALL), a single treatment regime (e.g., taking medication), or individuals in a single location. In addition, all but one study used parents and AYAs to generate the theoretical models. Further research is needed to determine if these findings cross diagnostic groups or treatment groups and are confirmed by AYAs from various diverse cultural groups. In addition, the two instruments reviewed were early in their development and need further evaluation in large-scale studies. The discrete choice experiment instrument especially holds promise to be used in precision health care for AYAs with a wide variety of cancers.

3.3.2 Medication Self-Management Behavior Studies

3.3.2.1 Descriptive Studies

Studies provide mixed evidence about context factors associated with poor MSMB in children and AYAs with cancer. Two studies found that age, gender, and race/ethnicity did not affect taking medications as prescribed [31, 32], but other studies found that AYA cancer survivors who were Hispanic [33], Black, uninsured, insured with CHIP or Medicaid [34], and more concerned about costs [35] may be at risk for having less optimal MSMB. Two studies concluded that MSMB was lower in adolescents compared with younger children [33, 34]. Greater mental distress, having more comorbidities, and not having a regular source for health care may be considered risk factors in the context domain [34, 35]. Other process factors associated with better MSMB included having greater family support [31] and more future-oriented goals [26]. Older AYAs are likely to be more future-oriented than younger AYAs [26].

Five studies [31, 32, 36–38], primarily focused on adolescents with ALL receiving maintenance treatment with oral chemotherapy, provided evidence about outcomes and patterns of MSMB. Methods to measure the rates of taking oral chemotherapy or other medications as prescribed include self-report, parental report, electronic monitoring of pill bottles with the Medication Event Monitoring System (MEMS), and bioassays of medication metabolites in the blood or urine. In one study [31], only half of adolescents on treatment and their parents endorsed perfect medication-taking behaviors. In other studies with adolescents on treatment, estimates of accurate medication-taking behaviors ranged from 59% to 95% [32, 33, 36, 37, 39], with evidence that taking these medications as prescribed decreases over time. Several variations in patterns of MSMB over time have been identified in AYAs. Rohan et al. [39] suggested three profiles of mercaptopurine (6MP) metabolites in children and adolescents with ALL or lymphoblastic lymphoma over 15 months. One profile (60%) showed low levels of metabolites, indicating sub-optimal medication taking, while the other two profiles (40%) showed adequate levels of metabolites. The sub-optimal profile group remained at lower levels over the 15-month period. McGrady et al. [36] examined the MSMB of six adolescents post-hematopoietic stem cell transplantation (HSCT) for immunosuppressant drugs and antibiotics. They identified three patterns of MSMB that reflected effective behaviors, variable behaviors, and delayed problems.

Bhatia et al. [33] followed 327 children and AYAs with ALL for a median of 3.7 years. Taking 6MP less than 95% of the prescribed time was associated with an increased risk of relapse.

In summary, many children and AYAs do not take medications to manage cancer or its complications as prescribed, especially over a long duration. Patterns of MSBM also vary. Adolescents with complex conditions, receiving complicated treatment regimens, and having limited resources may be at highest risk for poor MSMB. Racial and ethnic minority patients may also be particularly vulnerable. Most importantly, not taking oral chemotherapy as prescribed can affect cancer outcomes.

3.3.2.2 Intervention Studies

Four studies reported interventions related to MSMB. Interventions included: educational cards [40, 41], a smartphone medication reminder application [42, 43], and a video game [44]. The interventions involved health education and methods to increase disease knowledge, self-efficacy, decision-making, problem-solving, and participation.

Two studies used methods that would require health care workers or caregivers to assist in the delivery of the intervention. Cards containing information about cancer, recreational activities, and exercises focused on expressing feelings delivered by a researcher increased children's collaborative behavior during ambulatory chemotherapy requiring intramuscular injections. These behaviors were not maintained post-intervention, and the authors suggested that future studies should involve group interventions, caregivers, and health care workers. Bagnasco et al. [41] used Barrow's Cards tailored for AYAs with cancer to assist them to deal with complex problems to improve adherence to immunosuppressive therapy. Barrow's Cards is a case-based learning method originally developed to test decision-making and critical thinking skills in medical students. Preliminary data indicated no complications and no readmissions during the study period compared with two cases prior to the implementation of the Barrow's Cards. Families and adolescents were satisfied using this method which could also be delivered using a computerized platform.

In the study by Wu et al. [43], 70% of participants reported that a smartphone visual/audio medication reminder application (Dosecast) to improve medication related decision-making was useful to increase independence of MSMB. Although the intervention did not show overall improvement in MSMB, four MSMB phenotype patterns were identified [42]: (1) high MSMB before and during the intervention ($n = 13$); (2) low MSMB before with improvement during the intervention ($n = 3$); (3) low MSMB before and during the intervention ($n = 6$); and (4) high MSMB before and low during the intervention ($n = 1$). Adolescents with high rates of taking medication as prescribed prior to and during the intervention mostly reported scheduling/lifestyle problems as reasons for missing doses. An improvement in MSMB was more prominent among adolescents who reported forgetfulness as reasons for missing doses. Problems with accessing treatment were more frequently reported by adolescents with low MSMB and no marked improvement. Context factors that were identified as influencing MSBM included access to health care, the frequency of treatment (e.g., missing morning doses), and side effects. While medication reminders may increase MSMB independence, identifying MSMB phenotype patterns and considering contextual factors may further optimize MSMB interventions.

In a large RCT, a video-game (Re-Mission) intervention focused on behavioral issues, various self-care behaviors, and patient participation, increased MSMB, self-efficacy, and knowledge in the intervention group, although only 28% completely adhered to the prescribed 1 h/week [44]. Self-reported MSMB, stress, control, and quality of life did not improve. Knowledge and self-efficacy jointly accounted for the change in taking doses of trimethoprim and sulfamethoxazole (TMP/SMX), but not 6MP. Access to personal computers may limit the applicability of this intervention; African American participants had the highest non-use rates.

Educational interventions that address increasing disease knowledge, self-efficacy, decision-making, and problem-solving may improve short-term MSMB; however, no long-term data are available. Interventions directed at a single process (e.g., medication reminders/instrumental support only) do not appear to improve MSMB. MSMB phenotype patterns and context factors should also be considered when developing interventions.

3.3.3 Symptom Management and Therapeutic Regime Self-Management Studies

3.3.3.1 Descriptive Studies

Of the 11 descriptive studies in this category, three described SM behaviors used by children and AYAs with cancer to manage their symptoms. Nine studies described context and process variables from the IFSMT, and, in some studies, the relationship of the concept and process variables to symptom SMB and other outcomes were explored.

The three studies describing SMB used to manage symptoms did so by developmental stage (school age children and AYAs) and identified behaviors specific to cancer. The first study with AYAs used free text responses to two questions on the Computerized Symptom Capture Tool (C-SCAT) [45]. Responses were analyzed to determine the most common self-management strategies AYAs employed to manage individual symptoms or symptom clusters. AYAs indicated they used a variety of strategies, which were categorized into three overarching themes: “Things I Take-or Not,” “Physical Care Things I Do,” and “Psychosocial

Care Things." Participants reported strategies in each of these themes; however, medication-taking behaviors were addressed the most. Some strategies involved a health care provider (e.g., changing medication, dose, or route), while some were AYAs' independent behaviors (e.g., getting enough sleep, doing small amounts of exercise). Physical behaviors to address symptoms included "eating slower, taking naps, and wearing an eyeshade patch to keep it dark." Similarly, psychosocial strategies included "talking about it, spending some time in peace and quiet and doing simple fun tasks to distract me." The study of school-aged children used draw-and-tell interviews to identify both symptoms (e.g., nausea, fatigue, pain, and sadness) and SM strategies [46]. Children reported fewer medication-taking strategies than AYAs and focused on physical and psychosocial care strategies. Most described SMB they used when they were not feeling well. Children's physical care behaviors, such as those to manage energy balance and improve personal comfort, were common (e.g., lie down and rest). Psychological care strategies included distraction and behaviors to personalize and normalize their life. In the third study, AYA survivors who were at least two years from treatment used similar SM strategies to manage six late effects, including fatigue, pain, and depression [47]. The specificity of the behaviors to address symptom or symptom clusters by developmental stage provides rich although preliminary information for individually tailored care and future intervention research.

Of the nine other descriptive studies, seven described context and process factors/needs that were positively or negatively related to health promotion activities or treatment regime SMB in children and AYAs with cancer (e.g., healthy eating and physical activity), SMB used to manage symptoms of cancer or its treatment, and health outcomes (transition to adulthood). Two studies explored the relationship between context and process variables. Although there was some consistency across studies with age (context variable) [48–50] and positive attitudes (process variable) related to increased symptom SMB across several studies, generally the relationship of context and process factors to outcomes varied by the SMB or health outcome.

Across studies, context variables related to SMB included both risk factors (e.g., lack of resources, male gender, CNS tumor, negative social and environmental influences, cognitive limitations) and protective factors (e.g., being older, having a single parent, being female) [48, 49]. These context variables, however, were inconsistently supported across the studies. A recent German study found that the context variables of gender, religion, education, age, anxiety, and family atmosphere were not related to SMB [29]. In another study [51], being a childhood cancer survivor, when compared to those without cancer, was not related to implementing healthy nutrition and physical activity behaviors. These behaviors did not differ across ethnic groups; however, Hispanic survivors had a higher body mass index than Caucasian survivors. The authors concluded that there was much room for improvement in diet and lifestyle SMB, which could be expected to improve overall health in both groups.

Process variables identified as SM needs or factors related to SMB included disease knowledge and cancer care skills [48], knowledge and skills to support effective transition to adult health care, delivery of health care services accessible to adolescents with cancer, beliefs about illness, and supports for the adolescent with cancer [52]. Attitudes, both positive (optimism) and negative (negative thoughts and feelings) and social relationships were also related to SMB. Generally, health care provider relationships were not related to SMB [29]. Nonetheless, AYAs saw dependence on pediatric health care providers, less confidence in primary care physicians, and inadequate communication as barriers to transition to adult healthcare [48]. In contrast, age, confidence in and proximity to health care providers, good communications, and independence were perceived as facilitators of this transition. However, more AYAs when compared to older patients reported sub-optimal communication with health care providers and considered stopping treatment.

In studies examining relationships between context and process concepts, risk knowledge was not related to responsibility for SM or executive function [53]. While cancer-specific variables (e.g., intensity of treatment, time since end of treatment) were not related to self-efficacy [54], attendance at a survivorship clinic, having a regular oncologist, Hispanic ethnicity, religious/spiritual beliefs and psychosocial variables [55], optimism and health vulnerability were. Self-efficacy, especially confidence for managing one’s specific health care condition, was a major predictor of outcomes across ages and conditions. Understanding self-efficacy in managing symptoms of cancer or its treatment remains an area of research needing further exploration.

In summary, only two studies described SMB used by children and AYAs. The two developmentally based studies were excellent and generated a preliminary taxonomy of SMB in children and adolescents, but their findings need to be confirmed with diverse ethnic and disease populations. Even though a few studies found similar context and process variables related to symptom SMB, health promotion SMB, or transition to adult healthcare, no clear pattern across the majority of studies was present. Better understanding of the function of context and process variables in these outcomes is foundational to precision health care.

3.3.3.2 *Intervention Studies*

A small body of research addressed interventions to improve self-management behaviors in children and AYAs during the cancer trajectory. Most of these interventions involved health technology. AYA cancer survivors acknowledge unmet information needs related to cancer information, social support, and self-management; and that these needs can be partially met through eHealth and mHealth technologies [56]. A number of studies reported the development of mobile phone apps and Internet-based interventions to improve the self-management process of children and AYAs during and after cancer treatment (Chap. 8).

A few self-management interventions that incorporate patient-reported outcomes (Chap. 7) have shown efficacy to improve process factors or outcomes, including symptoms (Chap. 5). A heuristic app focused on symptom assessment improved self-efficacy and self-regulation for managing symptoms in AYAs receiving chemotherapy and also facilitated communication about symptoms with providers [57]. An Internet-based token system, along with in-person mentoring, was used to increase participation by children and adolescents in a home-based exercise program following completion of cancer treatment [58]. Although participants completed only some of the activities, the exercise program improved endurance, strength, and mobility. Jibb et al. [59, 60] developed and pilot tested a smartphone app for adolescents to report and self-manage their pain. Use of the app showed improved pain outcomes, including health-related QOL, pain intensity, and pain care self-efficacy. Williamson et al. [61] found that when children and AYAs used an electronic personal health record, such as SurvivorLink, they were more likely to return for long-term follow-up care.

Other technology-based programs and interventions were reported to be in early phases of development. Testing is needed to determine the efficacy of these programs to improve proximal and distal outcomes related to health behaviors, symptom management, and other health outcomes (See Chap. 8). Aldiss et al. [62] reported on the development of a symptom management system mobile phone app (ASyMS) for AYAs which will help them monitor and manage multiple symptoms by providing tailored symptom management information. The app was tested and found to be feasible and acceptable to AYAs. Stinson et al. [63] reported on the usability of an Internet-based SM program for adolescents with cancer and their parents ("Teens Taking Charge: Managing Cancer Online"). The 12-module program provides cancer-specific content, SM strategies, and social support. Other apps under development are focused on improving eating behaviors in children and adolescents following hematopoietic stem cell transplant (HSCT) [64] and pain management [65]. One app by Kock et al. [66] focused on providing tailored information about long-term effects from cancer treatment, with reminders and calendar functions to make future follow-up care appointments.

Although much of the evidence about these interventions comes from feasibility and pilot studies with small samples of AYAs, most of the interventions involve innovative technology, which should appeal to this age group. Some of the apps and programs show promise to improve process variables, such as knowledge, self-efficacy, and communication, as well as some short-term outcomes, such as symptom severity and engagement in health-related behaviors.

3.4 Discussion

The small number of diverse studies in each of the three major categories reported in this analysis (theoretical, MSMB, and symptom and other SM behaviors) makes drawing conclusions difficult. The theoretical studies related to SM focused on this population provide some specificity to the process variables included in the IFSMT. For example, decision-making is a core process variable in self-regulation, and McGrady et al. [26] provided insight into how AYAs with cancer make decisions about taking medications. Landier [24] specifically addressed the knowledge and beliefs of children and AYAs with leukemia and their parents as they take responsibility for taking oral chemotherapy.

In the context domain of self-management, multiple individual factors were considered, and many studies had heterogeneity in the ages of participants, cancer diagnoses, treatment regimens, and phases of survivorship. While some studies included infants and children and their parents, more is known about AYAs. A few studies with AYAs also included parents, but no studies with AYAs described caregivers other than parents, such as friends or partners. Most studies were conducted during the acute phase of survivorship—from diagnosis through treatment, but a few studies focused on self-management during extended or late survivorship.

Consistency in the study of process variables, including knowledge, self-efficacy, self-regulation (including decision-making), and social support, was greater in this body of literature. These process variables were also the primary targets of the interventions tested. For both MSMB and SM related to symptoms and other topics, interventions were typically psychoeducational and often used some type of technology, such as an app. Most interventions were described in pilot or feasibility studies with the exception of one randomized clinical trial that had a large enough sample to make a conclusion of efficacy [44]. In this study, a video-game intervention improved knowledge, self-efficacy, and medication self-management behaviors. Smaller quasi-experimental studies with other SM interventions demonstrated improvement in pain outcomes, strength and endurance outcomes, and self-efficacy for symptom management.

Studies that focused specifically on MSMB found that many children and AYAs do not take medications as prescribed, especially when prescribed for a long duration. Multiple context factors were suggested as risk factors, such as adolescence, racial or ethnic minority status, uninsured or underinsured, and poor access to health care. Several small studies suggested that interventions focused on improving process variables related to knowledge, self-efficacy, and decision-making may have promise to improve MSMB.

These studies related to MSMB provided important information for precision health. Two useful studies described the specific SMB that children and AYA used to manage their medications and other cancer treatment regimes. Better understanding of these SMBs is the foundation for precision health interventions to optimize outcomes. In addition, studies identified patterns of MSMB (labeled as adherence) that can assist the nurse in planning precision health interventions [36, 39, 42]. The study with the largest sample [39] called the three patterns "exemplary" (71% had positive MSMB nearly 100% of the time), "deteriorating" (17% had MSMB that decreased from 100 to 60%), and "chronically poor" (6% had consistently poor MSMB), while others described patterns in an intervention study as "consistently high, improving or impaired." In addition, an instrument in early stages of development by Kondryn et al. [28] holds promise of identifying those who are "low-risk" or "high-risk" to have problems taking their medications.

Although the lack of definitive intervention studies and inconsistent findings across descriptive studies preclude definitive recommendations, the studies reviewed do offer important preliminary information on which to build precision health. Particularly useful are the delineation of specific SMB used by children and AYAs with cancer and the patterns of MSMB.

3.5 Limitations

Although a librarian with expertise in literature searches assisted with this project, the use of limited combinations of search terms may have missed relevant studies related to SM, especially related to infants and younger children with cancer and their parents. However, the use of multiple databases should have reduced this possibility. The lack of high-quality studies yielding strong evidence limited the resulting recommendations for practice. Finally, the authors' approach to framing and reporting adherence as MSMB may be controversial and may impede communication about the problems of medication-taking behaviors in this population. However, this proposed approach should advance understanding of the comprehensive meaning of MSMB and inform future research in this area.

3.6 Evidence-Based Findings Derived from the Science of Self-Management in Pediatric Oncology Ready for Translation to Clinical Practice

This body of evidence shows the impact of several precision health factors specific to self-management for children and AYAs with cancer that address the individual, family, and their lifestyles. While few recommendations for nursing practice can be made with confidence, several suggestions to consider for practice do emerge from this literature. These include:

3.6.1 Medication Self-Management Behavior

- Many children and AYAs do not take medications as prescribed, especially during a long course of treatment.
- AYAs present with different MSMB patterns that are influenced by various individual and family factors. AYAs with complex conditions and treatments and with limited resources and support may be most at risk for poor MSMB.
- Nurses should complete a comprehensive assessment of MSMB. In addition to asking about taking the medication as prescribed, nurses should question how the child or AYA obtains their medications, whether they understand the name and purpose of each medication (especially long-term benefits), how they implement a plan to organize medications, and how they take action to prevent or manage adverse effects.
- Nurses should monitor for patterns of MSMB and plan interventions based on the pattern for a personalized approach. For example, children and AYAs who have optimal medication-taking behaviors may need continued reinforcement and reminders from the health care team. For children and AYAs with less optimal behaviors, providers need to identify barriers and explore other problem-solving strategies with the patient and family. Depending on the barrier, some children and AYAs may need more intensive interventions, such as a referral to

or consultation with a psychologist or a social worker.

3.6.2 Self-Management Behavior

- A child's or AYA's knowledge and beliefs, especially to connect cancer treatment with control of the cancer, a positive attitude, and strategies to integrate treatment into daily routines, tend to improve SMB.
- Instrumental and emotional support from family members and the feeling of being supported is important to foster SMB in children and AYAs with cancer.
- Environmental factors, such as access to health care and good communication with providers, facilitate SMB.
- Interventions to improve the SMB of children and AYAs with cancer should address the process variables of SM (e.g., knowledge, beliefs, self-efficacy) since these are the variables most amenable to change.
- Nurses and other healthcare team members need to collaborate with parents and caregivers of children and AYAs as well as with the other sources of social support, such as friends, partners, and teachers, to create a social environment that is supportive of effective SMB for each individual.

3.7 Future Research Recommendations to Advance the Science of Self-Management in Pediatric Oncology

Advancing the science of precision health to develop personalized approaches to self-management in children and AYAs with cancer will require research focused on multiple domains of self-management. Evidence is needed to fill gaps in knowledge so that nurses are able to deliver the "right intervention for the right person at the right time" [67]. The theoretical studies laid a good foundation for understanding the process of self-management in this population, but this insight is limited by the diagnoses studied and the diversity of samples. Although the descriptive literature added important information for nursing practice, it is limited by the lack of consistency identifying context factors. In addition, context and process factors need to be related to outcomes, especially distal outcomes, such as quality of life, cost, and achievement of future developmental milestones. The number of intervention studies related to SM in this population is especially limited, especially related to SMB outside of taking medications. Recommendations for future research:

- Studies need to use a conceptual or theoretical framework related to SM to systematically propose and organize research variables of interest.
- Concepts, such as adherence, need to be conceptually clear and defined. For example, many of the studies that reported on adherence actually included broader behaviors beyond just taking the medication as prescribed.
- Studies that focus on or distinguish a particular age group, cancer diagnosis, and phase of survivorship are needed to fill in the gaps of knowledge about this developmentally diverse population so that recommendations can be made for practice that are informed by more precise evidence.
- Studies are needed to explore SMB, especially over time, related to symptom management and general healthy lifestyle behaviors, building on what is already known from the interventions currently under development.
- Technology-based and mHealth interventions to improve SMB in children and AYAs need to be tailored using precision-health elements related to the individual, family, and the environment.

3.8 Conclusion

Cancer is a frightening diagnosis for a young person and their family and frequently requires lengthy and complicated treatment associated with acute and long-term consequences. Nurses can look to a growing body of literature focused on children and AYAs with cancer for evidence about how to support children and AYAs to successfully manage their cancer during and after treatment. Incorporating a focus on precision health care, guided by the specific components of the IFSMT, can assist nurses in understanding individual and family self-management for children and AYAs with cancer. Although further research is needed to better identify key concepts for targeted and individualized interventions and the relationships between the individual, family, and environment, the studies reviewed can provide nurses with preliminary guidance for precision care. Nurses need to contribute to the discovery of new knowledge about self-management in this population and translate the findings into practice to ensure optimal cancer and developmental outcomes. Promoting effective precision health care related to self-management is especially important for children and AYAs with cancer because the outcomes of this care can extend for decades into survivorship.

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4. Resilience in Pediatric Oncology

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Abstract

The focus on precision health in healthcare fits well with the recent shift from a traditional illness-focused model to a positive health approach. Precision health seeks to tailor treatment and supportive care to characteristics of individual patients in order to attain the best clinical outcome for that person. In order to achieve increasingly positive outcomes, it is helpful to understand why some patients and families thrive despite adversity, while others struggle. Therefore, resilience is receiving increased attention in research and clinical care. The science and understanding of resilience specifically in pediatric oncology is emerging with research efforts aimed at understanding and intervening with patients and families to promote health in the face of illness. Challenges remain, including the need for a single, agreed upon definition of resilience among healthcare professionals.

Keywords Resilience – Positive health – Strengths-based approach –

4.1 Introduction

In 2001, the National Institutes of Health endorsed the importance of a positive health approach to care. This fits nicely with the emerging focus on precision health, with its focus on improving individual outcomes by tailoring treatment and supportive care [1]. Positive Health focuses on four core concepts: (1) understanding ways individuals sustain or regain optimal health; (2) the presence of wellness as well as absence of disease; (3) primary prevention and positive health promotion; and (4) most relevant to this chapter on resilience, building on strengths to address problems [2]. Resilience is increasingly of interest to clinicians and researchers for several reasons.

- An understanding of protective factors that foster resilience addresses the question of why and how individuals and families rise above the adversities associated with cancer.
- Knowledge of resilience processes and outcomes is necessary to guide intervention development to help adolescents and young adults (AYAs) and their family learn effective ways to overcome the difficulties of receiving a cancer diagnosis and treatments and dealing with late effects.
- All children, AYAs, and families have some level of resilience protective factors, so thoughtfully assessing, enhancing, and adding to existing strengths may be an efficient and effective way to overcome illness-related distress and foster positive health outcomes.

Precision health approaches consider such aspects of a person as their genetics, environment, lifestyle, etc. and formulates a plan to optimize individual health [1, 3]. Precision health approaches encourage clinicians to consider the unique individual when planning care. Context and culture are variables to consider not only in cancer care but also in research. Resilience is particularly salient within the context of precision health with a focus on positive health. From a precision health perspective, assessment of the multiple risk and protective factors associated with resilience is necessary to first understand individual and/or family strengths and needs and then to foster these strengths through tailored interventions.

While no single definition of resilience is currently universally accepted, resilience is generally defined as positive adjustment in the face of adversity. A general definition developed in the context of cancer and other chronic illnesses is that “resilience is the process of identifying or developing resources and strengths to flexibly manage stressors to gain a positive outcome, a sense of confidence/mastery, self-transcendence, and self-esteem” [4]. Resilience is a particularly relevant concept in pediatric oncology because more patients are surviving cancer. Therefore, efforts to understand, foster, and promote resilience in patients and families undergoing cancer treatment are vital to long-term positive outcomes (Fig. 4.1).

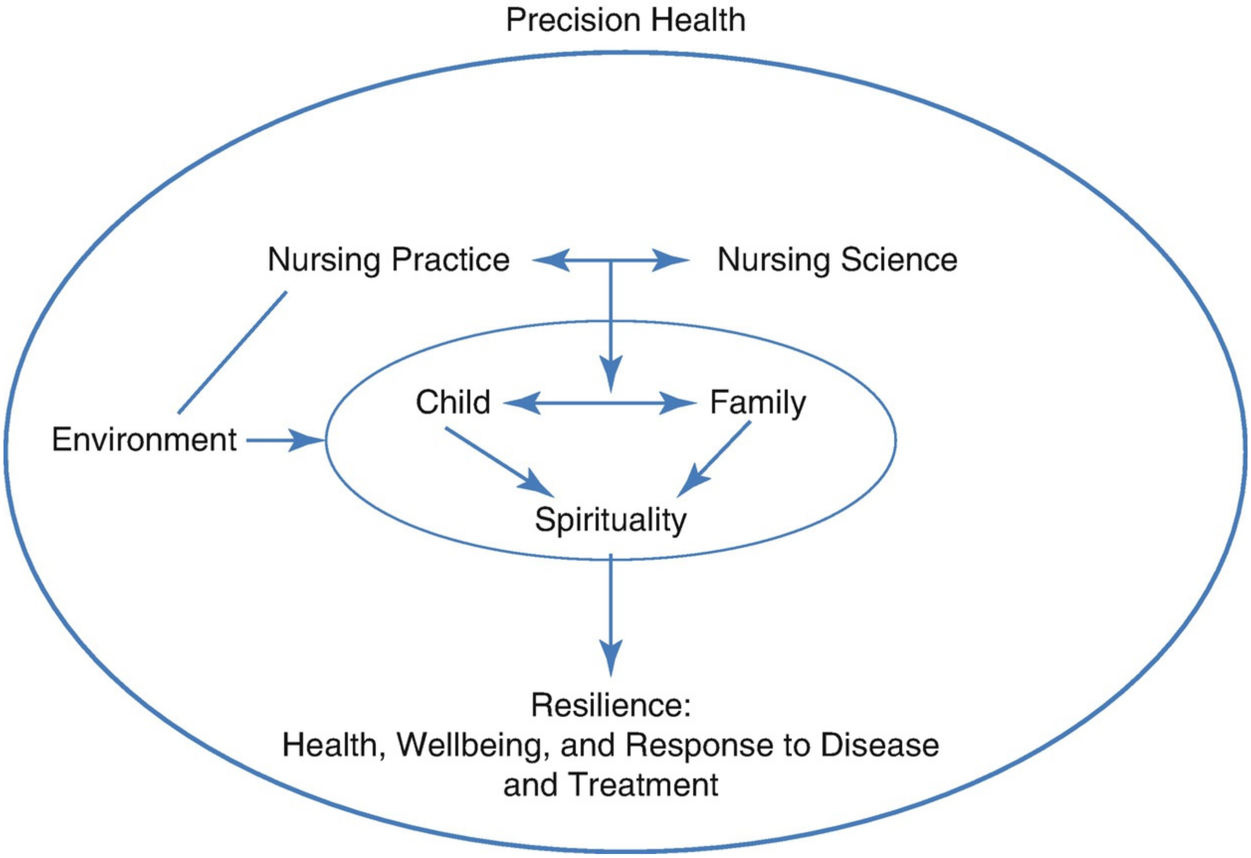

Fig. 4.1 Resilience in child and family health and response to disease (cancer) and its treatment within the context of precision health

Pediatric oncology nurses have long recognized the importance of resilience research and practice. The Resilience in Illness Model (RIM)

[5] was developed with adolescents with chronic illness, including cancer [6, 7]. In 2013, the RIM was adapted for use to guide all research conducted through the Children's Oncology Group (COG) Nursing Discipline and this adapted model, "Resilience in Individuals and Families affected by Cancer" now serves as the organizing framework for descriptive and intervention research within the Nursing Discipline of the Children's Oncology Group [8].

4.2 Review of Literature

4.2.1 Resilience Models

There are several commonalities among the current conceptual models of resilience. First, they focus on concepts that are rarely included or are underemphasized in deficit-oriented theories, specifically protective factors, assets, competence, and developmental tasks [9]. They also usually describe the influence and impact of risk factors on resilience outcomes. They indicate ways protective factors can foster resilience, even amid difficult life circumstances. And, they describe the underlying mechanism of interactions among protective and risk factors, as well as their contributions to resilience outcomes. Because factors that influence positive health are amenable to improvement, resilience models are useful to guide the development of positive health focused interventions.

4.2.2 Changing Perspectives of Resilience

Much of the early resilience research focused on common character traits (e.g., competence, self-esteem, extraordinary coping, and advanced self-help and problem-solving skills) that children who faced adversity either demonstrated or did not. Such traits are generally static and not easily modifiable through interventions. Beginning in the 1980s, conceptualizations of resilience were broadened to view resilience as a modifiable state or process, described by Rutter as "the ability to bounce back or cope successfully despite substantial adversity," [10] and researchers began to study family and social protective factors that influence resilience over time [11].

Resilience research has been predominated by psychology and nursing, examining resilience within and across multiple levels, from cells to societies. There are also focused efforts to holistically study and develop and test theoretical models of resilience [5, 12]. In contrast to the pathological and/or deficit-based approaches to illness that have guided healthcare for centuries, positive health and resilience are strengths-based approaches that emphasize the meanings of illness experiences and the influence of patterns and experiences of illness on individuals and their families.

While resilience is most clearly described at the individual level, individuals are social beings who have consistent interactions with the surrounding environment; thus, extrinsic factors such as family, social ecology, and culture significantly influence the ability of individuals, families, and larger groups to positively adjust to difficult situations [13–15]. Resilience research is evolving from a strictly individual-focused conceptualization towards a contextually and culturally embedded framework. This advance is parallel with the development of bio-social-ecological systems models of human development [16]. The premise for a multi-level focus is that a singular focus on individual-level factors alone is inadequate to understand or improve resilience significantly. Instead, researchers and healthcare providers must pay attention to the contextual and culture-related factors that influence individual resilience.

Risk and protective processes of resilience are labeled, defined, and measured in different ways across studies, so the proportion of participants in studies who are deemed to be "resilient" varies greatly [17]. This makes comparison of populations across multiple studies difficult. The terms "resilient," "resiliency," and "ego-resilience" are not recommended because they indicate a personality trait such as hardiness, instead of a process of adjustment, which is amenable to change.

4.2.3 Research on Resilience in Pediatric Oncology

At present, few models or measures of resilience have established reliability and validity in the pediatric oncology population. One notable exception, the Resilience in Illness Model (RIM), focuses on AYA with cancer. This model was developed from a positive health perspective to evaluate positive health processes and outcomes in AYA [18]. RIM was developed through a series of qualitative and quantitative studies conducted over 33 years. These studies used phenomenology, simultaneous concept analysis, and instrumentation methods to understand and measure AYA experiences of dealing with chronic illnesses (i.e., cancer, cystic fibrosis, asthma, and cardiac diseases) [6, 19–21]. In the RIM, resilience is defined in terms of both process and outcome. Resilience as a *process* is "the degree to which individuals identify, develop, and/or engage in protective resources" (i.e., spiritual perspective, social integration, family environment, courageous coping, and hope-derived meaning) to flexibly manage illness-related stressors (i.e., illness-related distress and defensive coping) in order to achieve the two-fold outcomes, resilience resolution, and self-transcendence [5] that lead to well-being [2]. Resilience as outcome is "the degree to which individuals (a) gain a sense of mastery, accomplishment, and competency related to managing the illness situation; (b) are motivated to continue to maintain and improve the situation and help and inspire others; and (c) acknowledge and accept that the illness experience contributes to but does not predominantly define oneself as a person" [5].

An important concept relative to the RIM is connectedness. This refers to an individual's sense of attachment and engagement with others, including family, peers, healthcare providers, and the community (including school, activities, and work as appropriate) [22]. This emerging concept is newly related to resilience in the pediatric oncology literature, but early research and extant literature note that children and adolescents who are more connected have better psychological outcomes following cancer treatment [23]. Thus far, connectedness has been studied in isolation, such as connectedness with healthcare providers [24] and connectedness at school and psychological outcomes [25]. Because children and adolescents do not function within single domains, it is important to assess connectedness across the interdependent systems (e.g., work, home, peers, school, healthcare) to gain a clear picture of how connected the individual is and how these connections can be facilitated to foster resilience in illness [22], for example, interventions conducted at the family or group level to foster socialization and peer support.

The "Resilience in Individuals and Families Affected by Cancer," based on the RIM [8] broadens the model to include family resilience and the environment and culture in the framework. Particularly in pediatric oncology, a focus on the individual AND family is crucial because care of the child or AYA with cancer occurs on multiple levels (see also Chap. 2, “Family-Centered Care in Pediatric Oncology”). The impact of cancer is felt by the entire family, and resilience can occur at the individual level with each family member and in the context of the family as a whole [8]. All the RIM factors are depicted within the inner circle of the COG Nursing Discipline framework. RIM was expanded into an ecological model by adding family and culture outer circles. In addition, cancer continuum constructs, individual biological variables, and family variables were added; these variables are impacted by and have impact on the individual’s resilience. Examples of these variables are individual and family ages, developmental levels, illness, and treatment characteristics and genetic characteristics [26]. This COG Nursing Discipline framework guides research on positive health perspectives by understanding the ways individuals and their families sustain or regain optimal health during the cancer experience, and by exploring and testing interventions to promote resilience and well-being for patients and families facing a pediatric cancer diagnosis [8] (Fig. 4.2).

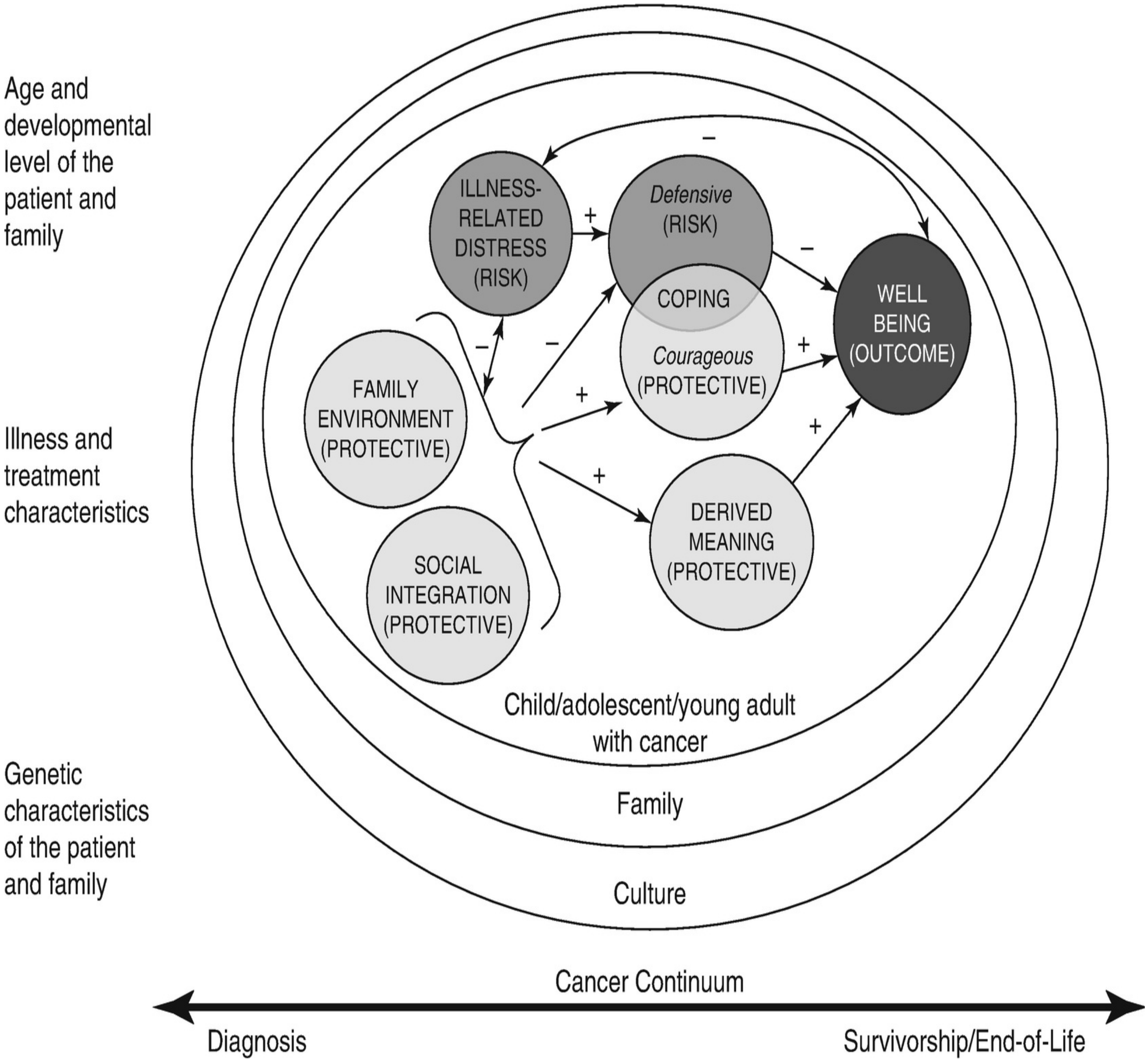

Fig. 4.2 Resilience in Individuals and Families Affected by Cancer

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4.3 Assessment and Measurement of Resilience

Central to the study of resilience is identification of factors that make a difference, i.e., what is necessary to help individuals meet challenges and adapt to adversity. Assessment of protective factors is important to understand and build on individual strengths to manage illness-related distress. Protective factors and resilience outcomes are not physically observable, so measurement is necessary [27]. Understanding the complex interplay between these factors requires study at multiple levels, from neurobiology to culture and society. Most studies of resilience have been cross-sectional. Since resilience is a dynamic process, it is also important to consider longitudinal (at least three time points) measurement to capture change [27].

Measuring resilience in individuals and/or families can be challenging. An ongoing challenge is developing measurement strategies that are sensitive to the dynamic quality of the concept. A further challenge comes when measuring resilience within a family, as each of the multiple members should be included in the assessment, measurement, and interpretation of results. As a result of these challenges, measurement of resilience in pediatric oncology is evolving. The RIM uses multiple, validated instruments to measure all protective and risk factors in children and AYA ages 11–26. Measures are assessed from the perspective of the individual, as well as the parent perceptions of the individual and family. More research is needed to assess resilience in younger children and in all individuals within the family, and in other cultures. In 2018, the AREA (Asia Resilience Enhancement for AYA with Cancer) Cooperative Group was formed to: evaluate the cultural appropriateness of RIM in AYA with cancer within each Asian country; compare the RIM across Asian countries, evaluate a composite Asian RIM model, and compare these models to the RIM developed in North America. The first aim of the group was to find translated versions or translate/back-translate versions of all RIM measures and all measures are now translated into Simple Mandarin, Taiwanese Mandarin, and Korean. Translation into Japanese is underway.

Because resilience is not directly observable, measurement of resilience often requires the use of latent variable modeling [28]. Latent variable modeling accounts for the unobservable aspects of a phenomenon by measuring the manifest (observable) variables as indicators of a larger construct [27]. For example, we cannot measure “health” directly, so we measure body mass index, heart rate, blood pressure, cholesterol, etc. Someone who is trained to assess “health” can look at these manifest variables and have a picture of one’s health. Latent variable modeling is a well-supported approach if the relationship between the latent and manifest variables is specifically defined.

While single measures of resilience exist, most have not been validated in pediatric oncology. The exception is the Connor-Davidson Resilience Scale which has been validated in parents of children with cancer [29]. The Connor-Davidson Resilience Scale [30] is a 25-item scale (there are also ten item and two item brief versions). It was originally designed to assess resilience in persons with post-traumatic stress disorder but has since also been validated in multiple populations, including caregivers [29]. It measures resilience in the following domains: personal competence, acceptance of change and secure relationships, trust/tolerance/strengthening, control, and spiritual influences.

Table 4.1 includes assessment tools which may have utility in pediatric oncology resilience research but have not yet been validated in this population.

Table 4.1 Resilience measures with potential for use in pediatric oncology populations

Assessment tool	**Appropriate age group**	**Number of items**	**Subscales**	**Who completes this tool**
Devereux Early Childhood Assessment for Preschoolers Second Edition (DECA-P2) [31]	Children: 3–5 years	38 items	Initiative Self-regulation Attachment/relationship Behavioral concern	Caregiver or teacher report
Youth Resiliency: Assessing Developmental Strengths (YR: ADS) [32, 33]	Adolescents: 12–17 years	94 items (10 factors, 31 subscales)	Parental support/expectations Peer relationships Community cohesiveness Commitment to learning School culture Culture sensitivity Self-control Empowerment Self-concept Social sensitivity	Self-report
Child and Youth	Adolescents	28 items	Individual	Self-report

Resilience Measure (CYRM-28) [34]	and young adults: 12–23 years		Relational Community Culture	
Resilience Scale (RS) [35]	Sixth grade reading level	25 items (also 14-item short form)	Individual resilience (personal competence and acceptance of self and life)	Self-report

The RIM measures each latent factor (e.g., courageous coping, family environment, social integration) with two to three measures and/or subscales and has a single measure of resilience as outcome developed in the context of chronic illness. This enables specific measurement of the concepts that foster resilience outcomes and gives a composite picture of resilience in the individual. Since some of the constructs involve family, measurement of individual family member perspective was done, but more research is needed to measure resilience of families as a unit.

4.4 Individual Resilience in Cancer

Resilience and vulnerability fluctuate throughout the lifespan depending on circumstances [30]. Resilience and vulnerability are not mutually exclusive concepts; they generally simultaneously exist within each person. People are complex and influenced by many internal and external factors. It is important to measure the constructs associated with resilience in multiple ways in order to obtain a holistic understanding of the individual's current level of resilience.

4.5 Resilience in Children with Cancer

Previous research has demonstrated that children with cancer are generally resilient and well-adjusted [22, 36]. One important note when considering child resilience is that resilience in a developing person is not circumscribed within the body and mind of that individual [37]. Resilience in children with cancer is influenced by and exists within the larger framework of the family and environment. Resilience is both complex and dynamic, particularly in children, because both the child and the context are continually changing as a result of their interactions with both people and environments. In addition, within each child there is the ever-changing environment over time [37]. Children are dependent on others for care, particularly when being treated for a life-threatening illness, like cancer. Research suggests that family functioning can act as a protective factor in the child's adjustment to cancer [7, 22, 36].

Concepts influencing resilience of children include the family environment (cohesion, adaptability, communication, perceived family strengths), characteristics of the child (coping, spirituality, spiritual perspective, and hope-derived meaning), and social integration (relationships with friends, within the community, and healthcare providers). Children less than 7 years old are often unable to complete measures for themselves, and thus proxy measures are necessary. This is challenging because research has demonstrated that proxy measures may not accurately reflect the whole of the child's experience since they are being completed by someone other than the child [38]. However, proxy measures are an important component to assessment of resilience in children [38].

Research addressing resilience in children with cancer is often inconsistent, in that sometimes studies explore age groups that include not only children but also adolescents. Additional studies may emphasize some, but not all, factors that may influence resilience. Comprehensive research into the resilience of children with cancer within the context of confirmed conceptual models of resilience is needed.

4.6 Adolescent/Young Adult (AYA) Resilience in Cancer

In pediatric oncology, much of the research addressing resilience has been conducted with AYAs. Haase's RIM model was developed with children and AYA, ages 11–26, primarily because of this populations' poorer health outcomes. The World Health Organization (WHO) defines an adolescent as any person between ages 10 and 19. This age range falls within WHO's definition of young people, which refers to individuals between ages 10 and 24. The Children's Oncology Group's Adolescents and Young Adults Committee defines the group as including ages 15–29 years while the NIH includes individuals from 15 to 39 years.

In adolescence, resilience is particularly important to assess and foster because of the unique developmental tasks facing adolescents, regardless of their illness. Investigations exploring the prevalence of positive changes in AYA with cancer found that most reported some positive growth, and that the ability to identify positive aspects of their cancer experience may help to protect patients from adverse effects of cancer and its treatments [39]. When AYA and their families respond in positive ways, they may obtain personal growth and positive effects [40, 41].

Most intervention studies have included AYA receiving treatment. However, many psychological challenges AYA experience occur after treatment has ended. The availability of psychosocial support is more limited, so there is greater need for positive health-focused psychosocial interventions. Another challenge to assessing effectiveness of psychosocial interventions is the length of follow-up. Because cancer treatment can last from months to years, adequate time is needed to evaluate the impact of psychosocial interventions over time. AYA may benefit from longer follow-up or booster sessions of interventions designed to promote resilience.

Due to the complexity of psychosocial well-being, most psychosocial intervention studies for AYA diagnosed with cancer used multiple outcome measures. Summarizing results, however, is difficult when different measures are used to study outcomes. Additionally, many psychosocial measures have not been evaluated in AYA. Because AYA with cancer has unique individual and social challenges, measures designed for adults with cancer may or may not be appropriate for AYA. This limited availability of validated measures on psychosocial health for AYA hinders researchers to measure changes in psychosocial well-being.

4.7 Resilience of Parents of Children with Cancer

Rosenberg and colleagues [42] proposed a model of resilience assessment—Resilience in Pediatric Cancer Assessment (RPCA)—for parents of children with cancer. This model was developed from a review of the existing resilience literature, qualitative interviews with bereaved parents, and quantitative measures of resilience. RPCA is a paper/pencil survey comprised of instruments validated among adults and/or parents of children with cancer. The survey has six domains: resilience resources, emotional distress, social function, health behaviors, cancer experience, and demographics. While constructed differently than the Resilience in Illness Model, the conceptual model proposed by Rosenberg and colleagues [42] accounts for the development of resilience over time. It is built on baseline characteristics (individual), evolves as patients and families adapt to their circumstances, and is affected by psychosocial outcomes. Overarching all of this are the individual's subjective perceptions and appraisals of strengths and stressors over time. These authors note that the appropriateness of different interventions is likely to vary based on where the patient is on the treatment trajectory [29].

A few models provide a framework for understanding resilience in parents. The only one specifically noted for parents of pediatric cancer patients is the Resilience Model for Parents of Children with Cancer (RMP-CC) [43] in mainland China; the exploratory study identified two protective factors (Social Support, Courageous Coping) and three risk factors (Emotional distress, Caregiver Burden, and Uncertainty in Illness). These five factors explained 58% of the variance in resilience in parents, which indicated that RMP-CC was a reasonable model to guide interventions for parents in mainland China [43].

4.8 Resilience in Families of a Child with Cancer

Cancer diagnosis in a child renders the entire family vulnerable to negative outcomes [44]. Diagnosis, treatment, and subsequent survivorship or bereavement all require the whole family to alter responsibilities. Responses of the family as a unit to the cancer diagnosis require individual members to deal with emotions and effectively communicate. Overall, most individual family members demonstrate resilience in the context of cancer, adjusting to the new demands of the cancer diagnosis over a short time [44]. However, sometimes family members struggle, and it is important to be able to assess and intervene with these families and their individual members at both the family and individual levels.

Research addressing the family as a unit of analysis is evolving [2]. A recent systematic review of existing literature on resilience of families experiencing cancer operationalizes family resilience as competent family functioning after exposure to a significant risk [44]. Most theories of family resilience identify specific aspects of family functioning that can impact child adjustment such as family cohesion, family conflict, adaptability, beliefs, communication skills, organizational patterns, problem-solving abilities, and social support [7, 45].

Families are complex and vary in their structure and function. Recent research demonstrates the diversity within families is complex and there are multiple pathways of human development within families [46]. In the context of resilience, there are three aspects of family environment: cohesion, adaptation, and communication [7, 44]. Cohesion refers to the emotional bond between family members, adaptation refers to abilities to adjust to changing circumstances, and communication refers to quality, relevance, and openness to discuss what is important. A review of the literature exploring resilience in families of children with cancer demonstrated overall increased cohesion within families after a child's cancer diagnosis (and into survivorship) with parents, children with cancer, and siblings all acknowledging this increase, although siblings experienced a peripheral role at times [47]. Resilient families balance cohesion to avoid the extremes of being disengaged or enmeshed.

When considering family resilience, recognition that families are made of individuals interacting within both the family and the environment is necessary. In these interactions, risk and protective factors are interrelated within the individual and across the family and environment [48]. Challenges of studying family resilience include differing views on whether resilience is a process or outcome for the family. (Practitioners tend to be focus on what strengths any particular family brings to a crisis while researchers often focus on the outcomes of resilience in the family [49].

Less is known about family strengths, particularly following the experience of pediatric cancer. A cancer diagnosis not only influences individual family members, but also impacts family relationships and function. Family is the basic unit of society providing care to children. When a child is diagnosed with cancer, families need to alter roles and responsibilities, communicate effectively, and work as a team to cope with this unpredictable stressor and take care of child and siblings. Therefore, understanding family resilience in its totality is important.

The concept of family resilience shifts attention from seeing family as a resource for individual resilience to a systematic perspective of resilience within the family [50]. The whole family is affected by adversity; family resilience mediates the adaptation of all family members and the family as a unit. Research at the level of family resilience following a pediatric cancer diagnosis is sparse. Studies describe the outcomes of family resilience from multiple expected functions of the family, including cohesion, adaptability, communication, family support, sense of belonging and meaning, and protection of vulnerable family members [44, 50]. Families who were deemed "resilient" were those who were able to return to, sustain, or achieve competent levels of functioning (i.e., cohesion, adaptation, communication, family support, and general family functioning) after being challenged by a pediatric cancer diagnosis [44].

Further theoretically based research on family resilience and factors predicting resilience outcomes is warranted and should include attention to measurement and statistical analyses [44]. Future family resilience research needs to involve multiple family members, consider collection of longitudinal data to assess changes in family resilience over time, and use mixed methods to examine the processes of family function, short-term and long-term outcomes. The mechanisms of family resilience are important to inform interventions. Healthcare providers should assess family functioning and resilience routinely and be aware of cultural differences when considering the family within the larger socio-ecological context.

Current extant literature supports the idea that everyone has a degree of resilience. This includes the micro-level of the individual, the family at a broader level and, finally, in consideration of the contextual impact of culture of origin and/or current locale of residence. However, many salient issues must be considered as one develops a study focused on resilience. First, patterns of resilience vary over time, both within the individual and the family. Second, the nature of the adversity needs to be considered. Within the care of the pediatric oncology patient and family, there are adversities central to receiving the cancer diagnosis, treatment, stem cell transplant, relapse, and survivorship. It is important to recognize that resilience can be fostered by assessing, drawing on, and enhancing the protective factors as an antidote to the adversities associated within each phase of the cancer journey. Starting with assessment of resilience at an individual level and then focusing outward is an appropriate approach. Intervention development is necessary at multiple levels after current status and needs are identified. The focus on strengths-based assessment is important to overcome the negatives inherent in the diagnosis, treatment, and late effects of childhood cancer.

While systematically assessing a child or family's resilience at diagnosis and other cancer milestones is ideal, daily assessment in usual clinical care should also include consideration of protective factors to address problems. As an example, an assessment of family support can help healthcare providers better understand family strengths and guide resources to strengthen family communication and help families adapt to having a child with cancer, and children and family members who are exhibiting defensive coping mechanisms can receive interventions to teach more positive coping mechanisms.

4.9 Neurobiological Basis for Resilience

Evidence for the association of specific biomarkers with resilience and that these biomarkers may represent the biological component of this phenomenon is growing. Biomarkers include the anxiolytic neuromodulators oxytocin and neuropeptide Y (NPY) [51, 52] as well as cortisol and dehydroepiandrosterone (DHEA) [53, 54]. In addition, oxytocin assists with social and emotional behavior in humans and rodents. Examples of such behavior are trust and bonding, as well as reducing anxiety [55]. A study in human volunteers exposed to psychosocial stress demonstrated that oxytocin had an anxiety-decreasing effect [55]. A growing body of literature also suggests that oxytocin aids in building and maintaining resilience [51].

In neurobiological research on resilience, studies conducted within diverse samples of children across the world are of particular relevance [56]. Luo et al. [57] conducted a study in female adolescents with different levels of exposure to the 2008 Wenchuan earthquake in China. Results showed that hair cortisol levels were elevated in girls with higher level of exposure, which may be a potential biomarker that provides a timeline of stress responses embedded in the hair as it grows [57]. It is possible that information gained from this study can inform stress response in cancer as well, although hair loss associated with many of the treatments for cancer may limit the utility of this approach. Additionally, many pediatric and adolescent treatment protocols include the use of corticosteroids as primary treatment or supportive care, thus requiring careful assessment of the role of cortisol in stress response in these populations.

4.10 Resilience in Different Cultures

Culture plays a critical role in resilience development. Although previous studies suggest there is a common set of characteristics and processes associated with resilience among adolescents across diverse cultures (such as family support, peer relationship, community/school support, and educational engagement) when people are in the midst of adversity, culture influences individual's interpretation of adversity [58–60]. Culture also influences coping strategies, evaluation of positive adaptation, expectations about what "doing well" means and strategies for promoting resilience [9, 56, 59, 61]. Cross-cultural research on resilience is important to evaluate how resilience is applicable across culturally diverse populations, understand ways resilience mechanisms work in local cultural contexts, and generate more universal and comprehensive knowledge about resilience. More importantly, research on resilience can drive innovations in methodology, theory, and interventions to enhance resilience in multicultural contexts [56].

The study of resilience in different cultures is in its early stages [13]. This includes the study of cultural similarities and differences in resilience among individuals with cancer and their families. Research focuses on understanding specific resilience-related factors in cultural context and how cultural background (i.e., culture identity, cultural values, language, beliefs, customs, norms, and religious rituals) helps individuals and communities overcome adversity [62]. A literature review of 72 studies examined cultural influences on pediatric cancer populations from Asia, North America, Europe, and the Middle East [63]. This review concluded that cultural factors impact many aspects of the pediatric cancer experience, including cancer representations (cancer stigma, conceptualizations, and attributions), cancer disclosure patterns, reaction to diagnosis, management of medical procedures, complementary and alternative medicine use, coping strategies, and end-of-life issues [63]. Just as religious beliefs can facilitate resilience in Western culture, they have substantial cultural influence on how people perceive and handle adversities. In the following section, we focus on cultural differences in Asia as an example of the importance of understanding cultural differences in ways to foster resilience.

4.10.1 Culture Influences People's Interpretation of Adversity

In traditional Chinese societies, three philosophies, Confucianism, Taoism, and Buddhism, influence responses to a cancer diagnosis [64]. The Confucian tradition emphasizes inner strengths and virtues, such as perseverance and tolerance, which are important to coping and adjustment. Risk factors are viewed as opportunities for growth [65]. Many traditional sayings convey the belief that people have the capacity to overcome adversity and people grow wiser and stronger through their hardships [66]. For example, one saying is, "When Heaven is about to place great responsibility upon a man, it will first temper his heart and mind, fatigue his bones and muscles with toil, expose him to starvation and poverty, harass him by troubles and setbacks so as to stimulate his spirit, toughen his nature and enhance his abilities" [64].

Taoism emphasizes that everything in the world has its own rules for development and inner strength. People should follow the rules and view adversity from a dialectic approach. A typical Taoism saying is "Good fortune follows upon disaster, while disaster lurks within good fortune." Therefore, adversity is viewed both positively and negatively.

Buddhism has the same goal of overcoming and transcending suffering as Confucianism. In this context, adherence to traditional cultural beliefs may enable parents and young people to cope with cancer-related adversities.

4.10.2 Cultural Influences on Resilience Factors

Across cultures, considerable cross-cultural variability exists regarding disclosure of a cancer diagnosis to a child. Most studies indicate that Asian parents do not inform children of their cancer diagnosis or discuss treatment and/or prognosis because parents viewed cancer as a severe disease, and they do not want to discuss difficult topics with children [67]. Instead, they want to protect the children from “bad news” to foster courage and hope [68]. Since parents have the right to make decisions for their children in Asian countries, physicians follow parents’ desires regarding disclosure of a cancer diagnosis or lack thereof to their child. With the improvement in medical treatments and survival rates of children with cancer, this phenomenon of non-disclosure is becoming less prevalent [69]. Awareness of these cultural differences is crucial to provide culturally sensitive interventions to enhance resilience.

Under the influence of collectivism, people in China attach great importance to interpersonal relationships with family and community [70]. For children, the family is the basic unit of society that provides care and social support [65]. Therefore, family capacity to foster resilience resources for children is critical and family protective factors may have greater influence on resilience in Chinese culture. When designing programs to promote resilience among Chinese people, relevant cultural strengths could be used to foster resilience, such as emphasizing strong family relationships and Confucian and Taoist approaches to adversity [71].

4.11 Examples of Resilience Research in Pediatric Oncology

A randomized clinical trial (RCT) of the “Stories and Music for Adolescent/Young Adult Resilience during Transplant” (SMART I) was guided by the RIM [72]. In this study, 113 AYA (aged 11–24 years) with cancer and undergoing a hematopoietic stem cell transplant developed a therapeutic music video intervention. AYA in the intervention group had significantly better courageous coping compared with the control group and better family environment and social integration [72].

In a follow-up RCT, “Stories and Music for AYA and Parents” (SMART II), parents of AYA with high risk cancer participated in an AYA/parent communication intervention delivered by nurses and focused on strategies to promote parent self-care, open dialogue, and active listening. The purpose of the study was to enhance the family protective factor and target the family circle of the COG nursing research organizing framework. At the time of publication, results were still being analyzed.

The Asia Resilience Enhancement for AYA with Cancer (AREA) Cooperative Group was established in 2018, with researchers from China, Korea, Taiwan, Japan, Singapore, and the USA. This group is studying resilience in AYA with cancer using the RIM to guide their research. The AREA Cooperative Group's vision is to foster resilience in all children with chronic illness worldwide and its initial long-term goal is to improve resilience in AYA with cancer and their families in Asia. Although RIM factors have been used to guide some research in each of these countries, many of the RIM measures and whole RIM have not been systematically evaluated in Asian countries. It is necessary to have psychometrically sound Asian versions of RIM measures demonstrating reliability, validity, cultural appropriateness prior to evaluating cultural differences in the RIM and to develop culturally appropriate interventions. The AREA Cooperative Group is presently evaluating the RIM measures and goodness-of-fit of the model in AYA with cancer and their parents in Asia. When the project is completed, the necessary information and infrastructure will be obtained to sustain Asian and country-specific research and international collaborations on positive health interventions to improve outcomes for AYA with cancer.

4.12 Evidence-Based Findings Derived from Research Addressing Resilience Ready for Translation to Clinical Practice

Within the field of pediatric oncology, resilience research is the most well defined and developed for AYA with cancer and to an extent, the family. The RIM was specifically developed and tested with AYA with cancer and can be used to evaluate individual resilience risk and protective factors. RIM can also be used to evaluate efficacy and effect of interventions in AYA populations that aim to improve resilience and resilience-related outcomes including self-transcendence and quality of life, defined as sense of well-being AYA population.

Recommendations for applying current knowledge to practice:

1. Incorporate concepts associated with resilience in daily care of patients with cancer and their families. For example, provide basic

spiritual care, encourage positive coping skills, and refer patients and families to needed support services.

2. Provide appropriate supportive care for symptoms to decrease illness-related distress. Reassess frequently and address needs as they emerge.
3. Assess support systems available to the family at the time of diagnosis and as needed through the cancer continuum.
4. Use clear, literature-based definitions in resilience research.
5. Apply the RIM model to resilience research with AYAs with cancer.
6. Work within a conceptual model, such as the RIM, for resilience research to continue to develop concepts and measures related to resilience in the child, adolescent, and young adult with cancer and their family.

4.13 Future Research Recommendations for Research Addressing Resilience

Further testing is needed on the Resilience in Individuals and Families Affected by Cancer model to understand the effect of a child's diagnosis and/or treatment on the family overall and/or individual members who are not in the AYA age group. Most studies measure family function from the perspective of a single informant, rather than collecting data from multiple family members, which was not adequate to assess family functioning [44]. Presently, four family-related variables are measured in the RIM inner circle, including Family Support, Cohesion, Adaptability, Perceived Family Strength, and Parent–Adolescent Communication. There may be other protective and risk factors influencing resilience in the family context. There is also a need to identify the outcomes of resilience in the family context.

1. Prior to using the COG framework in different cultures, it is necessary to evaluate the psychometric properties and cultural

appropriateness of all the measures and the goodness-of-fit of the conceptual model.

2. Using clear definitions, continue to build the knowledge base for resilience research for the individual child, adolescent, or young adult as well as their family.

4.14 Conclusion

A focus on protective factors that foster resilience is an important and promising approach to address cancer-related distress in patients and families. However, more research is necessary for full implementation of resilience assessment and intervention to be a reality for each patient and family. Gaps in evidence should not deter clinicians from assessing the strengths and needs of individual patients and families and take every opportunity to promote resilience by building on individual and family strengths to address identified needs.

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5. Symptom Science in Pediatric Oncology

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Abstract

Children with cancer experience a myriad of symptoms, often occurring as symptom clusters. These symptoms are the result of the disease, its treatment, and associated procedures, can hinder the child’s psychosocial and physical development, and have negative effects on the child’s and family’s quality of life. Routine symptom assessment and the application of evidence-based symptom management strategies are needed to address this problem. This chapter will apply a personalized health framework to the review of symptom science in pediatric oncology. Specifically, this chapter provides an overview of the childhood cancer symptom literature and reviews the personalized health factors influencing the symptom experience in these young patients: biology and genetics, growth and development, behavior, family connection, and the social and treating environment. Implications for the translation of symptom assessment and management knowledge into nursing practice, as well as needed research in the area, are highlighted to direct future nursing efforts to mitigate symptoms in children with cancer.

Keywords Pediatric oncology – Cancer – Symptom assessment – Symptom management – Personalized health

5.1 Introduction

Symptoms for children with cancer and their families are burdensome, distressing, and often difficult to control. Successful management of symptoms is imperative because of the potential for deleterious effects on the child's health and well-being. Experiencing frequent and/or severe symptoms is associated with lower quality of life and may hinder multiple aspects of a child's development. Symptoms may keep a child from engaging in social interactions, such as playing or being with peers, that are key to facilitating psychosocial development. Symptoms such as loss of appetite, nausea, and vomiting lead to inadequate nutritional intake, negatively affecting physical development. Most children experience multiple symptoms and/or clusters of symptoms. To improve the health and well-being of children with cancer, effective symptom management is critical. Using a personalized health framework, this chapter will describe symptoms/symptom clusters in children with cancer, discuss the effects of symptoms/symptom clusters on the child and family, and provide an overview of current evidence pertaining to effective symptom management approaches. A symptom is defined as a subjective manifestation of a disease or change in condition perceived by an individual [1]. A symptom cluster is defined as symptoms which occur together that may share a common underlying biological mechanism, a mediator pathway, and/or incrementally affect patient outcomes [2]. Symptom management is the care given to prevent or treat the symptoms of a disease, the side effects of treatment, and psychosocial and spiritual problems associated with the disease or its treatment [3].

The personalized health framework described in Chap. 1 will be applied to our presentation of the state of current knowledge and research findings poised for translation to care. Research has demonstrated that the symptom experience differs for each individual and cannot be entirely related to diagnosis or treatment regimen [4]. However, little is known about what causes these differences. We explore what is known about symptoms in relation to biology, genetics, growth and development, behavior, family connection, and social and treating environments in order to begin to formulate recommendations for a personalized approach to symptom management. Figure 5.1 displays where these factors are situated in the Precision Symptom Management framework.

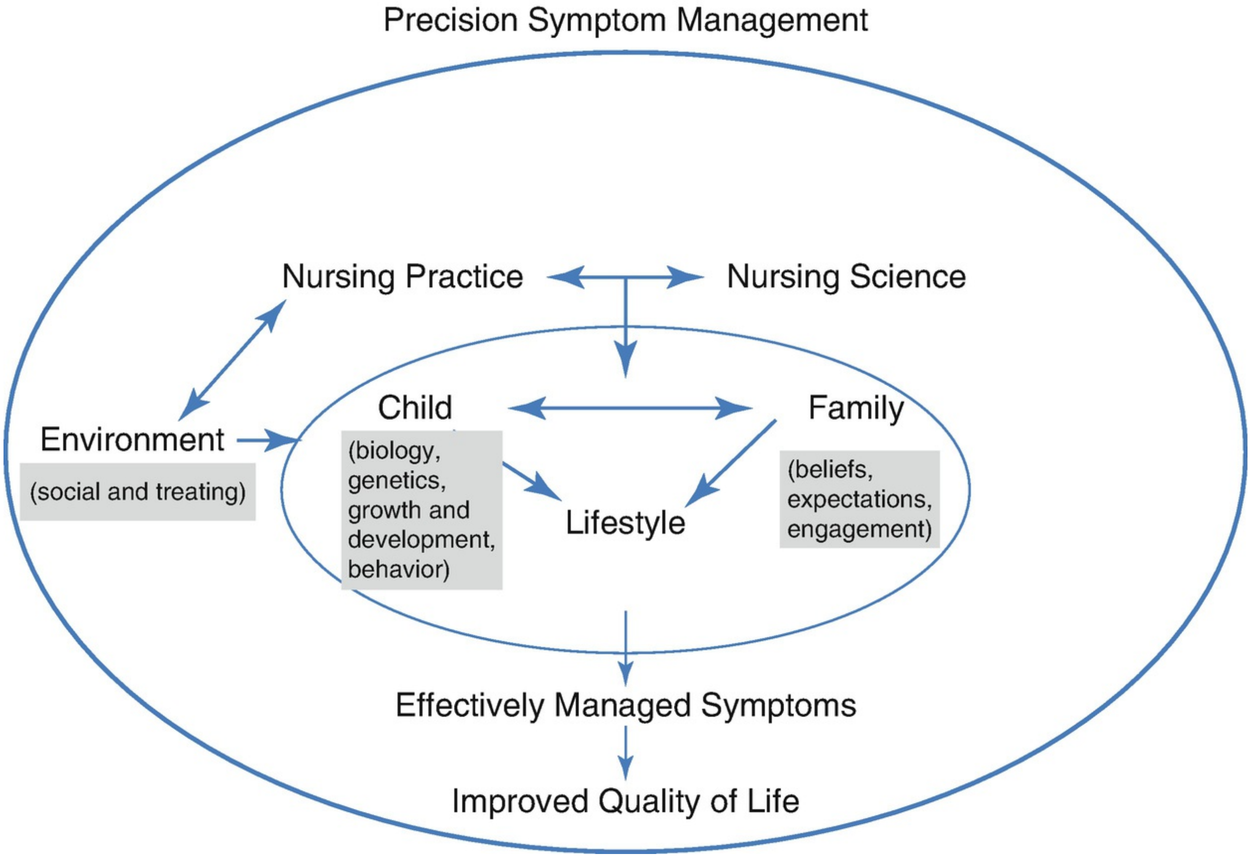

Fig. 5.1 The Precision Symptom Management framework with factors that influence the symptom experience for children and adolescents. These factors are listed in the grey boxes

Nursing science has been leading research efforts focused on symptoms/symptom clusters and symptom management in children with cancer over the past several decades. Nurses are on the frontline of assessing symptoms and helping children with cancer and their families manage symptoms. They hold the child and family at the center and work closely with them to improve symptom management. Nurses are providing care to children with cancer in numerous settings, including inpatient units, outpatient clinics, schools, home care, and supportive and hospice care. In these settings, nurses are assessing and managing symptoms on a regular basis and recognizing and responding to symptom changes.

5.2 Background on Symptoms

Children and adolescents with cancer experience multiple symptoms related to both cancer and cancer treatment [5]. Fatigue (often described as lack of energy or feeling drowsy), pain, alopecia, and gastrointestinal symptoms including nausea, vomiting, anorexia, and weight gain or loss are particularly common [5, 6]. Consistent relationships between specific cancer diagnoses and specific symptom experiences have not been identified nor have consistent relationships between ratings of symptom severity and symptom distress [5].

A symptom cluster is defined as two or more symptoms that occur together and are related to each other [7]. A variety of statistical approaches have been employed to identify symptom clusters in children with cancer, such as hierarchical cluster analysis, agglomerative hierarchy, and factor analysis [6, 8–11]. Symptom clusters have also been identified by self-report, including adolescents and young adults (AYAs) who have identified their own clusters [12]. The most common symptom clusters identified in childhood cancers both by self-report and statistical analyses are related to gastrointestinal symptoms (e.g., lack of appetite, nausea), mood (e.g., feeling sad, worry, feeling irritable), and energy (e.g., fatigue, sleep disturbances) [6, 13, 14]. Although these more common clusters were identified by both statistical analysis and self-report, the identification of other groups of co-occurring symptoms from the perspectives of the AYAs demonstrates their unique individual symptom experiences [4]. Relying solely on the statistical identification of symptom clusters could result in overlooking the individual symptom experience. Nurses can ask children who are old enough to self-report symptoms to identify which symptoms they perceive as occurring together, and develop a plan to address the multiple co-occurring symptoms. Consistent identical symptom clusters have not emerged primarily due to differences in samples (e.g., ages, diagnoses, treatments) and in methodologic approaches (e.g., measurement, analysis). The lack of consistency in identified symptom clusters inhibits the investigation of underlying mechanisms and the development of interventions to manage symptom clusters.

The trajectory of the symptom experience for children with cancer has been examined in very few studies, and the definition of trajectory often is study-dependent and/or lacking clarity. Given that some children will continue to experience symptoms after completion of treatment and into long-term survivorship, the definition of trajectory may need to extend into long-term survivorship; however, most research reviewed in this chapter focuses primarily on the symptom trajectory during treatment. In general, symptoms tend to decrease over time but some children continue to experience bothersome symptoms such as pain, fatigue, eating difficulties, and skin problems over the course of treatment [14–18]. Several researchers examined symptoms during a cycle of chemotherapy and found that while symptom severity frequently declined, a number of symptoms did not resolve completely [13, 19]. The evidence on individual symptoms, symptom clusters, and trajectories suggests that symptoms should be monitored frequently and managed aggressively throughout and beyond cancer treatment to minimize the effects of symptoms on those aspects of functional capacity and quality of life most salient to the individual child and family.

5.3 Factors Influencing the Symptom Experience

5.3.1 Biology and Genetics

Research regarding the influence of biology and genetics on the symptom experience is not far advanced. Most of what is known centers around the relationships between symptoms and certain biological factors, such as age, sex, and ethnicity. Research on symptom differences by age is also inconclusive [20], particularly in the case of pain, fatigue (e.g., [21, 22]), and nausea (e.g., [23, 24]). No clear differences have been found between adolescent males and females with cancer for the following symptoms:

sleep-wake disturbances, pain, nausea, and mood disturbances [20]. With regard to ethnicity, in one study, Hispanic children with cancer reported less severe symptoms [16] and in another, Hispanic children with acute lymphocytic leukemia (ALL) reported less pain [25].

Other biologic and genetic factors that affect symptoms are beginning to emerge although much of the research in the area has been conducted with adults. For example, the proinflammatory cytokines interleukin (IL)-1beta, and tumor necrosis factor-alpha (TNF), and IL-6 have been associated with anorexia, cachexia, sleep disturbance, fatigue, and depression [26]. A small number of studies in children with cancer have investigated some of these biologic and genetic factors. Vallence et al. [27] found significant associations between sleep disturbances and polymorphisms in IL-6 and TNF in children and adolescents with cancer. One of the characteristics of childhood leukemia is nitrosative and oxidative stress, which results from activation of the reactive nitrosative species (RNS)/reactive oxidative species (ROS) pathway. Protein 3-nitrotyrosin (3NT) is a biomarker of nitrosative stress that has been found to be associated with increased fatigue in children with cancer [28], as have other markers of oxidative stress [14, 29].

Carnitine is a micronutrient that is involved in energy production and carnitine levels decrease significantly in children with cancer receiving chemotherapy. Researchers have sought to determine whether lower levels of carnitine are associated with higher levels of fatigue in children with cancer, but the findings are mixed. No significant associations were found between carnitine and fatigue in children on treatment [17] or in a combination of children who were on and off treatment [30]. However, in children who were on treatment (not newly diagnosed) and had received previous treatment, low levels of carnitine were significantly associated with higher levels of fatigue [31]. Hooke et al. [17] suggest clinicians assess carnitine levels if the child is fatigued but they do not recommend assessment of carnitine levels on a regular basis.

Biologic mechanisms, such as certain proinflammatory cytokines and genetic polymorphisms, may contribute to the symptom experience. However, little is known about biologic mechanisms and many cancer symptoms. As Bellury and Clark [32] point out, much has been investigated about fatigue but we still know little about its etiology. Whether biologic mechanisms can be intervened upon is unknown, however recognition of explanatory mechanisms, which are often multifactorial (e.g., biological, social, environmental), has implications for intervening to reduce symptom burden.

5.3.2 Growth and Development

The symptoms experienced by children with cancer vary in terms of their prevalence, type, and severity across childhood and adolescence. The phenomenon was demonstrated in seminal work related to the development of the Memorial Symptom Assessment Scale (MSAS) 7–12 and 10–18 Scales [33, 34]. This work showed lethargy, pain, and insomnia to be the most common symptoms in 7 to 12-year-olds with cancer (symptom prevalence between 31 and 35%) and lack of energy, pain, and feeling drowsy to be the most common symptoms in 10 to 18-year-olds (symptom prevalence between 48 and 49%). Additionally, these symptoms were more severe in intensity in the older group of children. Other more recent research has likewise demonstrated differences in the cancer symptom experiences of children across the age spectrum. An electronic momentary assessment study of pain experienced by children with cancer aged 8–18 years over 14 days showed age to significantly predict increased pain experience with older study participants (≥13 years) reporting higher pain severity and more unpleasantness than their younger counterparts [35]. In addition, in inpatient children and adolescents 8–18 years of age receiving cancer treatment who reported the occurrence and severity of 15 symptoms, being of older age (i.e., 15–18 years) was associated with higher symptom scores [36].

Variation in symptom experiences may be due to differences in the epidemiology of cancer disease types across the spectrum of child ages. For instance, cancers originating in the bone are known to be particularly painful [37] and these cancers are more prevalent in adolescents. However, differences in cancer symptom occurrence and perceived severity may also be related to the various developmental stages of childhood and adolescence. For instance, a systematic review of the qualitative literature describing children's experiences of cancer care showed that younger children stressed the physical suffering associated with cancer-related symptoms, whereas older children highlighted the emotional and social burden of the disease [38].

Cancer symptom experience differences, as well as differences in the cognitive capacity to understand and describe symptoms, mean that both symptom assessment and symptom management techniques should be tailored to children according to their developmental stage. Special challenges related to symptom assessment and management in babies, toddlers, and preschool-aged children require consideration by clinicians and may be mitigated through partnerships with parents. Assessment of cancer-related symptoms for these pre-verbal and just-verbal children requires observations of behaviors (e.g., grimacing or wincing as indictors of pain) and/or verbal determinations using words that the child is familiar with (e.g., "ouchie" for pain), however validated tools to conduct these assessments are lacking. Future research oriented at the measurement of cancer-related symptoms in very young children is needed. Young children with cancer may be particularly vulnerable to undertreated symptoms because of their inability or limited ability to self-report their symptom experience and their reliance on parents and clinicians for symptom management support. This was shown in a daily diary study with children with cancer being treated on an outpatient basis which showed that child pain was undermanaged in terms of analgesic administration because parents did not recognize the signs of pain in their child [39]. Nurses should therefore be mindful of the need to utilize parents' expert knowledge regarding symptom signs in their children. Nurses should also partner with parents by empowering them with education related to the importance of symptom assessment and management and practical techniques to decrease symptom burden and improve quality of life.

Beginning at approximately 4 years of age, children can provide valid assessments of their symptoms [40, 41]. Therefore, general consensus in the field of pediatric symptom assessment is that measurement by self-report, as opposed to observation or proxy-report, should be conducted whenever possible for these children [42]. Report by proxy is important in cases where communication is limited by developmental stage, illness, or cognitive impairment. However, proxy-report is not always a reliable approximation of a person's symptom experience, and has been specifically shown as inaccurate in comparisons between parent and child reports of cancer symptoms [43].

A recent systematic review showed a dearth of self-report tools for children with cancer younger than 8 years of age [44]. In response, the mini-Symptom Screening in Pediatrics Tool (mini-SSPedi) has been developed to screen for the presence of 15 potentially bothersome symptoms in children with cancer aged 4–7 years [45]. The measure has been shown to be usable and satisfactory to cancer patients (see Chap. 7). In terms of cancer symptom treatment for children in this age group, research has shown their interest in partnering with clinicians to manage symptoms. For example, an observational study with these children showed that when they participated in cancer treatment-related procedures, they more often facilitated care by cooperating and helping [46].

Most older children and adolescents can provide valid and detailed descriptions of the symptoms they experience, and therefore symptom self-report is generally recommended [40]. To assess these symptoms, a number of psychometrically sound (i.e., evidence of good validity and/or reliability) multi-symptom tools exist. For instance, the MSAS 10–18 (assesses 30 symptoms) and MSAS 7–12 (assesses 8 symptoms) tools described previously assess the prevalence, severity, and distress caused by 30 common cancer symptoms in children and adolescents 10–18 years and 7–12 years, respectively [33, 34]. The validity of the Patient Reported Outcomes Measurement Information System (PROMIS) suite of symptom, function, and quality of life measures has also been demonstrated in children and adolescents 8–17 years [47]. In addition, the Symptom Screening in Pediatrics Tool (SSPedi) screens for the presence and bothersomeness of 15 symptoms in children and adolescents with cancer and pediatric hematopoietic stem cell transplant (HSCT) recipients aged 8–18 years, and additionally allows for the free-text recording of other bothersome symptoms not already listed [48]. A proxy-reporting version of SSPedi has also been validated for use with children and adolescents with cancer who are unable to self-report symptoms [49] (see Chap. 7).

A recent systematic review conducted by members of the Children's Oncology Group (COG) Nursing Discipline identified and synthesized barriers and facilitators to symptom-related communication with healthcare professionals by adolescents [50]. Results showed that barriers to symptom reporting on the part of adolescents are: negative expectations (e.g., symptoms were inevitable), health-related uncertainty (e.g., symptoms indicate disease progression), ambiguousness with assessments (e.g., difficulty to quantify symptoms), worry about others' perceptions (e.g., fear of being judged by healthcare professional), and healthcare professional approach (e.g., distant attitude on the part of healthcare professional). The sole identified facilitator of symptom communication was patient–healthcare professional rapport. On the basis of these findings, the authors of the review put forth practice recommendations to guide symptom communication with adolescents. Recommendations focus on the establishment of a therapeutic rapport with adolescents to promote open communication in a non-judgmental environment, the exploration of adolescent expectations related to symptoms, and the provision of symptom-related education to adolescents.

With respect to the treatment of symptoms, several qualitative research studies have shown that adolescents are keen to be involved in cancer-related care decisions, as well as the management of symptoms [38, 51, 52]. As such, supporting these adolescents to engage in symptom self-management may minimize symptom occurrence and severity and improve quality of life. Research related to cancer symptom self-management has begun to be conducted and has been shown to be amenable to adolescents [53–55]. For instance, a smartphone-based pain self-management app used by adolescents with cancer-related pain (12–18 years) for 1 month was shown to decrease pain severity and pain interference and improve quality of life [56]. In addition, use of a computerized symptom capture tool aimed at facilitating adolescents and young adults with cancer (15–29 years) to engage in symptom self-management resulted in improved feelings of self-efficacy and communication with healthcare providers [57].

5.3.3 Behavior

Behaviors are an individual's external reactions to their environment. Behavioral changes have been documented in children and adolescents with cancer particularly in the period of time following diagnosis. One study found that approximately 25% of children and adolescents who were in the early stages of their cancer diagnosis exhibited behavioral problems [58]. In another study of children and adolescents with cancer in Taiwan, parents reported more behavioral problems such as anxiety, social withdrawal, and somatic complaints in younger children than in adolescents during the first 6 months of treatment [59]. Although this is a time that the child and family are experiencing major stressful events from the new diagnosis, it is also a time of high symptom burden due to the intensity of treatment. Some children and adolescents with cancer continue to display aggressive and regressive behaviors beyond diagnosis [60]. Behavioral changes at end of life are less apparent, although some parents have noted behavioral changes such as being afraid to fall asleep [61]. Regardless of the point in the cancer trajectory, the symptoms children and adolescents experience may account for some of their changes in behavior.

Children's behavior can be negatively affected, and at times significantly, by the symptoms they experience. The behaviors they exhibit will depend upon their age and stage of development. The largest body of research on behaviors and symptoms arises from the literature on pain in children, but not exclusively cancer pain. For example, an infant in pain may display facial grimacing and feed poorly, a preschooler may display aggressive behaviors, a school-age child may engage in passive resistance or plea bargaining, and an adolescent may be stoic and be hesitant about reporting pain. Less is known about other symptoms. Hockenberry et al. [9] found that in children with cancer, higher levels of fatigue were associated with changes in behaviors manifested in interpersonal relations, stress, depression, anxiety, and sense of inadequacy, while in adolescents, higher levels of a cluster of symptoms that included fatigue and sleep disturbances were associated with changes in behaviors manifested in interpersonal relations, stress, and anxiety. In a qualitative study, Woodgate [62] explored children and adolescents symptom experience wherein they reported that symptoms made them act cranky and not like themselves.

Corticosteroids are a mainstay of treatment for a number of childhood cancers, particularly acute lymphoblastic leukemia (ALL). These medications unfortunately carry a heavy symptom burden including sleep disruptions, mood instability, increased appetite, and fluid retention, as well as significant changes in behaviors. Behavioral disturbances from corticosteroids are noted in all ages, but particularly in younger children, and are proposed to stem from the effects of the steroid on the hippocampus and neurotransmitters [63]. However, behavioral changes may also be a response to the distressing symptoms caused by the corticosteroids.

Though not a behavior, a child's temperament can influence their perception of a symptom. For example, in children with cancer, optimism was found to be associated with lower levels of pain and pessimism to be associated with poorer mental health [64]. Recommendations, though without strong evidence, are that children with serious illnesses such as cancer should be screened for low optimism/high pessimism and be referred for interventional services that could positively affect adjustment [64].

With the dearth of research on the relationship between cancer symptoms and behaviors, it is not surprising that much of the research on symptom interventions has not included behaviors as a factor. Symptom intervention studies tend to assess dimensions of the symptom, such as frequency, severity, and distress [21, 65, 66] which is logical. There have been psychosocial (see review by Coughtrey et al. [67]) and art [68] interventions that have aimed to reduce negative behaviors in children and adolescents with cancer but they have not focused specifically on symptoms.

In summary, the extent to which behaviors are directly or solely due to a specific symptom or symptoms is unclear. Although there are numerous descriptive studies on symptoms in children and adolescents with cancer, most have not examined whether symptoms are associated with or predict behaviors. In addition, most symptom intervention studies have not included behavioral changes as an outcome.

5.3.4 Family Connection

Transition periods in the childhood cancer symptom trajectory have been proposed as a framework for understanding not only the child's but also the family's experience of childhood cancer [69]. The child's symptom experience across the cancer trajectory impacts the child and the entire family and the family's quality of life [70]. Family beliefs and expectations, in addition to those held by the child, may contribute to symptom distress, such as the expectation that symptom control is not possible and the belief that symptom suffering is necessary if cancer is to be overcome [71].

Parents are actively involved in managing their child's symptom experience, for example, managing pain from disease, treatment, and procedures using pharmacological and nonpharmacological strategies [72, 73]. The importance of their involvement needs to be recognized and respected and the meanings families as well as children assign to the child's symptoms need to be understood [70]. In general, this parental involvement in symptom management is regarded as positive; however, one study suggests that lax parenting practices in combination with an increase in comforting activities and co-sleeping may contribute to child reliance on parental assistance to initiate or maintain sleep and thus actually increase sleep disturbance [74].

Parents of children on treatment report more distress [75] and more difficulty in family life [76] than parents of children who have completed treatment. This may be due to the focus on monitoring and managing the child's health status and symptoms during treatment [76]. Child symptom burden is positively correlated with parental report of restrictions on their work, studies, and leisure activities [77] and with parental depressive symptoms [78]. Parents who express greater self-efficacy for keeping their child calm before and/or during cancer treatment procedures report lower state anxiety, while those who express greater self-efficacy for keeping their child calm before procedures report fewer post-traumatic stress symptoms and those who express greater self-efficacy for keeping their child calm during procedures report less distress [79]. Pain, sleep disturbance, and fatigue in school-age children with leukemia impact not only patient quality of life but also family quality of life with parents also experiencing sleep disturbance and fatigue [80]. Among leukemia survivors, lower family cohesion, higher parental distress, and parental overprotection are associated with higher child symptom burden which is associated with lower child health-related quality of life, associated with more family strain [81].

5.3.5 Social and Treating Environment

Pediatric cancer symptom assessment and management occurs within a complex milieu of social interactions with children and adolescents' peers and healthcare providers. While research on how social environments impact the pediatric cancer symptom experience is lacking, the studies that do exist indicate that the effect may be appreciable. For instance, pertaining to peers, in adult oncology social support is effective at improving quality of life, decreasing anxiety and depression, and buffering the negative effects of stress [82]; however, many children and adolescents have limited access to this resource. This limited access is due to a lack of attendance at school and social events [83, 84], inaccessibility of formal social support programs [85–87], and the time associated with cancer treatment [88, 89]. In fact, adolescents with cancer have been shown to have fewer friends and smaller social support networks than their healthy counterparts [86, 90–92], which may negatively affect their capacity to manage the cancer-related symptoms they experience. In addition, an interview-based study of children 8–12 years with cancer showed that children perceived friendships as resulting in the establishment of mutual trust, understanding, and empathic actions, which could be leveraged for the development of interventions focused on symptom mitigation and health promotion [93].

Social interactions with healthcare professionals also have the potential to affect the symptom experience of children. Children with cancer have reported the positive therapeutic impacts of social relationships with nurses on sadness [94], pain [54], and insomnia [95]. Social interactions with healthcare professionals may also influence the validity of symptom assessments. In the case of pediatric pain, pain assessment has been suggested to be a social transaction occurring through the patient–provider interaction and impacted by the biological, cultural, social, developmental, and cognitive context surrounding both parties [96]. Through this social transaction model, symptom self-reports to healthcare providers must be considered in the context of the variables (e.g., power dynamics between children and adults) surrounding the assessment, especially when symptom management decisions are being made [96, 97]. In the pediatric oncology setting, nurses should strive to minimize these power dynamics by developing therapeutic relationships that empower children with information and the ability to participate in care and care-related decisions.

With respect to pediatric oncology treatment environments, the hospital has historically been the dominant site for care delivery and remains a critically important treatment venue for the routine and emergency care of children and adolescents with cancer. Symptom assessment in the hospital may involve the regular measurement of cancer-related symptoms, which enables the longitudinal tracking of symptom status and the appraisal of treatment effectiveness. Expedient access to trained healthcare professionals and treatment modalities in hospital settings further supports high-quality symptom management. Still, there are several problematic issues from the perspective of children with cancer and their families related to in-patent hospital-based care. A recent interview-based study indicated that, although the periods of hospitalization served an important social function that mitigated anxiety, children and parents felt substantial distress related to the impact of prolonged hospitalizations on siblings and experienced significant sleep disturbances [98]. Previous qualitative research with children with cancer has also shown negative impacts of hospitalization on children with cancer, including its capacity to act as a reminder of illness, become a barrier to engaging in usual activities, and negatively impact sleep [38].

However, due to improvements in therapeutic regimes, supportive care, and changes in the healthcare system, children are now spending less time in hospital and more time at home [99]. While outpatient-based care is often well-liked by families [54, 98, 100], it results in children and families being increasingly responsible for addressing symptoms in environments with less supervision from clinicians. Children with cancer may be more vulnerable in these environments as they and their families often lack the knowledge and skills needed to adequately react to symptoms and may ignore or inappropriately accept symptom changes [101]. Outside of the hospital environment, children also have an increased reliance on parents to know when to administer management interventions, when to seek medical treatment [39], and which treatment interventions to employ.

To inform symptom management and improve the health-related quality of life of children with cancer receiving care in treating environments other than the hospital, nurses and other clinicians critically require access to a valid, comprehensive picture of children’s symptom experience. Technology-based interventions have been proposed as solutions to address symptom assessment and management challenges related to the changing landscape of pediatric oncological care [102]. Recent adult cancer research has demonstrated the positive impact of electronically reported symptom assessment for outpatients on health outcomes, including overall survival [103, 104]. The unique challenges associated with childhood cancer symptom assessment and management mean that the development of interventions targeted at children with cancer and their families is required. See Chap. 8 for a review of research related to the development and evaluation of technology-based solutions to manage pediatric oncology symptoms outside of the hospital.

5.4 Translation to Practice and Future Research

Cancer is uncommon in children and represents less than 1% of all cancer diagnoses each year [105], a significantly lower incidence than in adults. The relatively low incidence combined with the heterogeneity of pediatric cancers and cancer treatment regimens creates challenges for conducting research on symptoms in children. Over the past two decades, the research on these factors has provided a fuller yet still incomplete understanding of symptoms and symptom clusters. The symptom experience is unique for each child with cancer. The most frequently reported symptoms include nausea, vomiting, pain, and fatigue. Commonly identified symptom clusters are related to gastrointestinal symptoms, mood, and energy. Symptoms generally decrease throughout treatment. During survivorship, new symptoms related to late effects may develop. While diagnoses and treatments may be associated with certain symptoms, they alone do not explain the array of symptoms each child experiences. In this chapter, other critical factors that affect the symptom experience have been reviewed, including the biology and genetics, growth and development, behaviors, family connection, and the social and treating environments.

A number of considerations for symptom assessment have been highlighted in this chapter and have important implications for translation, particularly for providing personalized healthcare. Symptoms should be monitored continuously and age-appropriately during treatment and managed aggressively. The factors that can influence the symptom experience should be assessed when possible, and considered in the context of the individual. The major points for each of these factors are as follows. Biologic and genetic factors such as cytokines and polymorphisms are associated with some symptoms and may provide explanatory mechanisms. Growth and development should guide symptom assessment, including facilitating age-appropriate communication about symptoms. Negative behaviors may indicate bothersome or worsening symptoms. The child's symptom experience affects the entire family. The family's beliefs and expectations may contribute to symptom distress. Social support is important to assess because it can be a key element for coping with symptoms but children with cancer are often isolated from their peers. The hospital environment can be supportive and clinicians are available continuously to help manage symptoms, but the hospital environment can also exacerbate symptoms. As children are receiving more outpatient care, the child and family are managing symptoms more often on their own, which can be challenging for them. The effects of symptoms on functional capacity and quality of life should be an integral part of symptom monitoring.

5.4.1 Evidence-Based Findings Derived from the Science of Symptoms in Pediatric Oncology Ready for Translation to Clinical Practice

A number of the findings related to symptoms, symptom clusters, and symptom management for children with cancer and their families are ready to translate to clinical practice. These findings include:

- Symptom experience differs for each child but consists of multiple symptoms/clusters of symptoms related to both disease and treatment.
- Fatigue, pain, alopecia, and gastrointestinal symptoms are common.
- Gastrointestinal symptoms, mood, and energy are common symptom clusters.
- Symptoms are distressing, burdensome, and affect psychosocial and physical development, functional capacity, and quality of life.
- Symptoms may abate over time but may persist over treatment and into survivorship.
- Assessment and management should be ongoing throughout the cancer trajectory into survivorship.
- Assessment and management must be tailored to age/developmental

stage due to impact on symptom prevalence, type, and severity.
- Symptoms should be managed aggressively to minimize effect on aspects of functional capacity and quality of life most salient to child and family.
- Symptoms may affect behavior, behavioral effects depend on age/developmental stage.
- The child's symptom experience affects the quality of life for the entire family.
- Family beliefs and expectations influence the child's symptom experience.
- Parents are actively involved in symptom management but continually need support and guidance.
- Social interactions with peers and healthcare professionals may affect the child's symptom experience.
- The inpatient environment may facilitate symptom assessment and management but also exacerbate some symptoms such as sleep disruption.
- The outpatient environment places responsibility for symptom assessment and management on the child and family but use of technology-based interventions may facilitate collaboration and communication with healthcare professionals.

5.4.2 Future Research Recommendations for Symptoms in Pediatric Oncology

What is known about the factors that influence symptoms that have been reviewed in this chapter is limited; however, the research to date illuminates the important roles these factors play in the symptom experience. Advancing the science to develop personalized approaches to symptom management in children with cancer will require research focused on increasing understanding of these factors and their relationships with symptoms. Based on the literature, there are a number of areas that require further study to generate translation-ready evidence. These areas are:

- Relationships between specific disease and/or specific treatment and specific symptom experiences.
- Relationships between symptom severity and symptom distress.

- Common symptom clusters and trajectories.
- Inter-individual differences in symptom experience unexplained by disease and/or treatment.
- Influence of biologic factors (such as age, gender, ethnicity), biologic mechanisms (such as proinflammatory cytokines, genetic polymorphisms), and genetics.
- Approaches to symptom assessment in pre-verbal/just-verbal/non-verbal children who may experience sub-optimal symptom management due to lack of self-report.
- Association of specific symptoms with specific behaviors.
- Change in behavior as an outcome of symptom management intervention.
- Effect of social interactions with peers and healthcare professionals on symptom experience.
- Use of technology-based interventions for child and family symptom assessment and management in the outpatient environment.

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6. Improving Care Through Patient and Family Education in Pediatric Oncology

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Abstract

Patient and family education in pediatric oncology provides knowledge that empowers autonomous decisions, which may ultimately affect health outcomes. Thus, patient and family education is an integral and crucial element of nursing care in pediatric oncology. Significant time points throughout the cancer care trajectory during which there is an increased need for delivery of information include the time of diagnosis, end of treatment, relapse, transition to survivorship, and end-of-life care. Because of limited evidence to guide best practices, patient and family education has recently been identified as both a clinical and research priority within the pediatric oncology community. Expert consensus recommendations have been developed to guide the provision of education to families of newly diagnosed patients. These recommendations include standardizing content, personalizing delivery methods, pacing and tracking delivery of information, and attending to the emotional needs of families. Gaps in knowledge regarding the delivery of patient/family education in pediatric oncology have been identified, and several research studies are currently addressing these gaps. Knowledge gained through current research will inform future evidence-based best practices for health care professionals, providing guidance for the delivery of high-quality patient/family education in pediatric oncology.

Keywords Patient and family education – Pediatric oncology – Best practices

This chapter is dedicated to Cheryl Rodgers, a pediatric oncology nursing leader who strived to improve the lives of children with cancer—your passion and dedication has inspired us to continue this important work in your name.

6.1 Introduction

Patient and family education in health care provides knowledge necessary for patients and caregivers to make autonomous decisions and take ownership of care that may ultimately affect health outcomes [1]. Decisions regarding health care, and ownership of that care, can potentially affect a broad spectrum of behaviors, such as identifying signs and symptoms that require attention by a health care professional, and adherence to medications and recommended health care practices [2].

In pediatric oncology, patient and family education is an integral and crucial element of nursing care (Fig. 6.1). There are significant time points identified along a child’s cancer journey when there is an increased need for the delivery of information. These time points include the time of diagnosis, end of treatment, relapse, transition to survivorship, and end-of-life care. Consistent across these identified time points is the significant variability in content and methods currently used to provide education [3]. There remains a paucity of evidence to guide best practices for delivery of high-quality, personalized patient and family education in the setting of childhood cancer. Thus, patient and family education has been identified as both a clinical and research priority within the pediatric oncology community [4].

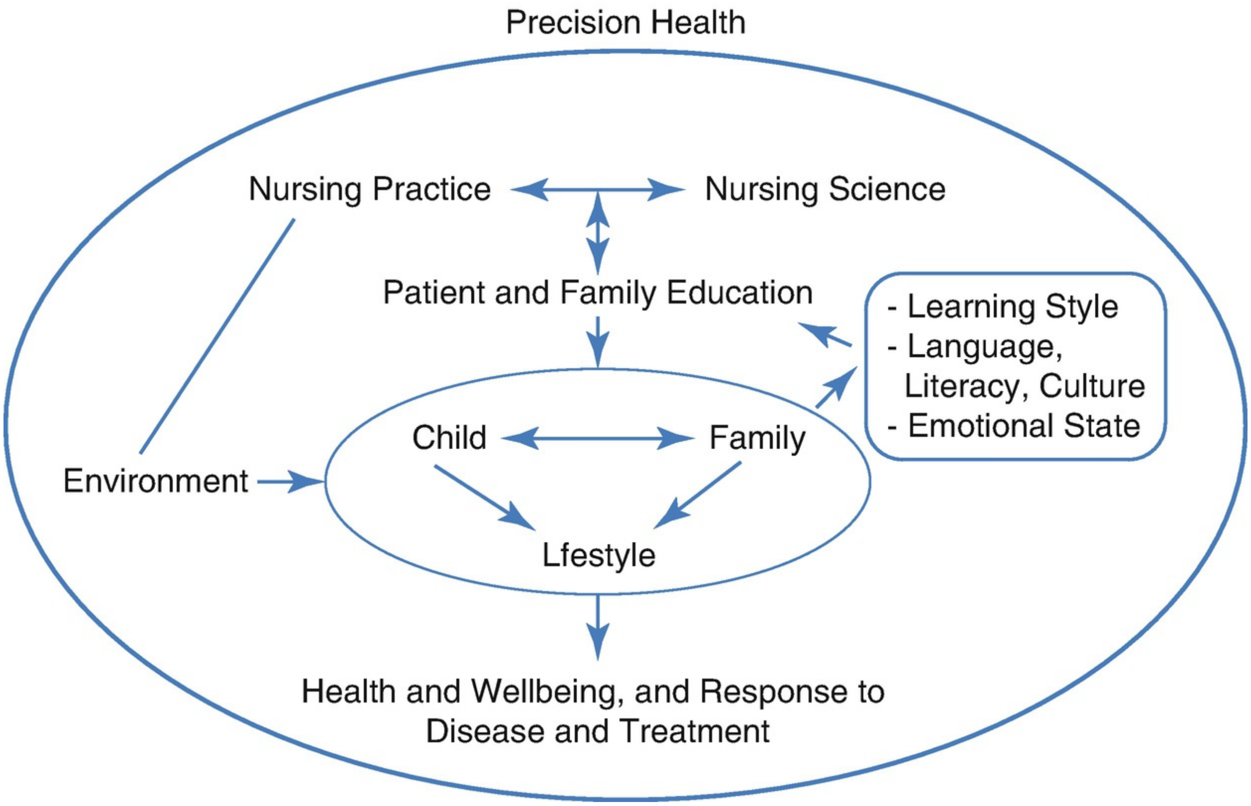

Fig. 6.1 Integration of patient and family education within nursing practice and nursing science and its impact on child and family health and response to disease (cancer) and its treatment within the context of precision health

This chapter includes a review of the current state of knowledge regarding optimal delivery of patient and family education in pediatric oncology, including content and methods, as well as ongoing and future research initiatives in this field with a particular focus on nursing care delivery.

6.2 Background

Much of the existing evidence for the provision of patient and family education in pediatric oncology is targeted to the time of initial cancer diagnosis. This underscores the overwhelming amount of new information that is often provided, in parallel with the need for families to gain a good understanding of the diagnosis and treatment in order to provide safe care for the child in the home setting. It also highlights the significant emotional impact of the new cancer diagnosis on the patient and family, and the resulting influence this will have on their ability to successfully absorb this important information.

To gain a better understanding of what and how information is provided to patients and families at the time of the initial pediatric cancer diagnosis, a systematic review of the literature was conducted by Rodgers et al. [5]. In this review, several key recommendations were identified. The recommendations focused on methods, timing, content, influencing factors, and effective interventions for providing education directed at newly diagnosed pediatric cancer patients and families at the time of initial diagnosis [5]. Methods were variable and included written materials, in-person education delivered by a health care provider, audio and/or video educational recordings provided by a health care provider, and Internet resources. An important finding was the variation in preferred methods reported by families, highlighting the importance of having quality education available in varying methods that address learning preferences and styles. Timing was identified as a crucial element in providing quality education. The review by Rodgers et al. [5] validated that families feel an intense emotional burden at the time of their child's cancer diagnosis and that this negatively affected their ability to learn. This suggests that the delivery of information should be paced and emotional responses addressed; however, no specific evidence was identified to support effective timing [5]. The systematic review also identified factors that might negatively influence the effective delivery of education. These included the delivery of large amounts of information (both written and verbal), use of medical terms in teaching, conflicting information delivered by different health care team members, and presence of the ill child during educational sessions [5]. Other factors found to have a negative influence on the effectiveness of education included the family's emotional distress, language barriers, previously experienced negative relationships with health care providers, the child's health status, and social concerns (such as worry over managing everyday care of siblings, transportation, work, and similar life issues).

The recommendations from the systematic review by Rodgers et al. [5] were limited due to the paucity of published evidence and the low quality of existing studies; however, the review highlights not only the significant practice variations in providing education for families of newly diagnosed pediatric oncology patients, but also identifies the critical gaps in evidence necessary for the development of evidence-based practice recommendations. A commitment to addressing the identified gaps in the evidence related to the effective delivery of patient and family education in pediatric oncology is evidenced by recent surges in research and quality improvement projects developed with this focus. A review of both completed and ongoing initiatives will be reviewed later in this chapter.

6.3 Development of Expert Consensus Recommendations

Recognizing the lack of evidence-informed approaches to patient/family education in pediatric oncology, the Children's Oncology Group (COG) Nursing Discipline convened a state of the science symposium in 2015 that included interprofessional experts from both within and outside the field of pediatric oncology, with the goal of developing expert consensus recommendations to guide patient/family education in the setting of a new diagnosis of childhood cancer [6]. During the symposium, topics presented included a review of existing evidence for the delivery of patient and family education [5], evidence highlighting the variation in institutional practices for the provision of education across COG institutions [3], the identification of essential educational content for families of newly diagnosed pediatric oncology patients prior to first hospital discharge [7], and family perspectives regarding the receipt of education in the setting of a new pediatric cancer diagnosis [8]. The symposium also included invited experts from other pediatric subspecialties who shared their expertise regarding the effective delivery of patient and family education in other pediatric fields. Critique and discussion were solicited from the audience, which was comprised of interprofessional pediatric oncology health care providers and patient advocates. Following the symposium, an expert panel that included representatives from nursing, medicine, behavioral science, and patient advocacy convened with the task of consolidating the existing evidence with expert opinion in order to develop consensus recommendations to guide current practice for providing education for families of newly diagnosed pediatric oncology patients. These expert consensus recommendations are presented in Table 6.1.

Table 6.1 Expert consensus recommendations for the provision of patient/family education to families of newly diagnosed pediatric oncology patients. With permission from Landier et al. [6]

1. In pediatric oncology, patient/family education is family centered
    - Include all individuals who are central to the patient's care
    - The family is considered an important part of the child's health care team
    - Teach more than one caregiver in each family, whenever possible
2. A diagnosis of cancer in a child is overwhelming for the family
    - Before the family is able to learn to care for the child, they need
        - Time to process the diagnosis emotionally and
        - A plan to manage ongoing life demands in light of the diagnosis
    - The psychosocial services team plays a key role in supporting the family
    - The family's learning priorities may differ from those of health care professionals during the initial timeframe
    - Address the learners' fears/concerns prior to proceeding with teaching
3. Quality of teaching determines family readiness to care for their child at home
    - Patient/family education for newly diagnosed families should be an interprofessional responsibility, with a focus on three key areas
        - Diagnosis/treatment
        - Psychosocial coping
        - Care of the child
    - Standardized educational content, but individualize educational methods
    - Pacing of patient/family education is important; the initial focus should be on the "essentials" (i.e., survival skills)
    - All health care professionals should receive training in the principles and practice of patient/family education in pediatric oncology
    - Consistent messaging across disciplines (e.g., pediatric oncology, nursing, psychosocial) and platforms (e.g., written, oral, electronic) is essential

- Assess family readiness to care for the child at home from multiple perspectives (parent, nurse, physician, psychosocial services team)

4. Patient/family education occurs across the continuum of care
    - Provide only essential education during the initial period following diagnosis
    - Provide education across care settings and transitions
5. A supportive environment is required to optimize learning
    - Focus on listening and avoid distractions while teaching
    - Provide education that is understandable and culturally sensitive
    - Provide anticipatory guidance (i.e., help the family to ask questions)
    - Reassure the family that initial learning is typically a gradual process
6. In pediatric oncology, patient/family education is family centered
    - Include all individuals who are central to the patient's care
    - The family is considered an important part of the child's health care team
    - Teach more than one caregiver in each family, whenever possible
7. A diagnosis of cancer in a child is overwhelming for the family
    - Before the family is able to learn to care for the child, they need
        - Time to process the diagnosis emotionally <u>and</u>
        - A plan to manage ongoing life demands in light of the diagnosis
    - The psychosocial services team plays a key role in supporting the family
    - The family's learning priorities may differ from those of health care professionals during the initial timeframe
    - Address the learners' fears/concerns prior to proceeding with teaching
8. Quality of teaching determines family readiness to care for their child at home
    - Patient/family education for newly diagnosed families should be an interprofessional responsibility, with a focus on three key areas:
        - Diagnosis/treatment
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    - Standardized educational content, but individualize educational methods
    - Pacing of patient/family education is important; the initial focus should be on the "essentials" (i.e., survival skills)
    - All health care professionals should receive training in the principles and practice of patient/family education in pediatric oncology

- Consistent messaging across disciplines (e.g., pediatric oncology, nursing, psychosocial) and platforms (e.g., written, oral, electronic) is essential
- Assess family readiness to care for the child at home from multiple perspectives (parent, nurse, physician, psychosocial services team)

9. Patient/family education occurs across the continuum of care
    - Provide only essential education during the initial period following diagnosis
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10. A supportive environment is required to optimize learning
    - Focus on listening and avoid distractions while teaching
    - Provide education that is understandable and culturally sensitive
    - Provide anticipatory guidance (i.e., help the family to ask questions)
    - Reassure the family that initial learning is typically a gradual process

6.4 Standardizing Essential Educational Content

The first step toward ensuring quality and consistency of education provided at the time of initial pediatric cancer diagnosis involves identifying and standardizing essential content. Using Delphi methodology that engaged a group of interprofessional pediatric oncology clinical experts, consensus was obtained regarding educational content that was essential to deliver to families prior to a child's first hospital discharge after the initial pediatric cancer diagnosis (Table 6.2) [7]. Consensus regarding the essential content by cancer type (i.e., leukemia/lymphoma, solid tumor, central nervous system [CNS] tumor) was also identified using Delphi methodology, addressing the uniqueness of expected symptoms and anticipated toxicities related to the specific diseases and cancer-directed therapies [7]. This expert consensus process has laid the foundation for ensuring that all newly diagnosed pediatric cancer patients and their families receive essential information necessary for the provision of safe care after first discharge.

Table 6.2 Multidisciplinary consensus of essential educational content for families of newly diagnosed pediatric oncology patients prior to first discharge home. With permission from Haugen et al. [7]

Topics for all newly diagnosed pediatric oncology patients

Educational topic	Rank order[a]	Mean-rank score[b]
Diagnosis	1	16.66
Treatment plan	2	14.18
Fever	3	12.23
Prognosis	4	11.43
Side effects of treatment	5	11.32
Who/how to call (e.g., days, nights, weekends)	6	10.98
When/why to call treatment team	7	10.70
Clinical trials	8	9.91
Managing medications	9	9.34
Central line care	10	8.98
Care of the child at home	11	8.89
Supportive care	12	7.73
Health care team (key members)	12	7.73
Preventing infection	14	7.20
Blood counts	15	6.68
Follow-up appointments	16	6.45
Fertility preservation options	17	5.84
Psychosocial issues	18	4.75

[a] 1 = most important; 18 = least important

[b] 18 points assigned for first-place rank position, 17 points for second place, and so on down through 1 point for a last-place rank

6.5 Personalizing Education for Families

Although standardizing content is essential in order to assure that all families receive the necessary information to safely care for their child with cancer, individuals vary in their learning styles and preferences. Therefore, the Children's Oncology Group expert consensus recommendations noted the importance of personalizing the delivery of education according to the learner's specific preferences (Table 6.3) [6].

Table 6.3 Personalizing the delivery of education to families based on learner characteristics and preferences. With permission from Landier et al. [6]

Learner characteristics	Suggested tailoring of education
Learning style	Assess preferred learning style, literacy, and health literacy prior to initiation of education Build a relationship with the learner Use techniques that enhance the learner's self-efficacy (e.g., involvement in the child's care during hospitalization, hands-on learning) Use a "teaching toolbox" that includes multiple modalities, including low- to high-technology options, developmentally appropriate content, and varied learning strategies (e.g., active learning-simulation, one-on-one interaction, video modules, web-based tools, hands-on training, written materials, COG Family Handbook)
Language/literacy/culture	Provide content in the learner's preferred language Use simple (non-medical) language (i.e., at or below a fifth grade level) Strive for cultural congruency when reviewing key educational content with the learner (e.g., dietary instructions)
Emotional state ("Feeling Overwhelmed")	Set appointment times for teaching, and create meeting agendas (i.e., "action plans") Keep educational sessions brief Provide information in small (i.e., "bite-sized") segments Repeat essential information over time Avoid giving families excessive amounts of written material (i.e., avoid "paper overload") For parents of young children, develop a plan to have the child cared for during teaching sessions so that the parent(s) can devote their full attention to learning

COG Children's Oncology Group

Multiple methods for delivery of informational content have been identified in the literature. These include materials in written form, as well as in-person teaching (one-on-one and classroom), audio and video sources, and websites [8]. Health literacy is an important consideration when choosing the method for delivering information [1].

Effective teaching techniques that have been identified as appropriate for teaching families, particularly in the setting of a newly diagnosed child with cancer, include “think forward”—which involves the caregiver envisioning scenarios related to the child’s care that may occur at home and developing pro-active plans to address them [9]—and “teach-back”—which involves having the caregiver explain or demonstrate their understanding of a particular concept or skill [10].

6.6 Tracking Delivery of Essential Education

The next critical step in ensuring the delivery of the identified essential content was the development of a tool to track the delivery of patient and family education. Using the content developed through expert consensus, a standardized discharge checklist was created [11]. To develop this checklist, nursing experts shared and critiqued existing tools from their clinical practices. An additional goal of this process was to develop consensus regarding the pace of delivery of information to patients and families. The essential topics were categorized as primary, secondary, or tertiary based on the necessary timing of their delivery, and incorporated into the standardized checklist (Fig. 6.2) [11]. The primary topics are the essential content that must be taught prior to the child’s first discharge home. Education regarding secondary topics should occur within the first month following cancer diagnosis. Tertiary topics are equally important, but delivery of this information can be paced throughout treatment, with all information designated for delivery prior to the end of the child’s cancer treatment [11].

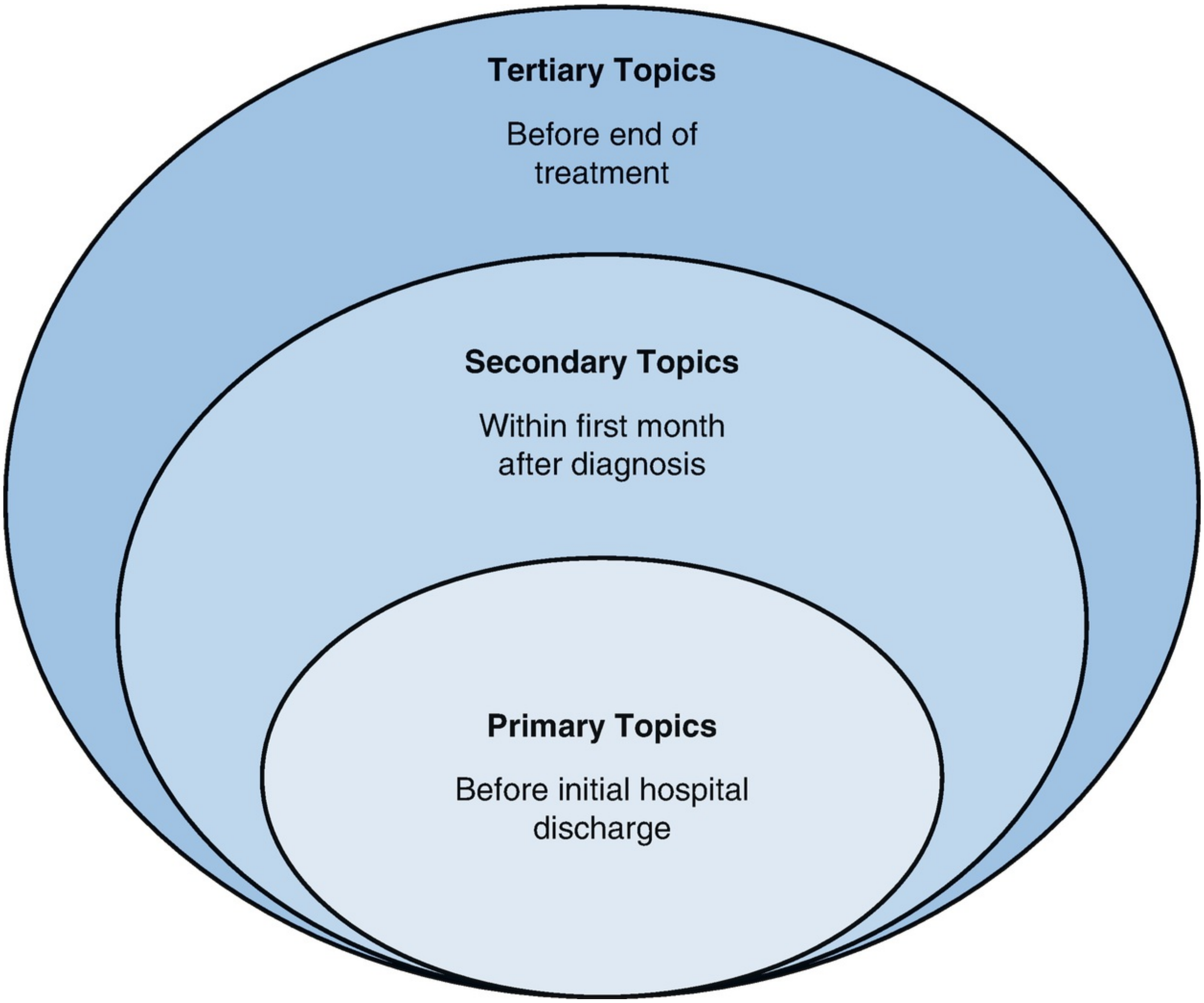

Fig. 6.2 Categorization of primary, secondary, and tertiary educational topics for families of newly diagnosed pediatric oncology patients. With permission from Rodgers et al. [11]

6.7 Available Educational Resources

There are numerous educational resources currently available for families of children with cancer. The Children's Oncology Group has developed a series of resources aimed to address the needs of families with a child newly diagnosed with cancer, including the *Children's Oncology Group Family Handbook* and *New Diagnosis Guide* (available in English, Spanish, and French), which are available at https://childrensoncologygroup.org/index.php/cog-family-handbook. The *COG Family Handbook* is also available in eBook format for multiple types of eBook readers. Summaries explaining COG clinical trials have also been developed for families, and are available at https://www.childrensoncologygroup.org/cog-clinical-trial-summaries. The Children's Oncology Group has also developed educational materials for childhood cancer survivors, known as *Health Links*, that address 43 health topics relevant to late effects of cancer treatment, as well as health promotion. The COG *Health Links* are available at www.survivorshipguidelines.org. The Association of Pediatric Hematology Oncology Nurses (APHON) also features numerous resources for patients and families, including diagnosis-specific informational guides, information about treatment (chemotherapy and radiation therapy), and guides to fertility preservation options. These resources are available at https://aphon.org/education/patient-family-resources. The National Cancer Institute has developed a library of educational materials about childhood cancer that can be accessed at https://www.cancer.gov/types/childhood-cancers. Numerous publications have also been developed internationally, such as those for families in the United Kingdom (https://www.cclg.org.uk/publications).

6.8 Implementing Expert Recommendations

Using the expert consensus recommendations, the Children's Hospital of Wisconsin and St. Vincent's Hospital/Prevea Health recently developed an initiative to improve the quality of education and support provided parent and caregivers at their institution [12]. Key education milestones were defined for delivery of essential information across the first 2 months following diagnosis of a child's cancer, and multidisciplinary role accountability was established for delivering the education and support to the family.

At Children's National Health System, a performance improvement initiative, *The Road to Home*, was developed to guide education at the time of a child's cancer diagnosis in order to increase family and nurse satisfaction with new diagnosis education and the discharge process [13]. This program included a visual, interactive display of essential educational topics, incorporating both institution-specific content and information from the Children's Oncology Group. Patient and nursing satisfaction was tracked, and sustained increased satisfaction scores related to discharge education and planning were reported following implementation [13].

6.9 Current Research

Research studies addressing patient and family education in pediatric oncology are currently in progress. A study funded by the American Nurses Credentialing Center (ANCC) is evaluating nurse-led parent educational discharge support strategies for children newly diagnosed with cancer. This multi-site study, led by Marilyn Hockenberry PhD, is testing the effectiveness of two different support interventions that enhance usual discharge education. The study is currently in progress at multiple Magnet hospital across the USA [14]. A single-site study funded by Alex's Lemonade Stand Foundation is evaluating caregiver readiness for discharge, perceived quality of education, and post-discharge coping difficulty before and after implementation of a standardized discharge teaching intervention based on the Children's Oncology Group's expert consensus recommendations [15]. Additionally, a recently completed Children's Oncology Group study, currently under analysis, is evaluating an adherence-enhancing intervention in children receiving maintenance chemotherapy for childhood acute lymphoblastic leukemia, with participants randomized between a multimedia educational program vs. a multicomponent intervention package [16].

6.10 Evidence-Based Findings Derived from the Science of Patient Family Education in Pediatric Oncology

Notable findings from research already conducted regarding patient education in the field of pediatric oncology should be incorporated into current clinical practice as follows:

1. *Providing information to families at the time of diagnosis*. Delivering quality education using varying methods that address learning preferences and styles is important when educating families. The delivery of information should be paced according to the family's ability to comprehend the information while experiencing strong

emotional responses to the child's diagnosis [6]. A standardized checklist of critical topics may help the health care team to appropriately pace the delivery of information for patients and families during the period immediately surrounding the child's diagnosis [11].

2. *Essential content to include during initial education*. Standardizing the content to be taught at diagnosis is the first step in providing quality and consistent education [6]. Expert consensus regarding the top ten essential educational topics for all newly diagnosed pediatric oncology patients are: diagnosis, treatment plan, fever, prognosis, side effects of treatment, who/how to call for help, when/why to call the treatment team, clinical trials, managing medications, and central line care [7].

3. *Influences on the effective delivery of education*. The delivery of effective education can be positively influenced by giving smaller amounts of information (both written and verbal) at several sittings, simplifying explanations instead of using medical terms, and consistent messaging by all health care team members. It may also be helpful to consider not having the ill child present during educational sessions. Factors found to have a negative influence on the effectiveness of education include the family's emotional distress, language barriers, previously experienced negative relationships with health care providers, the child's health status, and social concerns [5, 6].

6.11 Future Research Recommendations for Patient and Family Education in Pediatric Oncology

Although much progress has recently been made in defining critical aspects of the effective delivery of patient and family education in pediatric oncology, much work remains to be done.

1. *Assessment of informational uptake*. Critical to delivering essential content at the time of an initial pediatric cancer diagnosis is ensuring that the quality of delivery has resulted in successful uptake of

information by the patient and family. This will involve an assessment of each unique patient and family, leading to the creation of an education plan that includes the core teaching topics but that is tailored and personalized to the specific family needs and preferences. There is currently limited evidence regarding the assessment and the evaluation of successful uptake and understanding by patients and families.

2. *Evaluating implementation*. Future initiatives that describe the components of successful implementation of expert consensus recommendations and tools (such as the standardized checklist) in the provision of education by nursing and interprofessional teams for families of newly diagnosed pediatric cancer patients are crucial. Aspects of implementation that need to be studied include clarification of team member roles and expectations related to delivery of education, documentation of education delivered, and an assessment of the degree of successful uptake on the part of patients and families. It will also be important to measure the amount of resources required for successful implementation of standardized educational strategies and tools, as well as to measure the impact on the patient and family coping, adjustment, health care utilization, and health outcomes. These data will provide the evidence and guidance for programs to embrace the significant (and costly) resources required for implementation.

3. *Timing of education*. Education should start as early as possible for each stage of treatment and into survivorship. In focus groups conducted at the Dana-Farber Cancer Institute, an emerging theme was that adult survivors of childhood cancer did not feel adequately prepared to transition to independent adult medical care [17]. Survivors may struggle with knowledge deficits critical for optimal medical self-management. Adolescents perceived significant gaps in delivery of transition education and expressed a desire that the transition process start earlier in adolescence. Multiple formats are needed to facilitate the transition, including individualized, developmentally appropriate education delivered one-on-one by pediatric oncology providers and augmented with written and online

documents, peer support groups, and Web-based resources. This model of early introduction of patient and family education, and the provision of education using varying methods, personalized to each patient and family, with the ability to repeat and reinforce content, requires further validation at all critically identified time points along the pediatric cancer journey.

4. *Determining preferred delivery methods*. Multiple formats are needed to deliver the education, as not one method may be effective for all learners. Written materials are important [18], and educational games may be an effective alternate delivery method [19]; however, using multiple formats when providing education is best for sustained knowledge. Kunin-Batson et al. [20] used a randomized design to compare personalized cancer information made available using protected website access with standard of care education (in-person provider counseling at visits) in adolescents and young adult survivors of pediatric cancers. Findings indicate that knowledge gaps continue to exist, and that purely educational information in either format did not improve the knowledge deficit. In a large cohort of childhood cancer survivors attending a long-term follow-up clinic, significant improvement in the awareness of personal health risks was evident after each of the first three clinic long-term follow-up visits where provider-delivered education was tailored to the survivor's specific risk of therapy-related complications. Nevertheless, 60% of the survivors remained unaware of most of their personal therapy-related health risks despite repeated tailored education [21].

5. *Educating health care professionals*. Health care professionals also need to be educated in the process of delivering standardized education. Additionally, their comfort level with sensitive issues (such as risky behaviors) needs to be considered when educating the educators, as many health care professionals may be reluctant to engage in conversations regarding sensitive topics [22].

6. *Addressing language barriers*. A final important factor to consider is language barriers. Zamora et al. [23] when studying Spanish-speaking caregivers of children with cancer found that language

barriers likely contribute to the experience of suboptimal health care quality and communication difficulties, both in-person and over the phone. Families with language barriers may be more vulnerable to misunderstanding medical information. Additionally, caregivers with language barriers have demonstrated greater knowledge gaps, increased problems accessing care, and adverse impacts on the child’s schooling and the caregiver’s employment, compared with their English-speaking counterparts. Strategies for addressing literacy and language barriers in providing patient and family education in pediatric oncology are recognized as a priority.

6.12 Future Directions

By addressing the current knowledge gaps, focus areas for future research related to pediatric oncology patient and family education can be identified. Most research to date has examined the time of initial pediatric cancer diagnosis, and the survivorship phase. Further exploration is needed regarding educational needs and approaches during the phases between these two time points. This may include re-education of patients, beginning in adolescence, regarding information already discussed with the parent or caregiver but that now needs to be conveyed to the maturing child. Minority, lower income, and non-English speaking patients and families will continue to require special attention. Improvement of the uptake of childhood cancer survivors’ awareness of their therapy-related health risks is necessary, particularly for vulnerable subpopulations, such as those with cognitive and sensory impairment. The provision of education for patients and families will be optimized by considering individualized needs, using written and online resources and technology, and evaluating ongoing educational needs across the span of development (pre-school, school-age, adolescents, and young adults).

As we continue to optimize the process of addressing educational needs of patients and families in pediatric oncology, the needs of the health professional should not be forgotten. Clear and succinct guidance for health professionals regarding best practices for providing education to all patients and families will be a key to success.

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7. Patient-Reported Outcomes in Pediatric Oncology: The Voice of the Child

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Abstract

Children with cancer frequently experience disease-related symptoms and treatment toxicities that directly affect their ability to function in multiple domains and their overall quality of life. Understanding these effects of cancer and its treatment is essential to developing preventative treatments. Nurses' deepest understanding can best be gained when the ill child's self-reports of the subjective effects are systematically collected and considered throughout the treatment trajectory. Accurately recording the ill child's perspectives in symptom and toxicity screening, and in ongoing assessments of function and quality of life will also determine the effect of the preventative interventions. Proxy reporting has been shown to be important, particularly in those circumstances that the child is unable to self-report. However, inconsistencies between the ill child's self-report and the proxy report have been documented, with little attention to the reasons for the differences. Fortunately, self-reports from the ill child are increasingly being recognized as the primary source of subjective symptom, toxicity, function and quality of life reports, and these reports are supported by the existence of validated instruments for children with cancer.

Keywords Pediatric patient-reported outcomes – Symptoms – Quality of life – Function – Treatment toxicities – Child voice – Proxy reports – PRO measures

7.1 Overview

In this chapter, we address the essential contribution of the subjective reports from the ill child or adolescent about the cancer experience in order to more accurately determine the impact of disease-directed therapies and the outcomes of patient care. We summarize the current state of the science of patient-reported outcomes in pediatric oncology and identify the findings that are ready for translation into nursing practice and precision health. The evidence in this chapter is notably derived from both single site and collaborative research across nations. Most recent initiatives have been informed by guidance at the level of national and professional organizations' policy statements. A notable example of this is the 2009 policy statement from the Food and Drug Administration (FDA) [1] regarding patient-reported outcomes in which the requirement to have patient-reported outcome data included with every new drug or device request for approval was made explicit. The guidance indicated that patient-reported outcomes, including those from children whenever possible, must come directly from the affected patient without interpretation by skilled clinicians or caring family members. These direct child symptom and cancer treatment toxicity reports, when embedded in nursing practice, as well as the direct influence of symptoms and toxicities on the child's functioning and quality of life can contribute to improved (more accurate and complete) symptom and toxicity monitoring and reporting to national and international governments supporting cancer care (Fig. 7.1).

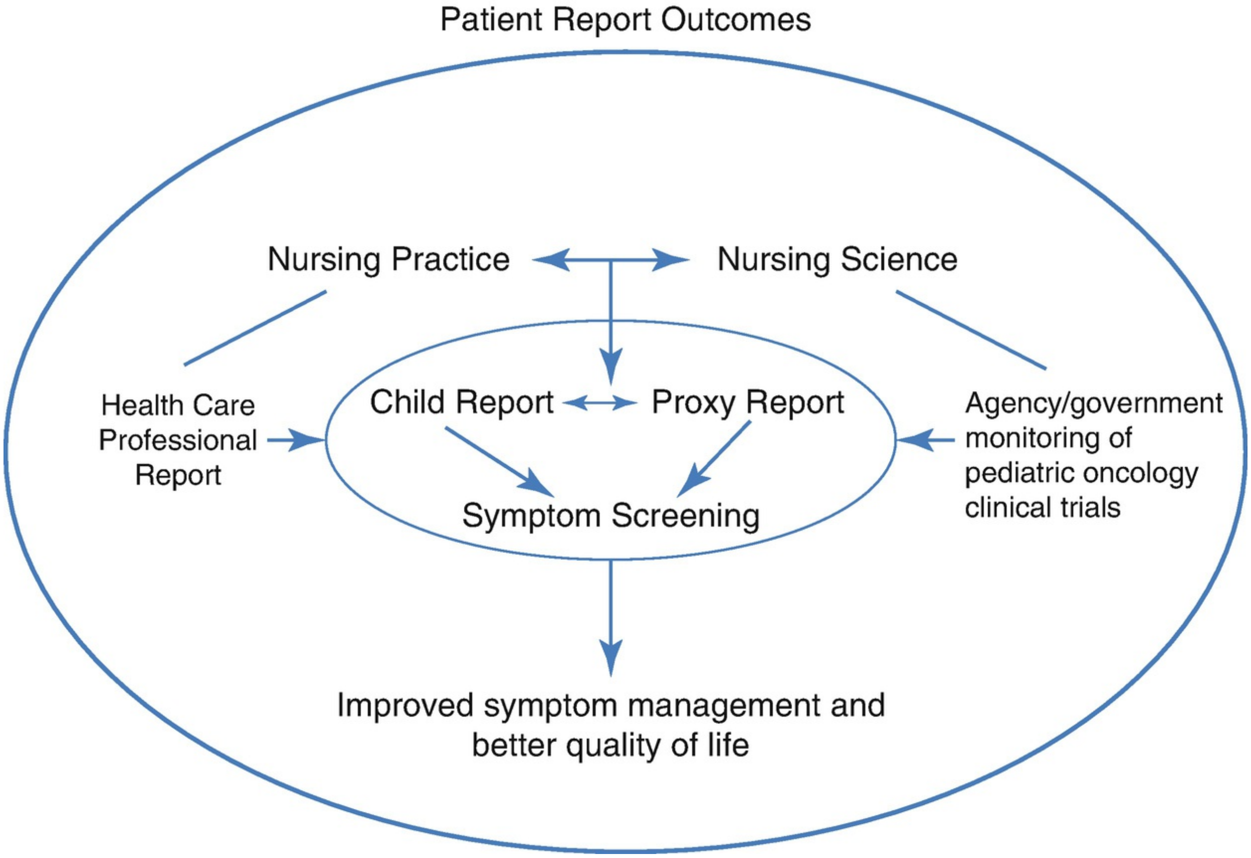

Fig. 7.1 Influence of nursing practice and nursing science on child symptom screening and management

Pediatric cancer treatment is usually associated with multiple co-occurring symptoms or toxicities that can result in a delay in scheduled therapies or a reduction in treatment doses [2], either of which can jeopardize treatment effectiveness. The multiple treatment effects have both subtle and visible effects on children, including behavior changes and quality of life impact [3]. Some of these effects continue or become more apparent following the completion of treatment [4, 5].

For at least two centuries, objective methods such as laboratory tests and diagnostic imaging, as well as physician clinical reports, have been widely used to understand children's symptom and toxicity burdens during cancer treatment. However, objective assessments of these burdens by persons other than the patient may not accurately reflect those symptoms and unobservable toxicities that could be more completely and sensitively captured by children's self-reported subjective treatment experience [6]. That is, an objectively observed symptom experience such as a vomiting may be more evident to parent or clinician report, but an unobservable symptom experience such as nausea is very likely best represented by a child's own self-report.

7.2 The Voice of the Child

Patient-reported outcomes (PROs) from adults with cancer facilitate patient–clinician communication and thereby contribute to improvements in symptom management, patient quality of life (QoL), and survival [7]. PROs are now considered an essential component of cancer care, both at an individual level for monitoring and improving symptom management and at a population level for collecting research and quality improvement data that could inform the next advance in cancer-specific therapies [7–10]. These important advances, secondary to incorporating adult patient reports into actual cancer care, have not yet been achieved in pediatric oncology, in part because of a persistent belief that children's self-reports are not reliable due to their developmental status [11]. This doubting of child-reported symptoms or treatment toxicities is also reflected in a continuing reliance *only* on clinician reports for both objective and subjective cancer treatment toxicities [12] and the use of certain symptom measures that rely on a parent or other proxy to interpret the ill child's symptom experience on behalf of the child [13].

The consensus definition of a symptom is that of a "subjective experience reflecting changes in the biopsychosocial functioning, sensations or cognition of an individual" [14]. The self-report of symptoms can include information on both the subjective and objective aspects of symptoms that are bothersome to the experiencing individual. Despite clinician or proxy reluctance to incorporate the child's self-report of symptoms into actual care, patient-reported pain has been recorded for more than three decades, most commonly through the use of the Numerical Rating Scale [15] and Faces Pain Scale [16]. Bolstered by several decades of research showing how children's own reports of pain influence patient care, more recent research includes children's self-report of additional symptoms. For children with cancer, their reports *specific* to QoL, fatigue, mucositis, nausea, loneliness, worry, or sadness have been solicited, and their reports to multiple symptom assessments in a single instrument have also been solicited [17–26]. The majority of these reports cover the age-span of 5–18 years.

In the past three decades, research funding has made possible the development and testing of new pediatric patient-reported outcome measures using advanced statistical methods such as item response theory. These efforts have resulted in multiple psychometrically sound instruments (e.g., the PROMIS pediatric measures) that are now available to measure symptoms and other patient-reported outcomes (e.g., function and QOL) in children with cancer (see Table 7.1). The initial use of qualitative methods directed at the lived experience of symptoms and treatment effects in children with cancer, a methodological approach consonant with the guidance from the FDA, has been contributory to the conceptual basis and content of many of these instruments [27]. As a result, new dimensions of the symptom experience have been identified; examples include the qualitative focus on mucositis [28], fatigue [25, 29, 30], and an overall symptom experience narrative [31–34].

Table 7.1 Example PRO pediatric multi-symptom and single symptom measures validated in children with cancer

Example multi-symptom PRO measures	Example single symptom PRO measures
Memorial Symptom Assessment Scale (MSAS)	Children's International Mucositis Evaluation Scale (ChIMES)
http://www.npcrc.org/files/news/memorial_symptom_	https://www.sungresearch.com/chimes

assessment_scale.pdf	
Pediatric Quality of Life and Evaluation of Symptoms Technology (PediQUEST)	Child Fatigue Scale (CFS) https://accpjournals.onlinelibrary.wiley.com/doi/abs/10.1592/phco.26.9.1221/
Symptom Screening in Pediatrics Tool (SSPedi) https://www.sungresearch.com/sspedi	Adolescent Sleep Wake Scale (ASWS) https://pediatrics.aappublications.org/content/115/Supplement_1/257/
Therapy-Related Symptom Checklist for Children (TRSC) http://iwbbio.ugr.es/2014/papers/IWBBIO_2014_paper_34.pdf	Child Sleep Wake Scale (CSWS) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5215091/
Rotterdam Symptom Checklist (RSC) https://www.umcg.nl/SiteCollectionDocuments/research/institutes/SHARE/assessment%20tools/handleiding_rscl2edruk.pdf	Child Depression Inventory (CDI) http://childhood-developmental-disorders.imedpub.com/childrens-depression-inventory-testing-measurement-invariance-for-the-hierarchical-factor-model-across-children-and-adolescents-in.pdf/
Symptom Distress Scale (SDS) https://eprovide.mapi-trust.org/instruments/symptom-distress-scale	Pediatric Nausea Assessment Tool (PeNAT) https://accpjournals.onlinelibrary.wiley.com/doi/abs/10.1592/phco.26.9.1221/
Advanced Symptom Management System (ASyMS) http://www.londoncancer.org/media/59987/asyms-study-2011.pdf	Perceived Symptom Severity (PSS) http://www.midss.org/content/perceived-stress-scale-pss/

Multiple studies have concluded that children as young as 8 years can reliably report on the majority of aspects of their health status, and younger children less than 8 years have reliably reported on one or more selected health domains using paper-based or computer-based methods [22, 35]. These studies reflect how more recently developed pediatric

PRO instruments (e.g., PROMIS pediatric measures) (https://commonfund.nih.gov/promis/websites) have been constructed and validated in consideration of children's cognitive status, reading ability, vocabulary, and language skills [36, 37]. An additional finding that supports the validity of the ill child's subjective symptom reports is the correlation of subjective and objective reports including for sleep [38], emesis episodes, and presence of neurological symptoms [20]. The complexity of symptoms and treatment toxicities from the perspective of children with cancer is readily apparent, bringing with it the realization that matching holistic, supportive care strategies need to evolve to minimize the symptom experience for these children as a group and as individuals (Fig. 7.1).

Although children with cancer, including those with incurable cancer and enrolled on a Phase I trial [22], are able and willing to report on the subjectively experienced symptoms or toxicities of their cancer treatment, they are unlikely to spontaneously report these experiences. Slightly more than 90% of children in treatment for cancer as reported in one study did not report burdensome symptoms until and unless directly asked to do so by clinicians [39]. Because these children are unlikely to report troubling symptoms, the risk is that clinicians and parents may conclude that the child is not experiencing such symptoms and thus may not probe such possibilities with the ill child [40]. This risk indicates the essential need for routine, ongoing symptom and toxicity and treatment impact screening using validated questions or measures administered to children to document their cancer treatment experience.

7.3 Proxy Voice in Pediatric Oncology

Parent-proxy reporting of subjective and certain objective symptoms has been considered necessary and legitimate in pediatric oncology. The parent-proxy report is particularly needed on behalf of younger children for whom validated self-report measures do not yet exist or those children who are nonverbal, for those who are more severely ill at the time of measurement and unable to self-report, and for those with cognitive impairment who are not able to understand the self-report measures [26]. When both patient self-report and their parent-proxy report of symptoms are collected at the same time point, the agreement between the two sets of reports tends to be low to low moderate [41–46]. This level of agreement indicates that the experiences differ for the two. Consequently, both the ill child's and the parent-proxy reports are important to fully ascertain the impact and the meaning of the actual cancer experience for the ill child and the parent.

Regardless of concordance or degree of difference between child and parent-proxy ratings, consensus is increasing toward the ill child's patient-reported outcomes being the primary outcome measure and parent-proxy reports being secondary unless the ill child is unable to self-report [47]. A proxy report is vulnerable to the proxy's mood. The validity of the proxy report is especially questioned for the ill child's subjectively experienced symptoms, such as sadness or distress and, most particularly, for such symptoms in older children [26, 48–50]. Ideally, the integration of both child self-report and parent-proxy report can be used to reflect their potentially unique perspectives [13].

7.4 Challenges to Studying Pediatric PROs in Pediatric Oncology

With any studies recruiting vulnerable populations, potential participants or their proxies may consider research participation to be too burdensome given the constraints of the illness and its treatment [51]. Barriers to recruitment in palliative care research, relevant to pediatric oncology research, have been reported to be: (1) defining eligibility criteria, which may include the wellness or stability of the child to participate while relying on the symptomatic child to ensure representativeness of results, (2) issues around gatekeeping where primary health care professionals may make the decision regarding approachability by a research team due to the vulnerability of the patient, (3) acceptability of study design including whether the eligible participant can accurately understand and evaluate risks and benefits of the study, and (4) logistical issues around access to participants [52]. These logistical challenges may include a preference for expedient clinic appointments or a lack of consistent availability of the parent of a hospitalized child to provide a proxy report. Other researchers have similarly reported on the challenges of recruiting adolescents with cancer to cancer research [53, 54] and have concluded that appropriate infrastructure and communication among the research team and clinicians may increase collaboration within health care teams to enhance participation in palliative care studies.

To study PROs in children with cancer, children experiencing symptoms and toxicities will need to be approached about the study. Study designs will need to include data collection points when symptoms are anticipated to be present and troubling as well as when symptoms are anticipated to be absent or minimally present. This could mean approaching pediatric oncology patients when they are in discomfort to invite them to participate in a study. Refusal to participate by the more symptomatic children may affect the overall results of reported symptoms or toxicities, thus making transparency in recruitment outcomes essential [55]. This threat to the validity of study findings means that a careful, detailed reporting of refusals to participate in such symptom studies becomes important enough to be a standard part of the dissemination of the study findings regardless of study design or methods.

7.5 Cross-Cultural Research in Pediatric Oncology

There is a new and developing literature regarding the possible impact of culture on patient-reported outcomes, including how children with cancer may conceptualize symptoms and rate the presence and interference of symptoms. Because culture is recognized as a dynamic process, clear use of terms in communication is considered key for any cross-cultural comparisons [56]. Liu and colleagues have successfully compared four PRO (PROMIS Pediatric) symptom measures (anxiety, depression, fatigue, and pain) across Chinese and American children with cancer and concluded that the measures were interpreted in a conceptually similar manner in both groups of children [57]. Current research is focused on translating psychometrically sound PRO measures for children with cancer, and successfully testing the psychometric properties of the translated versions [58–62]. The success with these studies will enable researchers to more confidently select and administer validated PROs to translate and use in their target study samples. The ability to study the same symptoms and other pediatric patient-reported outcomes in culturally diverse samples will likely yield new knowledge and in a very timely manner given that childhood cancer is a rare disease and enrolling sufficient participants to address pressing research questions is quite challenging. Of note, the studies described here are quantitative; qualitative or mixed methods studies completed in diverse geographic cultures that solicit the child and family experience of completing PROs will likely provide an important context regarding *the meaning* to a child or family of being asked to report own perceptions and experiences.

7.6 PROs and Clinical Trials in Pediatric Oncology

Since the US Food and Drug Administration released guidance concerning the use of PROs in trials to support drug labeling, PROs are included in those therapeutic trials in which the objective is cure [63]. This practice, however, is predominately more frequent in adult oncology trials than in pediatric oncology trials. A recently published study has confirmed the feasibility and acceptability of soliciting and documenting PRO endpoints in pediatric oncology Phase 1 or Phase 2 clinical trials [22]. However, to gain insights into the biological, environmental, and behavioral influences of cancer and its treatment on the lives of children, clinicians and scientists will need to integrate PRO measures into clinical trials. In particular, pediatric PRO measures will yield the most insightful information if aligned with the concurrent measurements of physiology, pathophysiology, genetics, and biology in pediatric oncology. A comprehensive analysis of relevant outcomes will bring new light to the interactions of symptoms, function, quality of life, and behavioral outcomes in pediatric cancers. With subjective and objective indicators measured simultaneously, clinicians will have the potential to identify those pediatric cancer patients who are uniquely susceptible to specific treatment toxicities. Having this more precise ability to identify such vulnerable patients will benefit the clinicians' efforts to support the individual patient's quality of life, improve symptom control, and provide tailored supportive care.

7.7 Health Care Professional, Parent, and Patient Responses to Pediatric PROs

Though acknowledged that children's self-reports are valuable in symptom, QOL and function assessments for research purposes and clinical practice, the potential discrepancies that result when child, parent, and health care professionals' reports are compared need to be carefully considered [13, 64]. A recently conducted systematic review focused on the discordance of pediatric oncology symptom reports among children, family caregivers, and healthcare professionals (HCP) [35], and noted that family caregivers' symptom reports were more closely aligned with children's reports than with the HCPs' reports. Influencing factors on the divergent symptom reports included the children's diagnosis, symptom characteristics, social-demographic factors, and family caregivers' psychosocial status. A second example of divergent reports was reported by Jones and colleagues [65] who summarized different importance ratings from survivors of childhood cancer, their parents, and health care professionals (HCPs): Clinicians rated five items in the pain interference domain and three items in the fatigue domain as more important than did survivors, but rated three items in the psychological stress domain and six items in the positive affect domain as less important than did survivor. In contrast, parents rated seven items in the positive affect domain as less important than did survivors. This divergence indicates that some differences are not limited to intensity or quality of the perceived cancer experience but to the perceived importance of certain aspects as well as to the ill child, parent, and HCP.

Finally, if the ill child is asked to respond independently to a PRO measure and has low literacy, the response ability may be affected even though the child may understand the PRO items when read to the child. Withycombe and study team members investigated the relationships among literacy, age, race, and their influence on a child's ability to understand and complete a PRO instrument during cancer treatment [66]. They found that, except for 63% of 7 year olds who required reading assistance, most participants (7–20 years) were able to complete the PRO that the team was studying. Even those children and adolescents with lower literacy skills were able to understand the PRO items, indicating that they knew the meaning of a word or phrase without recognizing it on paper.

7.8 Clinical Usefulness of Pediatric PROs

The anticipated improvements in care secondary to incorporating pediatric PROs into pediatric oncology clinical trials are additionally dependent upon clinicians using the ill child's reports to direct or alter actual care. Enhanced clinician awareness of the child's perspectives would be furthered by actual discussions between the clinician and the child as well as with the child's family. Research about the use of the ill child's PROs in pediatric oncology practice is limited, but one study does provide important insights into the future possibilities of such use. Wolfe and colleagues [67] conducted a parallel, multicenter pilot, randomized controlled trial to determine whether giving the PROs of children with advanced cancer to their oncology clinicians and their families improved the children's symptom distress and QOL. The results did not show significant effects on primary health outcomes, but a post-hoc analysis of surviving children 20 weeks after their PRO data were shared showed significant improvement in the emotional subscale of the PRO measurements and in an overall sickness scores, especially in children aged 8 years and older. Improvements were also noted in the perceptions of children and parents regarding talking to doctors, and in parents' understanding of their child's feelings. Clinicians expressed that they found useful and new information in PRO reports by children. Though limited at this point in time, these findings of the child's PROs being clinically useful are important indicators of the positive future use of pediatric PROs in pediatric oncology. The challenges documented in adult oncology to routinely embedding PROs in clinical practice, including little statistical support to analyze and interpret clinical meaning of results from the PROs, limited clinical site commitment of resources to the careful collection of PRO data, and the lack of quality enforcement of PRO data collection according to approved practices [68] would very likely be challenges in pediatric oncology as well.

7.9 Pediatric PRO Instrument Development

With the increasing recognition of the value of children's self-reports of symptoms, cancer treatment toxicities, and impact on QOL and functioning, the conceptual basis of pediatric PROs is of greater interest.

Certain pediatric PRO instruments that measure symptoms, QOL or functioning are created based on various conceptual foundations and with content input from various stakeholders. Anthony and colleagues [69] developed a PRO model to guide the content of pediatric oncology PRO instruments with four domains included: physical health, psychological health, social health, and general health. This PRO model can serve as an analytical lens for appraising the conceptual underpinnings of PRO instruments used in pediatric oncology.

Pediatric PRO measures include both generic and cancer-specific measures. While generic measures can be used in children being treated for diverse diseases, cancer-specific instruments tend to assess a range of possible consequences of treatment and disease, such as physical symptoms, emotional distress, body image, and cognition. Pinheiro et al. conducted a systematic literature review of existing instruments used to measure self-reported symptoms in children and adolescents undergoing cancer treatment and identified 38 self-report English instruments measuring approximately 81 different symptoms [6]. Differences among these instruments were detected including: symptoms assessed, cancer types, chronological age of the children being studied, number of items, recall period used, phrasing of questions, and number and type of response options. The pediatric PRO instruments most frequently cited in www.clinicaltrials.gov were the PedsQL 4.0 Generic Core Scales, PedsQL Multidimensional Fatigue Scale, PedsQL 3.0 Cancer Module, Fatigue Scale (Adolescent and Child version), and the Faces Pain Scale—Revised. Eight instruments had been psychometrically evaluated and found to detect significant changes over time in longitudinal pediatric oncology studies, including the Children's Depression Inventory, State-Trait Anxiety Inventory for Children, Children's International Mucositis Evaluation Scale, Fatigue Scale (Child and Adolescent versions), the Pain Squad App, the PedsQL 4.0 Generic Core Scales, and the PedsQL 3.0 Cancer Module [6].

An important consideration when selecting PRO measures is the alignment of the self-report of symptoms with prioritizing the corresponding supportive care. A recently completed systematic review [70] concluded that no pediatric self-report symptom measures assess all dimensions of the symptom experience that comprise the Theory of Unpleasant Symptoms (TOUS), i.e., intensity, timing, level of perceived distress, and quality. The TOUS is a notably complex theory [71] that has only recently had a majority of its components assessed quantitatively in a single pediatric study [21]. Augmentation of pediatric PRO instruments to reflect the dimensions of the concept being measured in a single measure or in a combination of measures is needed in order to assess the entire cancer subjective experience in children and adolescents.

When generic or cancer-specific instruments are used, several challenges persist in pediatric oncology PRO measurement. Literacy considerations understandably exist [66] and add to the concern that children might interpret the meaning of PROs differently across neurocognitive development stages [72]. Certainly pediatric PRO instruments need to carefully match content with children's cognitive development, reading ability, language skill, and vocabulary. Increasingly, evidence indicates that such concerns are pertinent to childhood cancer survivors. A final challenge is in research and care that extends over long periods of time and age of a pediatric oncology patient and age-specific PRO that a child may have completed at an early point in treatment but has now aged forward to a different age-specific version of the PRO. Linking these age-specific forms statistically is one approach to this challenge [73].

7.10 Patient-Report Measures More Commonly Used in Pediatric Oncology

Recent systematic reviews have reported that several PRO pediatric symptom measures have been validated in children with cancer and have been in use for 10–20 years [40, 74]. Certain of these measures have achieved strong reliability and validity coefficients and a few have additionally demonstrated the ability to sensitively capture symptom change over time [6]. Examples of pediatric patient-report measures commonly used in pediatric oncology are listed in Table 7.1, including multi-symptom measures and single symptom measures.

7.11 Development Process for Pediatric PRO Measures

The development of pediatric PRO measures follows a series of progressive steps that include a structured review of existing relevant measures, an early inclusion of children and adolescents who meet well-specified inclusion criteria including representativeness of certain characteristics such as age, gender, race, and ethnicity among others for purposes of item generation, refinement of wording of potential items, and testing of the psychometric properties of the developed measure across theoretically or empirically identified contrasting time points and/or samples. Each step can be repeated as needed [74–78]. Adhering to these well-tested progressive steps will have a high likelihood of the resulting PRO measure being sensitive to the ill child's treatment experience, valid and reliable (shown in Fig. 7.2).

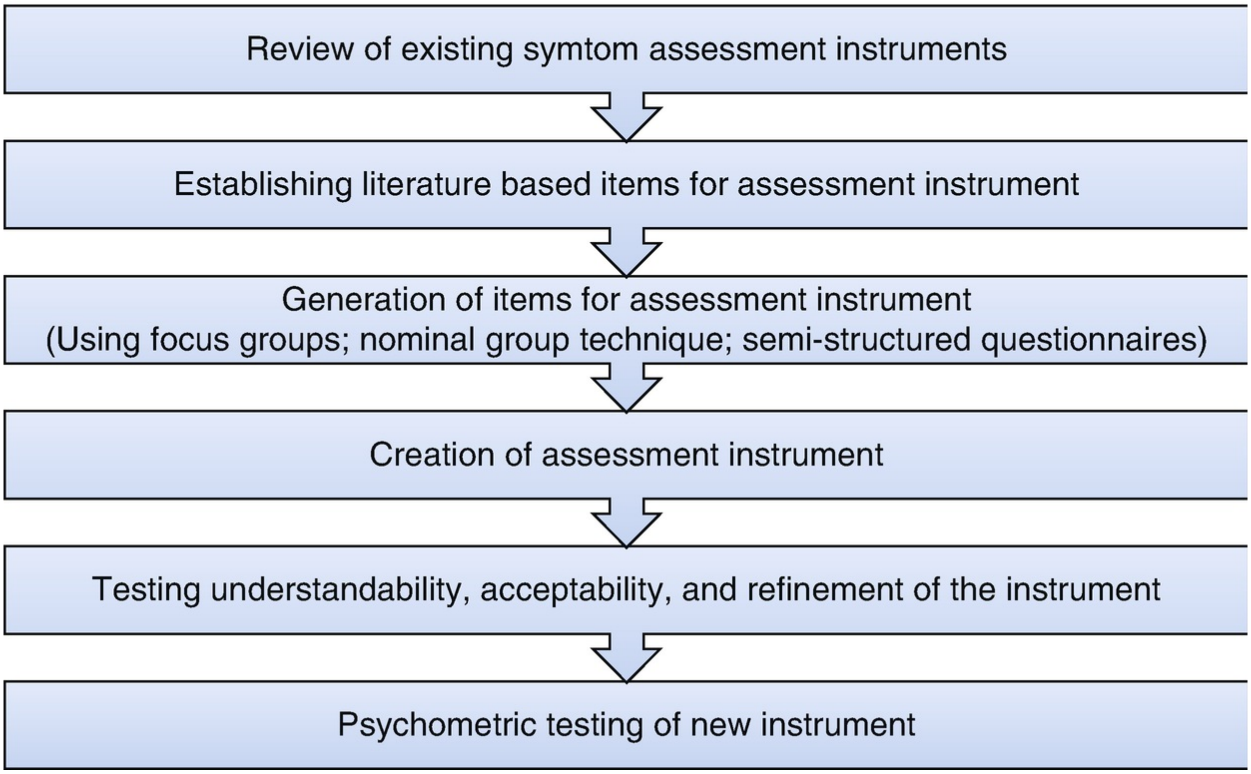

Fig. 7.2 Steps in the development of a PRO instrument (modified from Tomlinson and colleagues [79])

Two reviews of pediatric symptom screening PROs for children with cancer concluded that few ideal measures have been developed [40, 74]. However, two recently created and validated pediatric symptom and treatment toxicity patient-report measures, the Symptom Screening in Pediatrics Tool (SSPedi) and the Pediatric PRO CTCAE measure, represent the above described development steps particularly well.

7.12 Development of the Symptom Screening in Pediatrics Tool (SSPedi) and the Mini-Symptom Screening in Pediatrics Tool (Mini-SSPedi)

For the initial step in developing the SSPedi, a focus group involving 10 health care professionals with expertise in pediatric cancer symptom management and a patient advocate was convened. The group identified the optimal properties of a symptom screening tool for pediatric cancer patients, and existing symptom assessment scales were then evaluated against these properties [80].

A nominal group technique was used to identify the most important symptoms for inclusion in a new symptom screening tool, with 44 items generated by the group. Several items were subsequently combined, resulting in 25 items. A voting process established that 18 of these items were considered important by at least one participant. There was significant dialogue surrounding pain-related items. Clinicians questioned whether children would consider mucositis and headache to be forms of pain. Other group members suggested that all pain items be grouped as one item. However, the final consensus of the group was to retain three separate items related to pain in the tool: mucositis, headache, and other pain [80].

The 15 items most endorsed by the group members were retained and a draft of a self-report symptom screening tool for pediatric cancer was produced and named the Symptom Screening in Pediatrics Tool (SSPedi). The SSPedi has a recall period of “since yesterday” because the most relevant symptoms for the purpose of screening are current symptoms; this recall period was also perceived to be more accurately recalled by children. A 5-point Likert-type scale (0–4) was chosen rather than a visual analog scale because of ease of use. The final wording of the items and directions achieved consensus by group members [80]. A proxy version of SSPedi was also developed that mirrored SSPedi.

To formally test understandability and acceptability of the SSPedi to children, 8–18 years of age and diagnosed with cancer, children undergoing active cancer treatment and their parents were enrolled in an instrument study. Child and parent respondents completed the SSPedi/Proxy SSPedi once and responded to semi-structured questions. Then they rated how easy or difficult SSPedi was to complete. For items containing two concepts, respondents were asked whether concepts should remain together or be separated into two questions. Respondents were asked to indicate the importance of each item and to identify if any needed items were missing. Cognitive probing was conducted in children to evaluate their understanding of items and the response scale. This step used an iterative approach that reviewed responses after each group of participating 10 children and 10 parents to determine whether modifications were required. Thirty children and 20 parents were required to achieve a final version of SSPedi. Fifteen items remained in the final version with total scores ranging from 0 to 60 [81, 82].

The psychometric properties of the SSPedi and Proxy-SSPedi (test–retest and inter-rater reliability, construct validity, and responsiveness to change) were assessed in children with cancer and in stem cell transplant pediatric recipients. Results indicate that the SSPedi is reliable, valid, and responsive to change [19]. A final version of the SSPedi is shown in Fig. 7.3. A new self-report symptom screening tool for use in 4–7 year olds and derived from the SSPedi has now been developed and is named mini-SSPedi [83] (shown in Fig. 7.4). The new measure is pending assessment of its psychometric properties but will follow a similar approach as described above for the SSPedi.

Please tell us how much each of these things **bothered** you **yesterday** or **today** by ticking the circle that best describes the amount it bothered you:

	Not at all bothered	A little	Medium	A lot	Extremely bothered
Feeling disappointed or sad	○	○	○	○	○
Feeling scared or worried	○	○	○	○	○
Feeling cranky or angry	○	○	○	○	○
Problems with thinking or remembering things	○	○	○	○	○
Changes in how your body or face look	○	○	○	○	○
Feeling tired	○	○	○	○	○
Mouth sores	○	○	○	○	○
Headache	○	○	○	○	○
Hurt orpain (other than headache)	○	○	○	○	○
Tingly or numb hands or feet	○	○	○	○	○
Throwing up or feeling like you may throw up	○	○	○	○	○
Feeling more or less hungry than you usually do	○	○	○	○	○
Changes in taste	○	○	○	○	○
Constipation (hard to poop)	○	○	○	○	○
Diarrhea (watery, runny poop)	○	○	○	○	○

Please tell us about any other things that have bothered you lately by writing about them here.

Fig. 7.3 Symptom Screening in Pediatrics Tool (SSPedi) for 8–18 year olds diagnosed with cancer

Please tell us how much each of these things **bothered** you **today** by ticking the circle that best describes the amount it bothered you:

	Not bothered at all	Medium	Extremely bothered
			
Feeling sad	○	○	○
Feeling scared or worried	○	○	○
Feeling cranky or angry	○	○	○
Forgetting things	○	○	○
Changes in how you look	○	○	○
Feeling tired	○	○	○
Mouthsores	○	○	○
Headache	○	○	○
Hurt or pain (other than headache)	○	○	○
Hands or feet falling asleep or tingling	○	○	○
Throwing up or feeling like you may throw up	○	○	○
Feeling more or less hungry than you usually do	○	○	○
Food tastes different	○	○	○
Constipation (hard to poop)	○	○	○
Diarrhea (watery, runny poop)	○	○	○

Please tell us about any other things that have bothered you lately by writing about them here.

Fig. 7.4 The Mini-Symptom Screening in Pediatrics Tool (Mini-SSPedi) for 4–7 year olds diagnosed with cancer

7.13 Development of the Pediatric PRO Common Terminology for Adverse Events (CTCAE)

The National Cancer Institute (NCI) in the USA requires the reporting of cancer treatment toxicities using the Common Terminology for Adverse Events (CTCAE) measure in order to facilitate reporting and classification of toxicities secondary to cancer therapies, primarily chemotherapies. (https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf). This requirement has significantly advanced standardizing reporting and through that important step, documenting the real impact and safety of cancer treatments. The CTCAE contains more than 700 identified treatment toxicities that could be related to cancer therapies. A majority of these toxicities are objective in nature and assessed by laboratory-based measures. Such toxicities are reported and graded (1–5 with 1 being the lowest impact and 5 being death) by a clinician. However, nearly a third of the 790 toxicities are subjective in nature and would be most accurately reported by the individual receiving the treatment and experiencing the toxicity. This means that a patient-reported outcome version of the CTCAE, now in its fifth version, is needed. An adult PRO CTCAE (https://healthcaredelivery.cancer.gov/pro-ctcae/language.html) has been developed [84–88] and subsequently, a pediatric PRO CTCAE has also been developed. It is the latter that is described here.

The initial step was to have a 4-member panel of pediatric and pediatric oncology experts review the 790 CTCAE listed toxicities to determine which of these met the definition of a subjective toxicity experience. Consensus was iteratively achieved regarding 262 toxicities being subjective in nature. Seven collaborators from seven member sites of the Children's Oncology Group in the USA and Canada identified 187 pediatric oncology clinicians (physicians, nurse practitioners, nurses, and physicians) within their sites who met experience criteria and a Delphi research technique was used to invite each of these individuals to review the toxicities and indicate if they considered the toxicity to be subjective and if children as young as age 7 years could validly report on the toxicity (Survey 1). A total of 135 of the eligible clinicians (72%) completed one of the two forms and of the 262 items, 90 had a content-validity ratio (CVR) lower than the acceptable rate, indicating lower agreement among raters. Eight members of the study team reviewed these items for their clinical observability, i.e., addressing the likelihood of a clinician being able to see or identify the toxicity even if the child was not specifically asked about the toxicity, and retained 3 of the 90 for the second round survey. A second survey comprised of 79 CTCAE terms of the reviewed toxicities (Survey 2) was sent to the same respondents to Survey 1; the purpose of Survey 2 was to achieve consensus on the toxicities regarding the same two points above and to identify a core listing of toxicities that were considered common enough to be asked of pediatric oncology patients regardless of diagnosis or treatment. A total of 121 clinicians completed Survey 2 and consensus was achieved on 64 items, including 16 core items [89].

The next step was to translate the medical terms from the CTCAE for the 64 items into child-friendly terms and to confirm clarity and understandability of the items to pediatric oncology patients and their parent proxies. This was achieved using cognitive interviewing and involving 81 pediatric oncology patients ages 7–15 years and their parent-proxies from 7 pediatric research hospitals. Two rounds of cognitive interviewing were completed. Fifteen of the child-friendly items were revised after the first round of interviews and along with six other items found challenging were evaluated by patients and parents in the second round again with the collaborators using cognitive interviewing strategies with patients and parents. Overall, the 7-day recall period was *not* difficult for the 7–15-year-olds to understand and most children (with certain limited age differences noted) described the toxicity items to be “very easy” or “somewhat easy” to understand. Similarly, of the 42 parent proxies, all described the items as “very easy” or “somewhat easy” to answer. The outcomes included 62 toxicity terms in child-friendly wording and with wording in the stems of each question per toxicity that addressed toxicity presence, frequency, severity, and interference [37]. In a subsequent and similar cognitive interviewing approach involving 16–20-year-old patients, the collaborators were able to determine that this age group understood the toxicity items on the adult PRO CTCAE and thus could complete that set of items rather than the pediatric PRO CTCAE [90].

At the very same time of the cognitive interviewing steps described above, the 7–20-year-old participants were also asked to address how their body had felt during the previous 7 days, if any changes in their body had been observed by them and in particular, if any of their body changes had surprised them, and finally, to address their feelings of the past 7 days. This methodological approach allowed us to both confirm the relevance of the toxicity items to this age group and determine if any additional toxicity items needed to be developed and included. These face-to-face interactions with 96 age-stratified participants helped also to confirm or refine our items in consideration of the participants' cognitive development. The number of symptoms reported ranged from 0 to 7 per participating child; fatigue was the most frequently reported followed by nausea, aches or pain, and weakness. Among the least spontaneously reported were difficulty with sleep, change in hearing, swollen gums, and racing heart. Nearly 31% experienced surprising changes in their body including the most commonly reported type being skin changes. Emotions were not spontaneously identified by participants until directly asked. Findings support that children and adolescents in treatment for cancer are able to self-report clinically relevant physical and emotional concerns or symptoms. Only two new symptoms were identified that were not already on our toxicity list: constipation and diarrhea. Findings thus also supported the completeness of the list of cancer treatment toxicities as perceived by children and adolescents in treatment for cancer [39].

Concurrently, the collaborators completed an extensive review of pediatric PRO measures with a particular focus on recall period, item number, psychometric properties including ability to capture change over time, clarity of directions, and clarity of response options [6]. The validity assessments of the pediatric PRO CTCAE have addressed construct and concurrent validity as well as the measure's ability to capture change over time at the item level. These assessments include the data from more than 380 children, parent proxies, and clinicians. Additional papers in review include a mapping (assessing how the pediatric PRO CTCAE items and scores from participating children correspond with the toxicity grades completed on the CTCAE by clinicians for those same children) and a scoring paper, the latter explaining the scoring schema that was developed by the multi-site collaborators.

The Pediatric PRO-CTCAE consists of a library of 64 treatment toxicities assessed by 130 items [89, 90]. Though it varies by individual toxicity, the Pediatric PRO-CTCAE documents symptom presence, frequency, severity, and/or interference with daily activities. Each toxicity has four response options (Tables 7.2 and 7.3). The Pediatric PRO CTCAE is intended for use in clinical trials and differs from other pediatric PROs in three ways: it is designed as a library of items that can be used to assess a broad range of subjective toxicities that a child may experience during cancer treatment; investigators and clinicians can select the subjective toxicities from the Pediatric PRO-CTCAE library that they want to include in a clinical trial or for use with assessing clinical care concerns. Other pediatric PRO measures that have a fixed set of symptoms or functional domains. Second, the Pediatric PRO-CTCAE includes only a small number of questions per subjective toxicity to ascertain symptom frequency, severity, and interference with daily activities. This approach reduces patient and parent-proxy burden. Last, the Pediatric PRO-CTCAE assesses the *worst* experience of a subjective AE "over the past 7 days" to be consistent with CTCAE grading. Most other PRO tools assess an *average* symptom experience over the past week.

Table 7.2 Pediatric PRO-CTCAE treatment toxicity child-friendly terms

Arms and legs feel weak/weakness in your arms and legs	Feeling tired pain in your mouth or throat Sad or unhappy feelings
Bigger belly than usual	Food or drink taste different than usual
Pain or burning when you pee	Flashes of light that were not there when your eyes were open or closed
Bruise easily (get black and blue marks on your skin)	Hair fall out
Pee more than usual	See blurry (have blurry vision)
Burning feeling in your chest (heart burn)	Head hurt (headache)
Pee yourself on accident	Shaking chills

Change in the color of your pee
Pimples (bumps on the face or chest)
Changes in your voice
Poop yourself on accident
Cough
Problems breathing (shortness of breath)
Dizziness
Problems remembering things

Dry eyes
Problems sleeping (trouble falling or staying asleep)
Dry mouth
Problems with not being able to poop
Dry skin
Problems with paying attention (focusing on TV, reading, or school work)
Fall down
Problems with swallowing
Fart more than usual
Puffiness (swelling) in your arms, hands, legs, or feet
Feel hot all of a sudden (hot flashes)
Racing heart beat
Feel like you could not wait to pee
Ringing or buzzing in your ears
Pain in any bendable part of your body (knees, ankles, shoulders, or fingers)

Hiccups
Sneezing
Hoarse (scratchy) voice
Sore throat
Itchy red bumps on your skin
Stomach pain
Itchy skin
Sunburn more easily

Muscles hurt
Sweat more than usual or sweat for no reason
Nose bleeds
Think about hurting yourself
Not being able to sit still
Throw up
Not want to eat your meals
Watery eyes (tearing)
Numbness or tingly feeling in your hands or feet
Wheezing (a whistling noise in your chest when you breathe)
Open sores or red spots on your skin
Worried or nervous feelings
Pain
Feeling sick to your stomach (nausea)
Runny or watery poop

Table 7.3 Pediatric PRO-CTCAE question stems

Toxicity	Sample question	Response options

attribute		
Frequency	In the past 7 days, how often did your *head hurt*? (headache)	Never/sometimes/most of the time/almost all the time
Severity	In the past 7 days, how bad was your *sore throat*?	Did not have any/a little bad/bad/very bad
Severity interference	In the past 7 days, how much did your *itchy skin* keep you from doing things you usually do?	Not at all/some/a lot/a whole lot
Presence	In the past 7 days, did you have any *changes in your voice*?	Yes/no/I do not know

7.14 Enhanced Pediatric Precision Subjective Cancer Symptom Screening Through Symptom PRO Profiles?

Patient-reported outcome measures are increasingly becoming key outcome indicators in health care. However, how to integrate PROs as a routine part of clinical practice remains a question, as does how to interpret the PRO reports alongside all other aspects of a child's clinical status. Matching the pediatric PRO to the child's overall clinical situation merits careful consideration. Kwon and colleagues offered three important considerations when using PRO measures: (1) interpretation of contextual elements; (2) interpretation of PRO measures as an ongoing dialectical interaction; and (3) using PRO measures with openness and reflexivity [91]. To make a precision clinical decision informed by a pediatric PRO, then, requires knowledge of the ill child's overall clinical status over time and treatment, developmental and personal milestones, and knowledge of the PRO measure itself.

An additional consideration to increase the likelihood of pediatric PROs actually guiding clinical decision making with greater precision (meaning tailored to the individual child) means that the PRO scores must be manageable and interpretable by oncology health care professionals (HCPs). Too much information in terms of multiple individual PRO scores could prove too burdensome or confusing to HCPs, and thus the information would be less likely to be used to tailor supportive care or to alter treatment. To overcome this risk of too burdensome PRO details, a different approach is now being explored, that of PRO symptom profiles. The pediatric PRO symptom profiles are derived from PRO measures completed by different groups of pediatric oncology patients; two dominant profiles (low symptom suffering and high symptom suffering) have been identified in retrospective data analyses in children receiving chemotherapy and in children in survivorship [92, 93]. Though limited in number of such analyses, early findings suggest that children are highly likely to remain in their same suffering profile from beginning to end of a course of chemotherapy [93]. Further, in one study, children's response to a single pediatric PRO symptom item specific to fatigue had a high likelihood of predicting to which profile (high or low) a child belonged [93]. These findings indicate the likelihood of certain symptom PRO items being effective screening tools for clinical use to identify symptom suffering profiles at key treatment points. Knowing the patient profile would thus provide the opportunity for clinicians to alter the extent (increase, decrease, or alter) of supportive care for a specific child or adolescent based on the PRO score. That ability would greatly enhance the clinical usefulness of pediatric PROs in pediatric oncology and contribute to precision nursing care for such pediatric oncology patients.

7.15 Evidence-Based Findings Derived from the Science of Patient-Reported Outcomes (PROS) in Pediatric Oncology Ready for Translation to Clinical Practice

Certain evidence-based pediatric PRO findings have been confirmed in multiple studies or projects involving different pediatric oncology patient groups at different points in their cancer care. Researchers are strongly encouraged to seek opinions from experienced families and oncology clinicians regarding study design and methods when creating and implementing palliative care studies. Given the support for those confirmed findings, these findings are ready to be translated into routine clinical practice in pediatric oncology. The evidence-based findings include:

1. Children in treatment for cancer as young as 8 years of age (and some even younger) are generally able to understand and respond to patient-reported outcome measures regarding their symptom, treatment toxicity, and quality of life experiences during (including Phase I, II, and III clinical trials) and following cancer treatment. They are able to do so using paper or computer-based or interview methods.

2. If children in treatment for cancer are not asked to report on their subjective experiences, it is highly unlikely that they will spontaneously do so. Nurses and others in this specialty need to embed age-appropriate PRO measures into pediatric oncology care.

3. A growing number of pediatric patient-report measures have been validated in groups of pediatric oncology patients at varying times during treatment and survivorship, and a subset of these have the documented capacity to capture change over time. These measures are ready to be embedded into clinical trials as either primary or secondary endpoints.

4. Pediatric PRO measures validated in groups of children and adolescents in treatment for cancer can be sensitively used in screening for the presence and severity of symptoms or treatment toxicities and to measure the perceived impact of the cancer treatments on the ill child or adolescent’s functioning or quality of life. Therefore, the pediatric PRO measures known to have acceptable psychometric properties including capturing change over time are ready to be part of the best practice guidelines for screening and assessing cancer treatment impact in pediatric oncology.

5. Collecting both the child PROs and the parent-proxy PROs concurrently is possible and informative as the two sets of experiences likely differ from each other and collecting both is more informative of a family treatment experience. Validated measures in

both groups now exist and are ready to be embedded in standard practice.

7.16 Future Research Recommendations for Patient-Reported Outcomes in Pediatric Oncology

To continue the remarkable progress begun in developing and testing pediatric PROs in pediatric oncology to the actual routine embedding of PROs in clinical trials and clinical care, certain next steps are needed:

1. The clinical value of pediatric PROs in pediatric oncology at purposefully collected time points now needs to be established. Clinical value would be demonstrated in terms of clinician understanding of the meaning of the specific child's reports as evidenced in a change in supportive care or other forms of cancer treatment, or in a low burden, rapid clinical assessment of a patient's symptom, function or quality of life status that could then inform care efforts to reduce suffering specific to an individual child or to a group of children.

2. Documenting the collective clinical value of including patient, parent-proxy, and clinician reports in toxicity summaries to monitoring groups such as national cancer institutes across countries is an additional future research priority.

3. Continuing and extending the testing of psychometrically strong pediatric PRO measures across cultures and countries will result in unique benefits for pediatric oncology. Because pediatric cancers are rare, formal testing of interventions to reduce symptom or treatment-related toxicities can take an extensive period of time to enroll a sufficiently large study sample and the prolonged enrollment period can delay determining which interventions are acceptable and effective or not, and thus can also delay translating the effective interventions into practice. Confirming equivalence and cultural sensitivity of existing pediatric PRO measures across

countries could greatly speed up the ultimate use of clinically sound symptom, toxicity, and quality of life interventions. Because of this future benefit for pediatric oncology, the continued and expanded efforts to determine pediatric PRO measure equivalence need to be a research priority.

4. The study of refusals by children and adolescents to complete PRO measures is also recommended to determine the impact of such refusals on the actual findings. This careful, consistent attention given in a standardized manner across studies involving pediatric PROs in oncology would teach us which children are represented in our PRO study findings and which children are not.

5. When pediatric PRO measures are included in care guidelines, that actual use of the measures in clinical care needs to be assessed. As part of that research, identifying the conditions or the factors that are present when the PROS are or are not administered would also be important to assess.

6. Examining the impact of concurrently collecting the perspectives of the ill child, parent-proxy, and clinicians on different forms of care and cancer treatments is an essential next step.

7. Finally, as noted above regarding clinical value, expanding the study of symptom suffering profiles based on pediatric PRO measures will be especially valuable for both screening and treatment impact purposes.

7.17 Conclusion

The overarching motivation underlying the effort to develop, refine, test and refine again, and incorporate pediatric PROs into clinical research and care is to obtain a more complete and accurate understanding of the full impact of cancer and its treatment on the lives of children, and to minimize or prevent likely toxicities. To achieve these desired endpoints in pediatric oncology practice, pediatric PROs will need to be a routine part of pediatric oncology such that children and families understand the purpose of the PROs and can anticipate and complete them, and health care professionals can anticipate discussions with the child and family regarding the PROs. The time and effort given to reporting PROs by ill children will need to be regarded with much respect by HCPs and by the ill children's families. When their preferences cannot be honored, explanations to the children will be needed.

Health care professionals will be essential if a "pro-PRO" culture is to exist in pediatric oncology. Their role in soliciting and honoring PROs is substantial as is their role in clinically interpreting PRO data. A "pro-PRO" culture shift in health care will additionally need support from administrators of health care systems who are committed to supporting system change and resource provision to make PROs a routine part of care [68]. A current and comprehensive description of PROs' psychometric properties, previous applications, limitations, and administration and scoring guidelines needs to be compiled and made available for use by HCPs. Diverse methods for collecting and using pediatric PROs in pediatric oncology will also be needed. If we are to hear and to honor the ill child's voice in terms of subjective symptom, toxicity, function, and QOL experiences during and after cancer treatment, PROs need to become a routine part of clinical care in pediatric oncology.

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8. Technology to Support the Care of Children and Adolescents with Cancer

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Abstract

Technology-based innovations have transformed healthcare, including the care of children with cancer and their families. As digital natives, children and adolescents have grown up with technology as part of their everyday lives. Researchers and clinicians have the capacity to collect more personal details, with greater ease and accuracy from patients and their families to better define phenotypes and advance the science of precision health. These recent digital health advances may facilitate the integration of multiple aspects of cancer care into families' lifestyles, with novel options for communication, monitoring, and education. This chapter explores ways in which technology is being used to advance the science of precision health for children with cancer and their families by addressing technology for monitoring health status and technology used to deliver supportive care. The chapter also explores current applications of technology to support nursing education which may also contribute to precision health for children with cancer and their families. While multiple technology-based resources show promise for enhancing care across the cancer continuum, research is needed to identify best practices for implementing technology within cancer care, including strategies for analyzing digitally obtained data, and to evaluate the efficacy of technology-based resources to improve patient outcomes.

Keywords Technology – mHealth – Digital health – eHealth – Mobile technology – Mobile apps – Internet

8.1 Overview

Technology-based innovations have transformed the healthcare landscape. Mobile phone ownership is ubiquitous [1]. New terminology reflects the interface of technology and healthcare. The term mHealth for describing healthcare practices supported by mobile technology devices is used frequently [2]. Because not all technology solutions are mobile, the term digital health is more encompassing. Other common new terminology includes eHealth, wearables, ePatient, digital native, patient-generated health data, self-tracker, and smart everything. Nurses often interact with new collaborators including engineers, informatics specialists, and entrepreneurs. Large technology companies as well as countless start-up companies are stepping into the digital health arena [3].

By applying these technological innovations to the concepts of the precision health framework utilized by this text, the child with cancer remains at the center of the model. However, children and adolescents with cancer do not go through the cancer experience alone. The applicability of digital health interventions must be considered within the context of family. The input of parents or guardians as proxy is required for some patients (e.g., the very young or very ill). For many other families of pediatric cancer patients, symptom reporting involves the joint contribution of patients and their family members to glean a comprehensive viewpoint of the patient's condition.

In recent years, the degree of detail of daily life that is captured and shared via technology has increased dramatically. These details enable advances in precision health. As researchers strive to determine how specific genetic changes impact outcomes, a clear understanding of an individual's phenotype is needed. Many of the outcomes under study have subjective components and rely on self-report. With the aid of technology, researchers and clinicians have the capacity to collect more personal details, with greater ease and accuracy from patients and their families to better define phenotypes and advance the science of precision health. As knowledge of symptom management improves, these details can be used to promote more personalized and effective supportive care.

These recent digital health advances may facilitate the integration of multiple aspects of cancer care into families' lifestyles, with novel options for communication, monitoring, and education. Numerous factors may affect the usability and acceptability of technology solutions. As "digital natives", children and adolescents may have preconceived expectations of mobile apps, wearable devices, or web-based support. Some technology options are now expected by healthcare consumers, while others may be overly onerous or intrusive to be incorporated into patients' lifestyles.

This chapter emphasizes the use of technology to support the care of children and adolescents with cancer. A summary of the technology solutions covered in this chapter is provided in Table 8.1. This technology-based support includes technologies to promote self-care strategies along with more indirect aspects of support, noted by enhancing patient/family education, as well as staff education. The delivery of effective technology-associated nursing and self-care interventions relies on adequately prepared staff and patients and their family members.

Table 8.1 Summary of technology solutions in pediatric oncology

Types of technology	**Examples**
Technology to monitor health status	
Web-based surveys	Single or infrequently administered electronic surveys as well as eDiaries for daily or more frequent assessments
Mobile applications	
Passive health monitors	Fitness trackers; other wearable technologies are being developed but not yet commonly used in pediatric oncology
Technology to deliver supportive care	
Psychosocial support	Online chat, writing assignments with remote tailored feedback, video review, and creation
Self-care advice	Mobile apps with self-care advice, with or without “eDiaries”, educational videos available on mobile devices
Telehealth: real-time remote monitoring	Remote appointments may include audio only or videoconferencing services
Promotion of physical activity	Coaching combined with a fitness tracker
Promotion of medication adherence	Mobile apps with medication reminders, electronic monitoring caps
Procedural distraction	Playful robots to serve as distraction
Technology to deliver staff education	
Web-based learning modules	Synchronous and asynchronous learner–educator interactions
Simulation	Low-fidelity and high-fidelity scenarios

8.2 Technology to Monitor Health Status

8.2.1 Electronic Patient-Reported Outcomes

Children and youth with cancer experience high levels of suffering from physical and emotional symptoms and poor quality of life. The impact of cancer extends to family members, including caregivers and siblings. As described in Chap. 7, an increased emphasis on incorporating patient-reported outcomes (PROs) into routine clinical care as a means to enhance patient and provider communication has been seen in the past decade. These efforts can improve clinicians' awareness and ability to monitor symptoms/health status and health-related quality of life over time, as well as evaluate treatment outcomes and support shared decision making [4].

The term "app" refers to software that is designed for a single purpose with the intent of performing a single function. An estimated 1000 new health-related mobile apps for smartphones and/or tablet computers are released each month. Health trackers are among the most common. These apps may be used both for health promotion and for chronic illness management [5, 6].

eDiaries are a subset of apps that support daily reporting of health-related data. These apps offer potential benefit to the user as well as clinicians and researchers to discover patterns of symptoms, therapy use, and effectiveness of symptom management strategies. A few such apps have been designed for children or adolescents with cancer; however, these did not progress beyond the initial testing phase [7–9], as is common of most mobile health apps [10]. Obstacles to successful app deployment include difficulties in securing funding, institutional bureaucracy in the technology approval process, difficulties in compiling multidisciplinary teams with complementary skills and expertise, and the rapid pace at which aspects of technology can become obsolete.

Among the most common barriers to cancer symptom treatment is patient reluctance to report symptoms and ambiguity on the part of patients related to assessment techniques [11, 12]. These barriers are problematic because accurate symptom assessment is required to facilitate timely and effective symptom management and ultimately maximize health-related quality of life for pediatric cancer patients and survivors. Although a number of pediatric cancer symptom assessment tools exist [13, 14], these tools are often implemented in clinical and research settings using traditional paper-and-pencil or verbal methods.

These traditional methods mean that symptom assessments are subject to recall bias due to a heavy reliance on memory-based symptom recall, do not allow for symptom assessment in children's natural environments (e.g., home) or social contexts, and do not easily allow for longitudinal assessment to facilitate understanding of symptom patterns overtime and responsiveness to treatment.

Electronic solutions are well-poised to address the shortcomings of traditional methods of pediatric cancer symptom assessment. Electronic PROs (ePROs) come in a variety of formats from the single administration of an Internet-based survey to app-based symptom trackers capable of collecting single or multiple symptom reports on a daily or more frequent basis. Deployed on Internet-enabled devices, apps can support symptom reported in real-time in a variety of environments, which maximizes the validity of reported data [15]. Using electronic solutions also allows for the examination of symptom patterns, both within and between days. Children with cancer as young as 8 years are capable of validly and reliably reporting cancer-related symptoms on electronic devices [14–16]. Given the ever-rising prevalence of Internet access among children and adolescents, as well as their parents and clinicians, electronic reporting may be a viable means to collect high-quality pediatric cancer symptom data for clinical and research purposes.

Young people are digital natives, and technology is a part of their everyday lives [17]. However, the pediatric oncology setting has lagged behind the adult setting in use and implementation of ePROs. Reasons for this include the belief that children's reports of health information are unreliable and the complexities inherent in designing and developing technology across children's developmental stages. Furthermore, relative to adult oncology, few clinicians and researchers specialize in pediatric oncology, and thus the pool of available researchers and developers to advance ePRO technology is limited. Indeed, children are able to reliably report their health status (see Chaps. 5 and 7), and pediatric ePRO instruments need to carefully accommodate specific content related to children's cognitive development, their expectations of design features, as well as their reading abilities, vocabulary, and language skills.

Researchers may migrate existing validated measures to electronic platforms to collect PROs. As long as modifications to a previously validated tool during migration are minimal, the psychometric properties of the ePRO are expected to be similar to the paper format [18]. Wu and colleagues used existing measures on an electronic platform to assess symptoms, quality of life, and resilience among youth undergoing cancer treatment just prior to ambulatory treatment clinic visits [19]. In a convenience sample of 40 adolescents with cancer between 13 and 20 years of age, they found the computerized assessment was feasible in terms of high completion rates without delaying clinic schedules, acceptability, time to complete (30 min), and level of assistance required. Linder and colleagues successfully collected daily symptom reports using an electronic version of the MSAS 7–12 delivered via an iPad from 50 hospitalized children and adolescents receiving chemotherapy with minimal missing data [20].

The use of ePROs facilitates the incorporation of complex psychometric properties into instruments. For example, the Patient-Reported Outcomes Measurement Information System (PROMIS) includes computer adaptive testing (CAT) [21]. With CAT testing, survey items are adjusted as a result of the respondents' prior answers to create surveys that are potentially shorter in duration yet tailored to the individual than standard surveys. The PROMIS tools are available for a wide range of ages, languages, and patient conditions, and have been implemented worldwide. PROMIS items can be administered on paper but researchers can benefit from the CAT features when the items are distributed via computer or mobile application (http://www.healthmeasures.net/explore-measurement-systems/promis). Research teams developed a pediatric item bank for the PROMIS system using cognitive interviewing to evaluate item comprehension among children as young as 8 years of age [22]. To investigate these key issues, researchers must select instruments that demonstrate responsiveness to change. Hinds and colleagues provided evidence that several of the PROMIS pediatric items demonstrated responsiveness to short-term and long-term change among children receiving cancer chemotherapy [23].

Research teams recognized the need for a mechanism to characterize the subjective symptom experience of clinical trial participants and developed the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE), as described in

Chap. 7. The tool can be used in paper or electronic formats [24]. The initial version of the PRO-CTCAE was developed for adults. Analysis of cognitive interviews with adolescents with cancer confirmed that use of this adult version is valid down to an age of 16 years [25]. In addition, a pediatric version of the PRO-CTCAE has undergone extensive psychometric evaluation and will soon be available for use free of charge in clinical trials and observational studies (https://healthcaredelivery.cancer.gov/pro-ctcae/) [26]. This readily accessible, validated series of items allows researchers or clinicians to tailor questionnaires to particular projects or clinical situations to minimize participant burden with data sets that are comparable across studies. The items can be distributed via simple to use electronic survey systems such as REDCap with minimal effort and expense.

Taylor and colleagues reported the development and initial validation of a survey to evaluate the physical and psychosocial concerns of adolescents and young adults (AYA) with cancer, termed the BRIGHTLIGHT survey [27]. First, they developed a conceptual framework and conducted a review of the literature to develop the initial domains and items within the survey and then assessed the face validity of the survey. They then confirmed the acceptability of the mode of administration of the survey in focus groups of AYAs (14–25 years), parents, and siblings to refine the survey. In the final development stage, they conducted telephone-administered cognitive interviews with AYAs to refine the final survey capturing 15 domains and 169 items. The key message from this study was the importance of actively involving young people in survey development to create meaningful tools that reflect their patient experience and outcomes. A longitudinal project that utilized the BRIGHTLIGHT surveys enrolled more than 1100 AYA patients in the United Kingdom. Participants completed the surveys 5 times over 3 years with relatively high completion rates of 47–75% at each time point. After completing the initial survey via interview, participants completed subsequent surveys online using item branching to tailor questions based on prior responses. A preliminary report of the study methodology, recruitment, and descriptive data from the first waves of surveys has been published with additional analyses to come [28].

In recent years, a number of electronic methods to facilitate the tracking of patient reports of multiple cancer symptoms have been developed that make use of the multimedia features available on mobile electronic platforms. For instance, recently the paper-based Symptom Screening in Pediatrics Tool (SSPedi) has been translated into an electronic format for use by children and adolescents. The SSPedi tool assesses the degree of bother related to 15 cancer-related symptoms, as described in Chap. 7. The electronic version of the tool includes audio assistance allowing instructions to be read aloud to users, help menus for each item assessed, and child-friendly animations. The usability of the tool has been evaluated in 20 children and adolescents (8–17 years) with cancer, and its functionalities, including data saving, were found easy to use [29]. The reliability, validity, and responsiveness of child self-report and parent proxy-report of SSPedi have been demonstrated in large cohort of children and adolescents with cancer and those undergoing haematopoietic stem cell transplant (HSCT) [16, 30].

These studies suggest that ePROs can be administered at home or during routine clinical assessments. Nurses play a key role in integrating ePROs into clinical care by helping to review, interpret, and act on these assessments to optimize supportive care for children and adolescents with cancer [17]. While some evidence of potential benefit of ePROs in adult oncology has been demonstrated [31–33], there is a paucity of such research in pediatrics in general and less so in pediatric oncology.

Wolfe and colleagues evaluated whether providing feedback on PROs collected using the Pediatric Quality of Life Evaluation of Symptoms Technology (PediQUEST) computerized platform to providers and families of children with advance cancer improved symptom distress and health-related quality of life [34]. A parallel, multi-centered randomized controlled trial design was used where children (age ≥2) with advanced cancer and their parents were randomized to intervention group (*n* = 51) and were asked to complete weekly PediQUEST PROs which were also provided to their clinicians (oncologists and nurse practitioners) or usual care group (*n* = 53; no PRO feedback provided). The PediQUEST survey included age- and responder-adapted versions of the Memorial Symptom Assessment Scale (MSAS) [35], Pediatric Quality of Life Inventory 4.0 Generic Core Scales (PedsQL 4.0) [36], and an overall sickness question. In the intervention group, emails were sent to the patient's oncologist for scores above a pre-determined threshold. While average scores on each measure did not significantly change between groups, subgroup analyses of children ≥8 year who survived 20 weeks indicated that feedback significantly improved the PedsQL 4.0 Emotional Subscale and sickness item scores. The ePROs were valued by the children, their parents, and health care providers. Some providers initiated psychosocial consults as a result of these reports. Of note, the researchers did not provide clinicians with suggestions on ways to respond to reports, including scores that exceeded threshold values. Future work should address methods to provide clinicians with evidence-based recommendations in response to PRO scores.

A key issue limiting the successful implementation of ePROs into everyday clinical care is the clinicians' lack of knowledge of how to effectively utilize PRO data in their clinical encounters. An example of successful implementation of an ePRO is the KLIK "ePROfile" website. On this portal, which was developed in the Netherlands, patients and parents complete surveys at home prior to a visit. To support its implementation by clinicians, Santana and colleagues developed and evaluated a training program that included a 1-h group training with theoretical and practice parts comprising three short videos of real patient cases representing consultations and actual KLIK ePROfiles as well as supporting tools (paper with summary of information in ePROfile and decision tree to aid integration of PRO data) [4]. The KLIK program has been adopted in eight pediatric centers with more than 7600 consultations. Over 3 years, an average of 70% of patients/parents completed one or more PROs prior to consultation. End-users evaluated this program during its development to identify barriers and facilitators to real-world implementation that could be modified when introducing other technology-based assessments [37].

The Symptom Monitoring and Systematic Assessment in Young Survivors (SyMon-SAYS) is a patient-centered technology-based symptom monitoring system that alerts clinicians regarding patient symptoms in real-time to enable proactive treatment [38]. The feasibility and acceptability of implementing SyMon-SAYS in a pediatric oncology clinic, with initial focus on fatigue, was investigated in a group of 57 patients (7–21 years) and their parents. Patient–parent dyads completed weekly fatigue assessments over 8 weeks via the Internet or interactive voice response by telephone. Clinicians received alerts concerning fatigue reports that exceeded a predefined limit of 10 points (1 standard deviation) worse than the general population norm or 10 points worse than the participant's own score from the prior week. Patients, parents, and clinicians each had access to graphic reports of fatigue scores prior to clinic visits at 4 and 8 weeks. The majority of patients and parents felt SyMon-SAYS was easy and satisfying to complete and facilitated fatigue management; however, most also reported clinicians did not discuss child's fatigue at clinic visits. Clinicians reported insufficient time to read SyMon-SAYS reports, yet the majority were willing to receive monthly reports. Additionally, the majority of children and adolescents preferred to complete the survey via the Internet rather than by telephone.

Pain is one of the most common and distressing symptoms reported by children and adolescents with cancer [39]. The Pain Squad™ smartphone-based real-time pain app has been developed to better track its occurrence, intensity, and impact [15, 40]. Using a law-enforcement-based gamified method to encourage maximal adherence, children and adolescents (8–18 years) report pain twice daily. The validity (including responsiveness) and reliability of Pain Squad™ have been demonstrated, and the app is also feasible for use by children with cancer pain (e.g., satisfactory to complete, high adherence to pain reporting that did not decline over time) [41]. Pain Squad™ is now publicly available for download (https://itunes.apple.com/ca/app/pain-squad/id929781246?mt=8). The app also provides real-time advice including pharmacological, psychological, and physical interventions for pain management. A randomized controlled trial with the app is underway.

Pain Buddy is a gamified tablet-based app developed by Fortier and colleagues for children undergoing cancer treatment [42]. It includes both symptom monitoring capabilities and evidence-based cognitive-behavioural intervention training and a symptom trigger system which ensures healthcare providers are aware of problematic symptoms. Feasibility testing among 12 participants (8–18 years) confirmed the appropriate delivery of alerts to clinicians and the app's acceptability among patients.

The *Computerized Symptom Capture Tool* (C-SCAT) is delivered via an iPad and uses a symptom heuristics approach to facilitate a visual representation of the patient's self-reported cancer symptoms, how the individual perceives the symptoms as being related to one another, how the symptoms cluster together, the priority symptom in each cluster, and the potential causes of the symptoms [43–45]. The C-SCAT targets AYAs with cancer and includes the 32 symptoms included in the MSAS [35]. The app has been shown to be both feasible to implement into clinical practice (i.e., completed by AYAs in an average of 25 min, considered an accurate description of symptoms by AYA, few associated technical issues) and acceptable to AYAs [44]. In addition, C-SCAT has been used to collect data from a cohort of 70 AYAs (13–29 years) receiving chemotherapy and was successful in documenting the symptom experience of these young patients. A recently completed follow-up study including 85 AYAs (15–29 years) demonstrated that use of the C-SCAT improved self-efficacy for managing symptoms [45].

Recognizing the challenges of assessing cancer symptoms in young children, including those who may not yet be able to read, the Sisom computer-based animated symptom communication tool has also been developed and evaluated using a phased approach. Using Sisom, children can report symptoms and psychosocial concerns in multiple formats (i.e., as text on the screen, read aloud, as an animation in which a cartoon avatar experiences the symptom). The tool has undergone usability testing with Norwegian (9–11 years), American (6–12 years), and Canadian (6–12 years) children with cancer which has shown the tool to be easy to use and understand for this group [46–48]. Further psychometric evaluation has involved comparing children’s (7–12 years) and their parents’ capacities to communicate symptoms using Sisom to the more routinely used MSAS 10–18 tool [35, 49]. This comparison indicated that both children and parents were more likely to report a given symptom using Sisom, indicating a potential clinical utility advantage of the tool over traditional symptom assessment methods.

8.2.2 Passive Health Monitors

In recent years, the field of “wearable technology” has evolved. The most common form of this technology is the fitness tracker, but additional options include biosensors embedded in tattoos, contact lenses, tooth sensors, and textiles [50, 51]. An obvious advantage of wearable technology is the minimal burden placed on the user relative to the vast data that can be produced. However, passive data collection alone cannot lead to improved outcomes unless the data are reviewed, interpreted, and interventions are planned based on the data. In fact, some patients have commented on the insights and catharsis that are associated with the process of active monitoring (e.g., submitting electronic diary entries) [7].

Activity trackers are a subset of passive health monitors. Data from sensors (fitness trackers) and ePRO measures allow key indices of patients' functional status to be collected between regular clinic visits, supporting clinicians in the delivery of patient care. The benefits of physical activity prior to and following cancer treatment have been well documented and have been shown to improve symptoms such as pain, fatigue, anxiety, depression, and sleep disturbances [52, 53]. Many wearable activity trackers (e.g., "smart watches", "smart pedometers") are commercially available and can be used to help promote physical activity and capture this data to be integrated with other PROs. Most of these trackers include a pedometer to record steps and some also include measures of intensity of physical activity. Activity trackers can be useful in assisting patients in the self-monitoring and management of activity and sedentary behavior habits by promoting motivation to increase physical activity as described later in this chapter. Research assessing the accuracy of these trackers compared to research-grade devices, however, is limited [54].

Actigraphy is a non-invasive method of monitoring human rest and activity cycles. A small actigraph unit, also called an actimetry sensor, can be worn for a week or more to measure gross motor activity. The unit is typically worn on the wrist. The movements the actigraph unit are continually recorded and the data can be later read to a computer and analyzed offline or analyzed in real-time for some versions. Actigraphy is ideal for exploring the impact of interventions to improve sleep and well-being in children [55, 56]. However, the cost of these devices may be prohibitive for some research projects.

8.3 Technology to Deliver Supportive Care

Technology can be used to deliver supportive care by providing online psychosocial support or self-care advice. The Internet provides a mechanism of communication without time, or geographical constraints which can be beneficial to patients with chronic conditions [57–59].

Internet-based support has also been incorporated as part of interventions to support physical activity in children and families undergoing active treatment and those in survivorship.

Advances in treatment protocols have meant children with cancer are increasingly treated as outpatients in ambulatory settings. This change in treatment location has resulted in a shift in responsibility for care from healthcare professionals to patients and their families. Consequently, the importance and impact of self-care advice for these patients is growing. Specific technologies used to deliver self-care advice include tablet/smartphone apps, videophone, Internet, and fitness trackers.

8.3.1 Online Psychosocial Support

Specific mechanisms in which researchers have used technology to provide online psychosocial support for children with cancer have differed. Maurice-Stam and colleagues developed *OK Onco Online,* an online cognitive-behavioural-based group intervention for adolescent survivors of cancer [60]. An existing face-to-face program was adapted to an online program with the aim of enabling participation unlimited by geography. Adolescent cancer survivors participated weekly in six 90-min online chats and home exercises in four intervention groups each with three participants. The program taught coping skills including information seeking, relaxation, social competence, and positive thinking. Participants reported a preference for the online format although clinicians delivering the program acknowledged that conversations online took more time than face-to-face. As a consequence, fewer topics could be covered in the allocated time.

Seitz and colleagues developed *Onco-STEP* for adolescent and young adult survivors of cancer [61]. *Onco-STEP* contains two online modules: “Looking back” is designed to prevent post-traumatic stress symptoms resultant from cancer treatment; “Looking ahead” encourages participants to deal with fears of relapse and cancer progression. Over a period of 5–6 weeks, participants undertook 10 writing assignments each taking approximately 45 min to complete. Participants received tailored feedback to each assignment from their personal therapist via secure web-based messages. Of the 31 participants assigned the intervention, 20 fully completed the assignment. More than 80% of participants indicated treatment components were at least partly helpful and 90% would recommend to a friend in a similar situation. However, the study was limited by a small sample size, self-selection of participants (mainly well-educated females), and no comparison group.

Raj and colleagues' website "A Survivor's Journey" provides AYA survivors of childhood brain tumours with an opportunity to complete five self-guided web-based content sessions and weekly videoconferences with a clinician [62]. The intervention was designed after focus groups with pediatric brain tumour patients and their parents. It includes tailored sessions based on the survivors' developmental levels and teaches a problem-solving process. No results of subsequent evaluation of the program have been published.

JTV Cancer Support is a website which enables young people (11–25 years) to share their experiences with cancer primarily through uploading videos (https://jtvcancersupport.com/) [63]. Gibson and colleagues conducted a virtual ethnography by analyzing longitudinal video diaries of 18 young people. They evaluated how social media can be used by young people with cancer as well as whether this is a suitable method for understanding this population. Qualitative content analysis enabled identification of four typologies which reflected participants' cancer journey: treatment and unrelenting side effects; rehabilitation and getting on with life; relapse and facing more treatment; and coming to terms with dying. The authors reflected that the video diaries enabled intimacy and honesty in participation as well as relieved participants of potential constraints of questionnaires or interviews (e.g., being forced to focus on the researcher's priorities rather than on what matters most to the them). Video diaries were identified as a source of "natural data". Although the paper did not set out to explicitly describe the therapeutic benefit of video diaries on those creating or watching them, the authors reported that participants benefitted from practical, emotional, and social insights around dealing with cancer as a result. Some participants referred to the camera as a friend to whom they could express thoughts which would not otherwise be disclosed.

To address prolonged isolation, Higuchi and colleagues conducted a pilot project to evaluate telecommunication between children 7–14 years of age undergoing HSCT with their family, friends, teachers, and classmates [64]. Participants telecommunicated with the hospital school and their homes a majority of the days while hospitalized (64.6% and

68.0% of days, respectively). Furthermore, participants used this technology despite experiencing numerous transplant-related toxicities.

These papers suggest technology can be used to provide psychosocial support to children with cancer. Of note, most of these studies included AYAs. Online forums, however, may be less adaptable to younger children. Psychosocial support is likely to be most effective when utilizing social networks available through online platforms as have been demonstrated in two of these three papers. The Internet enables AYAs to select their chosen level of anonymity and match this with their chosen level of intimacy both of which facilitate provision of psychosocial support.

8.3.2 Technology-Based Solutions for Self-Care Advice and Patient/Family Education

In addition to symptom tracking apps, apps have also been developed to provide self-care advice and education to survivors of childhood cancer and families of those receiving treatment. *The Aftercare App* for smartphones was developed by Kock and colleagues with the aim of supporting long-term follow-up care to survivors of childhood cancer [65]. This tailored smartphone app was evaluated in a pilot study of 13 participants (aged 15–17 years) in Germany who had completed cancer therapy. The participants and their family members completed a quantitative survey and provided positive feedback. The *Oncology Family App* targets parents of children with cancer with information, management plans, and resources including “when to call”, “information”, “blood results table”, and “statewide hospital contacts (relevant to Australia and New Zealand)” available via smartphone [66]. The team tested the app with nine staff members and six families of children with cancer prior its release. Six months after the app’s release it had been downloaded 498 times. The team interviewed 38 parents (26 of whom had downloaded the app) for additional feedback. The most used modules were “when to call” and the “blood results table”. The parents provided some suggestions to improve the app but gave “overwhelmingly positive” feedback [66].

8.3.3 Telehealth

Remote appointments are growing in popularity for both primary and specialist care [67, 68]. Telehealth helps bring care closer to home for children with cancer and their families by linking patients with their health care team when they are not in the same location, using Internet-based videoconferencing. Members of the oncology team consult directly into family's homes allowing services to be tailored to patients' needs and ultimately to provide greater access to specialized care, reduce travel times, and shorten wait times. Potential benefits of telehealth services including reduced barriers to access, cost-savings in terms of travel, and time off work for parents reduced wait times for access to care and clinician travel time. These benefits are of particular relevance for individuals living in remote, rural communities, those with mobility issues, and situations in which parents are not readily able to take time off work.

In 2006, Bensink and colleagues found evidence of the efficacy of videophone technology via personal computer, webcam, and dial-up modem for reducing anxiety and distress in a child with cancer by improving social interaction between the patient and family during his prolonged hospitalization for a stem cell transplant [69]. In 2008, Bensink and colleagues used the same technology with eight families, with the purpose of connecting the families to healthcare providers in the initial weeks after the children's new cancer diagnosis [70]. The researchers used software installed on the families' home computers and their home phone line. The technology was used by seven of eight participants. All families were satisfied with the care delivery system and there were few technical difficulties. No detrimental effects on the nurses' workload were detected. However, the research team had to abandon attempts at conducting randomized controlled trials using this technology with pediatric palliative care patients due to recruitment difficulties [71]. This technology is now obsolete with the ubiquitous availability of smartphones.

Bradford and colleagues examined the cost of providing pediatric palliative care services via Home Telehealth Program (HTP) using video consultation in Queensland, Australia. Using a cost minimization analysis, they compared the HTP with costs associated with face-to-face consultation during either hospital-based or home visit consultations from the pediatric palliative care service. They found the videoconferencing in the home was the most economical means of providing consultation with the large cost avoided due to clinician and patient travel. Telehealth can ensure equity in access of care and minimal disruption to the hospital-based care teams [72].

Bradford and colleagues also examined the effectiveness of telemedicine consultations undertaken in patient's homes in the context of pediatric palliative care in a sample of 50 consults via telehealth compared to 50 face-to-face consultations. They found that telemedicine consults were just as effective as face-to-face consultations in terms of the key components of palliative consultations [73].

8.3.4 Technology-Based Interventions to Promote Physical Activity

Several studies have incorporated one or more aspects of technology to promote physical activity among children and adolescents undergoing cancer treatment and those who have completed therapy. Selected examples of interventions include use of activity trackers as well as web-based interventions with additional personal messaging (Table 8.2). Several research groups have demonstrated the usability, feasibility, and acceptability of fitness trackers as an intervention to promote physical activity in children and adolescents with cancer [74], including in conjunction with social media-based peer groups [75] or a health coach who monitors fitness progress and provides real-time feedback [76, 77].

Table 8.2 Technology to promote physical activity

Author/year	Name of technology	Type of technology	Description of intervention	Supporting evidence	Evidence of applicability up
Götte [76]	Fitbit One and Fitbit Flex	Fitness tracker	Sample: 40 pediatric oncology patients aged 8–17 years Compared intervention to usual care Activity	A significant increase in step goals and HRQL was found in the intervention group from T1 (during treatment) to	This study de and acceptab physical activ fitness tracke

trackers recording step counts, number of active minutes, daily walking distance, and calories burned (worn either in the pocket or on the wrist) provided to patients along with a personalized 6–8 week exercise plan followed by a 2 week transition to aftercare	T2 (shortly after treatment completion). A marginal but significant increase in the number of active minutes between T1 and T2 but that value remained relatively low. No significant differences were noted between the intervention and control groups at T2 for step goals or active minutes
Data uploaded to password protected website with a dashboard that summarized metrics. Participants' goals were determined by their baseline weekly average steps while striving for a pre-determined	The participants rated this intervention as meaningful (94%) and motivational (80%) and easy and simple (86%) The percentage of children scoring below normative values for strength was greater in

			increase of 10% per week	control group. Furthermore, the control group lacked assessments at T1	
Hooke et al. (2016) [77]	Fitbit	Fitness tracker	Sample: 17 children with ALL aged 6–15 years Fitbit combined with coaching to increase steps per day prior to corticosteroid pulse with the aim of reducing fatigue	Intervention found to be feasible for a subset of children A non-significant trend towards increased steps was associated with the intervention Significant negative correlations were noted between fatigue at the end of a 5-day steroid pulse and participants' step counts from the week prior to the steroid pulse and the steps during the steroid pulse	Difficulties w technology m implemented
Huang et al. (2014) [17]	Fit4Life	Text message and internet	Sample: 38 youth aged 8–18 years with BMI >85% who had	When compared to controls who received a 4-month phone	Widespread text messagi easier to imp

			survived ALL 4-month web, phone, and text message delivered weight management intervention for childhood ALL survivors. Weekly web-based informational materials were delivered along with twice daily text messages and weekly phone counselling sessions. Topics included calorie reduction, tracking food and beverage intake, food selection when dining out, and the importance of engaging in daily physical activity	and mail delivered intervention, improvements in weight, weight-related behaviour, and psychological outcomes were found among the older participants (≥14 years). Intervention reported as feasible	
Le et al. (2017) [74]	Fitbit	Fitness tracker	Sample: 19 youth and young adults with cancer	Non-significant increases in total weekly	High retentio feasibility. La groups neede impact

aged 15–35 years Fitbit records daily calories burned, number of steps, distance in miles, flights of stairs, and overall movement. An interactive website enables participants to monitor progress Participants completed baseline PROs, wore a Fitbit for 6 months, used an Actigraph accelerometer for 7 days, and participated in a cardiac stress test	moderate to vigorous physical activity and maximal volume of oxygen (VO2) were found. No change in barriers, preferences, and beliefs regarding physical activity Survey responses indicated no change in barriers, preferences, and beliefs regarding physical activity. Fitness trackers show promise in promoting physical activity in children and youth with cancer but studies with larger sample sizes and control groups need to be conducted to demonstrate

				impact on clinical outcomes	
Mendoza et al. (2017) [75]	FitBit Flex + Facebook	Fitness tracker and social media	Sample: 60 patients aged 14–18 years who were >1 year post-cancer treatment Fitness tracker (FitBit) combined with peer-based virtual support group (Facebook) to promote physical activity in adolescent and young adult childhood cancer survivors	Evidence of intervention feasibility and acceptability found. No significant differences in physical activity but modest changes in quality of life and motivation for physical activity	Results are a

Hooke and colleagues aimed to reduce fatigue resultant from a corticosteroid pulse by combining Fitbit technology with coaching to increase the number of steps taken daily by children with acute lymphoblastic leukaemia [77]. The refusal rate among eligible patients was 40%. The study participants had a baseline daily step count of greater than 10,000 steps/day and relatively low mean baseline fatigue levels. The intervention was found to be feasible for a subset of fairly active children. A non-significant trend towards increased steps as a result of the intervention was noted. Of note, the participants did not experience an increase of fatigue during a pulse of steroids, differing from prior studies without interventions to promote physical activity.

Mendoza and colleagues aimed to increase physical activity in survivors of childhood cancer [75]. They combined Fitbit technology to track physical activity, with a Facebook group which provided incentives and a forum for encouragement and discussion of physical activity. The intervention was feasible and acceptable for youth aged 14–18 years at least 1 year after finishing cancer treatment. However, the researchers detected no significant differences in physical activity as a result of the intervention.

Götte and colleagues evaluated the feasibility and impact of a home-based intervention using activity trackers in 40 pediatric oncology patients aged 8–17 years compared to a usual care group on daily steps and achievement of goals for active minutes, motor performance, and health-related quality of life (HRQL) [76]. Patients used either the Fitbit One (worn in the pocket) or Fitbit Flex (worn on the wrist). They found a significant increase in step goals in the intervention group, but active minutes remained low in both groups.

Le and colleagues conducted a feasibility study in which they asked 19 youth with cancer to complete baseline PROs, wear a Fitbit for 6 months, use an actigraph accelerometer for 7 days, and participate in a cardiac stress test [74]. Feasibility was confirmed with a high retention rate of 79%, and device worn an average of 19 days per month in months 1–3 and 15 days per month in months 4–6. Results included non-significant increases in total weekly moderate to vigorous physical activity and maximal volume of oxygen (VO_2). Survey responses indicated no change in barriers, preferences, and beliefs regarding physical activity.

Huang and colleagues developed *Fit4Life*, a weight management intervention targeting survivors of childhood acute lymphoblastic leukaemia (ages 8–18) using a combination of website, phone, and text messages [78]. The control participants received weight management materials via phone and mail. The educational materials were more often successfully delivered in the intervention group than the controls (80% vs 50% delivery rate). A subset of participants in the intervention group, those ≥14 years, demonstrated statistically significant less weight gain and more physical activity than control participants. All participants reported decreased negative mood. This pilot study demonstrated feasibility of the *Fit4Life* program.

The use of technology shows promise in promoting physical activity in children and youth with cancer, but studies with larger sample sizes and control groups need to be conducted to demonstrate impact on clinical outcomes.

8.3.5 Technology to Support Medication Adherence

Oral medication nonadherence is a well-documented problem among children and adolescents receiving treatment for cancer and those undergoing HSCT [79–82]. Reasons for nonadherence are complex and are described in greater detail in Chaps. 3 and 6. Because of the widespread adoption of smartphones [1] and that "forgetfulness" is the most frequently reported reason for nonadherence, medication reminder apps have been proposed as a solution to support adherence [83, 84]. Over 25 apps that address cancer therapy or cancer medication management are available through either the iTunes App Store, Google Play, or both [85]. Other non-cancer specific apps that provide medication reminders are also widely available to consumers at no or minimal cost.

Two reports from one study provide initial evidence regarding the potential utility of medication reminder apps [86, 87]. This study included 23 AYAs who were receiving at least one prescribed oral medication related to their cancer or its supportive care. AYAs endorsed the app as easy to use, and those with greater perceived overall adherence reported taking medications right away when receiving alerts [87]. Overall, participants' adherence did not change, however, the variance in adherence narrowed among AYAs with higher levels of adherence. One small subgroup of patients with low baseline adherence levels, however, did experience improved adherence following introduction of the app [86].

Electronic monitoring caps provide an objective measure of adherence, and several brands are commercially available. The caps are designed to fit commercially available medication vials and contain a sensor that records the date and time a vial is opened. At the conclusion of the data collection period, data are transferred from the caps via a near field communication (NFC) reader and then exported as a computer file for analysis. Users must also maintain a log for occasions in which a vial was opened but a dose was not taken to support an accurate assessment of adherence.

Two nurse-led studies including pediatric and adolescent oncology patients have used electronic monitoring caps as measures of adherence. These studies provide evidence regarding patients' perceptions of adherence. Landier and colleagues monitored oral medication adherence among 416 children with acute lymphoblastic leukaemia over a 4-month period [80]. When comparing self-reported to electronically monitored adherence, 84.4% of participants overestimated their adherence. More poorly adherent participants were also more likely to over-report their adherence. Linder and colleagues identified that 22 of 23 AYA participants missed at least one medication dose during a 12-week study period, and even some of the more highly adherent AYAs did not achieve a weekly average of 90% adherence [86].

8.3.6 Technology for Procedural Distraction

Finally, a novel technology is presented by Jibb and colleagues who tested the feasibility of an interactive robot which uses dancing and singing behaviours, or employs evidence-based cognitive-behavioural interventions, to reduce pain and distress in children with cancer undergoing painful procedures [88]. While the use of the robot did not decrease pain associated with subcutaneous port accesses among 4- to 9-year-old children, its use did decrease procedural distress and it was highly acceptable to children, parents, and nurses.

8.4 Technology to Deliver Staff Education

Technology to support education offers a growing range of opportunities to facilitate pediatric oncology nursing education and to expand the dissemination of that education. As an example, distance-based technologies are presently used by professional organizations, including the Association of Pediatric Hematology/Oncology Nurses to deliver educational webinars to national and even international audiences [89]. Options for education delivery include both a synchronous approach, in which learners participate in the learning activity as it is being offered, and an asynchronous approach, in which the educational activity is made available for learners to access at a time and place of their choosing. Despite the growing use of technology to support pediatric oncology nursing staff education, research addressing the effectiveness of technology-based modalities is sparse.

Vadaparampil and colleagues reported outcomes of an 8-week web-based training program to enhance nurses' knowledge of fertility and reproductive health issues for AYAs [90]. Nearly three quarters of the 77 participants had improved post-test scores. At 6 months following completion of the training, 54 participants reported practice-related improvements including review of institutional practices, provision of additional staff education, provision of new resources targeted at AYAs, and development of new policies.

The Children's Oncology Group (COG) Nursing Discipline developed multimedia educational modules to support nurses' access to education regarding clinical trials [91]. Modules were developed as portable document format (PDF) files that could be accessed asynchronously via the COG website. A survey of 106 nurses attending a COG annual meeting revealed that only 59 reported being aware of the modules, and only 30 had viewed at least one module. These nurses were more likely to be 40 years of age and older and hold a graduate degree. Nurses who had viewed at least one module endorsed their ease of use and satisfaction with the content. Lack of time was reported as a barrier by those nurses who had not accessed the modules.

Technology-based resources used by patients may offer opportunities to educate clinicians about patient's unique experiences. Clinicians including pediatric oncology nurses endorsed digital stories created by children and AYAs with cancer as impacting them professionally [92]. These professionals gained greater understanding of patients' backgrounds by "standing in the midst" of their stories. They also endorsed the potential for these digital stories to be of benefit as part of new staff education.

Low-fidelity simulation (e.g., the use of case studies, role play) and medium fidelity simulation (e.g., the use of static mannequins or human actors) have been an integral part of nursing education in pediatric oncology for decades. High-fidelity simulation has emerged in recent years, with the ability to incorporate computer-controlled mannequins that demonstrate physiologic responses. Few publications regarding the use of simulation among oncology nurses are available [93–98], but numerous posts about simulation can be located on the APHON Member Connection discussion board. The evaluation of simulation education programs is generally limited to student proficiency rates and improvement in post-test scores. The evaluation of patient outcomes after simulation education implementation is rarely studied. The complex nature of evaluating outcomes for rare patient events in hospitals that are implementing numerous changes undoubtedly contributes to the low rates of patient outcome assessments. For example, Page and colleagues reported on the use of simulation training to reinforce nurses' training of central line care [96]. Rates of central line associated blood stream infections (CLABSIs) were monitored, but the hospital introduced new policies for central line dressing changes and caps during the study time frame. High-fidelity simulation is not appropriate for all training situations. High-fidelity simulation is costly and labour intensive. Furthermore, inexperienced staff members may be overwhelmed during the training sessions and may feel frustrated if they respond inappropriately to the mannequins' cues.

Effective concepts of technology-based nursing education can be adapted for use in patient and family education. Currently, critical patient/family training may be delivered in less than ideal circumstances (e.g., in a rushed manner, with frequent interruptions, or delivered to a single family member). Technology-based solutions may allow nurses to reach key family members during teaching sessions, use strategies best-matched to an individual's learning styles, and more thoroughly assess learner comprehension.

8.5 Evidence-Based Findings Related to the use of Technology in Pediatric Oncology That is Ready for Translation to Clinical Practice to Support Precision Health

Electronically Delivered PROs Questionnaires and other PROs are commonly administered via websites that are accessible on desktop computers or mobile devices. Not all users prefer this method of questionnaire delivery, so paper tools may also be required in certain circumstances.

Use of Medication Reminder Apps Although evidence regarding the efficacy of medication reminder apps to support adherence is limited, preliminary evidence suggests they are likely to be appealing to AYAs. Because many are downloadable at no or minimal cost, it is reasonable to consider implementing these apps as an adherence-boosting intervention. Nurses caring for patients receiving oral medications need to be aware that reminders, in and of themselves, are not the solution but may be a part of the solution for some patients and families. Staff need to ensure that families are aware of how to manage entries within such apps so that the patient's schedule can be updated at home if medication plans change between visits.

Technology to Support Education Selection of a given type of technology for use in education should be guided by established best practices regarding teaching and learning, including considerations for distance-based learners. A given technology should be selected for its potential merits in achieving the objectives for the learning activity rather than its novelty or potential appeal alone.

8.6 Areas for Future Research Related to the Use of Technology in Pediatric Oncology Nursing to Achieve Precision Health Goals

Incentivizing Completion of Electronic Measures Despite the ongoing development of a number of digital health solutions in the context of pediatric cancer, issues related to their use and implementation in routine clinical practice and research studies exist. For instance, it is unclear how best to provide incentives children and adolescents (particularly those with significant symptom burdens) to regularly complete electronic symptom reports or interact with other digital health devices. Incentivization methods that have been proposed include monetary or gift reimbursements for completed assessments as well as gamification mechanics where game-like incentives (e.g., point gathering and levelling) are embedded in the assessment tool [99]. To date, no study, including in the field of pediatric oncology, has evaluated the relative effectiveness of these different techniques to maximize adherence. Issues related to child access to Internet-enabled devices have also been raised, but are becoming less problematic with the increasing prevalence of device use by children, adolescents, and parents [100].

Psychometric Evaluation of Digital Health Resources With regard to the development and evaluation of technology-based solutions for pediatric cancer patients, future research in several veins is needed. In particular, the majority of digital health tools have undergone usability testing, but evaluations of their psychometric properties (i.e., validity and reliability) or linguistic or cultural adaptations have not been conducted. The acceptability of health-related apps and other digital PROs requires ongoing assessment. End-users' expectations of digital solutions frequently shift as particular electronic features become mainstream.

Evaluation of the Efficacy of Digital Health Resources to Enhance Precision Health Outcomes More research is needed to address how technology may support achievement of precision health goals. This includes identifying how end-users, whether patients or parents, interact with apps to understand how these resources may or may not support improved utilization. Studies with larger sample sizes of patients who are more homogenous with regard to age, disease type, and stage of treatment are also needed to identify predictors of patients who are more likely to benefit from the use of the technology. Research is also needed to explore distal outcomes related to technology-based interventions, including quality of life, survival, relapse-free survival, as well as unanticipated outcomes.

Strategies to Support Analysis Generated from Digital Health Resources Some digital health solutions lead to vast quantities of data that invoke the need for complex statistical analysis. Indeed, the emerging field of "big data" requires new data storage and analytic procedures.

Implementation Studies There are also current knowledge gaps related to how well these tools can be implemented into pediatric oncology practice (e.g., impact on clinical workflow, privacy concerns, and the capacity to integrate with electronic medical records) and the best method to enable this implementation. Finally, evaluations of how these tools can empower communication between patients and clinicians about the child's symptom experience and the impact of these tools on symptom management are required.

Research addressing system-wide factors that may enhance digital health interventions is needed. Optimizing electronic health record (EHR) systems to support nurses in assessing and monitoring adherence has contributed to improved adherence among adults with cancer receiving oral chemotherapy [101]. A similar approach may also benefit children and adolescents and will likely involve interprofessional collaboration among informatics specialists. Additional directions for optimizing EHR systems include supporting interoperability of sources of patient-generated data within EHR systems. This process also includes mapping terms used within these measures to standards-based terminology that are included in internationally recognized databases such as SNOMED CT [102] and LOINC [103] to support comparison of patient-generated measures across settings.

Establishing Best Practices for Technology-Delivered Education More research is needed regarding learner preferences for the use of technology-based education as well as learner outcomes using different technology-based modalities. Additionally, research addressing achievement of longer-term patient-focused outcomes as a result of the educational activity is needed. Strategies to foster nurses' utilization of available educational resources are also needed.

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9. Exercise and Physical Activity

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Abstract

Physical activity during treatment is an important way to promote health and quality of life for children with cancer. Nurses play a pivotal role in creating and supporting physical activity interventions. In this chapter we present information on the impact of a cancer diagnosis and treatment on a child's activities and physical functioning. In addition, we offer evidence that nurses can readily translate into their practice to promote physical activity in this vulnerable population. By applying principles of precision health offered in this chapter, the nurse can identify the child, family, disease, and environmental factors that influence physical activity and use this information to develop successful interventions across the childhood cancer trajectory. The chapter also offers insights into the role that nurses play in mobilizing resources to address barriers to physical activity, including multidisciplinary care and family influences. Finally, we examine the state of the science about physical activity and childhood cancer and suggest avenues for nursing research to expand the frontier of this important field.

Keywords Physical activity – Exercise – Childhood cancer – Treatment impacts – Interventions – Precision health

9.1 Background

Child's play is an idiom, which according to Merriam-Webster, expresses an extremely simple task or something that is insignificant. Yet for children, play is a critical form of physical activity and for the child with altered health conditions can be anything but simple or insignificant. Physical activity is any movement that uses skeletal muscles and requires the body to expend energy. Among school-age children all forms of physical activity have positive associations with markers of physical, psychological, behavioral, and developmental health [1]. The benefits of physical activity in childhood are not limited to childhood but may have protective cardiometabolic effects that continue into adulthood [2]. Regular physical activity benefits cognitive development in children [3], and can improve executive function which plays an important role in social development and academic achievement [4]. Physical activity is also important for the development of gross motor skills needed to perform activities of daily living [5, 6].

9.2 Impact of Cancer Diagnosis

The diagnosis of cancer presents a challenge to the child or adolescent's ability to be physically active. The child/adolescent's normal routine is disrupted with time spent in the hospital and clinic. The loss of structure from physical education classes within the school day to loss of participation in organized community-based physical activity such as sports teams and classes such as dance and gymnastics contribute to a decrease in physical activity yet developmentally appropriate physical activity is part of normality during childhood [7].

Symptoms from the cancer itself as well as side effects and toxicities can deplete energy and a sense of wellness that normally contribute to an active life [8]. In examining the evidence on the impact of a pediatric cancer diagnosis on exercise and physical activity for this chapter, studies were included if 50% or more of the study sample had children or teens in active treatment or within the first year of completing treatment. Physical activity in the survivor population is addressed in Chap. 14.

Research has shown that over the trajectory of treatment, children and adolescents become less physically active than their health peers, and their physical performance is negatively impacted. Changes in physical activity and performance can occur early in treatment; the loss of physical function and activity can negatively impact other symptoms including fatigue and sleep as well as quality of life. Before being diagnosed with cancer, 130 children, adolescents, and young adults ages 4–23 years self-reported physical activity levels that matched healthy norms; after 3 months of treatment, there was a significant decrease in physical activity and exercise minutes [9]. In their study in which they assessed the feasibility of evaluating physical performance during the first three months of cancer treatment, Nielsen [10] found that children ($n = 31$) ages 6–18 with leukemia had significant decreases in lower extremity function while other diagnostic groups ($n = 44$) did not experience reductions. A relationship between physical performance and fatigue early in treatment was found in 16 children with mixed cancer diagnoses measured twice during the first three cycles of chemotherapy treatment. When children increased the distance they covered in a 6 min walk test, indicating improving physical performance, fatigue decreased from the first cycle of chemotherapy [11]. This group of 16 children combined with 14 adolescents was compared to healthy norms for age and gender; 86% were 2 or more standard deviations below the means for healthy children, with 28% greater than 4 standard deviations below the norm showing how deconditioned they were within months of starting treatment [11]. Levels of physical activity early in treatment may be protective from symptom distress in children with acute lymphoblastic leukemia (ALL). In a sample of 327 children ages 3–18 undergoing ALL treatment, those who were more physically active by self-report at the start of post-induction therapy had a decrease in the severity of the symptom cluster that included fatigue, sleep disturbance, pain, nausea, and depression, during the first year of treatment [12].

As treatments progress, deficits in physical activity and physical performance persist. Physical activity was evaluated by activity monitor in 80 children ages 5–18 years in active treatment for cancer and compared to levels in healthy matched controls [13]. In the home environment, children with cancer had 40% of the gait cycles of their healthy peers; this decreased to 23% during inpatient stays [13]. Among a cohort of 60 children ages 10–18 years in active treatment for mixed cancer diagnoses, over half were more than 2 standard deviations below the predicted VO_2 peak value for cardiorespiratory fitness [14]. Their level of physical activity measured by actigraphy was positively correlated with cardiorespiratory fitness and negatively associated sedentary behavior [14]. Additionally, children who were more physically active had significantly less fatigue [14]. The benefit of physical activity in decreasing symptom distress was also seen in a group of 36 children receiving chemotherapy for mixed cancer diagnosis; higher levels of physical activity measured by actigraphy over 7 days was associated with improved sleep quality and efficacy [15]. Understanding the trajectory of physical activity during treatment, and the correlation between diminished physical activity and distressing symptoms such as fatigue will help the nurse to make appropriate recommendations and offer guidance to patients and families.

In addition to a decrease in levels of physical activity and physical performance, side effects of treatment can impact on the functional capacity needed for physical activity. Barriers to effective walking and running include impairments in ankle dorsiflexion and ankle range of motion, motor proficiency, muscle strength, and coordination that can occur secondary to neurotoxic chemotherapy. During the first months after starting cancer treatment, children with mixed cancer diagnoses ages 5–18 were significantly weaker in all muscle groups and knee flexion compared to their age and gender-matched controls [16]. Their muscle weakness was significantly correlated with lower quality of life [16]. In a cohort of 18 children ages 5–10 years with leukemia or lymphoma and within 10 months of completing chemotherapy, the children with cancer performed significantly worse in the standing broad jump, shuttle run, and hand grip test than their healthy peers [17]. Juan et al. evaluated 15 children ages 4–10 years receiving maintenance therapy for ALL and found that children with ALL had significantly lower VO_2 peak, active ankle dorsiflexion and range of motion, and quality of life than their healthy matched peers [18]. When children with ALL ages 4–12 had motor skills evaluated over the trajectory of ALL treatment and compared to healthy, matched controls, children with ALL had problems with daily life motor skills [19]. Problems with balance were more prevalent during the first two months of treatment while manual dexterity became worse at the end of the first year of treatment [19]. A small group of 8 children ages 4–15 years with ALL were measured before delayed intensification and demonstrated significantly lower mean knee extension strength, ankle dorsiflexion strength, and slower timed up and go test than healthy, matched controls [20].

Researchers are beginning to explore interventions to improve functional capacity in children with cancer which is needed as a foundation for improving physical activity. A 4-month individualized physical therapy intervention program that included home exercises for children ages 4–15 years, in maintenance ALL treatment, resulted in significantly improved ankle dorsiflexion active range of motion and knee extension strength in an intervention group of 13 children compared to 15 control patients receiving usual care [20]. More recently, researchers evaluated outcomes of a proactive physical therapy intervention, ‘The Stoplight Program’, in children ages 1–22 years who completed interventions that included outpatient physical therapy visits and home exercises personalized by developmental level and three level of functional performance across the trajectory of treatment [21]. At the baseline during consolidation, a standardized test assessment of 52 children showed that 46% of 1–5 year olds and 67% of 6–22 year olds had abnormal motor function. Ankle range of motion deficits peaked during delayed intensification and improved by maintenance therapy. Forty-three children completed the program interventions and measurements; all successfully met normative standards for motor function for their age [21]. Further research is needed to expand personalized interventions to diagnostic groups beyond ALL and to remove functional barriers to physical activity. This includes addressing ankle dorsiflexion and ankle range of motion, motor proficiency, muscle strength, and coordination.

9.3 Precision Health Principles

There is no one-size-fits-all approach when it comes to promoting physical activity in children, and this is particularly true in pediatric oncology where disease and treatment variables are important considerations. We have discussed the role of disease and treatment on physical activity and now we will focus on additional individual considerations for the child with cancer. Consideration of the child, family, environment (including cultural/lifestyle considerations), and disease/treatment effects on physical activity is integral for provision of precision health recommendations (Fig. 9.1). Available research upon which to make individual recommendations about physical activity is growing but insufficient to make specific practice advice [22]. Exercise intervention studies have shown improvement in body composition, flexibility, cardiorespiratory fitness, muscle strength, and health-related quality of life, but are often small, limited to children with leukemia or lack sufficient study design to show definitive effects [23].

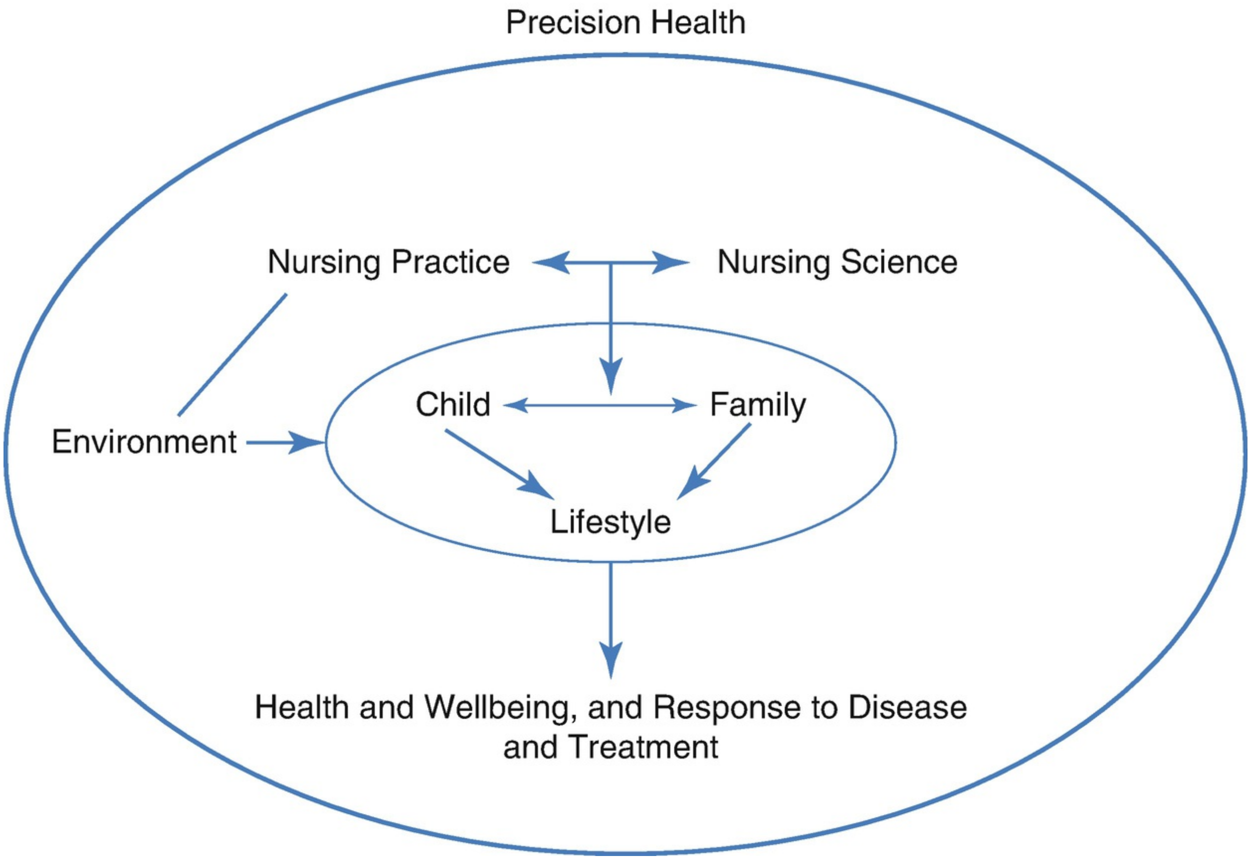

Fig. 9.1 Influence of nursing practice and nursing science on child and family health and response to disease (cancer) and its treatment within the context of precision health

9.3.1 Child Considerations

It is important to understand both the presenting and pre-diagnosis activity levels, which may be quite different. Children with cancer may present at diagnosis in a deconditioned state due to disease burden or complications. For example, children with bone tumors may present with pathologic fracture or soft tissue mass that has disrupted usual forms of physical activity [24], gait changes and mobility deficits often accompany the diagnosis of a childhood brain tumor [25], and baseline anemia or infection causing fatigue is a common presentation for childhood leukemia. Beulertz-Dipl et al. [26] reported that a targeted training schedule based on baseline function can significantly improve impairments in coordination, fine motor function, and in endurance and strength in children with cancer. Understanding and evaluating the present level of physical activity will be important for determining what recommendations should be considered early in the disease course.

Beyond the presenting level of physical condition it will be important to consider what the child's physical activity was prior to any disease symptoms. Sedentary lifestyles prior to treatment will likely be one of the most challenging situations and finding activities that are appealing to an individual child will be key in the nurses' strategy to promote physical activity. Children who were physically active prior to diagnosis will likely be the easiest to persuade to be active, but these children may find a decline in physical functioning during treatment disheartening and will require encouragement from family and staff. Discussing with the child and parent what was enjoyable and what goals they have for physical activity will help identify activities that are safe and appropriate in and out of the hospital setting. Understanding current and prior levels of activity will help the nurse determine the impact of the disease and treatment; therefore acknowledging inactivity as a side effect to be treated with the same consideration as any other acute toxicity [7].

Attention to physical activity changes throughout development, and consideratuin of the child's developmental level when recommending activities will be important. For example, the toddler who has only recently begun to walk may spend significant amounts of time in a crib for safety reasons during hospitalization. The lack of opportunity to practice this new developmental skill may delay or even diminish the ability to stand or walk independently. Nurses should be prepared to offer the family suggestions on ways to safely allow the toddler the opportunity to explore his/her environment and promote the gross motor skills necessary for development. The impact of inactivity during childhood cancer treatment is striking with up to 91% of children scoring below age/gender-matched normative data for important developmental measures of coordination, flexibility, speed, and strength at the end of the acute phase of treatment [27]. Further, deficits in fundamental movement skill attainment (sprint, side gallop, vertical jump, catch, over-arm throw, kick, and leap) are seen in children who have completed cancer treatment, potentially impacting the ability to maintain healthy lifestyles and development going forward [28]. Nurses can play an important role in monitoring the achievement and maintenance of developmental milestones during treatment.

Understanding motivation and anticipating barriers to physical activity for the individual child are other important components that nurses should consider when tailoring activities for the child with cancer. Motivation to be physically active can come in many forms; for some, the desire to achieve or maintain physical fitness is important while others may find it a distraction from treatment and therefore improves mood and brings a sense of normalcy. Further facilitators of physical activity during treatment will include access to equipment and space for activities. Significant barriers may exist and will require equal consideration including disease/treatment side effects, psychological impact (example frustration with current physical condition), and environmental constraints (example isolation and treatment interruptions) [29]. Self-efficacy (the belief in one's abilities) and physical activity are important considerations when tailoring physical activity recommendations for the child with cancer. Studies have shown that self-efficacy can be enhanced through physical activity interventions using theoretical frameworks, such as Social Cognitive Theory and Kolb's Experimental Learning Theory, where improvement in self-efficacy is associated with higher levels of physical activity [30, 31]. Physical activity in a group setting or adventure training with peers with similar fitness/skills are examples of activities used in the research setting that have been shown to have sustained effects on improving physical activity and self-efficacy in childhood cancer [32]. Nurses can impact the balance of motivation and barriers in numerous ways; for example, timing medications or infusions around opportunities for physical activity, recognizing, and commending the child's participation in activities and engaging the family and other providers in promoting the importance of staying active. In addition, nurses should consider engaging disciplines such as social work or behavioral psychology to develop individualized physical activity plans that focus on assessing and building self-efficacy.

9.3.2 Disease and Treatment Considerations

Encouraging physical activity, especially during treatment, will require support from all members of the health care team and family. Even in a structured research intervention, including nursing and physical therapy, it is difficult to impact physical activity early after diagnosis [33]. Despite the challenges of promoting physical activity during treatment there is evidence that interventions which include walking, running, or playing during treatment can have a positive impact on health-related quality of life [34]. The intensity of treatment and projected side effects are important considerations for recommending physical activity during treatment, lower intensity treatment times such as maintenance therapy for acute lymphoid leukemia presents an opportunity to introduce increasing physical activity levels. For example, a home-based exercise program with video instruction and coaching phone calls has been shown to improve flexibility, fitness, and motor function during maintenance therapy [35]. The potential impact of common disease and treatment side effects, as well as suggestions for appropriate actions and modifications that will allow the child to safely participate in physical activity are listed below (Table 9.1).

Table 9.1 Cancer impact on physical activity

Disease/side effect	Impact on physical activity	Suggested modifications and interventions
Anemia	Fatigue, limited energy	Transfusions as medically needed Balance of rest and activity, prioritize important activities
Thrombocytopenia	Risk of bleeding with activities	Transfusions as medically needed Avoid contact sports and activities with injury risk
Peripheral neuropathy	Numbness/tingling of extremities or muscle weakness make activities more difficult or painful	Referral to physical therapy for evaluation and treatment of muscle weakness Referral to occupational therapy for education about safety
Immunosuppression	Restrictions on group physical activities	Identify activities that limit exposure via close contact. Consider possible precautions such as masks or hand sanitizer. Plan activities that avoid nadir of blood counts
Pain	Some physical movements may increase pain. Pain medication may	Referral to physical therapy to recommend activities least likely to amplify pain. Schedule pain medications to maximize pain relief before activities

	make patient drowsy	and assess drowsiness to ensure patient safety
Balance/coordination dysfunction	Increases risk of injury and diminishes satisfaction with physical activity	Work with physical therapy/occupational therapy to identify any assistive devices that will decrease the risk of injury. Provide safety and emotional support as the patient trials physical activities that accommodate balance/coordination issues
Osteoporosis osteopenia/low bone density	Weight bearing physical activity essential to building bone density. Contact sports increase risk of fracture	Emphasize physical activity that focused on balance and strength training to reduce risk of fracture with falls

Adapted from Tanner and Thompson (2014). Practical Aspects of Physical Activity in Pediatric Oncology. Pages 61-102. In C. Chamorro-Viña, M. Keats, S. N. Culos-Reed (Editors). POEM; Pediatric Oncology Exercise; Professional Version, 1st Edition. Retrieved from: https://www.ucalgary.ca/poem/about-pro

9.3.3 Family Considerations

Family participation remains as a strong influence on physical activity of children [36]. Baseline activity level and attitudes towards physical activity and exercise are often woven into the fabric of family structure and culture. Understanding the family's baseline physical activity beliefs and influences is a good starting point for nurses as they work to promote physical activity in patients. The family that places high value on physical activity and regularly engaged in exercise and activity prior to diagnosis will have fewer barriers to re-instituting physical activity during or after diagnosis. Conversely, the family that was not previously active will have more difficulty in engaging in physical activity with and after diagnosis [37]. Nurses should consider asking the family about types of family activities, engagement in physical activities/sports, recreation activities, and preferences for family time as a means to gauge baseline physical activity.

Children often express interest in engaging in physical activity with family members and frequently report that they prefer the involvement of parents [36]. Engagement in physical activity as a family functions to foster relationships between children, siblings, and parents in times of psychological and physical challenge during treatment [38]. During treatment, children with cancer will often withdraw from participating in physical activities with their peers due to easy fatigue, fear of injury, strained social relationships, and safety concerns [38]. This provides the opportunity for families to function as a medium for physical activity by providing an inclusive environment tailored to the needs and abilities of the patient. Physical activities provide time with family outside of the caregiver-patient roles and allow parents and siblings to provide care and emotional support in new ways [38]. Interventional studies suggest that family-centered physical activities allowed parents to better understand the needs and abilities of their children while undergoing treatment [38]. Children with cancer readily recognize the importance of physical activity but believe that their cancer diagnosis creates safety barriers to engaging in exercise regularly [37]. Helping families overcome these presumed barriers and providing activity recommendations tailored to the patient and family unit will provide physical, psychological, and social benefit to patients.

Parents will understandably have some anxieties about their children engaging in physical activities due to their diagnosis. Oftentimes, children cite fatigue, concern for infection risk, gastrointestinal symptoms, pain, dizziness, and weakness as physical barriers to engaging in physical activities [36]. Psychological barriers to activity engagement of families include lack of energy, low moods, minimal motivation, preference for alternate activities, and fear of injury [36]. These physical and psychological barriers to family activities and exercise may be difficult to overcome in addition to organizational challenges of treatment introduced by the time constraints of treatment, physical equipment, lack of space, and lack of equipment. The nurse should be aware of these anxieties from families and patients when recommending physical activity and ensure that they ask parents and patients about their fears of activities and make safe and attainable recommendations that the patient and family have interest in. Nurses stand in a pivotal role in working with families to promote physical activity with their children while undergoing treatment for cancer. By understanding the influences on family physical activity and being able to articulate the benefits of activity as a family, nurses can assist in motivating and encouraging children to maintain physical activity.

9.3.4 Environmental Considerations

Treatment compromises the normal development and physical ability of children with cancer. Frequent hospitalizations and lengthy admissions interfere with time in which children can be active at home where they are most comfortable. A diagnosis of malignancy immediately interrupts and halts normal daily life for patients and families and changes the normal capacity for physical activity [7]. Children undergoing treatment for cancer live between the environments of home, hospital, and clinic, and sometimes school (depending on their treatment regimens and side effect profile). As such, nurses should consider ways to promote healthy and safe physical activity tailored to the patient's ability and environment.

Assessing the home situation requires inquiry of the parents or caregivers about the type of home (number of stories, stairs, size, presence of indoor/outdoor play space, individuals living in the home, resources for activities including pool, yard space, proximity to parks, sports equipment), preferred activities around the home, playmates nearby, and family activities. Research suggests that most school systems are unsure of their expectations with regard to promoting physical activity in children undergoing therapy [36]. They are often willing to increase exercise, but report communication gaps with the medical team in how to approach this goal safely. Nurses can help coordinate disciplines, for example, physical/occupational therapy and child life, to make appropriate recommendations for physical activity and ensure communication to the family and applicable community resources.

Organizational aspects of treatment like timing of medication administration, length of infusions, scheduled imaging or radiation, procedure prep and recovery time, and other constraints limit the time patients have to engage in physical activity. Medical equipment like central lines, intravenous catheters, IV poles, mobility devices, and splints/braces limit the physical ability for children to remain active. Furthermore, hospital environments are often not built with the goal of promoting physical activity and lack the physical space and resources to promote activity in children. Children report that they want to implement normal activities of life while in the hospital and will frequently report that hospitalization makes them feel restricted in their movements and activities leading to feelings of isolation and loneliness [7]. Families have also reported that they feel as though the medical team does not spend time engaging in education about physical activity in the hospital [36].

Promoting healthy physical activity requires the nurse to draw upon foundations of nursing education and skill; holistic patient care, time management, education, and health promotion. Research shows that in-hospital physical activity interventions are feasible and beneficial [39, 40]. A literature review including 10 studies with 204 pediatric oncology patients showed positive trends in health status in children who participated in physical activity interventions without any reported adverse events [41]. Another in-hospital exercise program for pediatric cancer patients resulted in improvements in muscle strength for patients with solid tumors [42] and a review of rehabilitation interventions aimed at physical activity in this population found improvements in functional mobility [43]. Just because in-hospital physical activity interventions are possible, does not mean they are easy to implement. Nurses will have to work with their patients to set individual goals for activity tailored to the physical ability of those they care for. This includes working with patients to identify times for activities, determine types of activities they can (and want to) participate in, advocating for physical therapy and occupational therapy involvement in care, and understanding the child’s functional limitations. Interventions to manage pain, discomfort, nausea, anxieties, and other symptoms should be provided prior to activities. Nurses should ensure that the activities in which children participate while in the hospital are safe, taking note of the patient’s platelet counts and immune function at the time. When patients transition back to home and school, nurses should work with parents and school staff to communicate expectations of physical activity and determine safe activities for patients. The nurse may need to also function as a motivator, and continue to promote physical activity at home and in the hospital; reminding patients of the benefits of physical activity and recruiting the appropriate team members and specialists along the way. Finally, as with any good intervention, nurses should make sure a member of the child's health care team is responsible for following up on interventions and routinely checking in on physical activity during treatment, regardless of the environment in which the patient spends their time.

9.3.5 Cultural Considerations

Multiple studies have shown that cultural factors and parents' perspectives may affect the physical activity levels of children with cancer [44, 45]. For example, Chinese culture is strongly influenced by the philosophy of Confucianism, which emphasizes the achievement of balance and harmony in everyday life through the concepts of "chung" and "yung" [45]. In this philosophy, cancer or other chronic diseases are regarded as "bad spirits" that are aggravated by physical activity, thus violating the rule of harmony [46]. Therefore, many parents of Chinese children with cancer may advise further rest and the avoidance of any high energy-consuming activities, including physical activity [47]. These children also have relatively low levels of body resistance and a high susceptibility to infection. Accordingly, many Chinese parents forbid activities performed outdoors or near crowded public places, particularly during seasonal outbreaks of influenza. These restrictions consequently affect their physical activity levels of children with cancer [44].

The Western literature also describes physical inactivity among children with cancer [29, 48, 49]. These children are often advised by their parents to take more rest and reduce physical activity, with the intent to avoid cancer- or treatment-related fatigue. However, these recommendations can actually accelerate fatigue, as physical inactivity induces muscle catabolism and atrophy [50] which may lead to a further decrease in functional capacity [48]. Nurses must correct these misconceptions about physical activity held by children with cancer and their parents and, most importantly, advocate the principle of regular physical activity for these children with the aim of enhancing their physical and psychological well-being.

9.4 Physical Activity Impact on Health and Well-

Being

9.4.1 Fatigue

Cancer-related fatigue is a debilitating and long-lasting adverse effect, and one of the most distressing physical symptoms reported by hospitalized pediatric cancer patients [8, 51, 52] and cancer survivors [44, 53]. Previous studies indicate that approximately 70% of cancer patients receiving treatment and up to 30% of survivors report a sense of fatigue [48, 54]. This clinical symptom is generally defined as a subjective and persistent sense of tiredness and/or exhaustion that cannot be relieved by rest [55]. Although the cause of cancer-related fatigue remains unclear, it is thought to be related to low-grade inflammatory responses elicited by the disease and treatments (e.g., chemotherapy and radiotherapy) [53].

Fatigue is a highly debilitating condition in children. This sensation can cause physical weakness and demotivate them from participating in daily activities, particularly physically demanding exercises [9, 56]. An increasing body of evidence suggests that a low- to moderate-intensity exercise program can attenuate cancer- or treatment-related fatigue, increase muscular strength and endurance, and improve physical functioning [49, 57]. Additionally, a study on the relationship between physical activity and fatigue revealed a significant association between these parameters. Specifically, a lower level of physical activity was found to be associated with a greater occurrence and severity of fatigue in children with cancer [58].

Numerous studies of children with cancer have described the adverse effects of cancer and related treatments on various aspects of physiological well-being, including cardiorespiratory function, muscle strength, and functional capacity [6, 8, 28, 59]. However, cancer and its treatments may also adversely affect the psychological well-being of children with cancer. Depression is one of the most commonly experienced psychological sequelae among children with cancer [60]. Previous studies of Chinese children with cancer revealed that more than half were potentially at risk of depression or presented with depressive symptoms [61]. These findings were consistent with previous studies of Western populations [62, 63] that observed a potential risk of depression in a majority of hospitalized children with cancer.

9.4.2 Depression

A study of the relationships between fatigue, physical activity, depressive symptoms, and quality of life has been limited to childhood cancer survivors; this research has revealed an association of a lower physical activity level with an increase in self-reported depressive symptoms [58]. However, scientific evidence indicates that exercise can stimulate the secretion of endorphins (hormones that trigger feelings of happiness) and thus reduce depressive symptoms during cancer treatment [64, 65]. Therefore, when promoting physical activity among children during cancer treatment, nurses should understand the psychological well-being of their patients and be able to detect any depressive symptoms.

9.4.3 Quality of Life

Increasingly, children with cancer are able to achieve curative responses. Therefore, the paradigm of care has shifted from acute treatment to a long-term emphasis on adverse treatment effects and quality of life [66]. To better understand the effects of cancer and its treatment from the patient's perspective, the National Cancer Institute in the USA emphasizes the importance of assessments and evaluations of patients' quality of life during and after active treatment [67]. The World Health Organization defines quality of life as an individual's perception of their position in life, including physical health, psychological status, level of independence, and social relationships, in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns [68]. The promotion of physical and psychosocial well-being, and particularly the quality of life, should be a primary concern of healthcare professionals with regard to children with cancer.

Numerous studies have described the benefits of regular physical activity in terms of improving the quality of life of children with cancer [69–71]. Specifically, scientific evidence indicates that regular moderate-intensity physical activity may ameliorate some of the adverse treatment-related effects experienced by children with cancer and could eventually improve their quality of life [34, 66]. In a study of the relationship between physical activity and quality of life, Lam et al.

observed markedly reduced current physical activity levels in children with cancer, compared with their pre-cancer situations [59]. Moreover, these children were significantly less active during physical activity and reported a poorer quality of life than their healthy counterparts. Additionally, a regression analysis identified physical activity as an important indicator of the quality of life in children with cancer. Therefore, nurses must promote regular participation in physical activity among children with cancer, with the aim of improving their quality of life.

9.5 Evidence-Based Findings Derived from the Science of Exercise and Physical Activity in Pediatric Oncology Ready for Translation to Clinical Practice

Development of Best Practices for Promoting Physical Activity

Over the past few decades, regular physical activity has been promoted increasingly among children with cancer and cancer survivors. Adequate evidence suggesting that regular physical activity can enhance an individual's physical and psychological well-being makes this an opportune time to translate this evidence into nursing practice [12]. Specifically, regular participation in moderate-intensity physical activity may ameliorate adverse treatment-related effects, such as depression, fatigue, and decreased muscle strength and endurance, and thus may eventually improve the quality of life of children with cancer [34, 66]. However, the abovementioned misconceptions must be corrected, and the benefits of regular physical activity must be promoted to children with cancer and their parents. Moving forward, research is needed to evaluate appropriate and effective interventions intended to promote the adoption and maintenance of a regular physical activity habit among children with cancer.

A review of the literature revealed that educational approaches are most commonly used to increase awareness of the importance of physical activity among children with cancer and translating these educational approaches into practice is an important step toward promoting physical activity [72]. However, a substantial body of evidence indicates that education alone is unlikely to change behavior [73] and further research is needed to identify new approaches to increasing physical activity beyond patient/family education. Some evidence suggests that a combination of adventure-based training based on experiential learning theory and an educational approach can effectively promote physical activity, reduce cancer-related fatigue, and enhance the physical activity self-efficacy and quality of life but has been only been evaluated in childhood cancer survivors [30, 74]. However, adventure-based training occurs in outdoor environments and involves activities that consume high levels of energy, which may be inappropriate for children in active cancer treatment and those with physical impairments due to cancer and its treatment. Furthermore, the sustainability of this type of approach is uncertain, and it may be costly to offer each participant the opportunity to participate in a 4-day program at a campsite.

Finally, Lam and colleagues developed a set of physical activities appropriate for children with different types of cancer and used experiential learning theory to enhance the children's physical activity self-efficacy [75]. In that study, children with cancer were encouraged to adopt a regular physical activity habit by participating in an integrated experiential training program comprising 28 home visits by coaches over a 6-month period. Notably, children with cancer who received the integrated program with coaching reported significantly lower levels of cancer-related fatigue, higher levels of physical activity and physical activity self-efficacy, greater right- and left-hand grip strength, and a better quality of life at a 9-month follow-up, compared to the participants who received usual care. The benefits of this approach are well documented and appropriate for translation selectively, depending upon child diagnosis and other factors. Although the integrated program may be appropriate for children with different types of cancer, the provision of 28 home visits by coaches within a 6-month period may be infeasible and could potentially require extensive resources. Moreover, the long-term effects of the integrated program on engagement in physical activity among children with cancer or cancer survivors remain uncertain. Future research looking at the feasibility and outcomes of physical activity programs that are integrated into the trajectory of cancer care is needed.

Translation to Practice

During cancer treatment, physical activity is associated with less symptom distress and is vital for ongoing development of the child during treatment. Nursing interventions to translate into practice when caring for children receiving treatment include:

1. Assess current level of physical activity and activity level pre-diagnosis
2. Identify inactivity as an acute toxicity of cancer and its treatment
3. Assess for barriers to physical activity including the home, hospital, and school environment, cancer symptoms and treatment side effects, attitudes of family and friends
4. Mobilize resources to address barriers including interdisciplinary health care and team and referral to rehabilitation services and
5. Identify activities patient and family enjoy and support them in developing goals for integrating them into family routine
6. Educate parents on the importance of physical activity in maintaining health during treatment and advancing development
7. Normalize physical activity as part of daily activities during hospitalization
8. Modify physical activity recommendation in response to the patient's disease and side effects

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9.6 Future Research Recommendations for the Science of Exercise and Physical Activity in Pediatric Oncology

Research is also needed to identify interventions that are innovative, cost-effective, and sustainable for promoting physical activity in the pediatric oncology population. Numerous interventions intended to promote physical activity among children with cancer have been discussed in the literature and throughout this chapter. However, no perfect or best practice has been identified. All interventions depend on the availability of resources and the nature of cancer, particularly in terms of the effects of the disease and treatment on the physical conditions of children. We must also consider cultural and environmental factors, as well as the children's and parents' perspectives on physical activity. Nevertheless, oncology nurses should continue to plan, develop, and evaluate appropriate interventions to promote physical activity that are innovative, cost-effective, and sustainable.

Some promising areas of inquiry that should continue to be pursued include family involvement, motivational interviewing, and the use of technology to promote physical activity (Chap. 8). Previous studies revealed that parents play influential roles in their children's participation in physical activity [76, 77]. Therefore, an alternative sustainable approach may involve encouraging parents to act as role models and promote their children's adoption and maintenance of a regular physical activity habit. Some evidence suggests that parents who participate in motivational interviewing (MI) can effectively promote behavioral changes, including those related to weight loss and eating habits, in their children [78, 79]. However, traditional MI is intensive and generally requires several sessions with durations exceeding 30 min. Therefore, MI is not feasible for busy parents. Alternatively, a brief MI that emphasizes the use of shorter and simpler strategies [80] could be proposed. Brief MI would share the same core as regular MI in that individuals would advocate the initiation and continuation of behavioral changes.

Current recommendations suggest the use of information communication technology (ICT); e.g., WhatsApp/WeChat, for brief MI and the provision of continuous support to parents as they motivate their children to engage in regular physical activity. ICT is increasingly used to promote health and deliver care. The World Health Organization defines new medical and public health practices and strategies supported by mobile devices as mobile health [81]. Instant messages delivered by mobile devices through services such as WhatsApp and WeChat are used widely to promote health and treatment compliance [82]. Instant messaging allows the rapid, direct, and continuous delivery of professional advice and support to parents and thus helps them to manage their child's level of physical activity. Brief MI can be performed instantaneously and accessed at the recipient's convenience. Instant messaging is also more time-saving and cost-effective than face-to-face meetings and offers a flexible platform for mutual communication through which parents can elicit feedback and interactions. Nevertheless, more rigorous empirical scrutiny of the effectiveness of brief MI and ICT for the promotion of physical activity among children with cancer is warranted.

Finally, nurses may need to expand their usual roles and form multidisciplinary partnerships with tertiary institutions and non-profit voluntary organizations, with the intent to sustain long-term programs promoting physical activity among children. Additionally, governments should provide more recreational and sport facilities to increase the accessibility of such programs.

9.7 Recommendations for Future Research

1. Develop and evaluate guidelines for physical activity during cancer treatment
2. Evaluate new approaches to increasing physical activity beyond patient/family education
3. Measure feasibility and outcomes of physical activity programs that are integrated into cancer care
4. Explore motivational interviewing interventions with parents to role model healthy habits with children.
5. Expand nursing roles in promoting physical activity as part of nursing care

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10. Treatment Decision Making

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Abstract

Treatment decision making (TDM) is complex due to the varying decisions which have to be made about diagnosis, treatment options, toxicity, and outcomes of treatment. Shared decision making is complicated by the triadic relationship of parent/caregiver, child and clinician typical in pediatric care. Increasing attention on how best to incorporate child and adolescent and young adult (AYA) voices in decision making is described. We review TDM from the various perspectives of those involved in making decisions about treatment, including parents, children, AYAs, family, and the health care team. Those involved in TDM bring with them their individual characteristics that include values, preferences, past experiences, and cognitive abilities. Interwoven with these influences are the person's environment, social determinants, and relationships. We incorporate into our discussion the available research literature concluding with what is ready for translation into clinical practice and recommendations for future research to fully understand the varying perspectives and factors which influence TDM and the nurse's important role in supporting children and their families.

Keywords Cancer – Communication – Decision preferences – Family – Patient–provider relationship – Pediatric oncology – Shared decision making – Treatment decision making

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There has been an explosion in the amount, complexity, and type of data available to care for patients in the twenty-first century. In previous generations, the health care team relied on relatively simple data that were easily obtained and processed including the history and physical exam. In simpler times, data included the personal knowledge of the patient's background, family, and living situation of which the clinician obtained from living in the same community. There is now recognition and incorporation of many more and varied sources of data that require accumulation, analysis, and interpretation, and ultimately consolidation into a better understanding of the patient from the perspective of one's specific disease, situation, and goals. This endeavor now encompasses the topic of precision health. Precision health incorporates data, not just from the traditional history and physical, but personal information such as behavior, preferences, environment, lifestyle, socioeconomic status, and culture. In addition, new technologies account for personal data, like genomics, proteomics, metabolomics, microbiomics, and new ‘omics yet to come. The ultimate goal of precision health is to prioritize and interpret every source of data possible to help the individual patient achieve optimal health and well-being, and treatment decision making (TDM) is one aspect of the pediatric oncology health care experience.

Throughout the cancer disease trajectory, there are specific time points when decisions are required, such as at diagnosis, disease recurrence, end-of-life, or for unforeseen complications. Pediatric cancer is no different. These decisions can be complicated by inexperience with cancer, uncertainty, risk, emotional stress, and the need to make decisions quickly. The decisions required in children’s cancer treatment can be difficult due to their high-stake nature and the vulnerability of the patient. Another group of decisions that has received less attention but are nonetheless important are the everyday decisions of self-care or symptom management. These decisions may be foreign at diagnosis, but the patients and families often develop a familiarity with them.

Research in the field of TDM has grown over the years and is necessary to optimally care for children with cancer and their families. It is now evident that TDM entails more than making a final therapy choice. It also includes the exchange of information that takes place throughout the decision-making process. In this era of precision health, designing personalized interventions in TDM must include the child, family, and their lifestyle at the core. While we acknowledge the child, adolescent, or young adult is part of TDM for cancer, his/her role is complicated and ever-changing.

Through application of the precision health framework, we will discuss current, well-developed approaches to TDM by illustrating the following roles and influential TDM factors for: (1) children, adolescents, and young adults, (2) parents and the family, (3) nursing and the health care team, and (4) environment and social determinants. We will also describe the evidence-based outcomes of TDM regarding child and family health and well-being. Additionally, we provide guidance on how to apply the current nursing science to practice, and provide suggestions on how we can advance science further through the lens of precision health.

10.1 Approaches to Treatment Decision Making

Several concepts have evolved in the field of TDM and are most applicable to personalized and precision health care in pediatric oncology. The most developed approaches include patient- and family-centered care, patient–clinician communication, and shared decision making (SDM).

10.1.1 Patient- and Family-Centered Care

The idea of patient-centered care began in the twentieth century. The Institute of Medicine [1] defines it as "care that is respectful of and responsive to individual patient preferences, needs, and values," and that it ensures "that patient values guide all clinical decisions" [2]. The value of patient-centered care has been well researched and recognized in TDM practice and research. For example, incorporating patient-centered preferences into decision making has been shown to increase satisfaction with decisions [3]. The Institute of Medicine [1] proposed that patient-centered care is an essential part of improving health care in the twenty-first century, and in 2012 the American Academy of Pediatrics issued a policy statement stressing the integral role that patients and their family members have on the health care team [2].

10.1.2 Patient–Clinician Communication

The National Cancer Institute of the National Institutes of Health recognizes that a core function of patient–clinician communication is making decisions and that communication is an essential aspect of patient-centered care in the cancer population [4]. Sisk, Mack, Ashworth, and DuBois [5] identify the content and characteristics of communication and the preferred roles of parents and children/adolescents as critical factors that clinicians must incorporate into oncology communication. The following are recommended strategies to facilitate patient-centered clinical communication: "(a) setting an agenda, (b) listening actively, (c) checking understanding, (d) offering opportunities for involvement, (e) endorsing patient participation in discussions and the decision, (f) accommodating patients' preferences, and (g) communicating empathy and warmth both verbally and nonverbally" [4] (p. 28). Refer to Chap. 13

for more detailed information on communication in pediatric oncology.

10.1.3 Shared Decision Making

“Shared decision making” was initially described in the early 1980s in the setting of informed consent, but its definition and use of the term have evolved with time [6]. The most common elements considered essential to SDM include: (a) presenting and discussing options (if options exist), (b) discussing the benefits and risks, (c) acknowledging patients’ values and preferences, and (d) making or deferring the decision [6]. Elwyn and colleagues [7] suggest a three-talk model of SDM after seeking input from SDM experts, interested community members, and clinicians: (1) Team Talk, (2) Option Talk, and (3) Decision Talk (Fig. 10.1). SDM has been described as the “pinnacle of patient-centered care,” as it is a method of incorporating the patient’s and family’s preferences, needs, and values into the decision-making process [8].

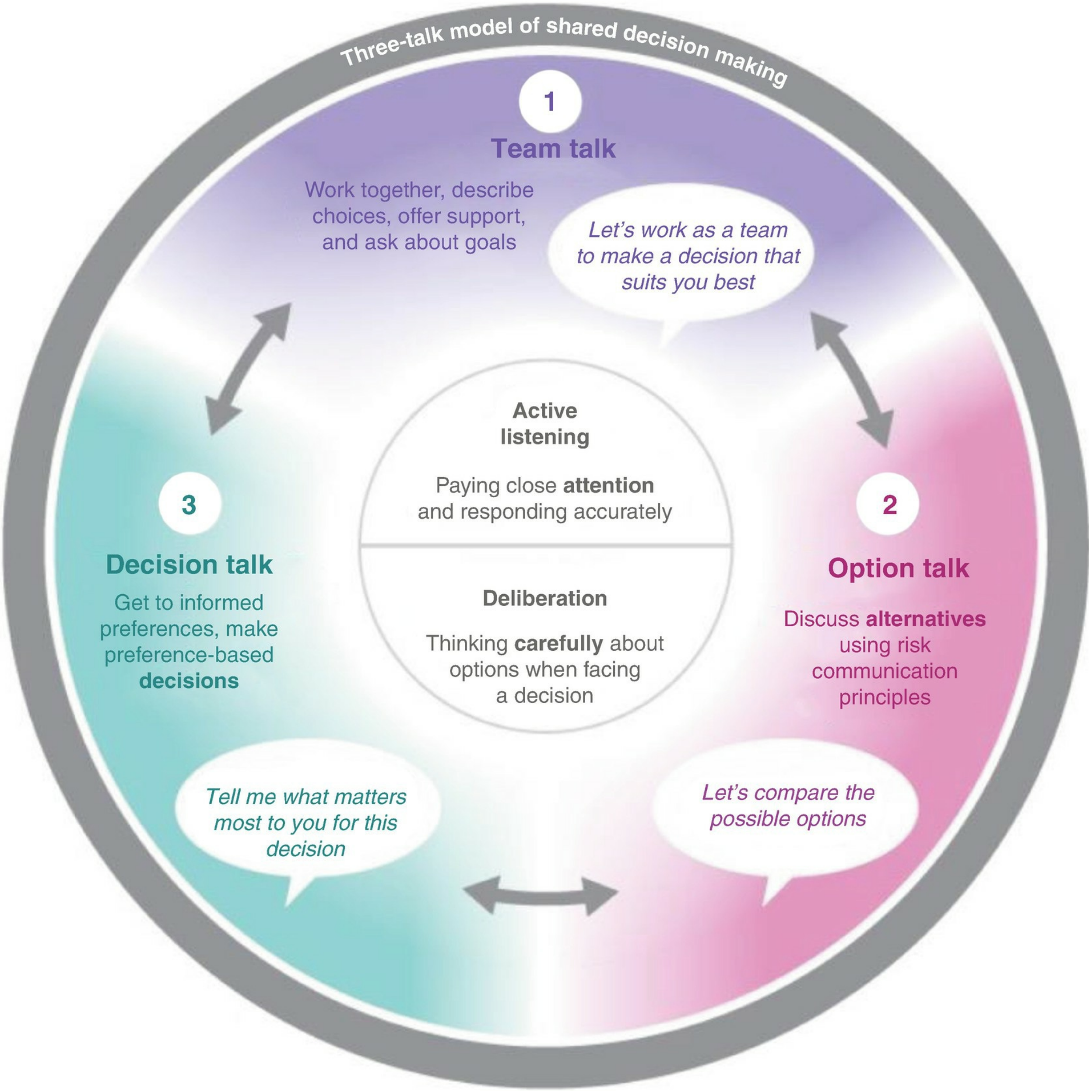

Fig. 10.1 Three-talk model of shared decision making [7] (p. 5)

Several authors recognize that SDM in the pediatric population is still in the early stages, and that it is unclear how to incorporate the child or adolescent [9, 10]. Opel [10] proposes a continuum of pediatric SDM and that SDM is not appropriate if there is only one medically reasonable option. When there is more than one option, the favorable medical benefit/burden ratio among options should be considered, and if there is a favorable option the decision should be physician-guided with a consideration of one’s preferences [10]. Morrison et al. [11] describe the amount of involvement by the clinician in SDM as “clinical directiveness.” They point out that in addition to the patient and family’s preference for involvement the health care team, quality of the decision, treatment, and seriousness of illness should be considered in determining the amount of clinician’s directiveness in TDM [11]. While Morrison and colleagues refer to the clinician taking the lead as “directiveness,” Whitney and colleagues [12] refer to it as “decisional priority.” Decisional priority happens when the clinician exercises a choice in a decision, but the priority may shift to the patient depending upon importance and certainty of the decision [12]. Figure 10.2 represents “decisional priority” in the pediatric oncology population [13].

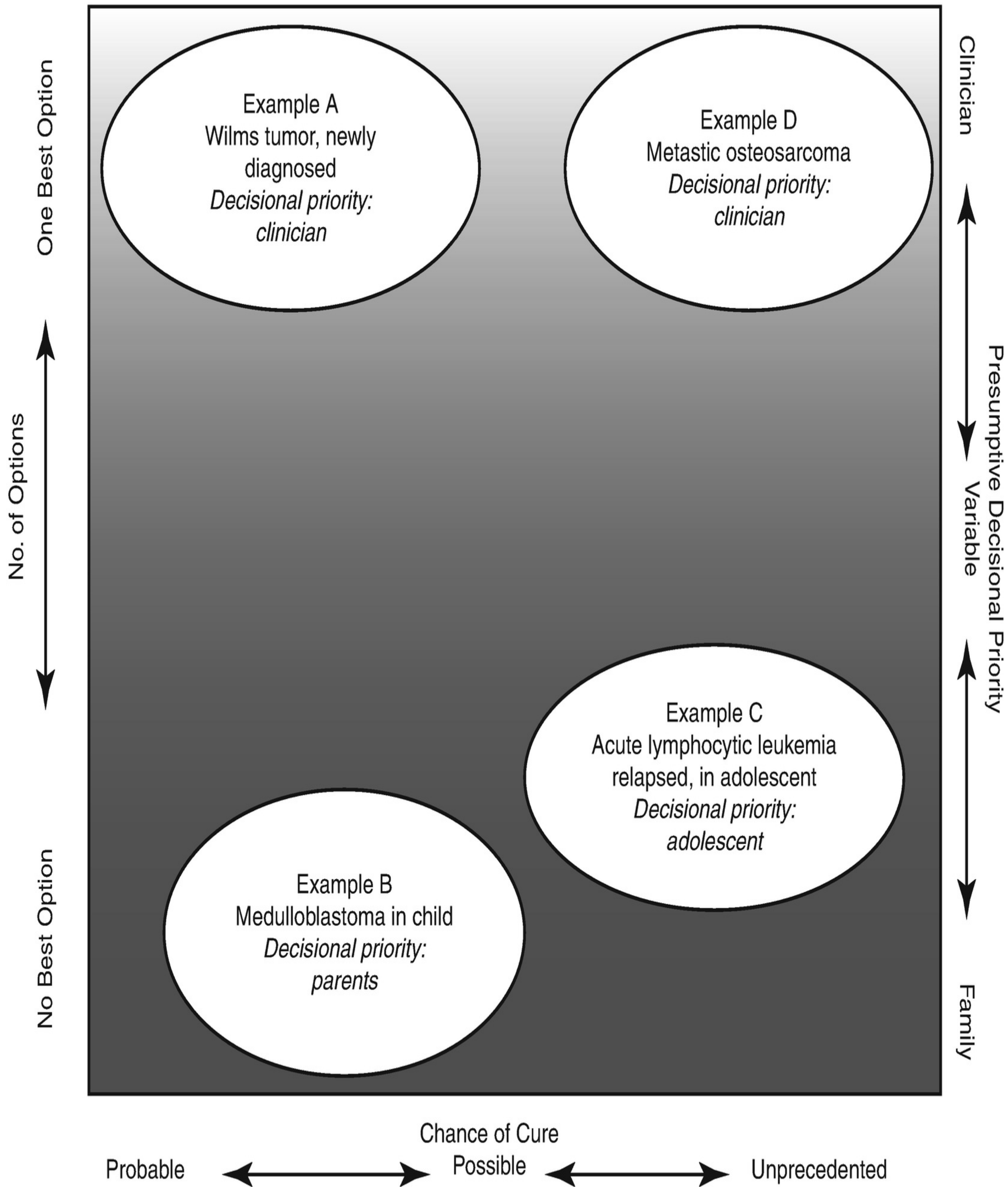

Fig. 10.2 The decisional priority in pediatric oncology model (Whitney, et al. [13], p. 162)

In caring for the pediatric oncology patient and their family, SDM describes the relationship between the family (parents), pediatric patient, and their healthcare team [14]. When there is only one viable treatment option, as may be the case in oncology, Pelletier et al. [15] suggest that “agreeing to a plan” may be a better description than SDM when describing the approach to care between the physician, patient, and family member. When there are options, Robertson et al. [16] provide the following suggestions to facilitate SDM in pediatric oncology clinical trials knowing that decision making is a process that occurs over a period of time and/or multiple occasions: (1) assessment and implementation of patient and family member’s preferences and needs, (3) encourage question asking and answer questions, (4) provide clear information, and (5) establish decision and psychosocial support.

There is some evidence that improved quality of these partnerships through SDM is associated with better outcomes for children and their families [17]. SDM may improve knowledge and expectations, satisfaction with and participation in care, and congruence of the decisions and choices of the family with their values. These, in turn, may improve the quality of care and patient safety [18]. In a recent Cochrane review though, no intervention studies promoting pediatric patient and family involvement specific to cancer decisions were identified [19]. Most of the current data as it relates to SDM and pediatric oncology is exploratory or descriptive in nature, and is elaborated throughout this chapter.

10.2 Children, Adolescents, and Young Adults

National and international organizations recognize the importance of youth being involved in their own health care decision making [2, 20–22] at a level appropriate to their age, capabilities, and experience. Guidelines promulgated by these organizations however are mostly expert opinion, with little empirical support. The term, youth, will be used to collectively include children and adolescents when used throughout the remainder of this chapter, and the phrase, adolescent and young adult (AYA), will encompass teenagers and people up to the age of 25 years.[1]

10.2.1 Involvement in Treatment Decision Making

Coyne et al. [23] (p. 274) define child and adolescent SDM as “the ways in which children can contribute to the decision making process, independent of who makes the final decision." Most studies of pediatric TDM in oncology are retrospective, cross-sectional studying research participation or end-of-life decisions, and focus on the parents' or clinician's perspective. Studies often mix child and adolescent results together, making it difficult to discern child from adolescent preferences and actual role taken in decision making. Few studies have focused only on AYAs [24]. Studies of youth or AYAs with cancer reveal preferences for involvement in TDM range from no involvement to leading the decisions [25–29]; however, they may not be involved in TDM in their preferred way [30, 31]. Adolescents, for instance, have been reported to be dissatisfied with their role in TDM and experience feelings of inadequacy [23]. They want support and prefer SDM with family and clinicians [25, 27, 31]. Wangmo and colleagues [27] found that this provided a safety net against erroneous choices.

Children have been reported to rely on their parents to protect and trust them to make decisions in their best interests [32]. Similarly, Kelly et al. [26] in their study of 29 children and adolescents aged 9–17 years with cancer found the degree of involvement in discussions was dependent on the youth's current illness state and the type of treatment decision being made. These youth felt less scared, happier, increased satisfaction, and more comfortable with decisions if they were involved either in the treatment discussions surrounding options or collaboratively making decisions with parents and health care professionals (HCPs). Through the development of their "Having a Say" construct, they demonstrated that children trust their parents and clinicians to act in their best interests, and depending on the circumstances may or may not want to participate in treatment discussions and decisions.

Older children and AYAs may want to be fully involved in TDM [33] and may make the final choice with help from parents [31]. In a Phase III clinical trial setting, Ingersgaard et al. [34] reported adolescents preferred to be the final or collaborative decision makers with their parents, in contrast to other studies where adolescents often abdicate decisions to their parents/physicians [31, 35–37]. In retrospect, older children and AYAs wished they had been more informed and/or more involved than they were in TDM [38, 39]. Robertson et al. [40]

investigated adolescents who were diagnosed within the previous year and found that they went along with their physicians' or parents' decisions, but still wanted to be informed and spoken to directly by physicians. In this study, they were satisfied with the treatment decisions because they believed the decision was the best choice or might help others.

Adolescents and young adults as a group are receiving more attention and study about their involvement in decision making. Pyke-Grimm et al. [41] in an integrative review of AYAs involvement in TDM identified five categories reflecting their involvement in TDM or influencing factors. These included: (1) AYAs' preferred/actual and/or perceived involvement, (2) age and cognitive maturity, (3) disease and illness factors, (4) information and communication, and (5) relationships, roles, and perspectives: parents and HCPs. Experience and individual circumstances might underlie the variation in AYA cancer TDM involvement and are likely to develop over time. Findings support that most AYAs rely upon parents and HCPs for advice [41].

Being autonomous in decision making was important to most AYAs studied by Pearce et al. [42]. In addition, Mack et al. [43] found no relation between level of decision-making involvement and decisional regret. Most patients between age 15 and 29 at diagnosis preferred shared responsibility. The youngest teenagers stated they wanted more autonomy than the older patients. This could reflect the adolescent desire for autonomy rather than a thoughtful decision. The majority felt their actual and preferred decision-making roles were congruent when dealing with their oncologist or parents.

10.2.2 Factors Influencing Treatment Decision Making

The involvement of youth in decision making depends on multiple variables including their chronological and developmental age, disease severity, experience with disease, urgency of the situation, and the type and enormity of the decision [29, 31, 32, 35, 44, 45]. Individual and family characteristics such as a child's health goals, style of coping, culture, family structure, and parenting in addition to how much the child is involved all influence TDM. Altruistic motives have also been identified as influencing youth's participation in specific contexts such as clinical research [28, 34–36, 42, 46, 47]. Below we describe the impact of development, relationships, and the type and timing of the decision on TDM involvement.

10.2.2.1 Development

Research on cognition and cognitive capacity has been the primary focus in exploring children's involvement in decision making [48]. The age when adolescents are competent to engage in the informed consent process (an important instance of TDM) is controversial [49, 50]. Weithorn and Campbell [51] suggest that children above 14 years of age are competent to understand the concept of consent. Children develop capacity to assent to care some time prior to 18 years of age [25, 52]. With help and supervision, adolescents are capable of actively participating in health care decision making at all phases of the treatment continuum, including decisions to participate in research studies and choices about fertility, advanced care, and end-of-life [36, 46, 53]. They should be able to understand the decision, consequences, and to some extent, weigh competing risks and values that underlie the decision.

Cancer-related treatment decision making is necessary while the child and AYA are experiencing ongoing developmental change in areas such as focus, memory, abstract thought and problem solving, ability to consider the future and to control impulsivity, and communication. In early adolescence, the frontal lobes develop slowly while deeper emotional areas such as the limbic system develop more quickly. This leads to an imbalance of power, with the decision-making priorities initially resulting in risk taking and stimulus seeking behavior [54]. Children and adolescents focus on the immediate here and now, so are therefore at risk for detrimental impulsive choices [55]. Cognitive maturation progresses, as prefrontal brain regions undergo synaptic pruning and myelination [56] with fronto-cortical areas developing dominance over executive processes such as planning and weighing of risks and benefits [57] resulting in improvement in executive functioning [58].

10.2.2.2 Relationships with Parents and HCPs

The participation of children and AYAs in TDM is complicated due to the triadic interactions and relationships between the child, their parents, and the HCP. Parents and physicians often act as gatekeepers to youth's involvement in health care [27]. Parents instinctively attempt to protect their child from the distress that they assume will be engendered if the child is burdened with information and requirement for a rapid decision [27, 45]. HCPs might not accurately assess the child's cognitive development (under or over estimate), and ability to understand and participate because they do not know the child well [25]. There is a wide range of opinions among parents and HCPs regarding how much involvement, if any, children should have in making decisions about their health care. The power differential between child, parents, and HCPs might mean their participation is not under their control. Protective parents might shield the child from information and TDM opportunities [52]. The autonomy of the adolescent is potentially limited by the parents' authority to overrule them, especially if the adolescent's preferences are not concordant with those of their parent [34].

10.2.2.3 Type and Timing of Decision

Decision points are common and vary throughout the child's disease trajectory. For example, a large number of children with cancer, approximately 70%, will participate in a clinical trial at some time during their cancer experience [59]. So not only is there a decision about treatments, but also about whether or not they pursue such treatments in the setting of a clinical trial.

There are situations when adolescents often prefer not to be responsible for making the decision, such as the time of diagnosis [33, 37]. Especially when initiation of treatment is time sensitive, TDM by youth and AYAs may be limited by the symptoms of their illness [31, 35]. There are other situations or decision points when they want to assume a more influential role [27, 36] or do not want to relinquish TDM control, such as at the end-of-life [36].

Preferences for involvement in decision making change over time and in the context of different decisions [60]. As youth journey through their disease trajectory, their preferences for involvement in TDM appear to change with experience. Around the events of diagnosis and initial TDM, parents often take control but as youth gain experience with cancer, they often want or demand to participate more actively in TDM [61, 62]. End-of-life decisions usually occur when the youth has become very experienced so it is no surprise that youth desire a high level of involvement in these decisions at the end of the cancer journey [63].

The enormity or life changing nature of the decision is a factor in youth's choice or preference to participate in TDM. In studies of SDM, for example, they are able to differentiate their participation between major (which they believe are not really decisions at all) and minor decisions (decisions about how care is delivered) [23]. Youth participate in supportive care type decisions or daily decisions related to their cancer treatment such as medication management (i.e., antiemetics, analgesics) [64, 65] and medical support during procedures (i.e., lumbar punctures, bone marrows) [66].

Coyne et al. [23] reported approximately half of the child participants preferred that major decisions be dealt with by their physician and parent(s) while the rest either wanted to share or control the decision [25]. Children did not want or could not make independent choices concerning major medical decisions such as those affecting the chance of cure [27]. Trust in their parents and physician was an important factor with children not wanting to make the "big" decisions yet they still wanted to be involved in the discussions surrounding these decisions [26]. Not having a say resulted in worry and feeling ignored when the child was not consulted on how the treatment was affecting them [26].

10.3 Parents and the Family

When a parent learns about his or her child's cancer diagnosis, they must make numerous decisions under conditions of intense emotional distress and uncertainty. They may decide where to go for treatment (although most stay at the diagnosing institution), what treatment is best for their child, and how to tell their child and other family members about the diagnosis. They also must identify options and decide about what to do about their job, childcare for siblings, and how to manage the child's treatment within their family life. Parents are also challenged by having to make life changing decisions for someone else, i.e., their child, which is very different from making a decision about themselves [67].

10.3.1 Parent TDM Across Phases of Their Child's Treatment

As with youth and AYAs, parents have varying preferences for and behaviors related to TDM across their child's illness course. These are described below.

10.3.1.1 New Diagnosis and During Initial Treatment

Parent TDM occurs either in collaboration with HCPs, independently, or having their opinions considered in the decisions of HCPs [68]. The relationship between parents and HCPs is an essential factor which influences their decision-making process [36, 68, 69]. Parents view TDM as a core function of "being a good parent" to their seriously ill child [70, 71] and strongly consider recommendations, opinions, and information provided by HCPs in their TDM [72, 73]. When parent decisions are contrary to HCPs' recommendations, parents are concerned about the potential for loss of support from the treating team [74]. Collaborative TDM is essential to ensure an optimal working relationship between parents and HCPs. Parental trust in HCPs is paramount [74] as is receiving appropriate information so that parents can make the best decision possible. Some parents prefer HCPs to make treatment decisions to reduce their distress [40]. Establishing a therapeutic relationship between parent and HCP can help parents cope regardless of their child's outcome [75].

10.3.1.2 Consolidation/Maintenance

As parents gain experience with their child's illness and treatment, their engagement in TDM grows as they come to understand the manifestations of their child's cancer, their options, and their child's responses [73]. With the passing of time, parents are exposed to numerous treatment decisions [74], especially those whose child has received multiple types of treatments or has had episodes requiring reassessment of goals and expectations. This experience instills confidence and empowerment in the decision-making process.

10.3.1.3 *Stem Cell Transplant*

Stem cell transplant can be an option or routine standard of care depending on the specific disease. The factors that influence the decision for this treatment vary between malignant and nonmalignant (i.e., sickle cell disease) diseases. Those with malignant disease have a sense of urgency to pursue transplant, while those with nonmalignant disease experience a stressful choice between options other than transplant [76]. Although anxiety provoking, stem cell transplant may be recognized by the patient and family as the treatment with the best hope of survival. Without a realistic alternative treatment choice, they rely on their physician when faced with transplant decisions [15, 76, 77]. Most families perceive there is no alternative decision to be made [15, 78], so in the situation of a sibling donor the potential donor sibling may feel excluded from the decision-making process [79]. Given the threat to their child's life, parents do not view these circumstances as decisions, but a situation where they have no choice but to proceed with the transplant to save their child's life. Pentz et al. [77] suggest that these circumstances should be framed as everyone "agreeing to a plan," rather than there being a "decision to be made."

10.3.1.4 *After Treatment Relapse*

When the disease recurs, a common decision is whether parents wish to have their child participate in experimental clinical trials, withdrawing treatment or other end-of-life decisions [80]. Parents also face everyday treatment decisions regarding symptom management. Parents who opt for participation in a Phase I clinical trial do so to pursue every option available [81]. They hope to improve the child's quality and quantity of life, reduce suffering, and hope for a cure [69, 73]. However, extending survival time or cure is commonly prioritized above quality of life by parents. Initially, at least, parents pursue cancer directed treatments even when the chance of cure is small [73], it is important that they believe that they have done everything possible to save their child's life [73].

10.3.1.5 *Withdrawing Care/Opting for End-of-Life Care*

Parents who ultimately choose end-of-life care do so to provide quality of life for their child and to respect their child's wishes [81]. Parents make these decisions based on their personal definition of "being a good parent" to their seriously ill child and consists of relieving their child's suffering [71]. Parent choices are dependent on where they and their child are in the illness trajectory [81].

10.3.2 Emotional Context: Impact on Parent TDM

The emotional impact of having a child with cancer is well known [82]. Parents make continuous treatment decisions for their child throughout the illness trajectory which leads to great emotional distress and turmoil [34, 68]. Parent TDM is influenced by characteristics of the family and the disease such as hope, uncertainty, and prognosis. Parental hope in TDM is well described in the literature. Parents may continue to opt for treatments in the hope for cure, increased quality of life, or to increase survival time even when there is less than 5% chance of cure [73]. Hope for a cure can outweigh the child's quality of life and survival time in decision making [73, 83, 84]. It is important in this context to acknowledge quality of life is subjective and what one parent may see as acceptable to their child's quality of life another parent may not.

Bereaved parents can regret the treatment decisions which they have made [85]. Parents may make different decisions prospectively depending on the information provided, their understanding of the situation, and how their child tolerated previous treatments.

Intertwined with hope is the reality of prognosis. Parents must have the necessary information to make informed treatment decisions based on realistic expectations of treatment and their outcomes. Hope is seen as an essential element in coping with having an ill child [84], however, the suffering caused by persisting in futile therapy raises ethical concerns about what is in the child and family's best interests. Ultimately, hope is a pivotal driving force in parental TDM and open honest discussions between HCPs and parents about the expectations of treatments and associated outcomes may help to support parents in choosing options which are realistic and provide quality of life for the child.

Parents' views of their child's prognosis are more accurate if their decision making is aligned with their preferences, social support, coping style, and sense of faith and meaning [86]. Alignment of parent preferences can provide an accurate perception of their child's prognosis resulting in informed decision making [80]. However, parents can continue to seek treatment due to previous experiences where their child had survived a recurrence [83]. Therefore, despite their child's prognosis parents can continue opting for treatments even when the chances of cure are low. Accurate prognostic information results in parents being well-informed which can reduce decisional regret in their treatment decisions [87].

10.4 Family Treatment Decision Making

Most research in pediatric cancer TDM has been conducted with individual family members such as the child, parent, or sibling, rather than the family as a unit or dyad. The lack of research on the family unit is likely due to the complex nature of the family unit and its many characteristics, such as socioeconomic status, structure, and function [88, 89]. Snethen et al. [29] described four patterns of decision making in families making decisions about clinical trials for children with cancer. These patterns were subsequently applied to describe family childhood cancer information sharing and decision involvement [37, 90]. The four patterns included Exclusionary (decision exclusive to the parents in hopes of protecting the child/adolescent), Informative (parents were open to talking with child/adolescent about treatment), Collaborative (treatment discussed collaboratively between parent and child/adolescent), and Delegated (parent did not feel the need to force or pressure child/adolescent to participate).

Kelly and Ganong [91] examined parent TDM in structurally diverse families (i.e., divorced, separated, or never married biological parents of a child with cancer). They further identified how the various parent roles (custodial, nonresidential, and stepparent) affected their decision-making involvement. Both biological parents and stepparents acknowledged the priority of the custodial biological parent to make treatment decisions for their children with cancer with the stepparents' role as supporting their partners, including participating in the treatment discussion or offering an opinion but deferring decision making to the biological parents.

The treatment team typically discussed treatment with the parent who was present for clinical encounters. In divorced or never married families, this was typically the custodial parent who might not always convey this information to the other biological parent. Stepparents were rarely involved in treatment discussions and were not always informed about the child's status or treatment plan, even though they might be responsible for the child's care during scheduled visits. Whether the child's parents live together or not, clinicians must focus on providing information to all involved parents and to engage them in treatment discussions. Parents identify e-mail communication as an effective way to assure effective communication among parents and the treatment team [91].

10.5 Nursing and the Health Care Team

In pediatric oncology, various members of the health care team play a role in TDM. While physician oncologists are the most common HCPs who directly interact with patients and family members during TDM, primary care physicians, other physician specialists, nurses, psychologists, social workers, and research coordinators may indirectly support the oncologist, patient, and/or family member(s) throughout the decision-making process.

10.5.1 Clinician Roles in Treatment Decision Making

Oncologists have been described as taking on the role of medical expert in TDM, including identifying the best treatment and options for patients [92–94]. Throughout the treatment continuum, oncologists are central to seeking and providing knowledge and information with the patient and family [95]. Sometimes this means the oncologist reaches out to discuss the child/adolescent's diagnosis and treatment options with other physicians, especially in the case of a rare disease or very ill patient [92, 95]. Nurses often view themselves as bridging the gap and supporting physician, patient, and/or family members [93, 96]. Furthermore, during the informed consent process, nurses describe their role as "witness," "advisor," "legal liaison," "interpreter," and "conduit of information" [94].

Nurses have described their role in cancer TDM as supportive and include patient education, advocacy, information sharing and gathering, symptoms/side effect management, and psychological support [97].

Most of the established health care team research in pediatric oncology focuses on the oncologist. While oncologists are the medical experts in the treatment of children and adolescents with cancer, the oncologists' level of involvement in treatment decisions seems to vary along the treatment continuum. Furthermore, studies from the parents' viewpoint have shown that physicians might not recognize the preferred level of involvement that children/adolescents with cancer and their family members desire in the various treatment decisions [70, 98]. Sisk et al. [70] found that oncologists accurately identify parental preference for involvement only 49% of the time. It is suggested that physicians not only ask patients and family members what their preference of involvement is in TDM, but also that physicians share information and help patients and family members to understand their individual values, needs, and preferences [70].

Miller [48] suggests the following strategies that members of the health care team can do to facilitate children's involvement in TDM: (a) turn taking, (b) soliciting questions, (c) asking for information from the child, and (d) checking understanding. When Day and colleagues [60] asked HCPs their opinion on the involvement of teenagers in TDM, they felt teenagers should be communicated with openly. Day et al. [60] further found that how and to what extent teenagers are involved depended on family communication style, stage of illness, and nature of the disease.

10.5.2 Factors Influencing Treatment Decision Making

The healthcare team recognizes the various types of treatment decisions along the childhood cancer treatment trajectory, and their TDM is influenced by the type and timing of the decision. They may approach TDM differently based on whether the decision is a part of diagnosis and initial treatment, everyday decisions, refractory or recurrent disease, or end-of-life care.

10.5.2.1 Diagnosis and Initial Treatment

In pediatric oncology, treatment is often combined with research, as the field is continually trying to improve survival while minimizing side effects. Except in the case of a rare cancer, a standard of care treatment usually exists, and a clinical trial comparing another treatment regimen to the standard of care may be available. When this is the case, the decision is a matter of receiving treatment on the clinical trial or receiving current standard of care. Often the treatment decision at initial presentation is a matter of survival with minimal time for decision making, in which case the physician assumes the responsibility for decision making [60, 99]. HCPs have described this type of decision making as doing the “right thing” [60].

10.5.2.2 Everyday Decisions

Once therapy commences, several other treatment decisions follow. Many of these decisions are smaller decisions that affect quality of life to make the child/adolescent and/or family more comfortable. Such decisions do not impact cancer therapy itself and include decisions such as whether the medication is delivered orally versus intravenously. Yet another decision may be which day of the week the medication is delivered to the patient. These decisions are elective decisions and oncologists feel most comfortable giving these choices to patients and families [27, 92, 100].

10.5.2.3 Refractory or Recurrent Disease

Often when a patient has refractory or recurrent cancer, the treatment includes the option of a Phase I trial. Oncologists have described the following as most important when discussing Phase I trials with patients and families: providing information about the study, explaining disease progression, and discussing the various treatment options [101]. Some of the obstacles physicians find are: (a) recognizing the patient and/or family member’s eagerness to try anything after relapse/refractory disease, (b) providing hope while being honest and accurate about the child/adolescent’s condition, and (c) reviewing the consent document due to the length of and language of the document [101]. The majority of physicians try not to influence the families’ decision in Phase I involvement [101]. In research discussions such as these, physicians recognize the value of assent from a child/adolescent, but view themselves as a protector of the children and adolescents [102].

10.5.2.4 End-of-Life Care

In the case of advanced disease or serious illness, physicians describe themselves as the “bearer of bad news” [95]. Stenmarker et al. [95] found the following assists oncologists in end-of-life care decision making: (a) obtaining knowledge and information from colleagues, (b) building a close relationship and using empathy with patients and families, and (c) keeping a distance from their own attitudes and beliefs about end-of-life and existential issues. At this stage of TDM, De Vos et al. [96] further describe the physicians’ focus is on providing medical information and explaining the team’s preferred course of action. Refer to Chap. 12 for more information on end-of-life care and treatment in pediatric oncology.

10.6 Environment and Social Determinants of Health

The healthcare team encounters a diverse population and environment when providing care, and such diversity can influence TDM. A person’s culture and the various social determinants may impact their thoughts, communications, and actions during decision making.

While this area of research continues to grow, and we continue to learn more about what these factors are and mean to the healthcare experience, it is precision health and patient-centered care that is exposing their significance. The following factors have been identified as important considerations in cross-cultural interactions related to healthcare decision making: race, ethnicity, religion, socioeconomic status, education, and geographic location [103]. Derrington and colleagues [103] recommend that the healthcare team should not only acknowledge the patient’s and family’s personal beliefs and values, but their own as well. It is critical that the health care team mitigates any bias or preconceived ideas (bias is impossible to remove; however, it can be identified and mitigated) throughout the TDM process.

Although limited, the data available on culture and social determinants in pediatric oncology TDM relate to the disparities that exist within healthcare such as disparity in clinical trial participation and end-of-life care. Other areas are studied to a lesser extent. Acknowledging such disparities and continuing to explore diversity in healthcare will hopefully reduce the current inequalities and improve patient outcomes. Few intervention studies promote healthcare participation in culturally and linguistically diverse groups with cancer [104]. The healthcare team should appreciate that culture and social determinants are complex, and TDM should be approached with an open mind and dialogue to meet the patient's and family's preference.

Wiener and colleagues [105] identified various cultural influences in decision making about palliative care in pediatric cancer treatment. Areas of the decision-making process that may vary between cultures may be child participation, involvement of extended family members, or input from religious or community leaders. For example, African American and Russian families often look to their eldest family member (often male), Native American individuals commonly look to their community leaders, and in Asian and Latino families the mother is the primary caregiver with input sought from the father [105]. Following are several studies specific to TDM in pediatric oncology addressing disparities in race and ethnic minorities, religion and spirituality, and socioeconomic status and education.

10.6.1 Racial and Ethnic Minorities

Latinos are more likely to enroll their child with cancer in hospice compared to non-Latinos [106]. In white and black pediatric oncology patients though, Baker and colleagues [107] did not find race to influence do-not-resuscitate orders and end-of-life discussions. They point out that if there is equal access to specialized pediatric oncology care, such disparity does not exist. Miller et al. [108] suggest that meeting these patients' and families' educational needs may improve inequalities in parental decision making. They found minority groups had lower perceived voluntariness in a treatment trial compared to the majority [108]. Key elements that influence African Americans participation in clinic trials include negative beliefs, lack of knowledge, influence of faith, friends or relatives, and HCPs influence [109]. Mack and colleagues [87] found that black, Hispanic, and individuals of other racial and ethnic minorities had increased risk of decision regret several weeks after parents of children with childhood cancer made a decision regarding initial treatment relative to whites. They suggest that providing high quality information, encouraging parental involvement, and being trusted as providers may help reduce regret [87].

10.6.2 Religion and Spirituality

Superdock and colleagues [110] found that among Christian parents, religion and spirituality influenced a variety of treatment decisions in pediatric life-threatening illnesses such as stem cell transplant, including initiation of therapy and life-sustaining therapy. The core themes associated with influencing these decisions included “Hope and Faith,” “God is in Control,” “Miracles,” and “Prayers” [110]. Furthermore, in a study of families from various religions, religion did not seem to influence consent for a do-not-resuscitate order [111]. In a group of parents representing Jewish, Islamic, and Christian religions, Druze families were the only group unlikely to sign consent for do-not-resuscitate [111].

10.6.3 Socioeconomic Status and Education

With information sharing being so important in TDM, socioeconomic status and education should be a consideration. Language proficiency also plays a role in decision making. A study in the USA demonstrated English proficiency was associated with better self-report of patient–provider communication and SDM [112]. Miller and colleagues [108] found that parents with less education perceived less voluntariness in treatment trials in children with cancer compared with those more educated. Similarly, Hileli et al. [111] observed that when one parent had greater than 15 years of education, do-not-resuscitate consent was more likely to be obtained compared with two parents who had 15 years or less of education. Those with a higher income were also more likely to consent to do-not-resuscitate consent [111].

10.7 Outcomes of Treatment Decision Making

The impact of the youth's cancer disease and/or treatment outcomes can influence the youth's or parents' perception of how they view their previous decisions. Satisfaction with treatment decisions can be influenced by the success of treatment [40] rather than the decision-making experience. Research related to the outcomes of TDM is much less developed than research focused on the actual processes of making treatment decisions with parents and their youth with cancer. However, important considerations from the current evidence base inform nurses' practice to support parent and youth, and support future research to improve practice and ultimately youth and parent outcomes.

10.7.1 Parent Outcomes

HCPs must help parents become well informed about the relevant risks, benefits, and potential outcomes of available treatment options. Parents require adequate time to process the flood of information to make an optimal decision that they will not regret. Decisional conflict, regret, and disengagement may result when these aspects are not considered [113]. Parent values and preferences are fundamental to how parents make treatment decisions for their children. When these values and preferences are not aligned with the decisions made, parents might experience decisional regret [87] which can have consequences for years after their child has died [113]. Demands by HCPs that a family take a more active role in decision making than they desire may cause significant stress and be associated with decisional regret [70].

10.7.2 Youth and AYA Outcomes

Youth's participation in cancer TDM might lead to improvement in youth's feelings of control, competence, confidence, autonomy, and even treatment adherence [23, 25, 26, 29, 35, 114–116]. Youth participation in minor decisions has been shown to sustain a positive mental attitude and cooperation with the treatment team [25] while congruence between preferred and actual TDM roles improves youth's trust in their HCPs and satisfaction with TDM [114, 117].

Decisions made throughout the treatment trajectory can be difficult and may lead to regret. The causes or influences of "decisional regret" are difficult to clearly identify and evaluate for causality. Mack et al. [43]

reported decisional regret in almost one quarter of AYAs. On multivariate analysis, the strongest predictor was trust in the oncologist; however, decisional regret was also related to the prognosis of the cancer. Those who were extremely likely to be cured at the time of diagnosis had the lowest decisional regret, while increased uncertainty at diagnosis was associated with increased decisional regret. In addition, patients who experienced relapse had a higher rate of decisional regret than those who had not. This is likely to be a complex interaction; however, it is possible that they are related because the less likely a cancer is to have a high chance of cure, the more likely the disease is to relapse, and the more likely there will be therapeutic options with no clear guidance about which treatment is superior. The relationship with the oncologist may become more important if the disease is one that does not have a clear choice of therapy because it has a poor prognosis. For those patients, the relationship with the oncologist might become extremely important in protecting the patient against decisional regret.

10.8 Evidence-Based Findings Derived from the Science of Treatment Decision Making in Pediatric Oncology Ready for Translation to Clinical Practice

Evidence-based findings within the field of TDM are available and ready to be translated into routine clinical practice. Many of the findings specific to pediatric oncology TDM are primarily descriptive but have been replicated in multiple studies. Application of such findings into clinical practice is the foundation to providing precision health care. These findings include:

1. The ability and inclination of youth and their families to participate in the TDM process varies based upon the numerous personal, family, cultural, and situational variables. Such variables should be continually assessed and taken into consideration with each decision to identify individuals’ preferences and ever-changing needs throughout treatment. Approaches to assessing individuals’ preferences and needs have been described by experts in the field.
2. Many decisional situations exist along the pediatric cancer treatment

continuum, and youth and family preferences for involvement vary based upon the type of decision being made. The situations range from the initial disease-focused treatment selection at diagnosis to the transition to end-of-life care in refractory or relapsed disease. Minor treatment decisions include the time of day to take medication whereas major treatment decisions include which therapy option to start. Clinicians should be aware that the desire for involvement in TDM may change depending upon the type of decision.

3. The role youth and family members take in the decision is likely based upon whether a clear best option leading to probable cure is present or whether no obvious option for cure can be offered. When a superior option exists, the physician should utilize his or her expertise and opinion to take the lead, and communicate clearly what is standard of care versus clinical trial treatments. If no obvious option is present, the child or adolescent with cancer, parent(s), and other family members may want to take more of an active role in the TDM process.

4. Studies have reported that clinicians often identify parents as the main decision maker but acknowledge that the child and adolescent perspective can be beneficial and should be a priority. Open communication promotes trust of clinicians, satisfaction with decisions, and adherence to treatment. Successful strategies to facilitate child and adolescent involvement have been described and should be employed to ensure optimal TDM outcomes.

10.9 Future Research Recommendations for Treatment Decision Making in Pediatric Oncology

Our understanding of the complexities of TDM in pediatric oncology has advanced tremendously. Future research on TDM will enable us to tailor care based on the health care team’s understanding of the variety of preferences held by parents and children and the specific preferences the individual patient and family may hold. HCPs will be better prepared for various decision-making preferences and situations where the parent and patient preferences are congruent or divergent [118]. The following are areas in need of research to advance the science further:

1. The cancer literature primarily reports individual decision making accounts and usually the perspectives of a single participant type such as parents or physicians or patients, few focus on dyads or other combinations of these individuals' perspectives. Focusing on family perspectives and family level analysis will assist with this understanding. Studying family decision making focusing on combinations such as the parent-child dyad could improve knowledge in this area and support interventions developed to assist with family TDM when using a personalized approach. In addition, the fathers' viewpoint is under represented in TDM research. Predominately, mothers, who are typically the primary caregivers for children, have been included as study participants, so studying fathers is also important.
2. Exploring the many factors that influence decision making including cultural, psychosocial, behavioral, developmental, biological, and illness contexts is recommended. Similarly, our diverse society requires specifics of race and ethnicity to be taken into account in healthcare. The area of precision health must do the same to eliminate the potential for disparities to exist. Awareness of these factors and their associations with specific preferences is essential to help understand these preferences and preference patterns.
3. TDM should be studied longitudinally over the course of the disease. Examining how parents and patients make treatment decisions over time will help to describe their overall experiences and provide potential opportunities to develop interventions to specifically assist with TDM.
4. The literature contains descriptions of approaches used to promote involvement in TDM. Despite these approaches described to facilitate decision involvement, there is little empirical evidence to support them. Implementing strategies and interventions to facilitate the optimal involvement of youth in TDM directed at healthcare team members, family and youth must be developed and

validated. Based on a precision health approach and previous research, interventions need to be developed to help children and AYAs participate in TDM with the goal to identify their preferences for participation and to enhance their abilities to participate according to their preferences. Interventions might also target HCPs and/or parents, to encourage their inclusion in TDM to the level that they prefer to be involved. Interventions might help children understand the various options, others might help them develop skills needed to participate, and others might educate parents and HCPs to support participation in TDM.

5. Research is needed to continue to develop and psychometrically test measures of TDM.
6. Examining both short- and long-term outcomes of TDM on health outcomes such as adherence and transition to adult healthcare is essential.
7. Evidence about communication and decision making in the pediatric oncology population is limited. Studies to answer the question of how best to facilitate communication and decision making between HCPs, patient (child, AYA), and families are needed. Focusing on how we might integrate children and AYAs into the communication and decision-making process is needed.
8. Finally, research is needed to study decision aids and other tools that support TDM. Decision aids would assist, for example, parents in clarifying factors which are important when making decisions [73]. Decision aids have been shown to be beneficial to patients by enhancing their knowledge, being informed of the risks and benefits of treatment options to make treatment decisions, and feeling empowered [119] as well as supporting parents who are deciding whether to opt for a Phase I clinical trial [16]. However, further work is needed to develop such aids for parents and children in various circumstances within pediatric oncology, for example, when opting for cancer-directed therapy or symptom management only.

10.10 Summary

Researchers are beginning to define the abstract and complicated phenomenon of TDM in children, AYAs, parents, and the health care team. Treatment decision making incorporates aspects of SDM, patient- and family-centered care, and communication. Researchers must begin to incorporate these critical concepts within an underlying theoretical framework to move the science forward, especially in developing interventions to improve the TDM process. Using the organizing framework of precision health, we summarize key elements of youth and family TDM processes and outcomes, including how nursing science contributes to the evidence base that informs nursing practice directed to supporting child and family TDM over the course of a youth's illness (Fig. 10.3).

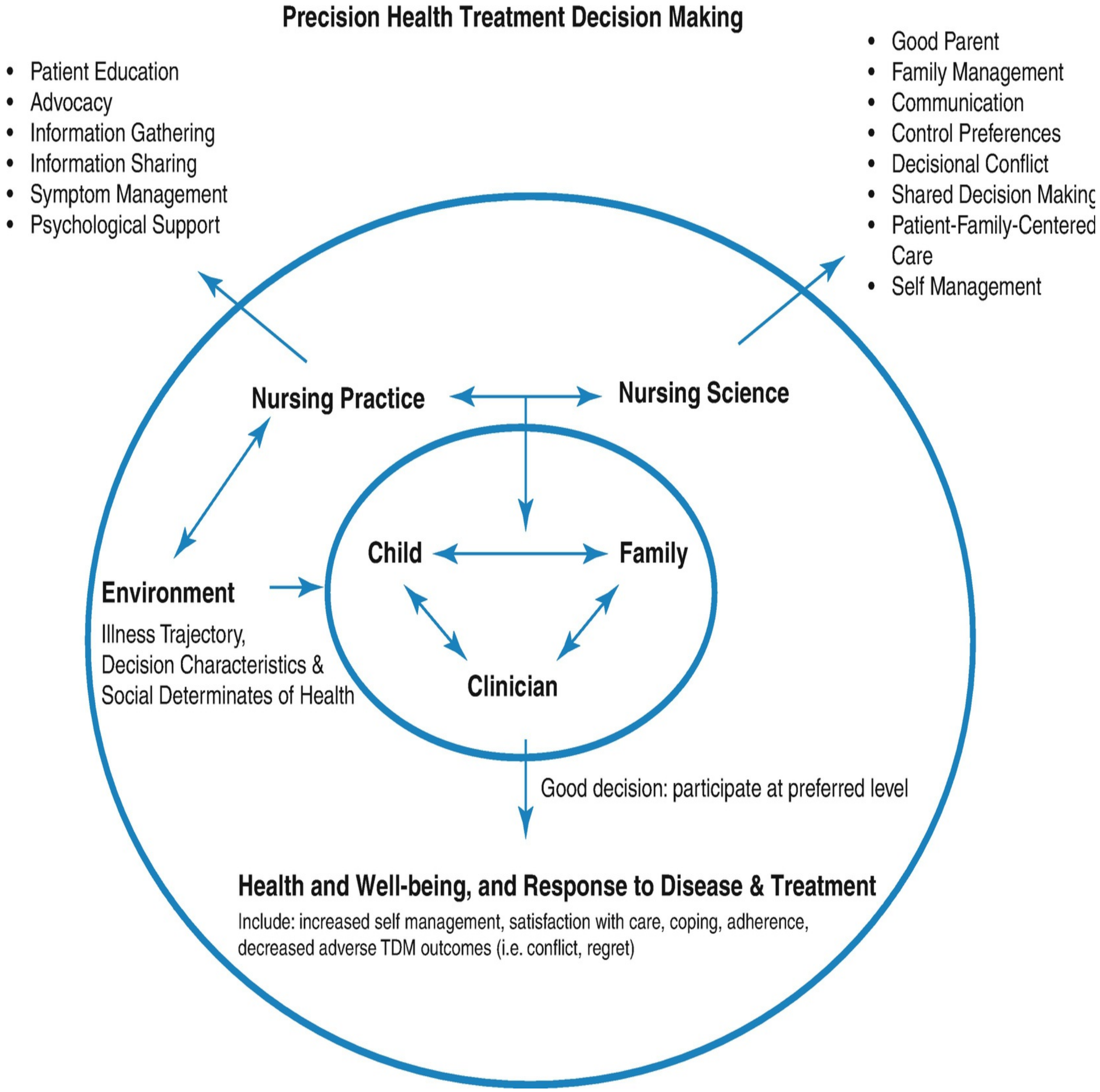

Fig. 10.3 Influence of nursing practice and nursing science on child and family health and response to disease (cancer) and its treatment within the context of the precision health

If we accept the hypothesis that improving the TDM process will lead to improved health outcomes and patient experience, then the need to improve our understanding of TDM and to design interventions to improve TDM is obvious. There are numerous opportunities to conduct research to support these goals across all healthcare disciplines to improve our basic understanding, and the skills and education of clinicians. Nurse scientists are especially positioned to support the design of future multidisciplinary, collaborative studies with the ultimate goal of implementing precision health to improve the outcomes of care for children with cancer and their families.

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Footnotes

1 The term youth is used to define a population of children. We understand there might be different interpretations of this word in some parts of the world; however, we feel it most useful in this context. We apologize for any offense this may inadvertently cause.

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11. Palliative Care in Pediatric Oncology

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Abstract

Pediatric palliative care (PPC) in oncology is the active total care of the child’s body, mind, and spirit and involves giving support to the family. Pediatric palliative oncology includes patients across the age spectrum from infancy through young adulthood, and can be embodied as a philosophy of care or applied by an interdisciplinary team of experts. PPC should be initiated at the time of a child’s cancer diagnosis and continued regardless of whether or not the child receives treatment directed at the cancer. PPC aims to prevent and relieve suffering across multiple realms (physical, psychological, social, and existential or spiritual) and enhance quality of life. PPC can be either primary (administered by the primary oncology team) or specialty-focused (administered by an expert or team of experts in PPC), depending on the unique needs of the patient, family, and health care team. Despite evidence demonstrating the benefits of PPC, numerous barriers to its implementation remain. Ongoing education and research are necessary to support consistent access for patients, families, and health care clinicians.

Keywords Palliative care – Quality of life – Interdisciplinary – End-of-life – Decision-making – Communication – Bereavement

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11.1 Introduction

Every year, approximately 300,000 children (ages 0–19) are diagnosed with cancer worldwide. While survival rates for children with cancer have risen dramatically in high-income countries over the past 60 years, nearly 80% of children diagnosed with cancer live in low- and middle-income countries where survival rates have lagged and linger at only 20% [1]. Even in countries with high survival rates, cure comes at a cost. Although treatments are evolving, most children are exposed to toxic, potentially life-threatening therapies. Such therapies impose risks that are both acute and chronic in nature, compromising the patient's current and future livelihood and quality of life. All of this is accompanied by uncertainty, which can haunt both the patient and family. Thus, an approach that minimizes the burden of suffering among all cancer patients and their families is desperately needed. "The field of pediatric palliative oncology has developed to help children with cancer and their families cope with this uncertainty and the physical, psychological, social and spiritual burdens of illness that begin at diagnosis and extend into the bereavement period" [2] p. 40.

Guided by the precision health framework presented in Chap. 1, this chapter will describe the development of pediatric palliative care (PPC) as a sub specialty and the interdisciplinary practices and research that have guided its development (see Fig. 11.1). Palliative care is deeply personal in nature, assessing the pediatric patient and his/her family holistically in a variety of different environments, recognizing the unique, inherent value in each person and his/her choices, in order to promote health and well-being. The foundations of palliative care including its focus on holistic symptom assessment and management, developmentally and culturally appropriate communication, goals of care, values, care coordination, end-of-life (EOL) care, and bereavement will be highlighted throughout the chapter.

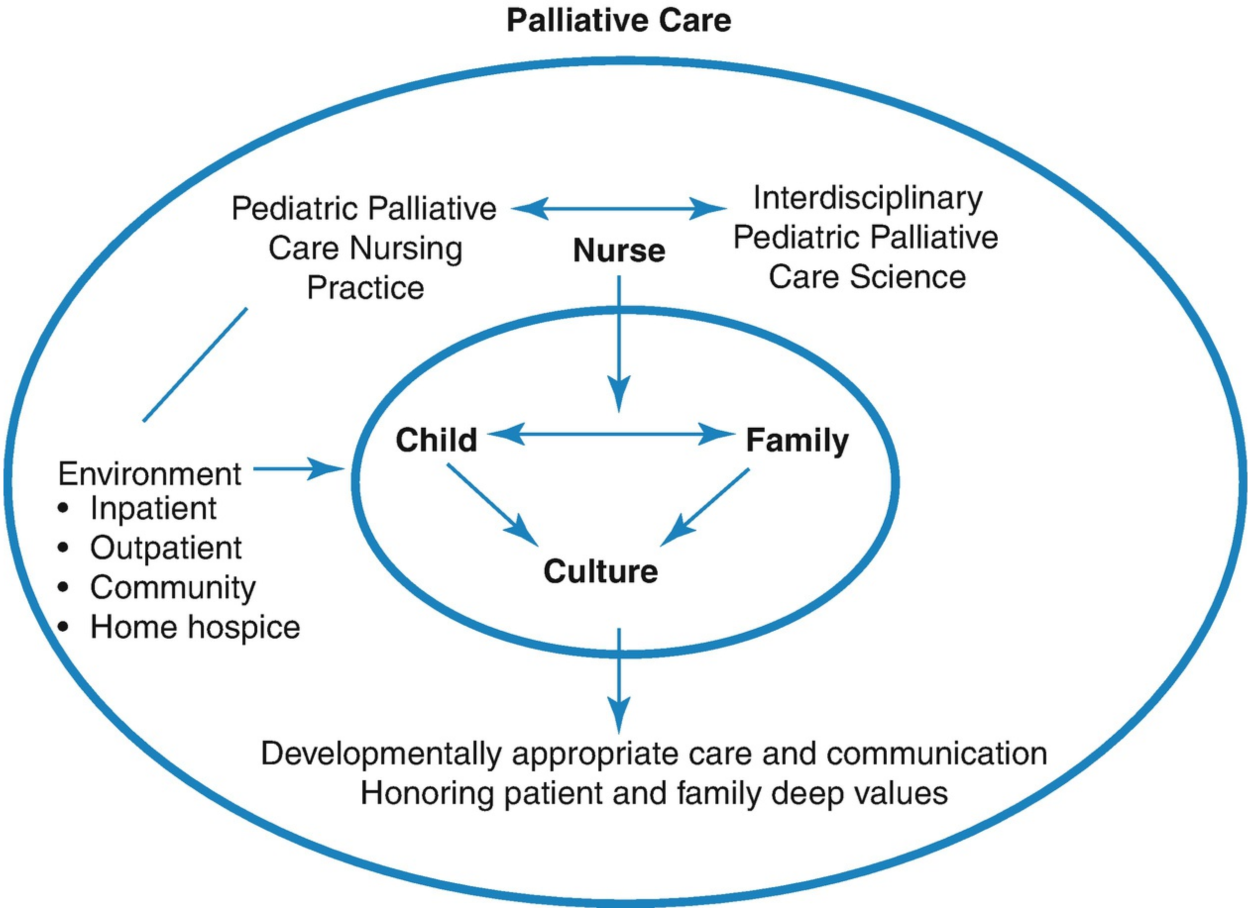

Fig. 11.1 Precision health framework in the context of palliative care

11.2 Development of Palliative Care as a Specialty

With its emphasis on holistic, compassionate, and individualized care, the hospice and palliative care movement was largely initiated by a nurse-turned-physician, Dr. Cicely Saunders. In response to the suffering and pain that Dr. Saunders observed in patients dying from advanced cancer, she embarked upon a career of observations, interviews, and investigations aimed at enhancing the quality of life of patients within this vulnerable population. Part of her work included the establishment of a free-standing hospice facility, St. Christopher's Hospice in South London in 1967. Dr. Saunders embraced the concept of interdisciplinary teams, advocating that a team effort was required to relieve the "total pain" of a dying person [3]. The concept of total pain extends beyond physical symptoms to include mental distress, social problems, and emotional difficulties occurring within the context of the patient's family. Dr. Saunders' great work and that of other pioneers in the field, including Dr. Elizabeth Kubler-Ross and Florence Wald, provided the foundation for the palliative care movement. In the late 1970s, Dr. Ida Martinson from the University of Minnesota's School of Nursing was among the first to apply such principles to children, documenting the experiences of caring for the dying child at home through a grant funded by the National Cancer Institute [4]. Over the last four decades, pediatric palliative and hospice care have grown considerably, but much work remains to be done to ensure that every child has access to the comprehensive services that are provided under this extra layer of care and support and advance the science of palliative care.

Nurse scientists were among the front runners in the field of pediatric palliative care within oncology [5–10]. Many of the early nurse-led studies focused on perspectives of parents caring for their children with incurable cancer [5, 7–10] or the challenges of confronting death for professional caregivers and chaplains [6]. However, Hinds also included the perspectives of children and adolescents with cancer, providing foundational understanding of the dynamism of hope and its importance within the context of a life-threatening illness such as cancer [11, 12], the importance of quality of life and the meaning of illness [13], and adolescent preferences for involvement in EOL decisions [14]. Nurse scientists have led [6, 7, 9, 13–15] or participated in interdisciplinary team research [16] since very early in the palliative care movement, underscoring the importance of incorporating interdisciplinary perspectives on how best to address the complexities of PPC within oncology.

Palliative care is currently defined by the World Health Organization

(WHO) [17] as “an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual.” PPC takes this one step further, and incorporates the unique and diverse developmental and physiologic variations of a wide range of diagnoses that are experienced by children with serious and life-threatening illnesses. Thus, PPC is the active total care of the child’s body, mind, and spirit, and involves giving support to the family. The word “child” in this context is a bit of a misnomer, in that, PPC generally includes patients across the age spectrum from infancy to young adulthood. Developmental assessment is a critical and unique aspect of PPC, and is informed not only by chronological age but also by the direct effects of the child’s condition and the experience of being ill. Each of these has the potential to impact the abilities of the infant/child (hereafter referred to as “child”) or adolescent/young adult’s (AYA) abilities to self-report one’s experiences, communicate preferences and values, and participate in decision-making, all critical aspects of navigating serious and life-threatening illnesses. When administered within the context of the care of children and AYAs with cancer, PPC can be referred to as pediatric palliative oncology.

11.3 Early Integration of Palliative Care

Leading health care organizations including the WHO and the American of Academy of Pediatrics [18] have endorsed that PPC should begin when a serious or life-threatening condition is diagnosed, and continue regardless of whether or not a child or AYA receives treatment aimed at comfort or cure. The early introduction of PPC principles was further endorsed as a psychosocial standard of care by an interdisciplinary group of pediatric oncology stakeholders, who developed evidence-based standards for psychosocial care in the pediatric cancer population [19]. Early integration of palliative care principles requires that clinicians evaluate and provide treatments that aim to (1) prevent and relieve suffering across multiple realms including the physical, psychological, social, and existential or spiritual; (2) improve the child and AYA's quality and enjoyment of life while helping families adapt and function during the illness and through bereavement; (3) facilitate informed decision-making by patients, families, and health care clinicians; and (4) assist with ongoing coordination of care among clinicians and across various sites of care. To provide such holistic care, an interdisciplinary approach that includes the family and makes use of available community resources even when resources are limited is required. While services vary based on available personnel and resources, PPC can be provided in tertiary care facilities, in community health centers, and even in the home environment. Ultimately, palliative care is a philosophy not simply based on physical location and availability of resources, but rather on attitudes and skills [20].

11.4 Models of Pediatric Palliative Care

Different models of PPC have developed in response to the recommendation that PPC be offered throughout the cancer journey from the time of diagnosis to survivorship or bereavement (see Fig. 11.2). To meet the needs of this expanded population, all pediatric oncology clinicians, including nurses, should embody the basic principles and practices of palliative care including (1) standard management of physical and emotional symptoms, (2) discussions regarding prognosis and goals of care, (3) reduction in suffering, and (4) initiation of advanced care planning. This is often referred to as "primary" palliative care. "Specialty" palliative care is then administered by individuals or teams of clinicians with formal training and education in palliative care when more advanced palliative care skills are required, such as complex pain and symptom management, expert communication assistance, and conflict resolution [21].

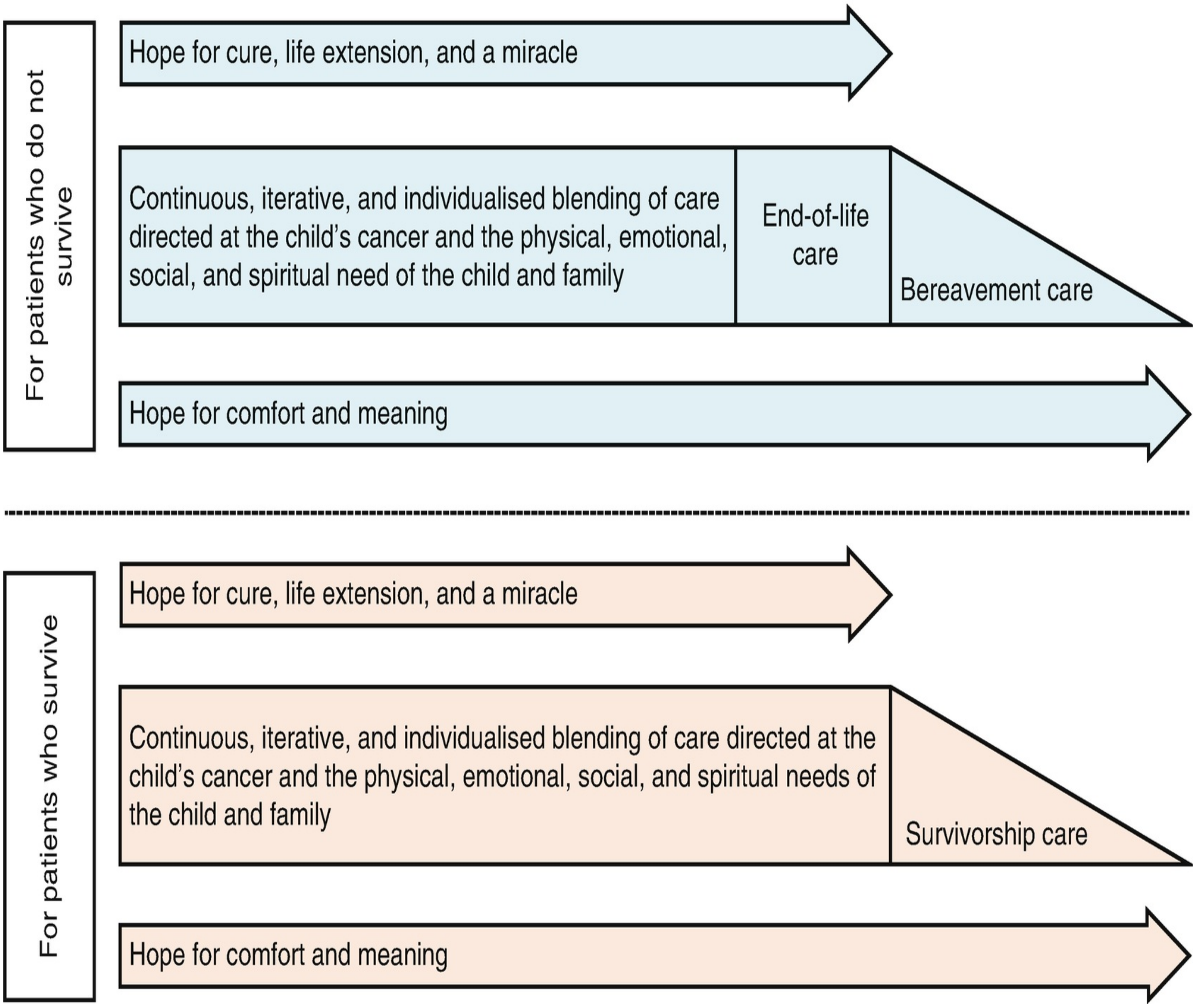

Fig. 11.2 Conceptual model of palliative care integration across the continuum for patients who do not or do survive. From [21]. Copyright 2017 by Elsevier. Reprinted with permission

In a recent international survey of medical settings providing care to children with cancer, 78% of respondents indicated having access to a specialized PPC team [22]. (Of note, greater than 80% of respondents were from higher-income countries.) The AAP and the American Academy of Hospice and Palliative Medicine recommend that interdisciplinary PPC teams include doctors, nurses, social workers, child life specialists, and spiritual advisors [18, 23], but team composition and the services available remain highly variable throughout different institutions and nations [24]. The size of the teams and services provided are thought to differ based on the maturity of programs, the resources available, and the populations the teams serve [25]. Although experts have recommended the embedding of PPC clinicians within pediatric oncology programs to optimize the early integration of palliative care, this model has not yet been widely adopted or reported [26]. Instead, PPC services are largely consult-driven. Many institutions have “triggers” in which palliative care consultation is suggested. Generally, such triggers are based on specific diagnoses or prognoses, care escalation metrics, length of stay, or re admission rates [22, 27]. Unfortunately, a consult-based model relies heavily upon primary oncologists and other specialists to make referrals. This reliance can serve as a barrier as oncologists and specialists do not always appreciate the benefits of PPC throughout the illness trajectory, or they may be unwilling to discuss palliative care with their patients and families and make actual referrals [28].

11.5 Symptom Management as a Foundation of Palliative Care

From the time of diagnosis, pediatric patients with cancer are at risk for experiencing high symptom burden and compromised quality of life [29–32], thus supporting the need for the early integration of PPC. (See Chap. 5 for a more detailed presentation of symptoms.) During the first month of therapy, a significant proportion of patients experience a constellation of different symptoms including nausea, loss of appetite, pain, anxiety, constipation, depression, and diarrhea, and report symptoms as causing a high degree of symptom-related suffering [30]. Although symptom prevalence and distress generally diminish over time, parents perceive that symptoms continue throughout treatment, and the more problematic symptoms may persist beyond the end of treatment [29]. Symptom distress and related suffering may be more pronounced in children with advanced cancer (i.e., those with disease progression, recurrent disease, or non-responsive disease). In a prospective study exploring symptom prevalence and distress among children with advanced cancer, children commonly reported having five or more symptoms at any given time point. Furthermore, when symptoms were present, they were generally regarded as highly distressing. Suffering appeared to be related to cancer and cancer-directed therapies and was reduced over time as the disease was controlled. These findings reinforce the need for more intensive symptom management particularly in complex cases when prognosis is uncertain, and patients, families, and clinicians continue to pursue cancer-directed therapies [32].

Profound suffering has also been reported at the end-of-life (EOL) with nearly 90% of parents in 2000 reflecting that they believed their child suffered “a lot” from at least one symptom at the end-of-life [31]. As the palliative care movement has gained momentum in the pediatric population, rates of suffering at the EOL appear to be decreasing. A follow-up study in 2008 demonstrated that although pediatric oncology patients at the EOL continued to have similar symptoms (e.g., fatigue, pain, dyspnea, anxiety), symptoms were less frequently reported as causing a “great deal” or “a lot of suffering” [33]. Thus, supporting the goal of palliative care to relieve symptom burden and promote optimal quality of life.

11.6 Developmentally Appropriate Care and Communication

One of the basic tenets of PPC is developmentally appropriate communication [19] across the trajectory of cancer. Communication must be adapted to meet a wide range of understanding from young children and their parents to AYAs. Palliative care communication incorporates discussions around prognosis, identification and management of symptoms, goals of therapy, life goals, advanced care planning, and EOL preparedness. Palliative care communication also includes determining preferences for involvement in decision-making and preferences for involving patients and/or parents or other support persons in care decisions. These difficult conversations are essential, particularly when prognosis is uncertain or cancer is advanced and/or incurable. However, knowing how and when to initiate such conversations is challenging, particularly in the clinical context of curative therapy. In addition, children and AYAs differ in their preferences for involvement in communication and decision-making. Whereas younger children (7–11 years old) tend to not want to be responsible for making big decisions and are satisfied with their parents taking the lead, older children (12–16 years old) have reported dissatisfaction with their limited role in shared decision-making conversations during cancer treatment, feeling a loss of control [34].

11.6.1 Prognostic Discussions

Prognostic uncertainty may be one of the most significant indications for involvement of PPC in pediatric oncology [35]. Studies have demonstrated discrepancies between parent–provider concordance regarding prognosis and goals of care [36] and AYA–oncologist concordance regarding prognosis [37]. Rosenberg and colleagues [36] surveyed 77 dyads of parents and providers, and found that parents were generally more optimistic, reporting that cure was still possible and describing cure as their goal when their providers did not. Similarly, only 31% of AYA patients with cancer were identified as having accurate prognostic awareness, while 62% of AYAs overestimated their likelihood of cure [37]. Open, honest communication throughout the disease course, facilitated by palliative care principles or a specialized palliative care team, can help heighten prognostic awareness, identify goals of the patient and family, and support informed decision-making. Kassam and colleagues [38] collected questionnaires from 75 bereaved parents, and found that respondents were more open to discussions regarding death and dying, guidance about talking to their children about death and dying, and sibling support, if a palliative care team was involved.

Historically, young people diagnosed with cancer were not included in discussions about their diagnosis, prognosis, and disease progression [39, 40]. This protective approach was intended for good as cancer was largely incurable in the 1950s [41]. In the seminal work of Myra Bluebond-Langner, dying children became aware of their own impending death through socialization [39]. Children and adolescents used non-verbal and verbal cues as they were dying to confirm or discredit their preconceived notions. In addition, children and adolescents would seek out their peers with similar diagnoses to determine what would happen next, if they could not get honest answers from their parents or health care clinicians [39]. See Table 11.1.

Table 11.1 Awareness and understanding of death[a]

Stages	Information about disease	Changes in

		self-concept
First stage: diagnosis	It is a serious illness	I am seriously ill
Second stage	There are medications for the illness with side effects	I am seriously ill and will get better
Third stage	There are special procedures needed to administer drugs; there may be additional treatments required because of side effects from the drugs. Each treatment and each procedure is a unique event	I am always ill and will get better
Fourth stage	The disease is a series of relapses and remissions. The medicines are not lasting as long as they are supposed to	I am always ill and will never get better
Fifth stage	The disease is a series of relapses and remissions. There are a finite number of drugs that can be used for treatment. When drugs are no longer effective, death occurs	I am dying (terminally ill)

From “Understanding quality of life in adolescents living with advanced cancer,” by C. J. Bell, 2011, Doctoral dissertation. Reprinted with permission

[a] Based on Myra Bluebond-Langner’s ethnographic study: the private worlds of dying children [39]

Since the 1950s, the pendulum has swung, and the standard of care is to inform pediatric patients with cancer of their diagnoses; however, prognostic disclosure and EOL discussions remain challenging. A more detailed discussion of EOL communication is provided in Chap. 12. With the significant advances made in cancer treatment over the past half a century, prognostication has become more challenging, and disclosure of prognosis remains complex as it is difficult to predict outcomes of any individual patient [40]. While reports of the perspectives of younger pediatric patients are limited, AYAs with cancer have indicated that knowing their likelihood of cure including numeric estimates is very important, and that, in general, such information is not upsetting. In fact, more extensive prognostic disclosure has been associated with greater trust in one's oncologist, greater peace of mind, and less psychological distress [37]. Furthermore, while younger children (ages 4–12 years) tend to stay in the background, AYAs prefer to be in the foreground for information-sharing discussions with their parents assuming a supportive background role [42].

Pediatric patients who have cancer with both good and poor prognoses and their parents prefer truth-telling and honest disclosure of prognostic information in a manner that conveys hope [43–46]. In a qualitative study involving 32 parents of children with advanced cancer, hope for a cure or a bright future coexisted with a realistic understanding of their children's poor prognoses [44]. Approximately 75% of the parents in the study acknowledged their hopes were different than their expectations or what was likely to occur. Coexisting goals and different types of hope are repeatedly described by researchers as they examine patient and parental communication, goals of care, quality of life, and suffering [30, 31]. These experiences are what make living with and managing the care of patients with life-threatening illnesses so challenging, but support the notion that palliative care is essential as an extra layer of support for patients, families, and health care clinicians.

11.6.2 Palliative Care and End-of-Life Discussions

Palliative care and EOL discussions should ideally occur across time, in a series of iterative conversations that prepare patients and their families of what is to come. Conversations include pragmatic discussions about symptom management and EOL issues, discussions about the grief and emotions associated with an uncertain prognosis or terminal disease, spiritual and existential struggles, and knowledge about what to expect as disease progresses [47–51]. As cancer advances, decisions about bone marrow transplant, discontinuation of therapy, or phase 1 clinical trial options may be needed [52]. Discussions that explore patient goals and preferences in light of goals of therapy are needed as disease progresses. Evidence exists to support patient participation in EOL discussions [53–56], EOL decisions, and life-sustaining treatment decisions [12, 57, 58]. However, longitudinal studies are needed to determine if and how preferences for decisional control and involvement of parents in decision-making change across time.

The theme of “protection” exists across studies examining palliative and EOL discussions; patients, families, and health care clinicians avoid conversations to prevent emotionally harming others [53, 59, 60]. Pritchard et al. refer to this as a “conspiracy of silence” ([59], p 2325). Patients look for cues in family members and health care clinicians to determine if talking about fear and sadness related to death and dying will be too upsetting or stressful [53]. Being present with young people who are processing intense emotions can be very difficult; however, these very conversations are critical as they can guide clinical discussions about goals of care. Establishing goals of care help the patient, family, and health care team to make treatment decisions that honor the patient’s deep values [48, 60]. Ongoing palliative and EOL preparedness conversations can also benefit patients and families by identifying age-appropriate support and meaningful activities [59, 61–64] and promoting optimal quality of life outcomes.

11.7 Decision-Making Preferences

While preferences for involvement in decision-making have been studied extensively in adult cancer populations [65, 66], very few studies have addressed child or adolescent preferences. More specifically, child and AYA preferences for involvement in decision-making across time or as disease progresses have not been well-documented. One study of children and adolescents 9–17 years old with cancer demonstrated that preferences for involvement in treatment discussions were dynamic and varied based on the type of decision, the timing of the discussion, and the symptom distress (physical or emotional) experienced by each child. Differences in preferences were not based on the chronological age of the child [67]. A systematic review of empirical research on decision-making in 13- to 19-year-old cancer patients provided evidence that adolescents do not have a clearly defined role in decision-making compared to their parents or clinicians [52]. Included studies reported the perspectives of adolescents, their parents and families, and health care clinicians, on their respective roles in decision-making. Across studies, parents viewed their role as multi-dimensional including that of advocate, expert, protector of the adolescent, and protector of family values. Physicians reported their role as experts, primary caregivers, providers of information, and advocates for the adolescents. Nurses reported their role as that of a liaison between parents and physicians with a key responsibility to inform adolescents, which sometimes led to conflict with parents [52]. The reported role of adolescents across studies was largely missing or reported as a passive role.

Lyon, Jacobs, Briggs, Cheng, and Wang aimed to elevate the voice and the preferences of AYAs with cancer in decision-making by engaging them in the process of family-centered advanced care planning (ACP) [54]. In this randomized controlled trial, AYAs with cancer (aged 14–21) were randomized to either receive three, 60-min sessions aimed at preparing the AYAs and their family members for future health care decisions (intervention arm) or a brochure on ACP (control arm). Results demonstrated that AYAs who participated in family-centered ACP were empowered to communicate their wishes about preferred EOL care choices in bad outcome situations as evidenced by greater congruence between AYA and family member decision-making in hypothetical situations. Furthermore, AYAs who engaged in the intervention were more likely to anticipate allowing their family members leeway to make decisions for them at the EOL.

Members of the palliative care team stand poised to assist with these conversations, helping to define and achieve EOL care preferences [33, 38, 68, 69]. Children and AYAs with cancer who are followed by palliative care teams are less likely to die in the intensive care unit, require mechanical ventilation near the EOL, undergo fewer invasive procedures at the EOL, and receive disease-directed therapy within the last month of life [68, 70]; all indicators of quality EOL care [71].

11.8 Supporting Patient-Family Values, Traditions, and Culture

Another important consideration in delivering palliative and EOL care services to pediatric oncology patients and their families is the incorporation of patient and family values, traditions, and cultural beliefs. Each patient and family have values, beliefs, and a culture that are unique to them. Family cultural values and beliefs may vary based on geographical location and/or spiritual, religious, or ethnic origin. Perceptions about information sharing and preferences for involvement in decision-making based on cultural values and beliefs have been largely understudied, particularly pertaining to PPC [56, 72, 73].

Many families have deeply ingrained cultural and religious beliefs that may influence palliative and EOL care preferences. Individuals from the same culture do not necessarily share the same religious beliefs [56], therefore a cultural assessment is crucial for delivering family-centered care. Palliative and EOL care preferences will only be understood through a mindful approach aimed at delivering individualized, culturally-sensitive family care that considers the spiritual or religious beliefs of patients and their families. A cultural assessment should include inquiry about origin of birth (country), ethnic or cultural identity, primary and secondary language, religious affiliation, dietary restrictions or preferences related to beliefs, health and illness beliefs, and customs/rituals surrounding death and dying [74].

In a systematic review on family communication in pediatric EOL care, parents desired respect for their religion and culture [75]. In some cultures, speaking of death is linked to giving up or the belief that talking about death may shorten life [56, 76]. Understanding cultural differences and gently guiding iterative conversations through honest disclosure over time is believed to be in the best interests of the patient and family [60]. In a study involving Mexican–American and Chinese–American parents of children requiring PPC, language and cultural barriers interfered with information sharing [72]. In some cases, parents described not being properly informed of available hospital services, such as interpreters and, therefore, were unable to fully understand and participate in discussion. Parents were frustrated that the cultural importance of family involvement was not respected or that communication was suboptimal. Frustration, anger, and sadness from these communication encounters lasted for many years after the child's death [72].

Cultural and religious beliefs influence decision-making, information sharing, communication about death and dying to children, the meaning of pain and suffering, the meaning of death and dying, and family preferences for location of death [56]. In some cultures, a death at home may be perceived as bad luck. In other cultures, if a patient dies in the hospital, his/her soul is believed to be lost [56]. Faith traditions also influence death and dying rituals, such as whether or not a body can be touched at the end of life or immediately after death. Religious beliefs may further influence decisions about burial, cremation, and autopsy, see Table 11.2.

Table 11.2 Major faith traditions, beliefs, and practices regarding illness, dying, and death[a]

	Buddhism [77]	**Catholicism [78, 79]**	**Hinduism [77, 80, 81]**	**Islam [77, 78]**	**Jehovah's Witness [82, 83]**	**Ju 79**
Illness/death rites or rituals	Family presence is important. May chant mantras as infant/child becomes seriously ill. The child's body should not be touched after death. Family may take the body home to prepare it for burial. The body should not be moved for 8 h after death.	Sacrament of the sick with anointing of oil, communion, and final blessing by priest	Ideal to be surrounded by family and friends who sing sacred hymns and say prayers or chant the dying person's mantra When death is near, the family spiritual leader is asked to conduct the final rites. The body should be as close to the ground as possible to help the soul absorb into the ground.	Body is washed three times. Muslim burial performed within 24 h. Cremation forbidden.	Prayer; reading the Bible.	Pra sic No Liv alw bo dea Bu aft po
Autopsy	According to individual situation	No restrictions	If required by law	Limited to medical and legal	If required by law	If r law

				reasons		
Existence of heaven	There are numerous heavens, hierarchically arranged and inhabited by joyous beings known as “gods” and “demi-gods.”	“Heaven” is a condition rather than a place; provides eternal fullness of life. Supreme happiness flows from intimacy with God.	Heaven is a place similar to life on earth, but without sickness, old age, death. A soul enjoys the rewards of his or her good deeds.	Heaven is described as a “garden” having several layers with the highest being directly under God’s throne. Souls are content.	Some people will go to heaven to rule with God and Jesus. The remainder of the righteous will enjoy paradise on earth.	He pla anx tra en Qu pea int act pla my life
Belief in reincarnation	Yes, all Buddhists believe in the notion of rebirth	No, it contradicts basic Catholic teaching	The notion of reincarnation and karma is a strong premise in Hindu thought.	No, there is only one life on earth	No, Jehovah’s Witnesses believe that at death life ceases to exist	Re tra of ess do tra Jev

From [56]. Copyright 2012 by Cambridge University Press. Reprinted with permission

[a] These are general, historical beliefs and practices according to some world religions. Always inquire with your patient and family about their individual preferences

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11.9 Challenges with Implementation of Pediatric Palliative Oncology Care

Despite the well-documented benefits of palliative care and the recommendation of its early integration, the timing of the introduction of palliative care varies substantially among patients, clinicians, and institutions. In 2008, only 6% of respondents from Children’s Oncology

Group institutions indicated having discussions about palliative care at the time of a patient’s diagnosis, and only 19% introduced palliative care when initial therapies failed [87]. Indeed, late palliative care and/or hospice referrals continue to be described in the literature as a significant problem for children with advanced cancer [35, 88, 89]. This variation in the introduction of palliative care is largely due to the following overarching challenges: (1) the association of palliative care with hospice and EOL care, (2) transitioning care from a primary focus on anti-cancer therapies to non-curative care, (3) availability of PPC services and training, and (4) integration of PPC teams into practice [90–92].

11.9.1 Association of Palliative Care with Hospice and End-of-Life Care

In general, the public and even clinicians remain uneducated about palliative care, its scope, and its availability. Many equate palliative care with hospice or EOL services, “giving up,” and/or an option that is only available when all curative therapies have been exhausted [28, 93]. Pervading western culture is the expectation that people with cancer are brave and always fight to overcome their cancer [94–97]. This expectation is particularly salient for children, as the death of a child goes against the natural life course. The association of palliative care with “giving up” and EOL is contrary to this expectation. As a result, pediatric clinicians are often slow to refer patients and families to PPC specialists, believing that (1) families will be reluctant to accept palliative care, (2) the clinician will be perceived as giving up on the child, and (3) families will be additionally burdened [92, 98, 99]. Consequently, PPC services are currently underutilized by patients and families [87, 90]. Evidence is now emerging that children with cancer and their parents do not oppose or perceive detrimental effects from the early introduction of palliative care, which should alleviate clinicians’ concerns [30].

A key method to overcoming the misconceptions of palliative care’s purpose includes the education of clinicians, patients, families, and the general public, and consistent use of palliative care terminology and definitions [91, 92]. This education includes lay literature, discussions with individual patients and families, as well as public displays of information [92]. Efforts must begin with clinicians, strategizing ways to reach clinicians who are hesitant to engage palliative care services because of the association between palliative and EOL care [99].

A second key method is for pediatric oncology clinicians to restructure the way care is delivered. Palliative care should be introduced to all patients and families at the time of diagnosis, and continued throughout the entire course of therapy regardless of whether or not patients receive treatment with curative intent. Creating the expectation that palliative care is part of the services provided to all children with cancer can enhance acceptance among patients and families, increase referrals to palliative care teams, and ensure that children have the opportunity to fully benefit from PPC services [99].

11.9.2 Transitioning Care from a Primary Focus on Anti-Cancer Therapies

The decision to shift a child's focus of care from primarily anti-cancer therapy to primarily non-curative care is heart-wrenching and one that children with cancer, their parents, and clinicians struggle with considerably [100]. "Survival work" refers to the cognitive and behavioral tasks involved with choosing to seek further anti-cancer therapy [101]. In contrast, "death work" consists of the tasks involved with preparing for one's death practically, emotionally, socially, and spiritually [102]. Palliative care can play an important role in both survival and death work due to its emphasis on symptom management and quality of life. However, palliative care features more prominently in death work because there is less focus on anti-cancer therapy.

Uncertainty in childhood cancer prognoses, parents' unrealistic expectations of their children's outcomes, and reluctance of clinicians and parents to discuss palliative care and/or hospice when cure remains the primary focus, all complicate the decision of when to transition away from a primary focus on anti-cancer therapies [100, 103–105]. Certain novel cancer-directed therapy options, including early phase clinical trials and expanded access therapies, are only available when no known curative therapies remain for a child's cancer. These options, while of uncertain benefit, are appealing to clinicians and families because of their novelty and the hope that the therapy will slow or stop the child's cancer [100]. However, experts have hypothesized that participation in early phase pediatric oncology clinical trials and other novel therapies may limit opportunities for palliation and death work, given their focus on survival work [94, 104, 106–109].

The literature is mixed regarding whether participation in early phase clinical trials impacts the palliative and EOL care provided for children with cancer. Although participation may not significantly impact location of death, unplanned medical visits or admissions, or the timing of ACP, enrollment on a clinical trial was associated with longer delays in the initiation of palliative care services [93, 110, 111]. Evidence suggests that clinical trial participation may impact how some parents manage their children's symptoms. The need to ensure that the child was not prematurely removed from the trial and did not miss doses of the investigational therapy was at times prioritized over the child's symptom management [100].

Children enrolled in pediatric oncology phase I clinical trials have a median life expectancy of 3.6–6.4 months [112–114]. This shortened life expectancy combined with receiving disease-directed therapy near the EOL suggests that families who participate in early phase clinical trials are at risk for losing opportunities to engage in death work [101, 108, 115]. These findings highlight the importance of providing effective palliative care concurrent with participation in early phase clinical trials and other novel therapies [109, 116]. Concurrent palliative and/or hospice care have been found to enhance symptom management and decrease psychological distress during this time [109, 117–122]. Initiation of concurrent care is best achieved by introducing palliative care early in the care of children with cancer and by including discussions of palliative care as part of the process when consenting patients to receive novel therapies [70, 106, 109].

11.9.3 Availability of Pediatric Palliative Care Services and Training

Palliative care teams are becoming more prevalent in medical centers that treat children with cancer, and yet, to meet the needs of early integration, more PPC clinicians and teams are necessary [22, 87].

Currently, most PPC teams are small, averaging 2.33 full-time equivalent personnel devoted to PPC services [24], and are hence challenged with managing the care of a large number of patients in diverse locations throughout different institutions. In settings where PPC services are not available, programs may use a PPC clinician to provide guidance and coordination of care to the patient's core team rather than directly providing care themselves [89]. Nurses, social workers, and other non-physician health care clinicians contribute significantly to palliative care services, improving access to care and alleviating dependence on physicians [104, 123]. Nurses, in particular, work on average appreciably more full-time hours for PPC teams than any other providers [24].

Specialized PPC training is necessary to effectively provide palliative care to children with cancer. Although significant advances have been made in palliative care education for all clinicians, access to universal training still needs to be improved [92, 103, 124]. This universal training should focus on palliative care concepts, advanced communication skills, managing prognostic uncertainty, facilitating EOL care, and improving symptom management [124]. See Table 11.3 for examples of currently available pediatric palliative and EOL care training for clinicians, including nurses.

Table 11.3 Pediatric palliative and EOL care training options for clinicians

Training program	**Provider(s)**	**Description**
End-of-Life Nursing Education Consortium (ELNEC) Pediatric Palliative Care	American Association of Colleges of Nursing (AACN) and the City of Hope, Duarte, CA	Provides undergraduate and graduate nursing faculty, continuing education providers, staff development educators, and nurses with pediatric palliative care training, including perinatal and neonatal content
Education on Palliative and End-of-Life Care (EPEC) Pediatrics	Northwestern University Feinberg School of Medicine in Chicago, Illinois	A comprehensive adaptation of the core EPEC curriculum designed to address the needs of children, their families, and pediatric oncology providers and other pediatric clinicians. Educates

		healthcare professionals of all varieties in the essential clinical competencies of pediatric palliative and end-of-life care
Initiative for Pediatric Palliative Care (IPPC)	Education Development Center (EDC), working in close collaboration with the National Association of Children's Hospitals and Related Institutions (NACHRI), the Society of Pediatric Nurses (SPN), the Association of Medical School Pediatric Department Chairs (AMSPDC), and the New York Academy of Medicine (NYAM)	An education and quality improvement effort aimed at enhancing family-centered care of children living with life-threatening conditions
Center to Advance Palliative Care (CAPC) Clinical Training	Center to Advance Palliative Care (CAPC), part of the Icahn School of Medicine at Mount Sinai	Provides health care clinicians and organizations with the training, tools, and technical assistance necessary to increase access to quality palliative care services. An important part of this mission is ensuring that all clinicians working with seriously ill patients have key skills, many of which are not yet taught in standard clinical education
Certified Hospice and Palliative Pediatric Nurse Certification Review Course	Hospice and Palliative Nurses Association (HPNA)	Designed to assist with preparation for the Hospice and Palliative Nurse certification exam. The educational content may also be used to increase the hospice and palliative nurse's knowledge of general palliative nursing
Hospice and Palliative Medicine Pediatric Educational Materials	American Academy of Hospice and Palliative Medicine (AAHPM)	Provides a variety of educational tools to enhance clinical practice. The pediatric tools include developmentally-appropriate care of pediatric and adolescent patients

PANDA Cubs Pediatric Palliative Care Training Program	Children’s National Health System	A specialized training program for clinicians who provide pediatric end-of-life care
Mastering Tough Conversations VitalTalk Course	VitalTalk	Innovative, interactive clinician and faculty development courses designed to improve communication skills on an individual and institutional level. Their verbal tools empower clinicians to communicate about serious illnesses empathetically and effectively, enabling them to feel less burned out in the process
Palliative Care Education and Practice (PCEP)	Harvard Medical School, Center for Palliative Care	Designed for palliative care specialists, champions, and educators, as well as generalist and specialist physicians and nurses who wish to gain additional competencies in palliative care. PCEP enhances clinicians’ skills in communication, teaching, and clinical practice. Includes a pediatric track.

11.9.4 Integration of Pediatric Palliative Care Teams into Practice

Best practices for integrating PPC into the care of pediatric oncology patients have not yet been established or adopted [91]. Most PPC teams in the USA function as consultative services, creating potential overlap in the roles of pediatric oncology clinicians and PPC team members [90, 92]. Pediatric oncology clinicians have expressed concerns that their patient relationships could be negatively impacted by the involvement of PPC teams, and that the goals of PPC teams may conflict with their own goals for their patients, hence disrupting the care provided to patients [92]. A clear model of care that respects and clearly defines roles and focuses attention on providing excellent comprehensive care to children with cancer and their families is universally needed.

Establishing and maintaining interdisciplinary PPC teams can be challenging [91]. Friedrichsdorf and Bruera describe the stages involved with achieving a well-funded and well-staffed interdisciplinary PPC team [125]. The authors advocate that a PPC team becomes fully established when it is (1) designated as an independent program (similar to pediatric oncology); (2) allocated dedicated space and team members; (3) assigned as a training rotation; and (4) actively consulted by clinicians throughout the institution [90, 125]. Pitfalls to becoming an established PPC team include hospital administrator and clinician denials of the need for a dedicated PPC team, lack of financial resources and staff necessary for the team to develop, and lack of referrals for patients with varying degrees of needs (i.e., not simply the most time-demanding and complex patients as this can exhaust the PPC team and its resources) [125].

Nurses are important providers of PPC. The role of nurses in PPC encompasses providing patient care; facilitating communication among patients, families, and members of the health care team; educating patients, family members, and other clinicians; ensuring patients and families have the resources and skills to manage at home; coordinating care among team members and other services; advocating on behalf of patients and families; and problem-solving issues that arise [24, 104, 126, 127]. Nurses can facilitate the integration of PPC teams into practice by advocating for early PPC team consultations for patients with poor prognoses, poorly controlled symptoms, or complex care requirements. For pediatric oncology patients who may not meet institutional criteria for a PPC team consultation, nurses can utilize PPC principles to guide patient care plans, thereby enhancing the care provided to patients and families and facilitating the future introduction of the PPC team, if it should ever be needed.

11.10 International Perspective

An estimated 21.6 million children with life-limiting and life-threatening illnesses stand to benefit from PPC services globally [128]. Yet, the availability of PPC and its services varies significantly from country to country, and PPC is not available in the majority of countries around the world (Fig. 11.3). Approximately 300,000 children are diagnosed with cancer each year worldwide, and 80,000 will die from their disease [129] with mortality rates the highest in resource-poor countries [130]. Thus, most pediatric cancer patients around the global do not have access to PPC despite WHO recommendations that palliative care is included as part of comprehensive cancer care [17]. In an international survey of pediatric oncologists, 46% of respondents reported access to specialty PPC services, 63% reported access to pain management, and 28% access to bereavement services [130]. Access varied by economic status of the country of origin with fewer physicians from low-income countries (LIC) reporting availability of programs in palliative care, pain management, bereavement care, and ethics. Respondents from LIC also reported fewer institutional policies and/or national laws to guide decisions regarding withholding and withdrawing of life-sustaining therapies.

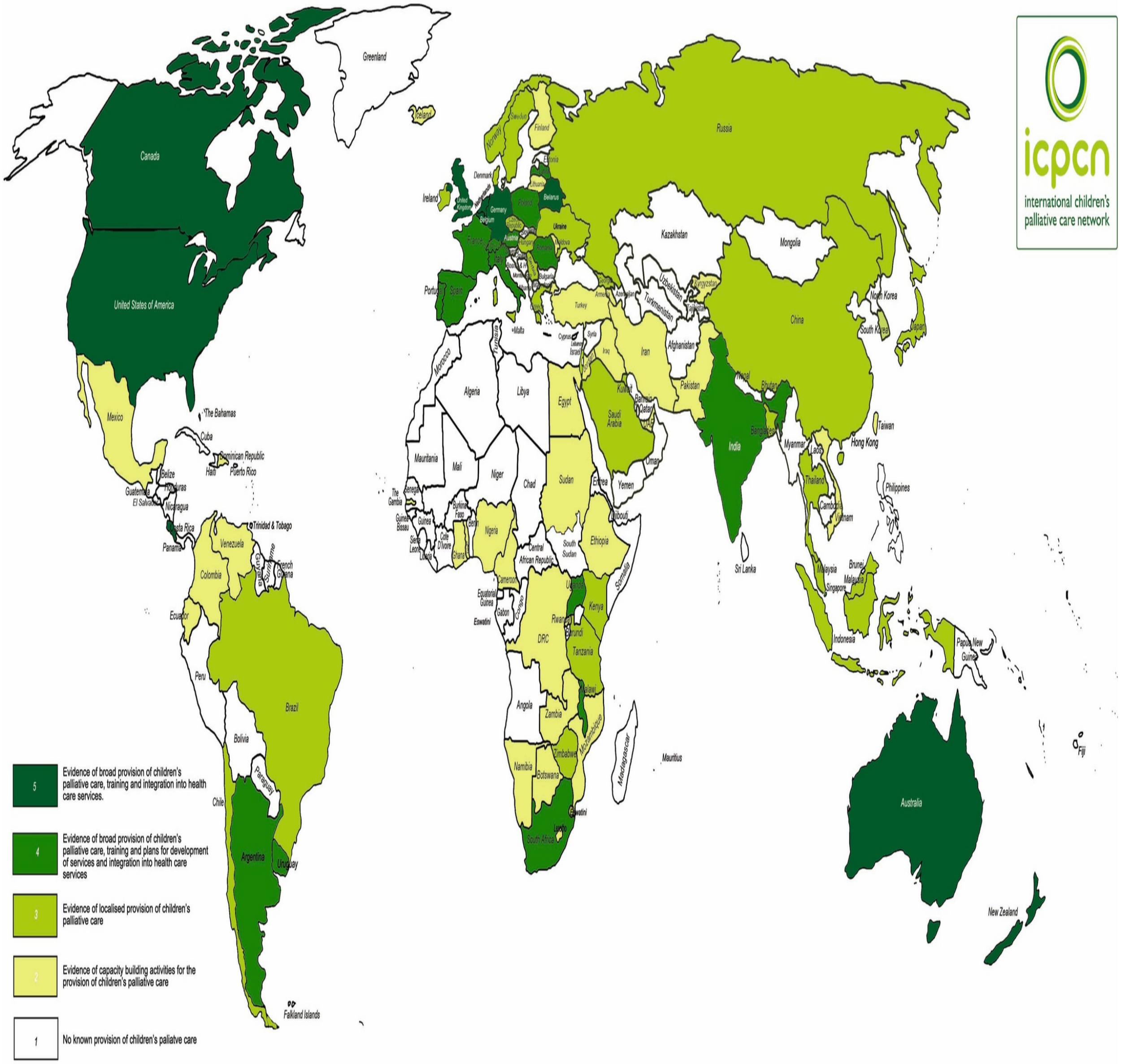

Fig. 11.3 Map showing the International Children's Palliative Care Network estimated levels of children's palliative care worldwide. From "Global levels of CPC provision: ICPCN estimated levels of children's palliative care provision worldwide [Internet]," by International Children's Palliative Care Network, 2019 [cited 2019 July 15]. Available from https://www.icpcn.org/1949-2/

A number of barriers to the global implementation of PPC have been cited [128, 131]. First, a general lack of understanding and awareness of the benefits of PPC among the general population as well as health care clinicians continues to limit expansion and uptake of PPC services. Subsequently, policies and procedures to support the growth and development of PPC are lacking. Without appropriate policies, support for PPC does not appear in government work plans or budgets, which limits availability and access within health care systems. Lack of clinical guidelines also limits expansion of PPC. Without clear rationale or referral guidelines, clinicians may be hesitant to use PPC services due to lack of knowledge or personal biases against PPC. Furthermore, if guidelines do not include direction on the utilization of appropriate and available medications, usefulness may be limited in countries where availability of certain medications including oral morphine and other adjuvant drugs for neuropathic pain are limited. Finally, efforts to integrate and expand PPC globally are limited by a lack of resources to support clinical care, education, and research.

Global access to PPC and hospice is urgently needed for the most vulnerable of patients, our children. Lack of access to PPC should be seen as a public health and human rights priority, and as such, advocacy is needed within all levels of health care systems and governments [128]. The International Children's Palliative Care Network (ICPCN, www.icpcn.org) is an international charity working globally for the rights of children with palliative care needs. ICPCN drives policy around the world, and ensured that the "Resolution of Palliative Care" adopted by the Worth Health Assembly in 2013 to develop, strengthen, and implement palliative care policies included provisions for children. Furthermore, recognizing the vast need for education, ICPCN has developed a free online, e-learning platform, www.elearnicpcn.org, that provides accessible palliative care education in multiple different languages. Finally, global research priorities have been established and include examining (1) children's understanding of death and dying, (2) managing pain when morphine is not available, (3) funding for and cost of PPC, (4) training needs, and (5) assessing the WHO two-step analgesic ladder [128].

11.11 Evidence-Based Findings Derived from the Science of Palliative Care in Pediatric Oncology Ready for Translation to Clinical Practice

While much of the research that has been conducted by palliative care nurse scientists and interdisciplinary teams has been exploratory and descriptive in nature, a number of the findings are ready for translation into practice. These findings include:

- All pediatric and AYA patients with newly diagnosed cancer should receive care that is grounded in palliative care principles from the time of diagnosis.
- Patients with poor prognoses, poorly controlled symptoms, and complex care requirements benefit from specialized palliative care.
- Communication among patients, families, and clinicians should be developmentally appropriate and oriented toward patient and family preferences.
- Parents and AYAs prefer that diagnostic and prognostic information be disclosed in an honest, but hopeful manner, regardless of prognosis.
- Parents report information needs throughout the cancer experience.
- Parents and patients, when appropriate, should be engaged in planning EOL care including preferred location of death.
- AYAs with cancer should be provided the opportunity to engage in facilitated ACP discussions.
- Goals of cure and quality of life are not mutually exclusive.
- Health care clinicians require additional training to better understand the basic tenets of palliative care and to feel confident and be competent in providing primary palliative care to all patients. Training should be interdisciplinary in nature.

11.12 Future Research Recommendations for Palliative Care in Pediatric Oncology

While the theoretical foundations of PPC are well established, great opportunity exists to generate meaningful data to further support the benefit of PPC upon patient, family, clinician, and health care system outcomes. Future areas of research include:

- Inclusion of the patient’s voice. Only a limited number of studies include the voice of the child. Recognizing and valuing the child’s voice in the different aspects of PPC are integral to providing care within a personalized health framework.
- Inclusion of culturally diverse perspectives on the different elements

and structures of PPC.

- Comparison of different models of PPC provision, including an embedded model, with attention to cost, staffing needs, scope of practice (inpatient, outpatient, community), and related outcomes.
- Evaluation of different models to expand access of PPC to children and AYAs in resource-poor countries.
- Examination of the role of spirituality in assessment and support of each patient and family unit.
- Examination of the role of complementary and alternative medications in the realm of PPC.
- Longitudinal and situational examination of child and AYA decisional preferences over the course of the illness experience.
- Establishment of quality metrics and outcome measures for assessment of PPC outcomes longitudinally. No pediatric-focused outcome assessment measures are consistently used to capture the impact and value of PPC.
- Description of the role of PPC in the transition to survivorship and outcomes related to the early integration of palliative care among survivors.
- Establishment of comprehensive, reproducible bereavement programs with measurement of psychosocial, emotional, and spiritual outcomes among parents and family members.
- Examination of parent treatment choices at EOL and association with decisional regret and other psychosocial outcomes.
- Description and examination of the impact of PPC practice on health care clinicians.

11.13 Conclusion

Due to its holistic groundings and person-centered approach, PPC has been identified as an essential component of comprehensive pediatric oncology care. Furthermore, the benefits of the early integration of PPC into the care of pediatric and AYA patients with cancer have been well described. With an emphasis on quality of life, PPC supports communication among patients, families, and clinicians, assists with complex physical and psychosocial symptom assessment and management, facilitates ACP and decision-making throughout the illness trajectory, and supports bereaved families. Through their training and holistic orientation, nurses contribute significantly to PPC teams by providing care, supporting education and research, and advocating for patients and families. Despite the described benefits of PPC, many and varied barriers exist worldwide, which prevent patients and their family members from consistently accessing PPC. Additional advocacy, education, and research are necessary to continue to raise awareness of PPC, document its benefits longitudinally, support clinical guidelines, and ensure universal access.

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12. End-of-Life Communication

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Abstract

Effective end-of-life (EOL) communication between pediatric oncology providers and child and family members is essential to minimizing unnecessary additional distress and to maximizing quality of life as care goals shift from curative-focused to comfort and end-of-life (EOL) care. EOL communication is information-sharing among children, family members, and health care providers regarding the child's illness, prognosis, and goals of care as the child transitions to the end of his/her life. Information-sharing comprises components of communication and types of communication within the context of the child's and family's lifestyle and culture. Communication experiences that occur at the diagnosis of cancer and early in the ill child’s illness trajectory can leave a lasting imprint and shape future communication experiences. Research indicates that offering the ill child, when appropriate, and family members the opportunity to engage in information-sharing that is direct, open, honest, and caring, optimal short- and long-term outcomes related to goal-concordant and high-quality care and bereavement are achieved. Health care providers are key participants and often the drivers of information-sharing with children and family members about the child’s condition. However, research demonstrates that pediatric oncology providers can struggle with barriers to promoting effective EOL communication. This chapter summarizes the scientific foundation related to EOL communication in pediatric oncology and includes recommendations for clinical practice to achieve optimal communication outcomes during EOL.

Keywords Communication – Palliative care – End-of-life – Pediatric – Cancer – Prognostic communication – Anticipatory guidance – Education

12.1 Introduction

Pediatric palliative care is an active, holistic approach to care for children with serious and/or life-threatening conditions that embraces the physical, emotional, and spiritual support needs of affected children, and the needs of their parents and other significant family members (e.g., siblings, grandparents). National organizations [1, 2] have recommended that providers who introduce the role of pediatric palliative and, when appropriate, end-of-life (EOL) care with parents should focus on the importance of enhancing the quality of life of the affected child and family. Enhancing quality of life includes planning and implementing strategies to manage distressing emotional and physical symptoms and offering emotional support throughout the treatment trajectory as well as bereavement support following a child’s death.

Children diagnosed with cancer and their families experience significant stress as they struggle with the effects of treatment, uncertainty related to prognosis, and dramatic shifts in their family life. High quality communication between pediatric oncology providers and the child/family is fundamental to minimizing unnecessary additional distress and maximizing overall child and family quality of life over the course of care. High-quality communication is particularly essential when a long hoped- and worked-for cure is no longer an option and care goals shift to comfort and EOL care.

The concept of precision health offers a useful framework for organizing our understanding of EOL communication in the context of childhood cancer, and thus guides the content of this chapter. First, this chapter addresses the importance of EOL communication, including tenets of national organizations highlighting the urgent need to improve palliative and EOL communication to affected children and family members. Next, this chapter provides a review of a recognized definition for communication, different components of communication (e.g., sender, message, and receiver), different types of communication (e.g., verbal, non-verbal, liner, circular), and cultural considerations. Following the broad introduction to communication, the chapter includes a synthesis of research and other evidence-based findings interpreted within the Precision Health Framework (Fig. 12.1). At the center of the framework is the interconnectedness among the child, family, and lifestyle. This chapter also addresses EOL communication perspectives of children and family members, the link between EOL communication and the child's and family's health and well-being and includes clinically useful recommendations for developmentally and culturally appropriate communication. The child, family, and their lifestyle exist within the complex interactions among the framework components of nursing, nursing science, and environment. These components influence one another as well as the child outcomes associated with their health and well-being. Therefore, this chapter also addresses EOL communication perspectives of pediatric oncology nurses and health care providers and discusses barriers and facilitators of EOL communication. Finally, this chapter offers strategies and resources to increase provider skill and competency in patient- and family-centered EOL communication and the importance of providing anticipatory guidance to both.

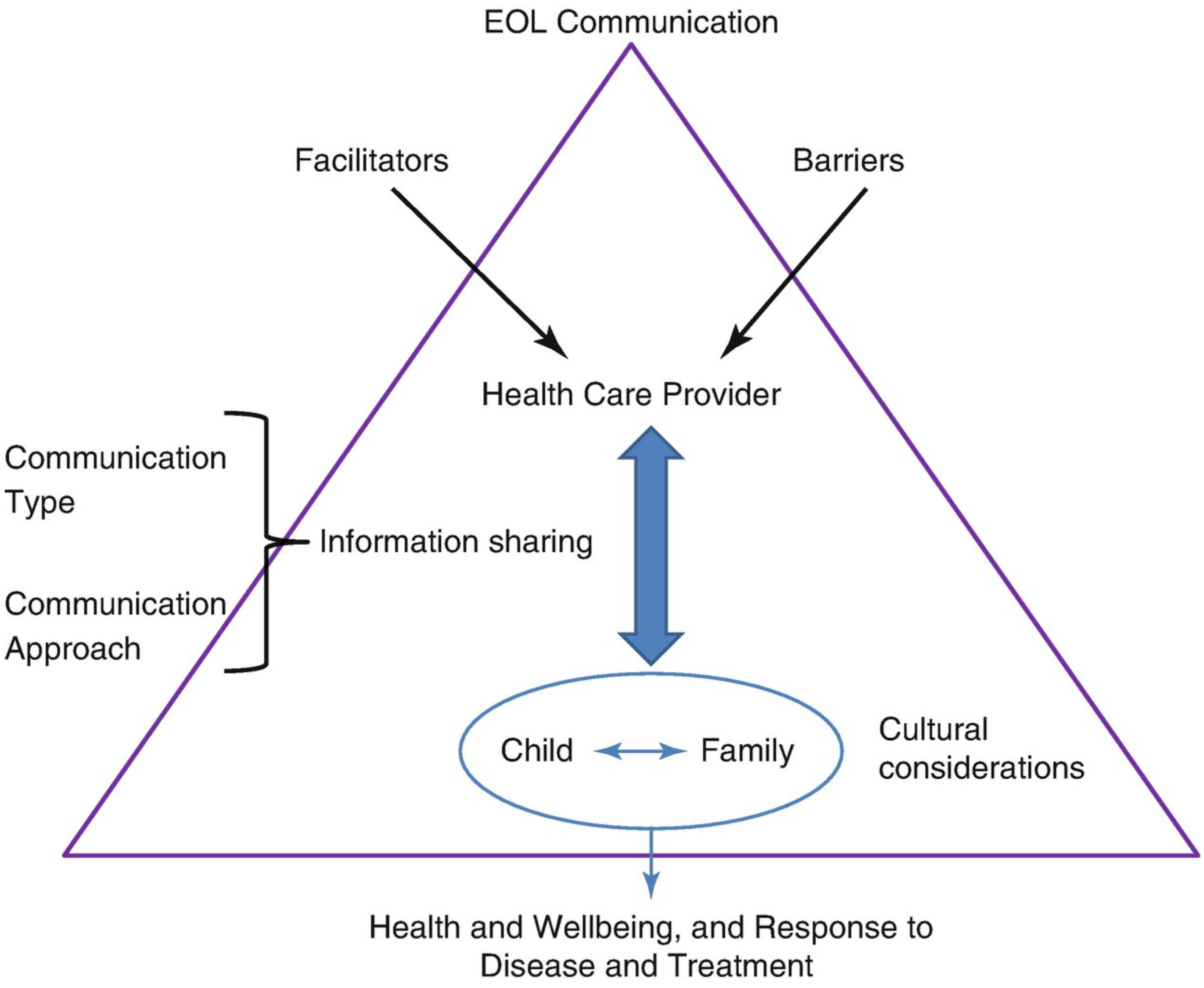

Fig. 12.1 End-of-life communication among the child, family, and health care providers within the context of precision health on child and family

12.2 The Importance of EOL Communication

Disclosing health information to parents related to a cancer diagnosis, treatment, and prognosis or a new EOL care recommendation is typically very distressing for physicians and emotionally difficult to be received by affected patients and their family members [3]. Understanding complex health care information about a life-threatening and life-ending illness, and subsequent health care decision-making can be a very difficult transition for parents. Parents of children with a cancer diagnosis experience emotional distress when receiving provider communication about implications of disease progression and the shift from a cure-oriented treatment focus to one of EOL care. Pediatric oncology providers have reported a perceived tension in parents when conveying a poor prognosis or when engaging in discussions about the benefits of a primary focus on quality of life and symptom management [4]. However, some research has shown that clear prognostic disclosure to parents is not associated with higher rates of parental distress, instead that the delivery of honest communication about prognosis is associated with greater parental peace of mind and trust in their child's physician [3, 5]. Research has also shown that when parents received complete and timely prognostic information about a child's cancer, they were more likely to report their child's physician made them feel hopeful [5]. These parents maintained higher hope over time [6]. Investigators have also reported that when providers engage in prognostic discussions, they are able to explore parental values, hopes, and fears about their child's future, before there is a health crisis requiring parents to make EOL decisions for their child [7].

12.2.1 Tenets of National Organizations

Numerous national health care organizations have declared that delivery of timely and clear communication about EOL care with patients experiencing a serious and/or life-threatening condition and their family members is a preferred practice by all health care providers (Table 12.1). These organizations also indicate that physicians and nurses have an ethical responsibility to inform parents of all treatment options, including palliative and EOL care to facilitate advance care planning and to honor parents' preferences for the location of their child's EOL care [1, 2]. Thus, a key component of palliative and EOL care is ongoing parent–provider communication and patient–family-centered decision-making relateds to goals of care during disease progression [8, 9].

Table 12.1 Recommendations from national organizations on palliative care

Organization	Title of document	Relevant recommendation(s)
American Academy of Pediatrics (AAP)	Pediatric Palliative Care and Hospice Care Commitments, Guidelines, and Recommendations	• Palliative care be initiated at diagnosis for children with a life-threatening condition • Providers should facilitate clear and honest discussions with patients and families about therapeutic goals and concerns, the benefits and burdens of therapies, and the value of

		advance care planning
National Institutes for Nursing Research (NINR)	Palliative Care: Conversations Matter®	• Identified palliative and end-of-life care for children with cancer as a research priority for the twenty-first century with a focus on improving health care provider communication with family members • Promote awareness of palliative care benefits for patients and their family members and to foster early palliative care discussions by providers with patients and family members
National Hospice and Palliative Care Organization (NHPCO)		• Palliative care and provider communication integrate the family's hoped-for goals into the pediatric patient's care plan
Institute of Medicine (IOM)	Dying in America: Improving Quality and Honoring Individual Preferences near the End of Life	• Improve health care provider delivery of palliative and end-of-life communication approaches to patients and their family members • Offer health care providers incentives and standards to deliver patient–provider communication • Leverage current health care related technology to allow electronic medical records to document and communicate patients' wishes across health care settings

Despite published national organization tenets about the need for health care providers to deliver early and clear communication about palliative and EOL care support for patients with a poor prognosis, there remains conflicting opinions by health care providers about the timing of such discussions with parents of children with cancer [10]. Several studies have provided evidence that pediatric providers often struggle with when and how to initiate early discussions about prognosis and EOL goals of care with parents because of limited palliative and EOL communication training [10]. The providers' struggle is compounded by their perceptions about parents' preferences and readiness to receive the difficult information about their child's condition [10]. Research has also provided evidence that early delivery of palliative care fosters more effective symptom management in pediatric patients with a poor prognosis and may help to reduce the emotional distress experienced by their family members [11]. Additionally, provider discussion of the benefit of early palliative care (a) helps minimize negative coping responses among parents, (b) facilitates making early advanced care planning decisions, (c) aids in receiving timely EOL care support for pediatric patients with a poor prognosis that have not benefitted from existing medical treatments, and (d) does not reduce parental hope [5, 12].

12.3 Definition and Principles of Effective Communication

Effective communication by nurses and other health care providers is essential to maintaining trusting and therapeutic relationships with pediatric oncology patients and their family members during all aspects of health care delivery to a child with cancer, and especially when heath care providers intend to initiate early EOL care discussions. To engage in high quality family-centered communication, nurses and other health care providers must be knowledgeable and competent in diverse communication skills from which to select a tailored approach for their planned discussions with patients and family members.

The most common communication behaviors used with another individual are either verbal or non-verbal forms. Verbal communication is typically defined as an exchange of specific information with one or more individuals and may also include sharing of an individual's thoughts, perspectives, and feelings [13]. In comparison, non-verbal communication is typically recognized to include one or more of the following physical behaviors: body movements (e.g., head nodding, hand movements, touch, displayed distance from others, etc.) and/or related facial expressions and behaviors (e.g., eye blinking, avoidance of eye contact, eye staring, facial smiling or frowning, etc.).

Patients and family members may focus not only on their providers' verbally delivered health care information but also on their provider's non-verbal behaviors. For example, providers initial non-verbal cues and body language behaviors when entering a private conference room to discuss a patient's health status with the patient and family members may adversely influence the perceptions held by patients and family members about the purpose of the meeting and influence the communication that follows [14]. Patients have reported that their assessment of a provider's subtle non-verbal cues (e.g., being unusually quiet, or distracted) may be interpreted as potential clues of receiving a negative report (e.g., cancer recurrence) about their health status [15]. Research has also provided evidence that patients with chronic conditions including cancer expect providers to display high quality communication skills (e.g., displaying patience, being honest, comfortable talking about sensitive topics, being treated as though they are valued, having their unique life histories acknowledged) during all professional encounters [16]. The potential implications of provider's subtle non-verbal cues and verbal communication during encounters with patients may influence how patients and family members respond to discussions about recommended health care options, such as the benefits of palliative care support and/or the transition to a focus from curative treatment to a focus on EOL care [14].

Use of consistent and sincere listening skills is an essential component of effective health care providers' communication with patients and family members [17]. Patient dissatisfaction with provider communication is often associated with the patient's perception of not being heard by health care providers. In contrast, health care providers' use of excellent listening skills is associated with establishing and strengthening the trust between a child and the child's health care providers [17]. Health care providers need to use the Best Ways to Listen and Learn about their patients to guide conversations (Table 12.2).

Table 12.2 Best ways to listen and learn

Best ways to listen	Example(s)
Be engaged and demonstrate your interest	Avoid technology distractions Turn off phones and pagers
Use of paraphrase responses	Echo expressed concerns, hopes, distress, or acceptance
Ask open-ended questions	*Please tell me more about how you are feeling*

Acknowledge their feelings and concerns	*It sounds like this was very difficult for you and your family*
Convey empathetic responses	*This must be very overwhelming to you*

Nurses and other health care providers can selectively use different types of patient- and family-focused questions related to the purpose and goals of discussions with patients and family members. Depending on the goals of planned patient- and family-focused discussions, health care providers may consider use of five types of questions: linear, circular, temporal, triadic, and/or mindreading questions [18]. Linear questions are typically used for gathering specific information about a patient's current and past health vital signs, history, and symptoms. In comparison, circular questions can be used for the following four different types of patient- and family-focused discussions: (a) questions crafted to help define an important concern or problem of an individual; (b) questions crafted to help evoke sharing perspectives about the impact of a sequence of health-related events; (c) comparison or classification questions crafted to help evoke sharing of perspectives about the impact of interactions or behaviors made by others; and (d) interventive questions crafted to help an individual consider changing a behavior. Temporal questions can also be used with patients and family members to help foster individual reflection and evaluation of past events that may have been helpful or less helpful and consideration of future changes that may be helpful to the individual. Triadic questions can be used to help foster reflection upon how the individual and other family members may respond to each other's emotional responses (e.g., being supportive when someone cries). Finally, mindreading questions can be used with patients and family members to help foster individual consideration and reflection about possible responses and reactions by others to different family situations. See Table 12.3 for a concise description of each type of question and an example format of applying each type of question approach when engaging in systematic questions related to palliative and EOL care discussions with pediatric oncology patients and their family members.

Table 12.3 Types and example communication approaches

Types of	**Description of**	**Example communication**

communication approaches [18]	communication approach	approaches
Linear questions	To determine specific information about an event or situation	How long (e.g., days, weeks, etc.) has your child been ill? Please share your child's current symptoms
Circular questions	To foster individual perspectives of the roles and relationships of their family members	Who in your family has been most affected by your child's symptoms and physical care needs? Please also share how? Can you share a little more about that?
Temporal questions	To evoke individual perspectives about a situation that may have changed or may change over time	I wonder if there is anything different about your child's past physical care needs compared to your child's current needs?
Triadic questions	To evoke comparisons of how the actions of two people might affect the mood or behavior of a third person or others	What would be your priority suggestions (or advice) to other parents who will be caring for a child with cancer in their home?
Mindreading questions	To evoke individual perspectives about a hypothetical situation and/or a health care role and what the individual might do or say related to the situation	What do you think would happen if your child was to receive care from a home care service and it was not clear to you who had the skills necessary to match your child's needs?

Effective and therapeutic health care provider communication practices involving patients and family members should include clear verbal communication with all involved individuals. For instance, when communicating with pediatric oncology patients and their family members about sensitive topics related to prognosis and palliative and EOL care benefits, it is important for health care providers to conduct an assessment of the patient's and family member's cultural background and health-related values, hoped-for goals, beliefs, preferences, and practices [19].

12.4 Elements of Effective EOL Communication

Essential care of the child with cancer and his/her family includes a commitment to open communication with family members and the child [20]. Communication experiences that occur from diagnosis and throughout cancer treatment can make a lasting imprint on the child and family. Even a single experience of insensitive communication may lead to unnecessary parental distress [21]. Communication is a critical component to the child's transition to EOL. Communication is central to care coordination, decision making, and symptom management. EOL communication is a difficult, yet a necessary element of care for children who will experience a cancer-related death.

12.4.1 Child and Family Perspectives

At the center of the Precision Health Framework is the interaction among the child, family, and lifestyle, which requires a comprehensive approach to communication during the highly vulnerable period of EOL. The interconnectedness children exhibit with respect to other family members should not be ignored. As a child faces death, he may grapple with his own role within the family structure and wonder how family members could go on without him [22]. The child and family face uncertainty during this life transition and throughout the EOL trajectory. Information sharing, allowing time to process, and decision-making are key processes of effective communication.

Providers may face a challenge early in EOL communication when determining who within the family structure should be included in information sharing. Health care and treatment-related communication with parents should include the pediatric patient with cancer, from the time of their initial diagnosis to the point that the ill child prefers [17, 23, 24]. The child preference may vary by topic and the child's health status [24]. Some parents may prefer to not include their child in any meetings with providers because of their attempt to protect the child; the risk of this protective behavior is that it may cause the child to experience emotional distress related to uncertainty about his/her health status. Evidence indicates that children are often aware of the seriousness of their illness [25, 26]. One recommended provider approach to support parents' comfortableness with having their ill child present during meetings is to pose an assessment question, such as “What are some of your concerns about having your child participate in our meetings?” [17].

Research has demonstrated that, when developmentally and culturally appropriate, the child should be offered the opportunity to participate in discussions surrounding prognosis and EOL [4, 20–24, 27–34]. Assessing what and how much the child knows and how much more the child would like to know about his disease, prognosis, and symptoms lays the foundation for the provider to proceed with communication. The same assessment should be completed for other family members, including the parents and the siblings [20, 21, 35]. Providers should be aware that information the child or family knows at one point in time and what they wish to know may fluctuate and change over the continuum of care as circumstances change [20, 24]. Once engaged in information-sharing, parents and children require clear and honest communication [4, 20, 21, 23, 33, 34, 36] that leaves them with a sense of preparedness for EOL [4, 21, 30]. Furthermore, parents value a trusting relationship and receiving information consistently from a primary oncology care provider [21, 30, 32]. When engaged in the information-sharing process, parents and children require room for hope while receiving concrete information about the reality of prognosis [21, 23, 29, 33, 34].

Having the knowledge, or understanding the importance of facilitating clear, direct, and honest communication, and the skill to communicate with compassion are both required to achieve optimal outcomes of effective EOL communication. However, research has shown that discussions of death and dying with the child and providing parents with guidance on how to speak with their child about death are two elements of palliative care delivery that are least provided by members of the health care team [37]. Access to palliative care specialists increases the likelihood of parents receiving guidance about death and dying [37]; these can provide mentorship in developing communication skills specific to discussing EOL with child and adult family members.

Several theories in seminal publications address a child’s understanding of death and related concepts. One theory describes children’s understanding of death occurs over a variable time span (Table 12.4) [38], and includes three major components: irreversibility, non-functionality, and universality [38]. A child’s ability to understand each component is generally achieved between the ages of 5–7 years [38]. However, it is unknown if the time it takes for a child to understand death differs for acutely chronically ill children.

Table 12.4 Components of death [38]

Component of death	Definition	Children's early views
Irreversibility	The understanding that once a living being dies, its physical body cannot be made alive again	Death is temporary and reversible
Non-functionality	The understanding that all life-defining functions cease at death	Dead beings do not possess all the functional capabilities of alive things or dead things have diminished capabilities for specific functions
Universality	The understanding that all living beings die	Death can be avoided through certain actions

Healthy children ages 4–7 have demonstrated a greater understanding of death and related concepts compared to what their parents believe them to understand [39]. Parents have been shown to generally speak with their child about the concept of death around 3 years of age [40]. Parents report greater levels of satisfaction when the explanation of death provided includes some type of continued existence after death, which may include reference to an afterlife or legacy regardless of religious or spiritual beliefs [40]. Within the context of childhood cancer, research has shown only one-third of parents who had a child die from cancer spoke directly with their child about death, compared to two-thirds of the parents who did not speak with their child about death [41]. For the parents who discussed death, none were found to regret doing so, while one quarter of parents who did not discuss death did voice regrets in not having the conversation [41]. With little empirical evidence outlining what children with life-threatening illnesses understand specifically about death and at what age, it is important for providers to tailor an approach to optimize direct, honest, and open communication.

12.4.2 Challenges to Effective EOL Communication

Challenges to communicating effectively during EOL have been documented in several studies. One challenge that creates a significant barrier for providers is when parents are unwilling to receive bad news [28]. Unwillingness to engage in communication about a child's prognosis and possible or likely death may be a behavior exhibited to protect the parent from difficult emotions associated with the anticipated death of their child. Unique considerations of pediatric palliative care and related provider communication with parents of children with cancer are a focus on the parent's ability and willingness to participate in information-sharing opportunities that can be emotionally difficult (Table 12.5).

Table 12.5 Unique considerations of pediatric palliative and EOL care communication with parents of children with cancer

- Understanding of the uncertainty of their child's prognosis
- Receiving poor prognosis information without experiencing increased anxiety, reduced trust in their child's provider, and decreased hope
- Receiving complex information related to their child's cancer diagnosis and cancer treatments
- Experiencing potential unpredictable symptom responses to cancer treatments and the risk of unsuccessful responses to received cancer treatments
- Changing developmental needs of a child with cancer and any siblings in the family
- Learning how to communicate effectively with multiple care providers involved in their child's cancer care over time
- Understanding the purpose of palliative care versus EOL care

Another challenge providers may face at the child, family, or lifestyle level is providing culturally appropriate communication. Receiving communication that is not culturally tailored can lead to distressing experiences for parents [21, 28]. Furthermore, receiving conflicting [4, 21], insufficient, or inappropriate information can contribute to negative experiences and a parent perception of not being prepared for what comes next [21, 42, 43]. An unexpected barrier to effective EOL communication is when a provider conveys excessive hope or optimism while delivering bad news [43].

12.4.3 The Meaning of Culture and EOL Communication

Cancer care for a pediatric patient and family holds specific consideration of family members’ individual beliefs, values, practices, and behaviors that may impact the child’s health care management in the home setting and family health care decisions for their child in the hospital setting. Additionally, the patient and/or family not speaking or understanding the primary language of the health care team and other language barriers can further complicate efforts to help parents participate in making informed decisions about the health care needs of their child, especially if the child’s cancer has a poor prognosis. For these reasons, providers must be knowledgeable about culturally competent patient–provider communication considerations when planning patient- and family-focused discussions.

An individual’s culture is often described as a system of beliefs, values, rules, and customs that may be shared in a group or the individual’s family system [19, 44]. To ensure effective communication with patients and family members, providers need to assess an individual’s culturally based values regarding medical and EOL care to facilitate providers’ understanding of culturally specific perspectives and behaviors.

Several tenets related to culture and their impact on communication with parents and children with cancer in culturally diverse families have been identified [19]. One tenet is that cultural aspects of a family system influence how children and adolescents diagnosed with cancer display and/or communicate symptoms and feelings [19]. A second tenet is that poorly shared or conflicting information by family members and/or by a child with cancer may be related to the family’s cultural beliefs about sharing their worries about their ill child [45]. A third tenet is that in many cultures, nondisclosure of malignant disorders to a child is the family’s practice [45]. A fourth tenet is that it may be more difficult for parents to comfort, support, and communicate with adolescents with cancer than with children of younger ages with cancer [19]. A fifth and final tenet is that mindful communication strategies may be helpful when providers need to engage in discussions about palliative care support with individuals across cultures [46]. Mindful communication strategies include providers being vigilant and practicing situational self-awareness and reflection of the timing, nature, and context of information that is selected to be shared with patients and family members [46].

Unfortunately, few studies have provided strong evidence regarding the role of culture and specific communication recommendations to use with culturally diverse family members of a child with cancer. Based on the limited and weak evidence about recommendations to guide health care providers in culturally specific communication with patients and family members, more rigorous and longitudinal intervention studies are needed. Until fully evidence-based guidelines are established, when planning discussions with culturally diverse pediatric oncology patients and their family members, providers need to use caring responses and integrate knowledge of a child's developmental stage, age-related differences, and cultural differences into all discussions [19]. A 2017 systematic review provided evidence that children and parents prefer the following communication approaches from pediatric health care providers: (a) ongoing communication about their child's illness throughout the trajectory; (b) honest, sensitive, empathetic, and hopeful communication responses from providers; (c) high quality communication to foster parents' peace of mind relative to uncertainty about their child's care; (d) engaging in communication and decision-making with their child's health care providers; and (e) recognizing that children may vary in their desire to be involved in decisions and to be included in meetings with providers [23].

12.4.4 Relationship Among Children and Family Members with Health-Related Outcomes

Palliative and EOL communication with children with cancer and their family members needs to be clear, effective, caring, and consistent by all interdisciplinary team members who will be with the family from diagnosis forward [4, 17]. Such communication by and within the child's health care team can foster a more positive experience for the child and family during treatment, and through the child's EOL care and the family's bereavement. Research indicates communication experiences during EOL are linked to the family's subsequent health and well-being, including goal-concordant care [47], parental ratings of care [4], and experiences of bereaved family members [21, 48].

Parents perceive experiencing goal-concordant care with quality decision-making and effective communication [47]. Through quality communication health care providers can provide clear and honest information about a child's disease and prognosis and can engage family members in dialogue to identify care preferences and goals of care. Understanding that preferences and goals may shift over time, communication is essential to optimize the child receiving goal-concordant care.

Health care provider communication and parental health and well-being have been linked to parental peace of mind, parents feeling acknowledged and comforted, and greater trust in the physician [23]. In contrast, emotional distress secondary to poor communication can lead to challenges with managing grief over time after a child's death [21, 48]. Positive emotional outcomes linked to quality communication can influence parental ratings of care satisfaction [4].

To ensure providers' delivery of consistent and effective communication to parents about their child's care in consideration of the benefits of palliative and EOL care support, the following strategies are recommended: (a) conduct interdisciplinary team meetings before family meetings to ensure the family receives consistent information from the team members; (b) reach consensus within the interdisciplinary team about the specific content related to the child's status and treatment response to be shared during family meetings; (c) reach consensus related to sharing any changes in the child's condition and recommended treatments during family meetings; (d) clarify the roles of all interdisciplinary team members during family meetings; and (e) allow the family to share any concerns about family dynamics or the pediatric patient [17].

12.4.5 Nurse and Health Care Provider Perspectives

Health care provider initiated high-quality communication across a cancer trajectory is influenced by a number of individual, team, and environmental factors [49–51], increasing the potential for miscommunication and emotional distress for families and health care providers alike [52]. Communication is a central component of patient- and family-centered care (PFCC), which is recognized by the American Academy of Pediatrics as a hallmark of pediatric health care (Table 12.6).

Table 12.6 American Academy of Pediatrics components of patient–family-centered care [53]

Listening to and respecting each child and his or her family. Honoring racial, ethnic, cultural, and socioeconomic background and patient and family experiences and incorporating them in accordance with patient and family preference into the planning and delivery of health care
Ensuring flexibility in organizational policies, procedures, and provider practices so services can be tailored to the needs, beliefs, and cultural values of each child and family and facilitating choice for the child and family about approaches to care
Sharing complete, honest, and unbiased information with patients and their families on an ongoing basis and in ways they find useful and affirming, so that they may effectively participate in care and decision making to the level they choose
Providing and/or ensuring formal and informal support (e.g., peer-to-peer support) for the child and family during each phase of the child's life
Collaborating with patients and families at all levels of health care: In the delivery of care to the individual child; in professional education, policy making, program development, implementation, and evaluation; and in health care facility design
Recognizing and building on the strengths of individual children and families and empowering them to discover their own strengths, build confidence, and participate in making choices and decisions about their health care

Central to achieving quality PFCC is the role of relationship-based care [54] which promotes the role of authentic human connections and therapeutic relationships between patients and caregivers as the basis for safe, quality care delivery. Numerous studies of pediatric oncology nurses, physicians, and psychosocial care providers cite the necessary relationship between the patient/family and providers as both a source of professional satisfaction and of distress [55–62].

Despite the importance of communication in maintaining trusting relationships with patients and families as well as within the interdisciplinary team, little formal communication training is provided in medical and nursing professional educational programs, leading to wide variability in communication skills across health care providers as they enter practice [63, 64]. Lack of interdisciplinary education regarding team-based communication can lead to discrepant information-sharing with children and families that can result in role confusion, miscommunication, and conflict among providers and family members [65, 66]. Physicians and nurses rank communication related to illness and treatment as one of the most important competencies in their practice [64, 67]; however, both groups report being less competent in addressing emotional needs of their patients as well as engaging in difficult conversations involving serious information, including EOL issues [63, 67–70].

Studies have identified several provider characteristics that create barriers to effective EOL communication. Mack [52] interviewed physicians and parent dyads and identified 20 of 29 relationships reported as difficult by both the parent and provider. Core issues leading to perceptions of difficult communication involved problems of provider–family connection and understanding, confrontational parental advocacy, parental mental health issues, and structural challenges (physical environment, care standards, etc.) to care. Parents who described the relationship as difficult reported feelings of distress, vulnerability, anger, mistrust, and a belief that the physician did not care about their child. Physicians reported feelings of frustration, lack of trust in parent, and distress/anxiety.

An integrative review of studies about parents' perspectives of nurses' delivery of family-centered care in intensive care described experiences where parent respect and dignity seemed low as evidenced by perceived lack of compassion, cold/callous communication, inappropriate body language, feeling judged by nurses, hearing insensitive comments, and lack of empathy [71]. Perceived family-related barriers to effective provider–family communication regarding EOL care include families with faith or cultural values different from those of the care team, angry or demanding families, parents who research information on the internet and challenge the treatment plan, and families who continue to pursue disease-directed treatment despite disease progression and the child's declining quality of life [52, 72, 73].

Treatment for childhood cancer involves adherence to complex treatment protocols, managing treatment side effects as well as unexpected complications and crises, and attention to the emotional and supportive care needs of patients and families in home and treatment settings. Parents and providers traverse the treatment landscape within a complex undercurrent of hope for cure and fear of death or disability. As such, the physical, mental, and emotional demands on pediatric oncology providers over the child's trajectory of care have been associated with experiences of burnout, compassion fatigue, moral distress, and grief [57, 59, 60, 74]. While these experiences have varying definitions and characteristics (Table 12.7), collectively, they are often interconnected and exacerbated by the emotional demands that occur in the patient–provider relationship [74].

Table 12.7 Experiences of provider distress [57, 59, 60, 74]

Burnout	Difficulty coping with stress and demands of the work environment
Compassion fatigue	Effect of witnessing suffering, tragedy, and loss within nurse/patient relationships
Moral distress	Result of situations where nurses recognize a moral or ethical issue in the care of patients but are unable to resolve the dilemma
Grief	Process of mourning deaths of children with whom providers have had a close personal and emotional connection

The most common sources of distress in providers center around difficult conversations related to shifting goals of care from cure to quality of life at EOL, managing the emotional challenges of supporting families, conflicts around demands for non-beneficial care and resultant suffering, as well as interprofessional team issues related to blurred and overlapping professional boundaries, devaluation of professional roles, challenging workloads, and sorrow over patient deaths [74–76]. Providers who experience distress related to their caregiving role and relationship with patients may experience decreased empathy and become distant and task-focused, which in turn erodes effective communication and guidance as well as overall quality of care.

Davies [77] interviewed families of children with complex medical conditions, including cancer, and their health care providers across several clinical sites to determine best practices in provider–parent interactions. Key components of best practice interactions between providers and parents included a broad world view, commitment to authentic engagement and connection with patients and parents, and expertise in clinical care and attunement to patient and parent needs over the illness trajectory. Some parents of children with cancer have reported that they appreciate their oncologist's focus on the clinical care of their child but did not feel it necessary to discuss emotional issues with the oncologist [58, 72]. Additional high quality communication skills employed by oncologists include use of open-ended questions, clarifying perspectives of the patient and family members, checking understanding, and acknowledging and responding to patient and family emotions [67]. Parents of technology-dependent children identified several key components of effective PFCC and communication that involved providing clear information, involving parents in the care of their child, engaging in reciprocal trust and respect with parents, maintaining caring attitudes, and advocating for the child [78]. Interviews with hospice nurses engaged in EOL decision-making with parents identified contextual awareness, attentive listening, creating a safe space for EOL, setting goals of care, and being honest as key aspects of assisting parents during their child's EOL journey [79]. Eliciting the perspectives of nurses, clinicians, and parents is essential in identifying characteristics of effective EOL communication and opportunities to assess and optimize anticipated barriers in pre-communication planning.

12.4.6 Health Care Provider Training in EOL Communication

Health care provider deficits in high quality communication skills have led to the development of a variety of communication training methods [63, 67, 68, 80]. Role modeling is an employed method that involves trainees "observing" more experienced practitioners who in turn are observed by the practitioner role model. However, studies have shown that although this is the most common form of communication skill development, formal training and learner feedback are often absent [67].

Several dedicated communication training programs and curricula have been developed that focus on topics such as difficult conversations, death and dying, or addressing goals of care [81–83]. VitalTalk (https://www.vitaltalk.org/) provides evidence-based training to interdisciplinary providers caring for patients with serious illness. Both the End-of-Life Nursing Education Curriculum (ELNEC) [83] and the Education in Palliative and End of Life Care—Pediatrics (EPEC) [81] provide didactic content on communication skills as part of a larger curriculum on various pediatric palliative care competencies. Such curricula often use videos, case studies, small group, and other experiential learning activities to reinforce communication skills.

Simulation using standardized patients is another means of enhancing provider communication skills [84–86]. Providers are given topical patient care scenarios and then enter a simulated patient encounter with the goal of engaging in communication around a challenging patient clinical issue. This technique is most useful in conjunction with didactic and clinical experiences to increase communication skills [68].

To facilitate quality provider–patient relationships and communication, organizational leadership should model excellence in service and create a healthy work environment that promotes caring and healing for patients and health care providers [54, 77]. Health care workspaces that provide ample space for team members to work in close proximity had been shown to facilitate face-to-face interprofessional collaboration and communication between team members [87]. Attending to environmental factors such as dimmed lighting and comfortable seating arrangements in workstations, patient rooms and conference spaces promote longer conversations and facilitate social interactions among the interdisciplinary teams [87, 88]. In addition to creating opportunities for health care providers to interact more efficiently and effectively, health care institutions should also take steps to assess and address providers work-related distress. Examples of organizational support include supporting providers to attend ongoing communication training, implementing standardized approaches to debriefing and support after patient deaths or other emotionally charged experiences, as well as creating opportunities for providers to enhance personal self-care skills [56, 89, 90].

12.5 Strategies to Promote Family-Centered EOL Communication

Optimal EOL communication begins with optimal disease and treatment-related communication throughout the child's illness trajectory. Anticipatory guidance is an important aspect of care planning and coordination over the course of an illness trajectory [67, 91, 92], which is best accomplished by trusted providers who know the child and family, have familiarity in managing children with the same or similar conditions, and are knowledgeable about treatment options and outcomes [93].

Facilitating the transition from cure of a child's cancer to a focus on palliating symptoms and maximizing quality of life requires skilled assessment of child and family beliefs and values, understanding of disease progression and management of symptoms, and the family's preferences for care at the EOL. Early integration of palliative care can be accomplished through the use of a "day two" talk [92] that can occur in the days to weeks after initial diagnosis, as well as during times of crisis or confirmed disease relapse, recurrence, or progression. This intervention is focused on meeting with the family a few days after a difficult conversation regarding a change in treatment or the child's condition to explore the family's view of their child as a person separate from the cancer, their understanding of the information they have received, eliciting their worries and fears, and identifying sources of support for the family. The conversation closes by summarizing the discussion and clarifying any misunderstandings, followed by a discussion regarding how the team will move forward with management of the child and family's needs and a commitment to re visit goals as circumstances change.

In addition to the "day two" talk, there are a number of resources to explore the child's and family's wishes for treatment including at EOL; however, the majority are aimed at adolescents and young adults (AYA) (Table 12.8) [94, 96, 97]. These resources are best facilitated by a provider who is familiar with the child and family and has adequate time to engage in the discussion. Psychosocial providers such as Social Workers, Psychologists, Chaplains, and Child Life Specialists are ideal for introducing activities to children and families. A plan should be established identifying how to communicate important preferences to the treating oncologists and other members of the child's team. Unfortunately, data on the frequency of use or clinical effectiveness of advance planning tools for children and AYA are limited [96].

Table 12.8 Provider tools to facilitate advance care planning and EOL communication

Advance care planning tools	Description	Available languages	Recommended use
Family-centered advanced care planning survey [94]	Assesses readiness to engage in advance care planning discussions	English Spanish	Adolescents
Voicing my CHOiCES [95] (https://ccr.cancer.gov/Pediatric-Oncology-Branch/Psychosocial/education)	Advanced care planning document created for adolescents and young adults	English Spanish	Adolescents Young adults
5 Wishes (https://fivewishes.org)	Legal advanced directive document written in everyday language	English Spanish	Adolescents Young adults Adults
My wishes (https://fivewishes.org)	Booklet that helps children express how they wish to be cared for if they become seriously ill	English Spanish	Children
Go wish (https://gowish.org)	Card came that allows children and adolescents to find words to discuss what is important to them during times of serious illness	English	Older children Adolescents Adults
This is my world (https://ccr.cancer.gov/Pediatric-Oncology-Branch/Psychosocial/education)	Workbook with activities to address family, friends, coping, and loss during times of chronic or life-threatening illness	English	Children Adolescents
ShopTalk (https://ccr.cancer.gov/Pediatric-Oncology-Branch/Psychosocial/education)	Therapeutic game to help therapists lead conversations about emotional issues related to illness	English	Children Adolescents (ages 7–16)

12.6 Evidence-Based Findings Derived from the Science of EOL Communication Ready for Translation to Clinical Practice

To achieve quality communication during EOL, health care teams must work collaboratively to create a supportive environment.

1. The clinical environment should be guided by policies and clinical practice guidelines to promote effective EOL communication as well as to achieve optimal outcomes for children and family members.
2. Evidence-based recommendations for clinical practice are summarized in Table 12.9. Guided by science, the 12 recommendations provide a foundation for health care leaders to evaluate in comparison to the current state at their institution. Performing such gap analyses can be helpful in identifying institution-specific strengths and priority areas for future work.

Table 12.9 Recommendations for effective EOL communication

- Reflect on one's personal knowledge and comfort level in communicating with children and family members about EOL
- Engage in learning and training opportunities to enhance communication skills
- Conduct a team meeting before engaging the child and family members to ensure consistent information
- Consult palliative care specialists to develop an approach to communication
- Assess previous communication experiences and cultural preferences of the child and family members for engaging in information-sharing about EOL
- Re-assess communication preferences of the child and family members over time, as the child's condition changes
- Communicate openly and directly with the child, when culturally and developmentally appropriate, and family members
- Allow time for the child and family to process information following difficult conversations
- Provide anticipatory guidance clearly and honestly to children and family

members

- Provide clear information about the child’s health status while allowing room for hope
- Select listening and questioning approaches that matches the purpose and goals of EOL discussions
- Select developmentally appropriate communication tools to engage children and family members in EOL discussions

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12.7 Future Research Recommendations for EOL Communication in Pediatric Oncology

Implementation of evidence-based recommendations is one of two essential steps to improve the quality of EOL communication delivery. The second step is to continue to generate new knowledge related to EOL communication. Based on the science outlined in this chapter, there are several recommendations for future research, including:

1. Use of prospective and longitudinal study designs,
2. Continued emphasis on mixed methods designs to capture quantitative and qualitative data,
3. Development and testing of an instrument to measure effective EOL communication,
4. Exploration of the linkages between EOL communication and patient-, parent-, and provider-reported health-related outcomes,
5. Development and testing of interventions targeted for patients, parents, and providers, and
6. Utilization of implementation science methodology to move existing and new evidence into clinical practice.

A clear deficit in the science is the over reliance of data from retrospective and cross-sectional designs. Movement towards integration of prospective and longitudinal measurement, with attention paid to mitigating the risk of burden, is warranted to describe communication experiences across the EOL continuum. Continued use of mixed methods to describe patient, parent, and provider experiences is essential due to the absence of a valid or reliable tool to measure effective EOL communication. Furthermore, because communication is a complex phenomenon, involving multiple individuals and occurring over time, qualitative data may capture experiences or views that may be missed from a traditional instrument. The science demonstrates an initiation of intervention research aimed at promoting effective EOL communication at the patient and child level, as well as increasing the knowledge and skills of providers who are engaged in EOL communication. These lines of investigation should continue with the recommendations to (a) employ longitudinal designs to test intervention effects on related outcomes over time, (b) test interventions in larger-scale studies or randomized controlled trials, and (c) inform conceptual models by developing an effective communication measure and evaluating positive or negative relationships with patient-, parent-, and provider-reported outcomes.

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13. Genetics and Genomics: Precision Health in Pediatric Oncology

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Abstract

The completion of the Human Genome Project revolutionized our understanding of precision health care. Currently, patients have numerous genetic and genomic testing options including predictive and diagnostic screening. Genetic/genomic screening provides precision medical care based on patient classification, such as disease susceptibility to understanding of disease etiology, as well as understanding an individual response to treatment. This chapter describes genetic and genomic precision health care, as well as the interaction of the individual's environment, family, and lifestyle. This vastly changing care environment has a significant impact on nursing practice, as nurses promote potential benefit while respecting the patient and family decision-making process. Within the precision health care environment, we, as nurses, must take responsibility in supporting the well-being of our patients and families, while fostering new knowledge.

Keywords Genetics – Genomics – Precision health care – Nursing practice – Pediatric oncology

13.1 Overview

Completion of the Human Genome Project established a new era of advanced technology. Despite advances in molecular genetics and genomic medicine, however, the etiology of pediatric cancer remains vastly unknown. A recent study found cancer predisposing germline mutations in 8–12% of the pediatric patients who had genomic sequencing [1]. While research continues to explore the etiology of pediatric cancers, the most significant advances in genetic/genomic precision health care are the individual approach to care and monitoring of disease.

This chapter describes how genomic sequencing may assist in customizing patient care in improving the patient's response to disease and treatment. Thus, nursing science must stay abreast of the rapidly changing environment of genomic precision health care, with translation of knowledge into nursing practice. Subsequently, nursing practice must promote the principle of "do no harm" within the construct of the patient's environment, family, and lifestyle, especially among patients identified as having heritable cancer predisposition [2]. Nursing science and nursing practice influence the health and well-being of the child and family through understanding of the cancer diagnosis, understanding of genomic sequencing, thus facilitating a positive response to treatment. The framework for genomic precision healthcare for the child with cancer will include the concepts of cancer diagnosis, genomic practice environment, genomic nursing practice, and nursing science and the influence on the child, family, and lifestyle, ultimately impacting the child and family health and well-being, and the child's response to disease and treatment (Fig. 13.1). Table 13.1 defines terms that should be understood in genomic nursing practice.

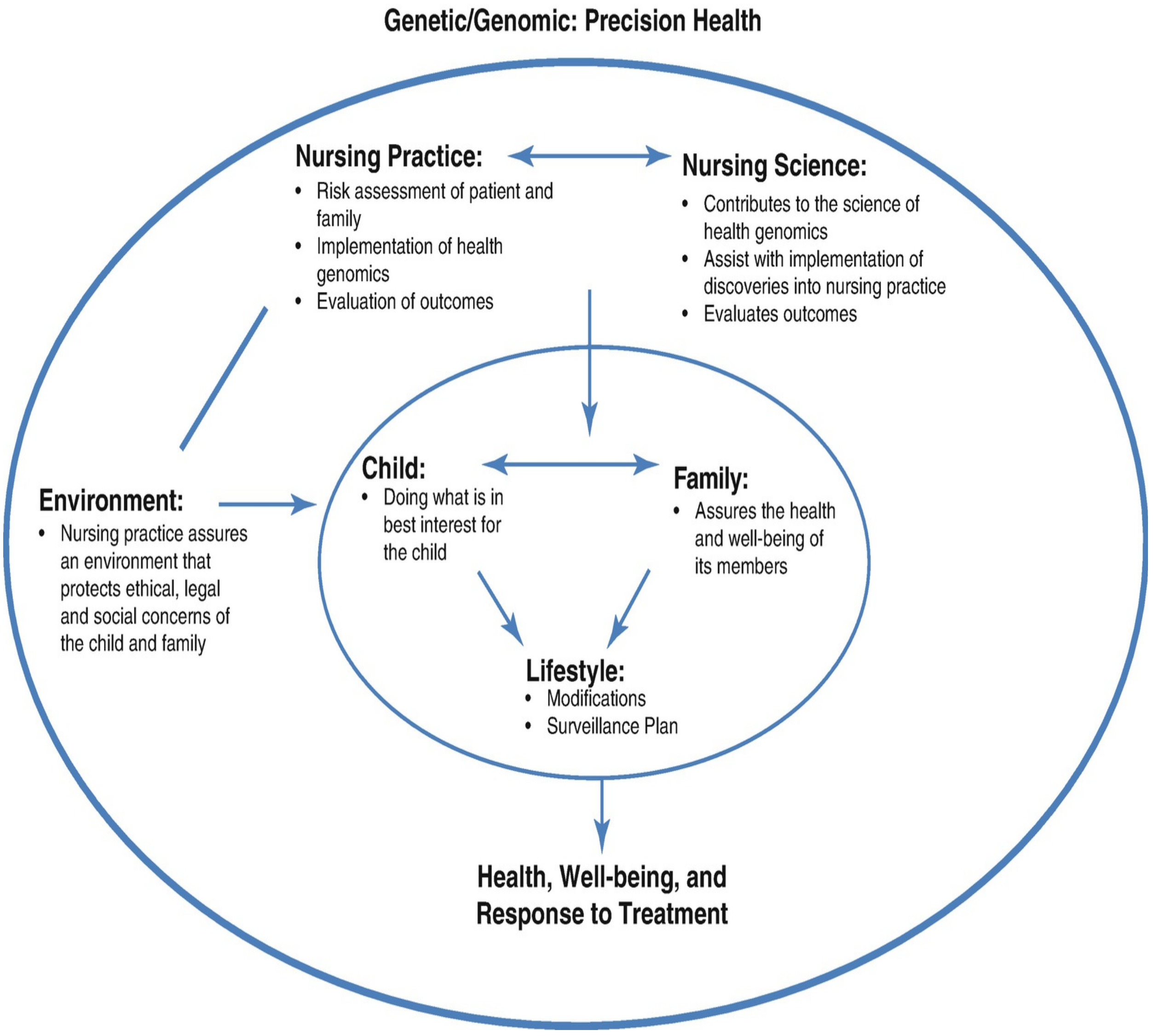

Fig. 13.1 Influence of nursing science and nursing practice on the health-care environment for the child and family, improving health, well-being, and response to treatment

Table 13.1 Term definitions

Gene: a specific sequence of DNA that serves as the instructions to tell the cells of the body how to function

Genetics: the study of specific genes and their effects on human health and development

Genetic testing: examination of specific bits of DNA that have a known function, or are associated with a specific disease

Genome: genetic information across all 23 chromosome pairs

Genomics: the study of all genes and their interrelationships to identify their combined association with disease

Pharmacogenetics: screening a single gene's role in a patient's response to a drug

Pharmacogenomics: the study of how genes affect a patient's response to drugs, it encompasses the patient's response to drugs, the entire genome, and gene–gene interactions

13.2 Cancer Diagnosis

13.2.1 Family History and Physical Exam

At the time of cancer diagnosis, a comprehensive family history is key to identifying children and adolescents with a potential heritable cancer predisposition. The family history is instrumental in altering the nurse of a potential cancer predisposition syndrome, requiring referral to a genetic specialist for counseling, genetic testing, and possible surveillance. The history should consist of three generations—grandparents, parents, and patient, with the patient identified as the proband, with an arrow (Fig. 13.2).

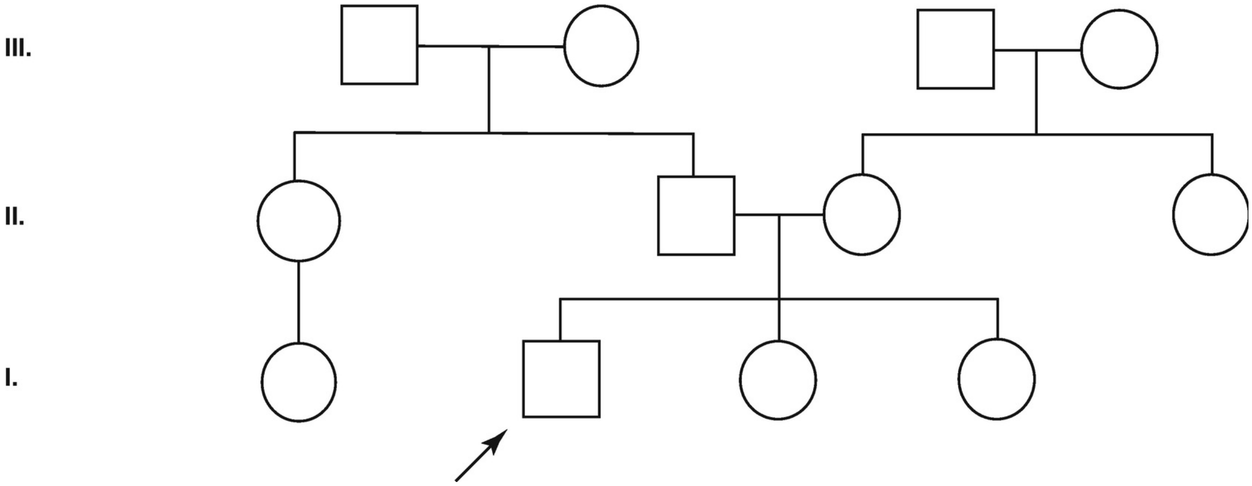

Fig. 13.2 Three-generation pedigree, arrow indicates the patient or proband

The nurse should be knowledgeable of potential features suggestive of an underlying cancer predisposition [2]. These include the pattern of cancer occurrence within the family: three or more relatives with the same, or related, cancer(s) on the same side of the family, one or more first-degree relatives with cancer (patient, sibling, parent), and cancer occurring at an earlier age than would be expected for the cancer. Other features include adult cancers occurring in children, multifocal cancers, or patients having multiple primary cancers. The patient's ethnicity should be considered, including Ashkenazi Jewish ancestry. Consanguineous relationships may also result in an increased risk of cancer syndromes that are transmitted in a recessive manner. Although a cancer predisposition syndrome may be suspected, many family histories are noncontributory [3]. This underscores the importance of pediatric oncology nurses' identification of red flags in the patient's family history, awareness of suggestive physical features, and understanding of when to refer a child for a genetic evaluation.

In addition to the family history, the nurse should be aware of physical findings associated with cancer predisposition syndromes. While the list of potential physical findings is lengthy, the more frequent findings should be noted. These findings include café-au-lait macules, hypopigmented macules, penile freckling, neurofibromas, facial dysmorphism, growth abnormalities (overgrowth and growth retardation), malformations of thumbs and forearms, abnormalities of the teeth and nails [3].

Examples of children whose condition warrants additional evaluation for and underlying cancer predisposition syndrome include:

- A child presenting with an optic pathway glioma, 6 café-au lait-spots, and short stature warrants a genetic referral for Neurofibromatosis type1.
- A child presenting with bilateral Wilms tumor, birth history of hypoglycemia, macroglossia, and leg length discrepancy warrants a genetic referral for Beckwith Wiedemann syndrome.
- A child diagnosed with juvenile myelomonocytic leukemia (JMML), short stature, heart defect, and blue sclera warrants a genetic referral for Noonan syndrome.

13.2.2 Genomic Understanding and Cancer

Cancer is well recognized as a genetic disease caused from one or many dysfunctional coding sequences within deoxyribonucleic acid (DNA), ribonucleic acid (RNA), messenger RNA, housekeeping RNA, regulatory RNA, and small non-coding RNAs. Most human DNA is non-protein coding and, for years, was thought to be "junk" DNA, having an unknown purpose [4]. The completion of the human genome sequencing advanced our understanding of DNA and has allowed the development of platforms for quick and accurate genomic analysis. The 2012 ENCODE project has further changed our understanding of the human genome with evidence that more than 80% of the human genome is biologically active [5]. Previously known as "junk" DNA, cis/trans-regulatory elements, introns, pseudogenes, repeat sequences, and telomeres are transcribed in non-coding RNA comprising functional RNA molecules [6]. A recent study is also exploring the role of mitochondrial DNA mutations in the development and progression of pediatric cancers [7].

Beyond the DNA nucleotide sequence, gene expression is also known to be influenced by epigenetic changes. The epigenetic changes are inheritable variations in phenotype (individual characteristics) without changes in the DNA genotype (DNA code), resulting from over or under expression of the given gene [8]. Epigenetic changes can be influenced by age, environment, and disease. Several mechanisms are now recognized as initiating and sustaining epigenetic changes. These mechanisms include DNA methylation, histone modification, and actions of non-coding RNA.

In contrast to adult cancers, pediatric cancers have fewer nonsynonymous somatic mutations (altered amino acids of proteins) and lower immunogenicity, resulting in pediatric cancers being less likely to respond to targeted immunotherapies [9]. Therefore, the impact of our understanding of molecular pathways driving cancer on the therapeutic approach to childhood cancer will be seen in the next decade and beyond. This is anticipated by the recent success of synthetic immunotherapies including monoclonal antibodies and chimeric antigen receptors now included in front-line and refractory pediatric treatment protocols.

13.2.3 Genomic Sequencing

To understand the current state of genetic and genomic science, the nurse should understand the basic concepts of screening, thus improving the nurse's competency and ultimately improving patient knowledge and satisfaction. There are three methods of genomic testing: cytogenetic, biochemical, and molecular. These methods may detect abnormalities in chromosome structure, protein function, and DNA sequence. Testing may include *somatic (tumor), germline (normal cells unaffected by cancer),* or both, as demonstrated in Fig. 13.3. Each cancer has a distinctive arrangement of genetic changes, and somatic sequencing is a process to identify these distinctive DNA changes. The identification of somatic (tumor-specific) variants has the potential to offer diagnostic information and inform selection of potential targeted therapies that may be added to the treatment regimen. If a somatic (tumor) variant is also found in the germline (normal) cells, further screening will determine if this is a de novo (present only in the patient) or inherited (from a parent) variant.

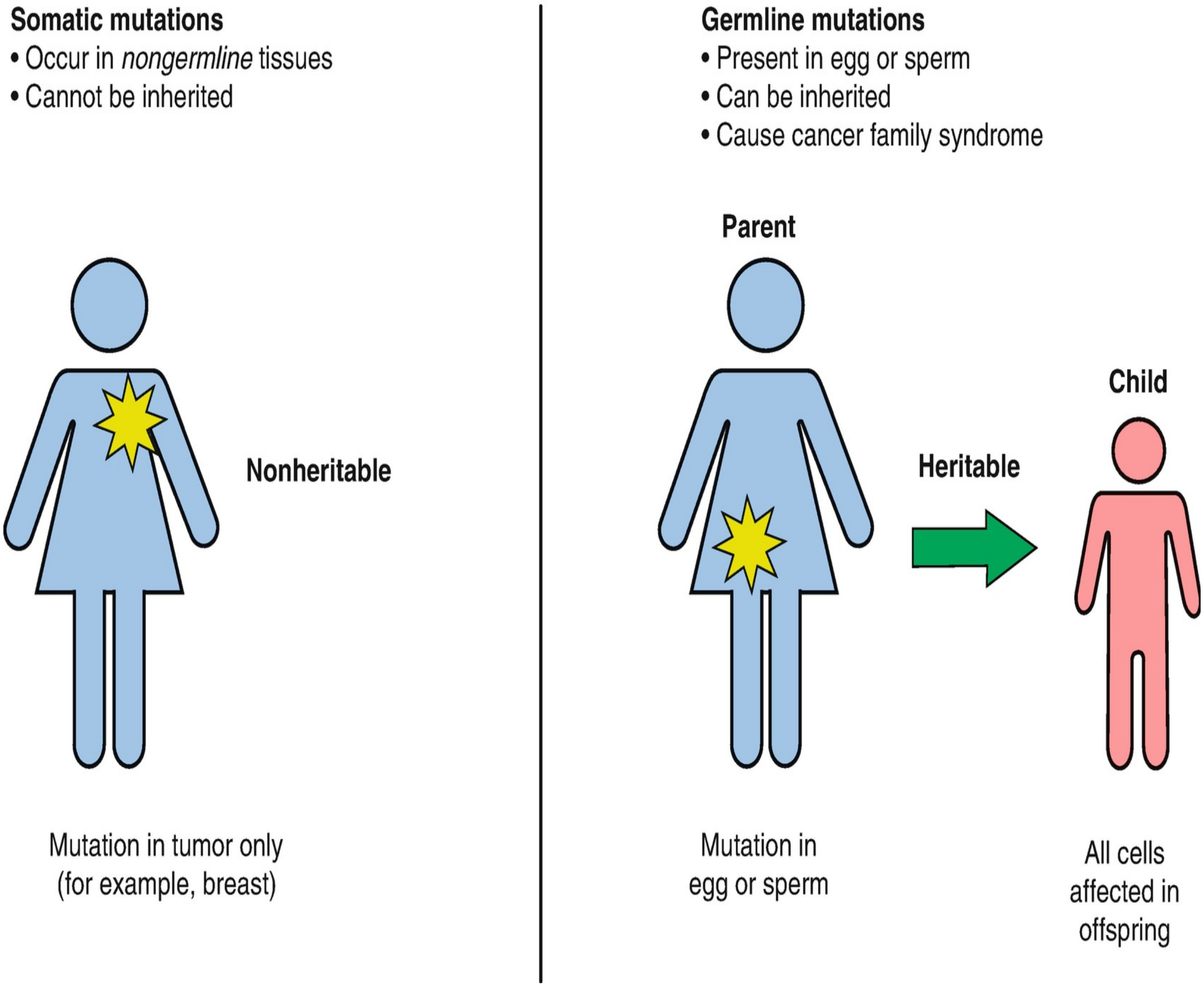

Fig. 13.3 Somatic and germline illustration

If the somatic and germline sequencing is positive for the variant, the patient and family should be referred for genetic counseling and further testing. Commonly reported cancer predisposition genes in pediatric patients are described in Table 13.2. Somatic and germline sequencing has proven clinical utility beyond the patient’s scope of care and may require genetic testing of family members, initiation of a cancer surveillance protocol, and preventive strategies (e.g., sunscreen, diet) in the presence of a cancer predisposition syndrome and, in some cases, changes in the patient’s cancer treatment (e.g., elimination of radiation therapy). For example, a child diagnosed with Li–Fraumeni syndrome (LFS) will require abdominal ultrasounds and blood work (testosterone, cortisol, androstenedione, DHEAS, DHEA, and 17-OH progesterone) every 3 months until the age of 18 years to screen for adrenocortical carcinoma (ACC). Germline variants may also explain non-cancer phenotypes and predict how the patient will respond to medications (pharmacogenetics). Numerous drug metabolizing genes may be tested in making drug therapy decisions for patients.

Table 13.2 Common cancer predisposition genes and associated cancer predisposition syndromes

Gene name	Cancer predisposition syndrome
APC	Familial adenomatous polyposis (FAP)
DICER1	DICER1 syndrome (DICER1)
ETV6	Familial leukemia
NF1	Neurofibromatosis type 1 (NF1)
PTCH1/SUFU	Gorlin syndrome
PTEN	PTEN hamartoma tumor syndrome (PTEN)
PTPN11/SOS1	Noonan syndrome
RB1	Hereditary retinoblastoma (RB1)
SMAD4	Juvenile polyposis syndrome, hereditary hemorrhagic telangiectasia (JPS; HHT)
SMARCB1	Rhabdoid tumor predisposition syndrome (ATRT)
TP53	Li–Fraumeni syndrome (LFS)
TSC1	Tuberous sclerosis complex (TSC)
WT1	WT1-related disorders: Denys–Drash syndrome; Frasier syndrome; WAGR syndrome (WT1)

13.2.4 Genetic Variants

Genetic screening assesses for changes in the DNA sequence, referred to as genetic mutations or variants. Many types of genetic variants can occur and result from DNA sequence substitution, insertion, deletion, or termination. The sentence, “The big fat cat ate the rat” will be used to illustrate each genetic variant.

In a *missense* variant, one DNA base is substituted for another, changing the meaning of the DNA code.

The big fat cat ate the **b**at.

An *insertion* variant occurs when an additional DNA base or multiple bases are inserted into the DNA sequence.

The big fat **c**ca tat eth era. (Frameshift)

The big fat **ccc** cat ate the rat. (Non-Frameshift)

In a *deletion* variant, DNA bases are deleted. This type of variant takes away information from the DNA sequence.

The big fat ___ ate the rat.

A *duplication* variant occurs when a DNA sequence is duplicated or repeated, one after the other. This is like writing the same word twice in a sentence.

The big fat **cat cat** ate the rat.

In a *nonsense* variant, changes in the DNA sequence stop the DNA code, inserting a period into the sentence. This premature ending is also referred to as truncation.

The big fat cat ate **(STOP)**.

In a *translocation*, a portion of a chromosome is relocated. The DNA sequence may relocate to another position on the same chromosome or become incorporated into a different chromosome.

The described genetic variants may or may not result in disease. Another genetic variant, *variants of unknown significance* may be found during genomic sequencing. The patient's risk for disease associated with variants of unknown significance is unknown.

13.2.5 Next Generation Sequencing

The development of next generation sequencing (NGS) including whole genome sequencing (WGS), whole exome sequencing (WES), and RNA sequencing has rapidly advanced our ability to explore genome and the molecular mechanisms potentially associated with cancer development and progression. The genome can be compared to a biological biography, or book, the book chapters are chromosomes made up of DNA. The DNA is organized into smaller units called genes. The genes are the sentences which instruct cellular function (Fig. 13.4).

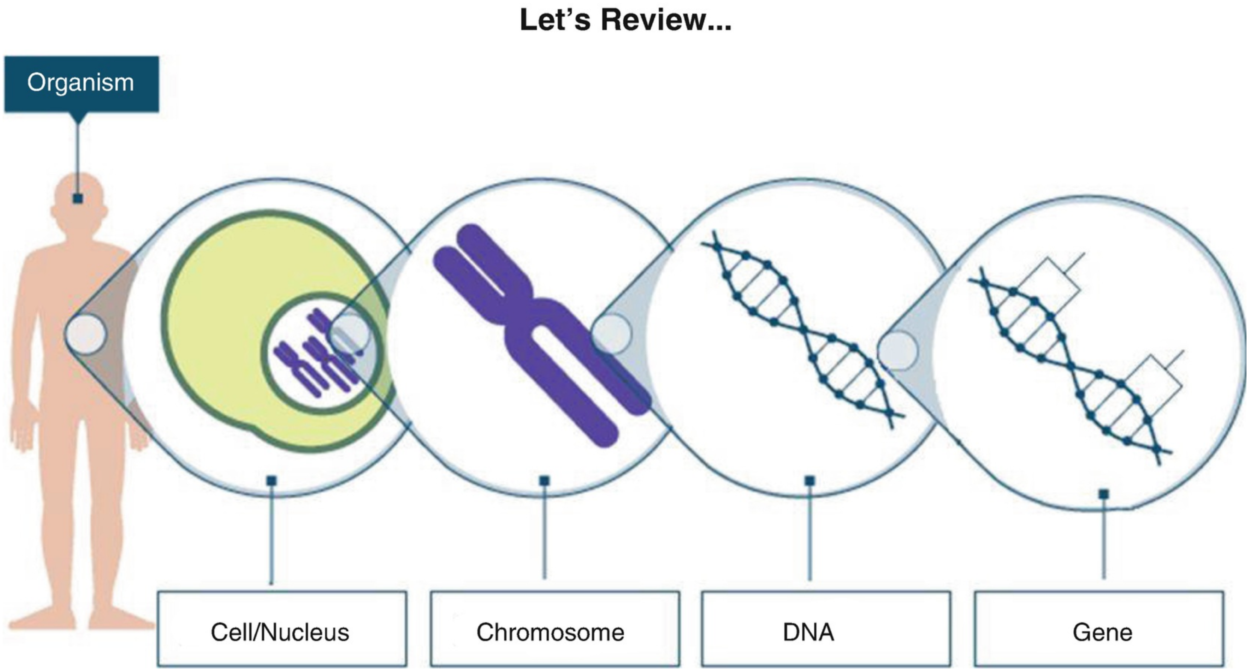

Fig. 13.4 Cell, chromosome, DNA, gene

Whole genome sequencing (WGS) allows for exploration of the entire DNA genome including exons (DNA coding regions) and introns (non-coding regions) which are removed by RNA splicing. WGS reads every letter of the genetic code, including all introns and exons within genes, and the large spaces of DNA that lie between genes.

Whole exome sequencing (WES) allows for exploration of the portion of the DNA that is comprised of exomes (DNA coding regions) and transcribed into RNA. WES sequencing is equivalent to reading the abstract of a book, where the most relevant sentences are combined to create a summary (Fig. 13.5).

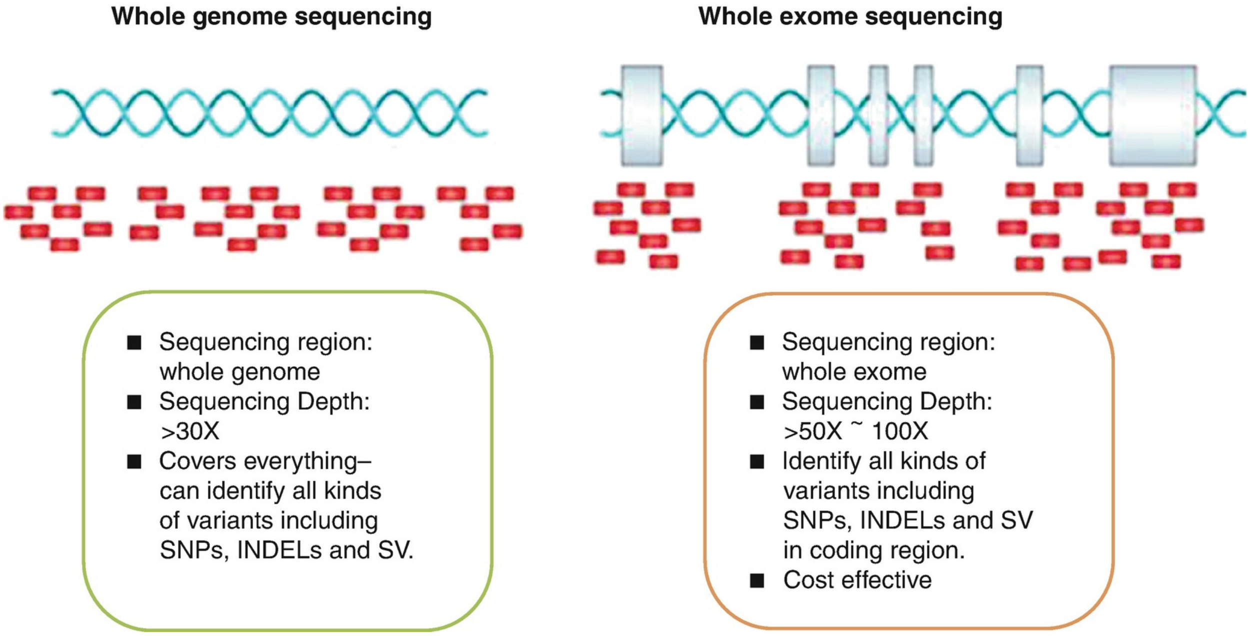

Fig. 13.5 Whole genome vs. exome sequencing

RNA sequencing allows for exploration of the transcriptome. The transcriptome is the complete set of the mRNA and non-coding RNA and is the product of the genome.

13.3 Environment

Genetic nursing practice began as a public health initiative in prenatal and neonatal screening, known as newborn screening. In 1976, the Genetic Diseases Act provided prenatal and pediatric genetic services, thus integrating genetics into clinical nursing practice. To practice in the genetic services system, nursing recognized a need for continuing education, support for patients and families diagnosed with a genetic disorder or at risk, and development of public health policies on behalf of the patients and families. As genetic implications advanced, so has the knowledge and clinical experiences within nursing. The practice of genetic nursing has expanded in the neurosciences, behavioral sciences, complex disorders, and oncology. Further discussion of the genetic/genomic environment will be focused within the environment of cancer care of the patient and family.

13.3.1 Data Privacy and Insurance Concerns

Parents have described concerns when proceeding with genetic/genomic testing for their child with cancer. Overwhelmingly, the concerns have included data privacy and data sharing of their child's genetic/genomic report, as well as insurance coverage. Knowing these concerns, the informed consent should specifically address privacy and insurance; however, the issue of genetic/genomic data privacy is less clear than that of insurance coverage.

Genetic information is protected health information (PHI) and is protected as other medical data. In the content of data sharing, the minimum necessary standard requires Health Insurance Portability and Accountability Act (HIPAA)-regulated entities to use, disclose, and request PHI parsimoniously in releasing the minimal amount of PHI that is reasonable in achieving the intended purpose (Id. at § 164.514(d)(3)(i) and at § 164.514(d)(4)(i). However, the minimal necessary standard is poorly understood and inconsistently implemented. Only HIPAA-regulated entities are regulated by the standard, the healthcare provider may generate, obtain, and store the data for treatment purposes, and data use is dependent upon the levels of privacy protection [10]. The participant may sign an individual authorization or exercise their right of access to their data, thus having individual control access to their data. In exercising this right, the individual's data is not subject to the minimum necessary standard.

In 2008, the Genetic Information Nondiscrimination Act (GINA) was signed into law. This act protects individuals against health care coverage or employment discrimination based on their genetic information. GINA does not protect against private life insurance coverage discrimination. Genetic information may be legally used in underwriting a policy, as is individual health information and family history of disease [11]. Patients and families have refused genetic/genomic screening due to insurance concerns; however, during the informed consent process patients and families should be made aware that the preexisting cancer diagnosis will exclude the patient from private life insurance eligibility. Genetic information or previous cancer diagnosis does not preclude enrollment in employer sponsored life insurance coverage.

13.4 Genomic Nursing Practice

The genetics/genomics nurse should focus on providing client-centered nursing care, education, and research based on the understanding of the underlying based on the genetics/genomics of individuals, families, and population. The American Nurses Association (ANA) and the International Society of Nurses in Genetics (ISONG) in the *Genetics/Genomics Nursing Scope and Standards of Practice* outline competencies for the basic and advanced-level nurses [12]. Both levels of nursing require genomic knowledge in risk assessment, outcomes, interventions, and evaluations; however, they are distinguished by the level of education. Nurses practicing at the basic level should have formal genomic clinical instruction and clinical experiences from their nursing training or on the job training from a genomic advanced nurse or medical faculty. The nurse should participate in genomic continuing education and credentialing in genomics is encouraged. The basic nurse should have fundamental genomic knowledge in cancer risk assessment including family history and construction in family pedigree. If the patient is found to be at risk, the basic genomic nurse develops a referral plan, provides psychosocial support, evaluates the intervention, and assesses the patient's understanding and ability to implement the plan of surveillance.

Nurses practicing at the advanced level have completed an accredited graduate (masters or doctoral) program including didactic genomic and clinical experiences. The educational curriculum should include human, molecular, and population genetics, as well as technological lab-based training. The advanced nurse should also have a strong understanding of ethical, legal, and social implications associated with genomic testing. Additionally, the advanced nurse should have ongoing training under their supervised genetic expert. For nurses considering advanced training, the National Institute of Nursing Research (NINR) offers a tuition-free genomic training program for students, faculty, or clinicians. The advanced nurse should maintain continuing education and credentialing.

The advanced genomic nurse conducts a more detailed family history, associated risk factors, and a detailed examination including a dysmorphology assessment, thus providing patient information regarding the appropriate genomic screening and enabling the patient to make a well-informed testing decision. Once the genomic results are returned, the advanced nurse interprets and explains the genomic results and if desired, develops a plan to assist the patient in disclosing to other family members. The advanced nurse discusses potential risk reduction options, surveillance plan and communicates with other health care providers to carry out the intervention.

13.4.1 Facilitators and Barriers in Genomic Nursing Practice

Although genomic health care is recognized as important, nurses have reported low competency and confidence in their genomic knowledge, as well as confidence in practice [13–18]. The role that nurses play as a patient advocate and educator, as well as their unique role in planning consistent care, enables them to serve as an essential partner in translating genetic and genomic results [19–22]. However, it is unclear if nurses are sufficiently trained in assisting with individualized health promotion and surveillance plans relevant to testing results. Nurses should be knowledgeable in promoting genomic health care, while advocating for equitable policies regarding access to genetic services, confidentiality of genomic data, and reimbursement for personalized healthcare [23]. Nurses should be positioned as a resource and coordinator of care, which requires the nurse to be knowledgeable of genetic and genomic methodology, concerns of and implications for patients and families, and policies governing practice [21].

National nursing organizations recognize the need for genomic knowledge among nurses. Competencies have also been defined to guide the use of genomics among practicing nurses [24, 25]. Globally, nursing organizations and leadership are actively incorporating genetics and genomics into education and practice [15]. Despite the nursing workforce expressing need for genetic and genomic knowledge, little has been done to overcome the educational gap [14, 16, 26, 27]. Nurses report the patient-and family-centered relationship as a motivator in obtaining genomic knowledge and understand the significance of maintaining genomic education and keeping abreast of testing advances and implications for patient treatment. Nurses understand their ethical responsibility as a patient advocate and the importance of understanding results, implications, and privacy [28, 29].

Nurses have reported numerous barriers contributing to their lack of confidence. Rapid advances combined with the lack of genomic hospital-based educational opportunities limit the role of nurses as patient educators and advocates [30]. This lack of educational opportunity is a significant barrier for the nurse when providing genomic education. Time is another barrier, with nurses reporting insufficient time for completion of a family history and pedigree [31–33]. Most significantly is the nurses perception of nursing leadership, with nurses perceiving their senior nursing leadership as placing little value in genomic nursing [13].

Several resources are available for genetic/genomic nursing education. The International Society of Nurses in Genetics (ISONG) is the leading academic and professional society in the field of genetic/genomic nursing. ISONG and the American Nursing Association have co-published the scope and standards of genetic/genomic nursing practice, providing the scope of practice [12]. ISONG also provides additional educational resources such as on-line webinars. The National Institute of Nursing Research (NINR) recently launched the Omics Nursing Science and Education Network (ONSEN https://omicsnursingnetwork.net/) website in collaboration with the National Human Genome Research Institute (NHGRI) and the National Cancer Institute (NCI). ONSEN provides resources to learn omics science, opportunities for training, and collaboration with other researchers.

13.5 Nursing Science

The Human Genome Project revealed whole sequence of human genome and enabled genomic association study to discover relationship between human gene variation and phenotype. Genome wide association studies have facilitated the discovery of candidate genes for common multifactorial disease [34]. This knowledge should be integrated into novel prevention and treatment strategies as an essential element of precision nursing [35]. Along with the development of prevention and treatment strategies, nursing scientist should be active collaborators in the study of genetics and genomics. Current nursing science places an emphasis on genetic/genomic research, the human phenomena, and the connection to nursing practice.

Nursing scientists may initiate genetic/genomic research questions specific to genotype–phenotype correlations associated with patient response to treatment or outcomes or describe association studies of a symptom phenomenon. One such example is the work by Goel et al. [36], listed as one of ten researches in "Notable Advances 2011–2015" by NINR. The study reported an association between a single nucleotide polymorphism (SNP) in catechol O-methyltransferase gene (*COMT*) and individual vulnerability in chronic partial sleep deprivation. Numerous studies investigating genetic associations with symptoms have subsequently been published. Nursing science also has the responsibility in conducting research surrounding the ethical, legal, and social issues associated with implementation of genomic science into patient care. It is not only imperative that nurses contribute to the science of health genomics, but we must assist in the implementation of these discoveries into nursing care. This includes the evaluation of outcomes for our patients and families [37]. Nurses should actively participate in assessing and assuring genomic literacy among their patients and families, specific to the consenting process and disclosure of results. Ongoing research questions should be developed exploring how the implementation of genomic health care impacts the patient and family health-related outcome. Lastly, the findings should be integrated into nursing practice through evidence-based practice.

13.6 Family

The primary function of the family is to ensure the health and well-being of its members [38]. The integration of genomic sequencing in clinical practice has potential implications within the family. Soon after the child's cancer diagnosis, parents and patients at the age of majority are offered and asked to provide consent for somatic and germline sequencing. Somatic sequencing facilitates the detection of tumor-specific genomic mutations that may responsive to targeted therapies as clinical care or incorporated into a research trial [39]. However, germline sequencing may identify a hereditary cancer predisposition gene, variants of uncertain clinical significance, or a non-oncological gene variant [40]. While the proportion of patients having an actionable somatic variant is small, families should be adequately informed of potential risks and benefits associated with germline sequencing.

When offering somatic and germline sequencing to patients with cancer and their families, nurses should assist in providing an environment that promotes informed decision making. Somatic sequencing of the tumor is a difficult concept and may be misunderstood; therefore, a detailed informed consent is imperative. Patients and parents assenting and consenting to somatic tumor sequencing should have the understanding that there will likely be little clinical benefit for the patient, but acquisition of generalizable knowledge. A recent study found most parents understood the primary goal of somatic sequencing as research and benefit for future patients, while one third of the parents believed the somatic sequencing would benefit their child [41]. To improve patient and parent understanding, a two-phase consent process conducted by a designated study nurse provided both repetition and improved understanding of somatic and germline sequencing. Although the surveyed parents endorsed improved knowledge and understanding at the second visit, somatic and germline terminology continue to be difficult concepts to comprehend [39]. At the time of assent and consent, the patient and family should understand they have the option to proceed or decline somatic and/or germline sequencing. If patients and parents proceed with germline sequencing, they should also understand they have the option to be informed or not be informed of the sequencing report [42].

In addition to diagnostic testing as previously described, families may consider predictive genetic screening for conditions having unpredictable onset in childhood or adulthood [43]. Families described as "cancer families" often proceed with predictive screening for Li-Fraumeni syndrome (LFS). Families with LFS, a cancer predisposition syndrome caused by pathological variants in the *TP53* tumor suppressor gene, often express anxiety and concern for their child's cancer risk. The majority of individuals with LFS will develop cancer in their life time and 20% will develop cancer by 20 years of age [44]. Predictive screening has not been found to have a negative impact on the child [45], but has been found to improve outcomes through cancer screening and early detection [46].

13.6.1 Return of Genomic Results

Little is known of how best to return genomic results; however, there is strong consensus that patients and families should be informed of whether results will or will not be returned, what results the family wants returned, and the opportunity to decline receipt of results for themselves or their child [3]. Patients and families should also state and consent to their position of being contacted should future genomic variants be found pathogenic. Due to the complexity of returning actionable genomic results, genetic nurse practitioners and genetic counselors are the preferred member of the care team to communicate the results to the patient and family [3, 47]. Furthermore, health care providers do not have the expertise in assisting the family on informing other family members who may be at risk for cancer predisposition.

13.7 Child

The societal and professional worldview of genetic/genomic testing is the principle of doing what is in the best interest of the child [48]. Genetic/genomic testing of children is not common, except for newborn screening. The American Academy of Pediatrics and American College of Medical Genetics and Genomics do not support genetic/genomic screening of children for adult-onset disorders, thus allowing the child to make an informed decision and consent at the time of majority [49]. Therefore, children are not typically screened for adult-onset disease, including predictive testing for cancer predisposition syndromes that present in adulthood (e.g., breast cancer).

At the time of parental consent, assent should be obtained according to the institutional policy. Parents may request that the genomic results not be disclosed with the child, or in other situations, the child may request that they not receive the results [50]. The disclosure of results should be resolved prior to testing; however, the family should understand that their change in decision will be honored until the time of disclosure. The adolescent patient should be included in the disclosure of results conversation and concur with the disclosure plan [49]. Parents should also be made aware that the genetic results belong to the patient and a plan should be made with sharing the results at the time of disclosure or a defined time in the future. In a study of parents of children with LFS, parents verbalized the importance of including the involved child in testing conversations; however, only half of these parents disclosed the positive results with their child. The reason for non-disclosure was age of the child, with parents wishing to defer result disclosure based on developmental age [51].

Parents should be aware of germline disclosure benefits and harm. Psychosocial benefit includes reduction of uncertainty and anxiety, the ability to make proactive life plans and sharing of information with family members [49, 52]. Reproductive benefits include avoidance of an inherited cancer predisposition syndrome. Psychological harm includes alteration of self-image, anxiety, change in perception of self and others, family stress associated with sharing with other members within the family, and need for family testing [49]. For persons known to have a cancer predisposition gene, reproductive choices may be influenced by family and social pressures.

13.8 Lifestyle

Patients found to have a germline cancer predisposition gene are at risk for the development of multiple primary cancers, as well as therapy related cancers. Patients known to harbor germline mutations including *RB1 and TP53* should avoid radiation due to risk of secondary cancers within the radiation field. In addition to changes with primary therapy, patients found to have a cancer predisposition gene variant should be advised in lifestyle modifications and surveillance. Lifestyle modifications include those known to be associated with a healthy lifestyle and include use of sunscreen, diet with fruits and vegetables and lean protein, exercise, no smoking, and limited alcohol consumption. Patients should also limit radiation exposure from environmental factors and diagnostic imaging such as computed tomography scan (CT scan).

In addition to lifestyle changes, persons found to have a cancer predisposition gene variant should have a customized cancer surveillance plan developed by a medical oncologist, including physical examination, blood work, and imaging studies with magnetic resonance imaging (MRI). The surveillance protocol will vary according to the patients age and sex. While the surveillance protocols may be stressful, parents have described the knowledge and surveillance as “being proactive” [51].

13.9 Health and Well-Being

Literature describing the health and well-being of children and adolescents enrolled in genomic sequencing during their cancer treatment is limited. Most of the current literature describes the process of consenting and parental understanding, as well as parental expectations. A recent qualitative study interviewed adolescents 12–25 years of age in families with LFS regarding their perspective of genetic testing [45]. All endorsed that genetic testing should be offered but proceeding with testing should be optional. The adolescents felt testing provided knowledge of risk status, allowed a plan for disease prevention, and reduced uncertainty and anxiety. Potential negative emotions associated with testing results were a disadvantage. Furthermore, the adolescents felt parents should make the decision over the child in decisions of young age and high-risk disease. Among the adolescents tested and aware of test results, all described no negative impact on their well-being and agreed testing was the best decision.

13.10 Response to Disease and Treatment

The integration of genetic and genomic sequencing into clinical practice is now considered standard of care and is improving clinical outcomes. At the time of diagnosis, patients with cancer are screened for variants (polymorphisms) in genes that encode drug-metabolizing enzymes that influence the uptake, metabolism, and elimination of drugs used in cancer treatment. Such screening assures improved treatment efficacy and decreased toxicity. Somatic (tumor) sequencing can facilitate the identification of targetable molecular pathways improving clinical outcomes through the addition of targeted therapies. Germline (normal) tissue sequencing can determine the presence of a heritable cancer predisposition syndrome, potentially changing the treatment scheme and reducing the risk of secondary cancers. Families found to have a cancer predisposition syndrome may now be offered screening for family members, along with surveillance plans improving health outcomes.

1.

13.11 Evidence-Based Findings Derived from Genetic/Genomic Science Ready for Translation to Clinical Practice

As genetic/genomic healthcare is translated into clinical practice, nursing plays a pivotal role in advancing precision care implementation.

Recommendations for the nursing role in precision healthcare implementation include [53]:

1. Participate in policy development and implementation of precision care within the research and clinical setting.
2. Ensure that the electronic medical record connects the results of genomic tests to recommended pharmacological and non-pharmacological therapy, as well as patient outcomes.
3. Collect genetic/genomic data including three-generation pedigree and social determinants.
4. Provide genetic/genomic continuing education to nurses and other healthcare professionals.
5. Assure that patients and families understand the benefits, goal, and limitations of precision healthcare.

13.12 Future Research Recommendations for Genetic/Genomic Science

Numerous obstacles hinder the translation of precision health care into clinical practice. These include the method of data collection and management with the electronic medical record, data sharing, privacy and discrimination concerns, and health literacy. Nursing plays an important role in resolving these obstacles.

Recommendations for genetic/genomic science within the nursing profession include [53]:

1.

Contribute to an understanding of the benefits and challenges of precision health care implementation, as well as ethical issues.

2. Integrate data within the electronic medical record, providing genomic testing results to healthcare team in an interpretable format.
3. Address knowledge gaps in what patients, research participants, and the public need to know when implementing precision healthcare.
4. Advocate for training, resources, and continuing education on precision heath care including patient education, health literacy assessment, data security, decision with genomic results, and support for acting upon clinically actionable findings

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13.13 Conclusion

Nursing science and nursing practice have a responsibility to assist patients and their families through the cancer experience, which now includes the integration of genetic and genomic sequencing. As genomic health care is implemented into practice, nursing science must assure that patients and their families understand the potential health and psychosocial implications. Research should include assessment of health literacy and genetic knowledge at the time of consent. Nursing science must be at the forefront of understanding the potential impact on the patient and family well-being as described by the patient and family, as well as measuring outcomes associated with response to disease and treatment. It is only through the continued endeavors in genetic and genomic research and education, that nurses are enabled to be vital advocates for their patients and families in understanding the enormous benefits and challenges of genomic health care.

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14. Cancer Survivorship in the Era of Precision Health

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Abstract

Survival after treatment for most types of childhood cancer has improved dramatically. However, life after curative treatment is not without late effects, some of which are life-threatening. Pediatric oncology nurses, advanced practice nurses, and nurse scientists have been in the forefront of program development for systematic follow-up for long-term childhood cancer survivors (CCS), studying determinants of—and interventions to ameliorate—late effects, and implementing a risk-based approach to follow-up care. Survivorship is a dynamic process, and nurses have adapted to this changing landscape. With the evolution of precision health (including genetics and genomics), the landscape will evolve, and nursing needs to be at the forefront of integrating this new information (big data) to provide comprehensive survivorship care. Nurse scientists now have opportunities to leverage the advances that have been made in precision health to both lead and contribute to informatics' solutions for data collection and data analyses with the unique nursing perspective derived from our decades of survivorship experience, and nurses in clinical practice and education are well positioned to translate research into clinical care to improve survivors' lifetime health. The goal of nursing science is the translation of evidence to improve population health. The prospects for nurse scientists to move the pendulum for all CCS' care toward a precision health-based framework from which to provide care are vast. Challenges remain in how best to reach many survivors who are not engaged in long-term follow-up care, as it is this type of precision health care that the survivors need most.

Keywords Behavior – Childhood – Family – Follow-up – Screening – Survivorship – Tailored

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14.1 Background

Over the past 50 years, survival after treatment for most types of childhood cancer has improved dramatically, such that the population of childhood cancer survivors (CCS) is approaching 500,000 in the USA [1]. Survivors' lived experience has taught us that life after curative treatment is not without complications, usually referred to as late effects, some of which are themselves life-threatening.

For nearly 50 years, pediatric oncology nurses have been in the forefront of program development for systematic long-term CCS follow-up, studying determinants of—and interventions to ameliorate—late effects, and implementing a risk-based approach to care [2]. Over this same time period, an age of scientific discovery has unfolded, particularly in the evolution of precision health. The goal of precision health is to provide a plan for health-promoting behaviors over a lifetime by taking into account the variability of individuals' genes, their environment, and lifestyle in designing targeted interventions [3, 4]. Precision health and survivorship have in common an emphasis on individualized care and health education that foster survivors' optimal health after cancer treatment.

In this chapter, we discuss advances in survivorship knowledge development and translation science, intentionally utilizing a case exemplar selected to illustrate care considerations for a survivor with very complex health needs,[1] along with recommendations for future survivorship research, recommendation for evidence-based translation of knowledge into practice, and identification of challenges and opportunities for nurses who are leading survivorship care and/or research in the era of precision health.

14.2 Case Study

EZ is a 17-year-old diagnosed with medulloblastoma at the age of 3 years. His treatment consisted of a gross total resection with placement of a ventriculoperitoneal shunt (VP), chemotherapy (alkylating agents/heavy metals), and craniospinal radiation therapy (CpRT) (3600 centigray (cGy); boost to the posterior fossa-5580 cGy). The case highlights significant late effects, but is not a comprehensive review of late effects and their known risk factors.

Organ/system affected	Response to treatment
Neurocognitive	EZ has neurocognitive dysfunction with impairments in many areas of functioning. He has an individual education plan (IEP) to optimize his academic potential

Sensorineural	EZ has sensorineural bilateral hearing loss requiring hearing aids, accrues excessive dry cerumen in both canals. He has difficulties with balance
Endocrinopathies	EZ had growth hormone (GH) deficiency and remains on adult growth hormone replacement; he has thyroid nodules necessitating annual endocrinology follow-up visits. Gonadal axis evaluation reveals elevated gonadotropins, but normal testosterone levels in the adult male range. He has poor bone density
Subsequent malignant neoplasms (SMNs)	EZ is at risk for skin cancers and secondary brain tumors, both benign and malignant
Cardiotoxicity	EZ is at risk for cardiovascular disease
Stroke	EZ is at risk for a stroke
Psychosocial–emotional	EZ's psychosocial–emotional issues require pharmacological treatment and cognitive behavioral therapy. He self-medicates using alcohol and marijuana. He has limited social outlets, no friends, and most of his time is spent with his family. While he wants to be independent, EZ does not demonstrate insight as to why this is not a realistic goal

What follows are descriptions of the physiological and psychosocial–emotional late effects outlined in the case study exemplar for this chapter to illustrate the impact of childhood cancer treatment in a growing child.

14.3 Physiological Outcomes

The majority of children with medulloblastoma are treated using surgery, chemotherapy, and radiation therapy (RT) [5]. Medulloblastoma survivors and their siblings from the Childhood Cancer Survivor Study (CCSS) treated from 1970 to 1986 were evaluated [6]. At 30 years post-treatment, common physical late effects consisted of chronic neurosensory impairments including tinnitus, hearing loss, seizures, as well as balance and coordination issues. Numerous studies have shown lower educational attainment and job security among survivors compared to their siblings without a cancer history [6–8]. In addition, the burden to families in relation to the late complications experienced by this population warrants assessment and support [9–11].

14.3.1 Neurocognitive Sequelae

The exemplar case study features a pediatric brain tumor survivor exposed to a high dose of cranial radiation (CRT) at an early age. Radiation can have deleterious effects on learning outcomes [12]. The difficulties most commonly reported are problems with attention, processing speed, working memory, and executive function [12, 13]. Executive function is essential for regulating decision making, mood, and task completion; anxiety and depression are common symptoms exhibited in survivors with executive function impairment. This population typically has lower levels of educational attainment and social achievement compared to peers [14–16].

Children who received methotrexate for acute lymphoblastic leukemia (ALL) also have been shown to have altered fatty acid saturation resulting in a decline in cognitive function [17]. While we are highlighting an exemplar in a brain tumor survivor, it is important to recognize the impact of CNS-directed therapy for ALL. A randomized control trial of an intervention aimed at preventing neurocognitive problems done with 57 children diagnosed with ALL revealed improved scores on both math abilities and visual working memory in the intervention group [18]. Investigators suggested further studies in this area using virtual (technology-based) methods to enhance family and child access to these services.

14.3.2 Sensorineural Hearing Loss

Hearing complications are common following nasopharyngeal and/or cranial radiation and/or platinum-based chemotherapy; children at younger ages at radiation exposure are most susceptible [19]. Treatment with platinum agents is known to cause high frequency sensorineural hearing loss that may affect learning, communication, and language development [20, 21].

Whole brain RT doses given in the range of 30 gray (Gy) and higher can have a damaging effect on the cochlear nerve which may be exacerbated in the presence of a VP shunt [22, 23]. A boost of RT to the posterior fossa increases the risk of hearing loss in CCS due to the increased exposure of the cochlea to the damaging RT [24]. Exposure to cranial radiation may cause an increase in dry hard cerumen, which may also affect hearing. Routine follow-up by a pediatric audiologist is required to monitor hearing aid functionality, replace ear molds as the child grows, and remove impacted cerumen.

14.3.3 Endocrinopathies/Metabolic Syndrome

Childhood cancer survivors, particularly those treated with cranial RT for brain tumors, can experience significant endocrine complications [25–27]. Endocrinopathies and metabolic issues (metabolic syndrome) may arise that require lifelong follow-up, depending on treatment-related exposures [28, 29]. Metabolic syndrome, other endocrine factors, and dietary changes can increase risks for obesity [30, 31]. Metabolic syndrome—with its associated obesity, abnormal glucose, and dyslipidemia—increases the risk of cardiovascular morbidity and mortality [25].

Radiotherapy doses used to treat brain tumors such as medulloblastoma have a direct effect on the hypothalamic–pituitary axis. Growth hormone deficiency is the most common impairment among medulloblastoma survivors [32] followed by thyroid impairment in CCS exposed to cranial spinal radiation therapy [27, 32]. Follow-up with a provider knowledgeable in endocrinopathies is warranted.

14.3.4 Subsequent Malignant Neoplasms

Survivors treated with both chemotherapy and radiation have increased incidence of subsequent malignant neoplasms (SMNs) at 15 years post-treatment compared to CCS who received chemotherapy alone [33]. Another study reported that among 5-year survivors of medulloblastoma who received both radiation and chemotherapy, the cumulative incidence of SMN was 12% at 20 years [34]. Subsequent malignancies reported for pediatric brain tumor survivors included gliomas (all grades), benign meningioma, nonmelanoma skin cancer, thyroid carcinomas, and soft tissue sarcomas. Hematological malignancies may occur sooner (within the first 5 years) after completion of treatment [34]. Hence, long-term follow-up in a cancer survivor focused program may be necessary.

14.3.5 Cardiotoxicity

Anthracyclines and RT are the most common treatment exposures implicated in cardiac dysfunction in CCS [35, 36]. Cardiovascular dysfunction following CpRT include but are not limited to valvular injury, coronary artery disease, myocarditis, pericardial thickening, conduction issues, and cardiomyopathy [35–37]. Factors affecting cardiac function post-radiation include the total dose, fractionation, and volume of heart irradiated. The onset of cardiovascular disease following radiation is usually 10 or more years post-treatment [35, 36]. Routine risk-based screening is warranted in subsets of CCS.

14.3.6 Stroke

Several studies have shown pediatric brain tumor survivors are at increased risk for stroke and/or transient ischemic attack (TIA) [38–40]. Treatment with cranial radiation may produce late vascular changes along with other chronic health conditions associated with stroke risk such as obesity, dyslipidemia, hypertension, and type 2 diabetes. This underscores the importance of health promotion behaviors and long-term follow-up.

14.4 Psychosocial–Emotional Outcomes

14.4.1 Health-Related Quality of Life (HRQL)

Psychosocial outcomes vary depending on cancer type and length of time since completion of treatment [41] as well as the characteristics and resources of the survivor/family. In studies of childhood brain tumor survivors, HRQL has been shown to be diminished compared to healthy peers and even of other CCS [42, 43]. A history of CRT and the presence of cognitive dysfunction were both found to be risk factors for lowered HRQL, which can impair educational attainment, occupation, and social skills [43–49]. Brain tumor survivors have poorer mental health outcomes compared to siblings without a cancer history, age matched controls, and to survivors of other childhood cancers [12, 50]. Subgroups of CCS have been found to exhibit risk-taking health behaviors including self-medicating with drugs/alcohol and to experience suicidal ideation [51, 52].

Nurses have taken the lead in exploring the effect of central nervous system (CNS) therapy on life satisfaction [53], hopefulness, self-esteem, HRQL [54, 55], and parental engagement and peer support [56]. Nurse clinicians and scientists are engaged in inquiry and translation of evidence regarding HRQL screening [44, 47, 57–59] and assessment for correlates such as fatigue, pain, and sleep problems [48, 58, 60].

14.4.2 Post-Traumatic Stress Disorder (PTSD) Syndrome (PTSS), and Growth (PTSG)

Post-traumatic stress disorder (PTSD) and post-traumatic stress syndrome (PTSS) are present in subsets of CCS [61–64]. In a study exploring PTSD in survivors, 16/78 (20%) of the sample of CCS screened for PTSD met the DSM-IV criteria for PTSD [63]. The presence of PTSD and/or PTSS can impact HRQL and decision making in subsets of CCS [59, 65–68]. Brain tumor survivors are particularly at risk for symptoms such as distress, anxiety, and depression, which can actually worsen over time [69]. Psychosocial symptoms may begin early in survivorship [13, 62, 69], necessitating regular screening and referral for mental health services [59, 69, 70]. Post-traumatic stress growth (PTSG) has been explored in a study of adolescent and young adult (AYA) CCS in the first 6 months following completion of cancer therapy [71]. In this study, most AYA survivors reported post-traumatic growth which was positively correlated with both post-traumatic stress and psychosocial functioning [71].

14.5 Framework for Survivorship Care in the Era of Precision Health

The nursing metaparadigm [72], with its broad domains of person-environment-health-nursing, offers a framework for nursing research and nursing practice in the context of childhood cancer survivorship and precision health. Today, according to Founds, “*Nursing* interventions centered on the *person* within the *environment* can be conceptualized as affecting the complex human organism at the molecular level to influence *health*” [72]. This is where precision health—personalized disease prevention and treatment based on an individual’s genetic/genomic and other health risk information—intersects with the essence of survivorship care: understanding determinants of health, risks associated with organ and system effects of cancer and its treatment, as well as nursing interventions that impact health outcomes. These overlapping relationships are depicted in Fig. 14.1.

Fig. 14.1 Survivorship care in the era of precision health

Family-centered care remains the hallmark of pediatric oncology nursing, and this construct extends across the lifespan for survivorship care. Childhood cancer survivors live within the context of their families [73] and the family environment [74, 75]. Risk-adapted or personalized patient/family health education has been largely the province of nurses, using guidelines based on available evidence and expert consensus, to reduce modifiable risk factors for optimal health.

Over the past decade, genome-wide association studies (GWAS) have been undertaken in pediatric oncology [76]. Genome-wide association studies data are being used to design treatment protocols targeted at specific polymorphisms, to better understand/predict factors that may affect acute and late toxicity or treatment efficacy (e.g., drug metabolism, cardiac toxicity), and susceptibility to comorbid conditions (e.g., cardiovascular disease, depression). Other datasets that also may inform precision health include biomolecular data, and the "omics" such as the microbiome and proteome. Increasingly, preventive interventions for the post-treatment phase of survivorship, based on findings from GWAS, omics, and other studies of health determinants, will be available for precision health application in clinical practice so that nurse clinicians can tailor care to the individual's variations at baseline and over time [4]. (See Chap. 13 for more detail about GWAS and pediatric oncology.) Essential aspects of GWAS and other "big data" studies of health determinants are that there need to be data repositories that can be shared, and appropriate precautions for privacy need to be in place.

14.6 Key Principles of Survivorship Care

The etiology of late effects in CCS is multifactorial. Risk factors include treatment exposures (what, how much, which organs/systems are affected), genetic susceptibility, and survivors' lifestyle behaviors, as well as social determinants of health as outlined in Healthy People 2020 [77]. New screening techniques based on biomarkers and genetic/genomic factors are emerging, as is the evidence base for health promoting behavioral interventions. The multifactorial and dynamic nature of survivorship care means that one size does not fit all, and that CCS ideally need annual appointments for cancer-focused risk-adapted follow-up care over their entire lifetime.

14.6.1 Survivorship Programs Provide the

Framework for Care

Advances in pediatric oncology have resulted in growing numbers of long-term survivors, and medical and psychosocial after-effects were first reported in CCS. As early as the 1970s, pediatric oncology nurses began coordinating survivorship care and participating in surveillance for survivors' treatment and disease-related side effects [2, 78]. Pioneers in pediatric oncology nursing focused on the identification and description of late effects, role development, and models of care. Nurses were instrumental in the development of formal survivorship programs [79–84], and were actively engaged as members of interprofessional teams that characterized disease and treatment-related symptoms, and tested interventions for improving symptom surveillance and management [2].

Nursing contributions to survivorship care grew as the number of CCS continued to increase in the 1980s and 1990s, and roles included serving as specialty care advanced practice provider, program manager, educator, researcher, and consultant [81]. Programmatic goals focused on systematic evaluation, identification and intervention for late effects, assisting the survivor and family to cope with the new "normal" of living with late effects, as well as assisting CCS and families to be vigilant for signs and symptoms of late effects. Within the Children's Oncology Group (COG), survivorship programs increased to 155 (87%) compared to 53% of institutions 10 years earlier [85]. However, many of these programs lacked dedicated staff time for program development [86]. Survivorship programs in the global community also expanded [86–88]. As a result of this growth, a need for standardizing and harmonizing standards of care was recognized; nurses participated in developing evidence- and consensus-based guidelines to direct the care of CCS in the early 2000s.

14.6.2 Long-Term Follow-up Guidelines Shape Survivorship Care

With the proliferation of survivorship programs, guidelines were needed to standardize surveillance for follow-up care across institutions and among all health care providers. The first set of guidelines, developed by investigators in the United Kingdom Children's Cancer Study Group, were therapy-based recommendations for follow-up care; a revised edition was published in 2005 [89]. In 2004, the COG published its first set of risk-based, exposure-related clinical practice guidelines, which were jointly developed by representatives of the COG Nursing Committee, Late Effects Committee, and the Patient Advocacy Committee [88]. Version 5.0 is available at http://www.survivorshipguidelines.org/. These guidelines represent consensus from a multidisciplinary panel of experts who rated the level of evidence; the COG Guidelines are thus consensus-based and are not, strictly speaking, evidence-based clinical practice guidelines.

Additional global efforts to address the need for risk-based guidelines have included the Late Effects Group of the United Kingdom Children's Cancer and Leukaemia Group (UKCCLG) (http://www.cclg/org/uk), the Cancer and Dutch Childhood Oncology Group (http://www.skion.nl/workspace/uploads/vertaling-richlijn-LATER-versie-final-okt-2-14_2.pdf), and the Scottish Intercollegiate Guidelines Network (SIGN) (http://www.sign.ac.uk/guidelines/fulltext/132/index.html). International interprofessional collaboration continues among pediatric oncologists, nurses, and other health care professionals and has resulted in the establishment of the International Late Effects of Childhood Cancer Guideline Harmonization Group (IGHG) [87, 90].

14.6.3 Health Education and "Survivorship Literacy"

Nurse clinicians and researchers have recognized that educating CCS about health risks and about effective self-care is based on understanding their knowledge gaps. Studies by several investigators revealed that most survivors knew general information about their diagnosis and treatment but lacked specifics such as drug names and radiation dose [91–93]. Researchers have successfully demonstrated that those individuals who attend a survivorship program are more knowledgeable than those who do not attend, and program participants have a better understanding of their future risks which may improve cancer screening and ultimate health outcomes [94–98]. The vast majority of nursing studies examining knowledge gaps included convenience samples of survivors during face to face survivorship clinic encounters [94, 95, 99]. Still, the majority of CCS do not have access to their treatment information (documents) and are not getting prescribed follow-up care despite attendance at survivorship programs [100]. Greater parental knowledge of the late complications of therapy and screening recommendations is associated with more knowledgeable CCS, although findings from these studies underscored that parental knowledge of their child's history was often greater than that of the survivor [99].

14.6.3.1 Survivorship Care Plans

Survivorship care plans (SCPs) were first created by pediatric oncology nurses as a method of educating CCS about individualized treatment information and recommended follow-up for CCS self-advocacy. The Institute of Medicine report, *Lost in Transition*, recognized the importance of every survivor having a SCP [101]. The key elements of the SCP are a treatment summary, a list of risks for late effects, and follow-up guidelines. More recently, the Passport for Care, a web-based SCP system, was developed including tailored surveillance recommendations [102]. Several barriers exist that inhibit full implementation of SCPs, including insufficient resources to input and update information needed to generate a SCP [103]. Even though there is limited evidence to date that SCPs have improved CCS knowledge, SCPs are considered to be a fundamental need in survivorship care. It is particularly important to have updated SCPs with information tailored for the individual CCS at increased risk for complications such as breast cancer [94, 104].

14.6.3.2 Education and Behavior Change

Despite nurses' decades-long engagement in educating survivors and their families, identifying effective methods for health education, especially if CCS behavior change is required, remains a definite challenge [2, 86]. Tailored or risk-adapted education has yielded early sustained outcomes [94, 105], supporting the need in survivors for personalized follow-up care. Adolescents and young adult cancer patients and survivors in general are technologically savvy and may benefit from educational interventions that utilize easily accessible technology [106].

Phone applications (apps) [107], phone calls [108], phone texts [109], and website materials and patient health record portals [110–112] have shown both feasibility and positive impact on patients' and survivors' engagement in follow-up care and screening. Wearable devices, including the Fitbit™ [113] and activity monitors [114] have been used to promote increasing physical activity; they may offer additional opportunities to promote follow-up care and screening. Fostering risk-based follow-up and screening requires multi-pronged approaches. Investigators recommend that technology-based interventions should be coupled with face to face interactions to amplify their effectiveness [110, 111, 115, 116]. Unfortunately, there is a plateau of knowledge gained with interventions such that over time knowledge decreases [94]. This finding is concerning and reinforces the importance of CCS survivorship program participation, and the need to have a variety of mechanisms to reinforce survivors' learning for best self-advocacy and health promotion behaviors.

Nurses' support of healthy lifestyle choices can empower CCS with evidence-based activities that can improve their late effects risk profile [2, 117–120]. Health promoting behaviors can significantly affect health outcomes and are critical for CCS because of their elevated risks for chronic conditions [30, 121–124]. A nurse scientist developed a predictive model outlining the vital personal and mediating factors of risk-taking behaviors and ultimately health outcomes [125, 126]. Murphy summarized the findings of health behavior studies and concluded that key factors in mobilizing survivor compliance with health behavior changes included tailored health promotion and survivor peer support [127]. Adolescence is a time of rebellion and risk-taking behaviors not unique to CCS [119, 122, 128–131]. Nurse scientists noted that survivors of pediatric brain tumors may have limited competence in independent, good decision-making practices that may affect their health. As a result, research has been done to measure how best to teach CCS the steps to making good decisions. Use of a decision-making framework by nurses with CSS augments the identification of predictors of poorer decision making and described how that reduced risk-taking behaviors [119, 128].

The health behaviors most targeted by nurses for modification include sun protection, smoking cessation, nutrition, physical activity, and metabolic dysfunction. Skin cancer is one of the most common subsequent malignancies [132], and the risk increases with time since diagnosis and advancing age. An interventional study done to improve sun protective behaviors in CCS showed improvements the use of sun protection at 1-month post-intervention in participants [133]. Other studies using multiple approaches to behavioral change concluded that peer counseling, web-based strategies, and social support consistently improved smoking cessation [118, 134]. These findings support the multimodal approach to educating survivors and changing behaviors. Survivors that smoked had peers who smoked or had smokers in their household; thus, exposure to smokers increased the likelihood that a CCS would smoke [122]. These findings underscore the need for family-centered approaches to risk reduction in smoking.

Consuming calorie dense food during therapy and limited adherence to US dietary guidelines may create unhealthy eating patterns post-treatment [135]. Poor dietary behaviors [135, 136] and excessive caloric intake with poor calcium and vitamin D intake have been found in CCS [30, 137], and are of particular concern in the exemplar case in this chapter.

Physical activity can play a significant role in improving bone density, body mass index, and cardiovascular health. Subsets of CCS may have comorbidities that impact physical activity such as poor balance, hearing loss (by affecting communication in team-based sports), amputation, or cardiovascular dysfunction [138]. Wherever possible, physical activity is encouraged because participating in regular physical activity can positively impact weight, bone mineral density, and mental health in CCS [139]. Nurses have been involved in several investigations that have had positive outcomes regarding physical activity and healthy weight management in CCS [140–142]. Various platforms have been used to deliver the intervention including face to face (personal) format and have demonstrated positive outcomes. The Fit4life program, designed for overweight and obese survivors of ALL, found that tailored intervention resulted in weight reduction and increased participation in physical activities following the 4-month intervention in the treatment group compared to the control group [140]. The Survivor Health and Resilience Education (SHARE) program was developed to change multiple behaviors including sun protection, physical activity, diet, and bone health among adolescent CCS. This program consisted of an in-person (face to face) half-day session to educate survivors regarding risk factors and prevention [133, 139]. Many studies demonstrate efficacy and short-term changes in behaviors such as using sun protection, healthy weight management and participation in moderate to vigorous physical activity on a regular basis, and healthy nutrition practices. More work is needed on a larger scale, using multiple modalities (face to face, technology-based). Future studies must be longitudinal in nature to determine whether health promoting behaviors are sustainable.

14.6.4 Special Risk-Adapted Considerations

Survivors with certain risk-based follow-up needs such as CCS treated with anthracycline-based chemotherapy are strongly encouraged to participate in follow-up [143–145]. One method employed by nurses engaged in long-term follow-up care that has shown some evidence in improving rates of cardiac screening includes the provision of telephone counseling by advanced practice nurses (APNs) following risk-based clinic visits [108]. While telephone calls cannot replace face-to-face engagement, personal engagement and communication using APNs improved screening practices [108, 146].

Nurses play a vital role in updating family histories at least annually and should have a strong knowledge base of cancer genetics/genomics, and cancer predisposition syndromes (CPS), as a basis for educating CCS and their families [147, 148]. Risk-based screening for survivors and families with CPS such as Li-Fraumeni (TP53 mutations) requires a tailored approach to follow-up [149]. These CCS have a significant risk of developing one or more cancers in their lifetime. CCS and their families perceive much benefit in cancer genetic screening and may experience reduced anxiety with genetic counseling [150, 151]. Survivors and their families with CPS require lifetime surveillance and periodically updated genetic counseling.

For CCS at increased risk of developing breast cancer, using a tailored approach [90, 94] and consideration of individual factors such as motivation have been shown to improve breast cancer screening in several studies [152–155]. In addition, pediatric oncology nurses create positive environments in which to have conversations with CCS at risk for breast cancer that will in turn promote adherence to regular breast cancer screening [156].

14.6.5 CCS Benefits from Participation in Survivorship Programs

Improved outcomes for CCS who attend survivorship clinics include fewer emergency department visits, better health behaviors, lower distress levels, more appropriate use of the health care system, improved knowledge, and improved detection of late effects [96, 97, 157]. The scholarly inquiry of pediatric oncology nurses has resulted in identification of several key predictors of long-term follow-up participation. Early involvement of parents in follow-up care has been shown to foster survivor attendance [158–160]. Reasons offered by survivors' mothers for attendance at follow-up clinics include needing more information, concern over their children's health, needing to provide transportation for the children to the clinic, and upholding a family tradition [161]. Potential benefits of attending survivorship care as a family unit and ongoing parental involvement include closing the knowledge gap between parents and CCS [99] and continued participation in survivorship health surveillance and healthy behaviors [158, 159, 162].

Survivors who have undergone more intense treatment regimens report a greater need for long-term support and resources [163]. Higher health care self-efficacy was noted in CCS who regularly attend a survivorship clinic [99]. To underscore the work that nursing has done in HRQL and survivor education, oncology nurses use the face to face clinic visit to facilitate the psychosocial development and enhance childhood cancer survivors' self-care and ultimately HRQL for survivors who attend follow-up care [54].

Childhood cancer survivors have been found to be more likely to participate in long-term follow-up clinic if they have received treatment with anthracyclines and radiation [144, 145]. A comprehensive review of patterns and drivers of health care use, such as CCS attendance at a childhood cancer survivor program (CCSP) found that greater attendance at specialized care programs by survivors was associated with higher income, private insurance, at least one chronic health condition, prior radiation, female sex, and older age at time of study

[163].

Despite the evidence underscoring its benefits, most survivors do not attend specialized survivorship programs or participate in follow-up care in general [164]. A study of 80 young adult survivors who had already transferred out of pediatric care revealed that only 55% endorsed cancer-focused follow-up. They reported that communication and the content covered during their primary care (adult) visits varied from no content to too much information that resulted in excessive worry [165].

Researchers have found that male sex, lower socioeconomic status, lower education level, race (specifically minorities including African American and Hispanic CCS), being uninsured or have federally subsidized insurance, treatment history, longer time since diagnosis, limited transportation options, longer distance from clinic, and work/school time commitments predict limited clinic attendance [90, 100, 101, 165, 166]. Where geographic proximity is not an issue, participating in survivorship clinics may be most affected by limited health literacy and education, financial hardships as a result of lower educational attainment, federally subsidized health insurance, and potential lack of transportation for CCS with neurosensory and/or neurocognitive dysfunction. Other nurse investigators have reported lack of attendance at survivorship programs may be more likely in rural regions. Survivors who do not have cancer survivorship programs or specialty services within a reasonable catchment area may not be receiving adequate follow-up, and location may predict attendance at survivor clinics [144, 167]. Research to identify effective methods of providing care to CCS outside of the face to face environment is critically needed.

Post-traumatic stress disorder and PTSS also have implications for CCS decisions to attend survivorship clinic. In several studies, the specific psychological reasons for non-attendance included fear and anxiety [146, 165], PTSD [168], desire to return to normal life, and lack of perceived self-efficacy [169]. Some CCS employ avoidance behaviors and do not attending survivorship programs or adhere to screening recommendations because they want to put their cancer experience behind them [70, 153]. Institutional barriers have included lack of a specialized program due to time and financial issues [86, 166, 170].

Gaining a more robust understanding of the impact of PTSS/PTSD and other psychological–emotional barriers to participation in survivorship care, such as social determinants of health, is paramount due to the impact of follow-up clinic non-attendance on CCS lifetime health risks.

14.7 Interprofessional and Collaborative Survivorship Care

Subspecialists, generalists, and other health care professionals have become increasing important partners in the long-term care of CCS as part of interprofessional survivorship programs [171]. For example, the recent American Heart Association scientific statement that CCS are at risk for cardiac dysfunction underscores the importance of education of all care providers who will care for CCS [143]. In addition, the Preventive Cardiovascular Nurses Association recently endorsed the 2018 American College of Cardiology/American Heart Association/multi-society cholesterol guideline and the US Department of Health and Human Services' physical activity guideline as key to the primary and secondary prevention of atherosclerotic cardiovascular disease [172].

As treatment changes and the roster of risk factors for late effects and comorbid conditions evolves, the need for different subspecialties is also expected to vary. With the advent of precision health, it will be advantageous for survivorship-focused nurse clinicians to partner with nurse scientists to conduct research and to translate the research evidence into CCS clinical care and education of health care providers.

14.7.1 Primary Care Providers

Most childhood cancer survivors receive their health care through their primary care provider (PCP). Therefore, educating primary care providers about late effects and risk-adapted survivorship care is important. Several studies have examined PCP knowledge of CCS' health care needs and explored the information most useful for PCPs to best manage their long-term follow-up care [173, 174]. Continuing education unit (CEU)-focused educational programs and online education for PCPs have been the focus [173, 175]. A PCP-based clinic could successfully meet the needs of adults with a history of childhood cancer [176].

Primary care providers caring for CCS want access to clinical care guidelines coupled with a letter from the primary oncology team with surveillance recommendations to assist them in managing the care of CCS [175].

14.7.2 College-Based Health Care Providers

A recent innovative approach to foster long-term follow-up care for CCS attending college is to work with health care providers on college campuses [177–179]. In one study, college health care providers were connected to survivorlink (www.cancersurvivorlink.org) and had access to key health documents [177]. Although the providers reported no change in self-perceived comfort with caring for CCS, their knowledge increased as did their referrals of other college students to survivorship programs. Investigators and clinicians educated college health care providers using a series of inservices, and college health providers reported an increase in knowledge and greater confidence in caring for CCS [179]. In addition, the college-based health care providers indicated they became more familiar with the local resources available to the CCS.

14.8 Survivorship Education and Lifelong Learning for Healthcare Providers

Survivorship after cancer in childhood or adolescence should become part of the curriculum for all future care providers [180]. The authors, while not specifically addressing pediatric cancer survivorship education, described the state of survivorship education and future directions for all disciplines at varying levels of education and practice, along with critical curriculum content. Because childhood cancer survivorship is multidimensional, education should include cancer screening and prevention, HRQL, support services and resources, adult health education principles, and ongoing care in the event of recurrent cancer. Despite the availability of continuing nursing education via professional organizations such as the Oncology Nursing Society and the Association of Pediatric Hematology/Oncology Nurses, potential state funded initiatives, and the American Cancer Society, not all nursing students and health care professionals have ready access to this information. Most professional organizations require a paid membership in order to access their continuing education programs. In addition, the continuing education programs are not offered in a systematic approach as is done in formal nursing education curricula, which facilitate foundational learning.

Other examinations of formal medical education included the evaluation of an education program for pediatric resident physicians who reported an increase in their knowledge of childhood cancer survivorship [181]. An integrated cancer survivorship training was reported for fellows, but to date only feasibility outcomes have been published including comfort in talking about survivorship issues including late effects, knowledge in survivorship in five cancer types, and the confidence to explain a survivorship care plan with survivors [182]. Further analysis of the program’s long-term success is pending. Educational initiatives are underway to better prepare PCPs in the care of CCS. The shared care model whereby the oncology specialist partners with the PCP in an effort to improve adherence to long-term follow-up (LTFU) guidelines holds promise [183, 184]. Offering CEUs and online education for PCPs is feasible to increase their knowledge. By supporting the PCP in caring for the survivor, we could potentially reduce some of the barriers that survivors face—such as distance from the clinic—when trying to access cancer survivorship-focused care.

Because targeted therapies and precision health are changing the landscape of survivorship care, lifelong learning is essential for nurse clinicians and nurse scientists engaged in survivorship care. Standards for nursing practice in the rapidly evolving field of genetics/genomics have been published [185], the Genomic Knowledge Matrix has been developed as a blueprint for nursing research that incorporates genomics [186], and roles of nurses and nurse scientists have been described [187].

14.9 Preparation of CCS in Transition to Follow-up Care

Nurses have been involved in the development of best transition practices for adolescents [188, 189]. The transition experience for children with special health care needs has been widely explored [190, 191], including CCS [192–195]. Nurses have a critical role in the preparation of AYAs for transition (readiness training), self-care skills acquisition, and in the development of transition programs by virtue of our role in health care [190, 191, 196, 197].

14.9.1 Methods of Transition Preparation

Standardized frameworks or models have been examined to address the most appropriate approaches to meet the transition needs of children with chronic conditions, their families, healthcare providers, and the healthcare system [194, 197–199]. The socioecological model of adolescent readiness to transition (SMART) integrates many survivor, parental, and healthcare provider constructs critical to a successful transition for these populations [199].

Models of transition specifically to adult care for CCS also have been explored [98, 199–202]. No one model fits all, but rather a tailored, risk-based follow-up approach for CCS is likely to be more successful. Individual organizational structures, financial issues, and available resources often impact which model will best suit each health care system. Using a global perspective, one study surveyed stakeholders to identify models of survivorship care [203]. Due to their different health care systems, models of survivorship care varied across countries. Further studies are needed of family-focused gradual approaches to the transition of CCS using developmentally appropriate education, which are tailored to meet their unique needs [159, 160, 188, 192, 193, 195, 196, 201, 204–206].

An advanced practice nurse and colleagues have outlined a step-by-step approach for transitional survivor care between an academic medical center and a children's hospital [207]. The program focuses on the needs of the CCS, defines an interprofessional approach to education, and provides navigation services to facilitate the program's long-term success and sustainability. Another nurse-led initiative in the United Kingdom developed benchmarks for successful transition of care from pediatrics to adult care [208]. The multisite, multi-staged project identified key components of a transition program for young adults using primary data from stakeholders, healthcare providers, and young adults and secondary data collection via national policies, guidelines, and other resources. Because of the complexity of medical care needed for CCS and other children with chronic conditions, participation of all entities involved in the transfer of care is necessary to develop best practices in transition.

Nurse scientists have been involved in interprofessional efforts in examining the challenges faced when addressing CCS transition to adult care [193, 196, 204, 206, 209, 210], and nurses have been engaged in testing interventions to overcome these challenges. A transition workbook to help prepare AYA cancer survivors for transition was piloted, and the investigators reported that face to face education and follow-up telephone calls over a 6-month period resulted in improved readiness to transition [196]. A telemedicine-based approach has been explored in practice to educate survivors about their cancer history and transition to primary care [211]. Survivors and healthcare providers reported increased knowledge and ease of use; only equipment difficulties caused negative feedback. Because of the nature of nurses' role in educating, counseling, advising, and coordinating the care of children, a nurse-led transition program for children with special health care needs was developed incorporating the components of education, anticipatory guidance, counseling, case management, and surveillance that are key to a successful health transition program [191].

While nurses have a significant and important role in the survivor transition team, survivorship care and transition also require an interprofessional approach. Further investigations are needed using randomized, longitudinal clinical trial designs to determine the sustainability of the interventions and models of care over time.

14.10 Summary

These reported outcomes, and challenges for CCS (in particular, brain tumor survivors) who were exposed to multimodal therapy underscore the need for routine long-term cancer surveillance. The chapter has outlined the role that nurses have played in the development, sustainability, and coordination of care and in investigations into the myriad of long-term difficulties these CCS face as they move into emerging and later stages of adulthood. The evidence is clear that nurses are integral to sustainable and successful survivorship programs and coordination of care as well as in the research focused on how best to optimize health outcomes in this population.

14.11 Evidence Available for Translation into Practice

Review of nursing research related to childhood cancer survivorship and transition points to evidence that is ready for translation into clinical practice. The evidence clusters into three key areas: Survivorship program development and interventions around established late effects, survivor/family engagement in LTFU (including transition) and survivor literacy, and targeted assessment for enhanced HRQL, and risk-based screening and health promoting behavior change. Table 14.1 summarizes the evidence in these areas. The evidence of nursing involvement in survivorship program development is embodied in the continued success of CCSPs and the holistic approach that nursing has taken in the care of these CCS and their families. Table 14.2 identifies the areas of precision survivorship research needing further study.

Table 14.1 Evidence ready for translation into practice

Key domains	Topic area	Examples of evidence	Sources
(I) Survivorship program development and interventions around established late effects	(A) Survivorship program development, coordination of care, and sustainability	The efforts on behalf of these pioneers in childhood cancer survivorship have included designing the infrastructure for survivorship programs, and clearly establishing that the nurse is central to the sustainability of all aspects of survivorship care coordination	[2, 78–84]
	(B) Role development in survivorship	The efforts on behalf of these nursing pioneers in childhood cancer survivorship have directly led to the development of nursing and advanced practice nursing leadership positions within childhood cancer survivorship programs Defined the roles of nurses in	[2, 79, 81, 82, 84]

		survivorship care and coordination	
	(C) Identification and attenuation of neurocognitive deficits	Intensive neurocognitive intervention for math abilities over a sustained period at least once a week (1–2 h) for one year improved math abilities in children with ALL	[15, 17, 18]
	(D) Interprofessional research collaboration to address the many late effects of CCS using evidence-based and consensus-based guidelines for care	Engagement of nurse leaders in long-term follow-up guidelines development (national–international) to facilitate risk-based screening and survivorship care using an interprofessional framework	[86–88]
(II) Survivor/family engagement in LTFU	(A) Clinic attendance	Parental engagement in and follow-up care for CCS facilitates the CCS' attendance at survivorship visits	[73, 75, 158–160]
	(B) Survivorship literacy	Parental attendance at LTFU is associated with CCS survivorship literacy	[10, 73, 94, 95, 97–99]
		Parental survivorship literacy influences CCS' survivorship literacy	
	(C) Transitions of care	Developmentally appropriate, gradual and personalized approach to transition of care enhances transition readiness in CCS	[98, 99, 191, 196]
		Workbooks, technology, parental engagement may facilitate successful transitions in subsets of CCS	
	(D) Decision-making capacity	Intentional focus for CCS with neurocognitive deficits and	[82, 94, 125, 126,

		decision-making capacity	128, 212]
(III) Targeted assessments and screening for CCS	(A) Screening and assessment for HRQL, PTSD, PTSS, and as part of an interprofessional research teams	Routine screening and assessment using standard measures over the course of survivorship trajectory are critical due to the variability in HRQL over time in this population and their families Regular screening for HRQL, PTSD, and PTSS using validated measures over time have shown to identify subsets of CCS (specifically brain tumor survivors) who may require ongoing screening and possible intervention The constructs of HRQL, PTSD, and PTSS are dynamic and require a lifetime of screening, assessment, and warrant tailored interventions for CCS	[44, 60, 64, 65, 68–70, 171]
	(B) Assessment and interventions for health promotion and risk-behaviors	Face to face and telephone counseling and follow-up over short term enhance intent to change behaviors and behavior change in CCS Peer to peer counseling may also increase behavior change	[117, 118, 133, 139, 140]
	(C) Cancer screening	Screening behaviors among women for both breast and cardiac screening can be increased following LTFU (face to face environment), and using a positive, holistic approach to education Having LTFU visits may predict increased screening	[108, 146, 154, 156]
	(D) Family-centered approach to interventions in	Family environment and family demands may serve as the framework from which to develop	[10, 11, 56, 75, 82, 128,

	behavior change in subsets of CCS	successful interventions to improve behaviors in subsets of CCS Consider health beliefs about CCS' condition and decision-making capacity	212]

Table 14.2 Areas of nursing research opportunities

Area of focus	Questions for nurse scientists moving forward
Genetic risk for physiological late effects in CCS	Over the past decade, genome-wide association studies (GWAS) have been undertaken in pediatric oncology [76], along with studies focusing on genetic risk factors for late complications in pediatric survivorship [213–215] What is the role of nurse scientists in the engagement of interprofessional genomic/genetic investigations to design precision health guided interventions to thwart the impact of the genetic risk factors for developing late complications?
Neurocognitive deficits and impact on educational attainment, occupational, and social outcomes	Childhood cancer survivorship is a public health/policy issue in many ways. Access to healthcare (insurance, transportation), career/vocational training, and accommodations at school and work (mandated by law) for identified disabilities are not luxuries, but reasonable organized efforts that nurses (public health and oncology) can lead What role does nurse-led, interprofessional collaboration for interventions focusing on helping CCS and their families attenuate the full negative impact of neurocognitive deficits of cancer treatment (specifically CNS directed radiation)? Interprofessional collaboration in symptom science should be incorporated into these investigations to identify biomarkers for increased neurocognitive impairment
Risk-based screening for second cancers, risk reduction behaviors, and survivor literacy	As part of the NINR's Strategic Plan, nursing research should address "*promoting health and preventing illness*" [216]. The investigations go beyond prediction to prevention including obesity, healthy lifestyle behaviors like physical activity, and screening for cardiomyopathy in

	this population. Landier et al. [94] reported that without repetition and tailored approaches to survivorship care, health promotion, and self-efficacy, survivors' knowledge will not be sustained over time Nurse-led large-scale, longitudinal, interprofessional collaborative investigations are needed to examine the sustainability of the tailored approaches already addressed to educate CCS about their risks, optimize health promotion behaviors and risk-based cancer screening practices What will be the impact of reinforcement of health behaviors and screening practices over time in health outcomes in this population in the context of precision health? What role will technology play and how can it be best used to either augment face to face interventions or be used exclusively in CCS as part of improving our outreach to subsets of this population who currently do not receive LTFU care?
Psychological/Emotional impact of the cancer experience and the ripple effect on LTFU care	Interprofessional, longitudinal, multisite, tailored approaches and sustainable interventions are needed that enhance the HRQL of CCS and their families How can nurse scientists align their expertise and efforts in an interprofessional team to design and implement successful interventions to enhance the HRQL for CCS and their families over time? In the context of precision health and symptom science, contributions of nurses in this area using biomarkers of fatigue, stress, and cognition should be incorporated into research The use of mobile technology-based resources, including tablet computers, to assess HRQL at visits for ease of capturing and analyzing this information for prompt intervention should be studied
Formal education and lifelong learning for health care providers due to the rapid evolution of the science of precision health in	Large-scale, longitudinal interprofessional research and education-focused investigations in a collaborative academic-clinical practice-based format are needed How should formal education be integrated into nursing and medical curricula with focused content in childhood

relation to childhood cancer survivorship	cancer survivorship? What are the critical competencies in survivorship that should be established and used as benchmarks? Ongoing education and resources need to be identified and updated regularly to ensure the curricula are keeping up with new knowledge in precision health

14.12 Opportunities for Nursing Investigations in the Context of Precision Health

Nursing scholarship encompasses the generation, synthesis, translation, application, and dissemination of knowledge that aims to improve health and transform healthcare [217]. Paradigm shifts have been seen in the technological capabilities for capture/secure storage/analysis of massive amounts of data (big data science), as well as in the evolution of precision health concepts and terminology. Given the large and growing population of CCS, evolving treatment approaches with associated changing patterns of late complications, and the data that will become available through precision health/big data research, rich opportunities are opening for nurse scientists to advance nursing scholarship in survivorship. The exemplar case study presented earlier in this chapter will be used as part of the determination of what nursing knowledge gaps remain as yet unaddressed.

14.13 Implications for Nursing Practice

Cure is not enough for CCS and their families who deal with the myriad of late physical and psychosocial–emotional effects of cancer treatment [217]. This chapter outlined the role of nurse clinicians, scientists, and educators in successful survivorship program development and sustainability for CCS and their families. Evidence supports the need for nurses to use tailored approaches to improve educational outcomes, HRQL, survivorship health literacy, and screening and health behavior practices in CCS. These tailored approaches should include various methods (e.g., face-to-face, technology-based) consistent to the unique needs of CCS and their families.

Parental involvement in the lives of CCS increases LTFU clinic attendance, improves survivorship health literacy, and facilitates CCS' adoption of health-promoting behaviors. Encouraging CCS to allow their parents to continue to be part of all aspects of their survivorship care while balancing self-management skills and autonomy are critical nursing responsibilities in the trajectory of CCS care. Parents have lived through the cancer experience with AYA survivors, and can serve as advocates and provide support and guidance throughout the cancer survivorship journey.

Information and re-enforcement of the importance of CCS' sustained participation in LTFU and screening, and engagement in health promotion and health maintenance practices in a repetitive format over time are key nursing roles in survivorship programs. Foundational and continuing education for pediatric oncology nurses, physicians, and ancillary staff who are actively involved in the care of children with cancer and throughout the trajectory of the children's cancer therapy is warrented. Continuing education is essential to provide state-of-the-art care in the era of advances in pediatric oncology, survivorship, and precision health. Ultimately, our goal is to achieve the best possible health outcomes for CCS and their families. Figure 14.2 depicts the many key principles of survivorship care in the context of precision health–nursing science and practice and the environment in which the survivors/families life.

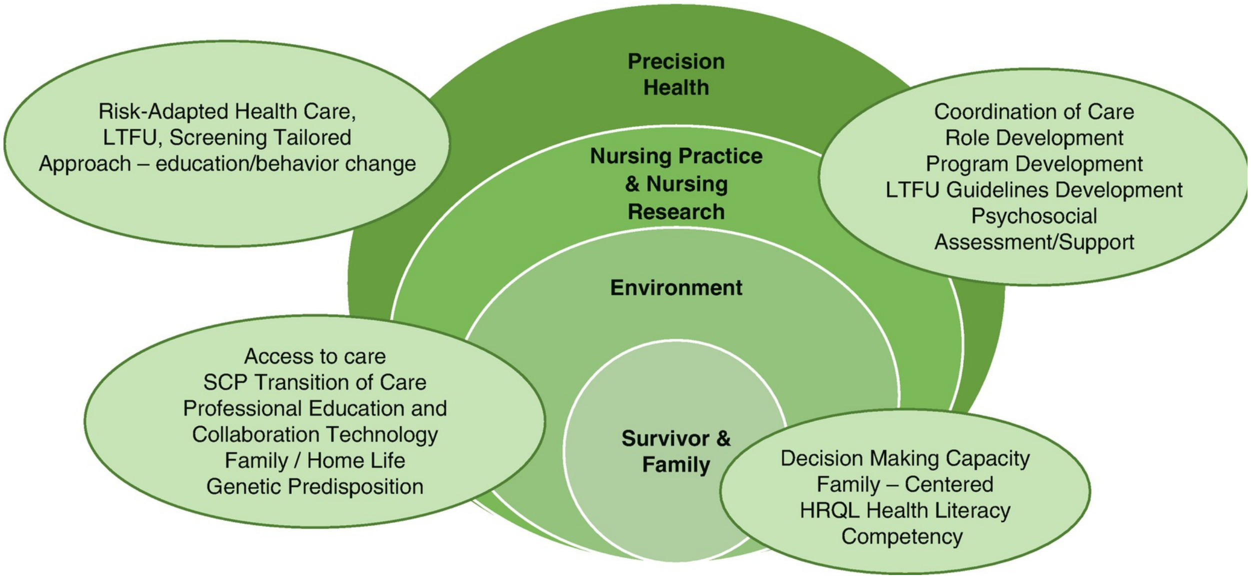

Fig. 14.2 Precision health and nursing care for survivors of childhood cancer

14.14 Conclusion

This chapter has presented many challenges that CCS face and the integral role of nurse clinicians and nurse scientists in optimizing long-term health outcomes in this vulnerable population. The successful development, care coordination, and provision of health care in CCS have been at the hands of skillful, passionate nurses who recognized the necessity of providing comprehensive care to CCS and their families. The evidence clearly speaks to the role of nurses in the development and coordination in all aspects of survivorship care, survivor literacy, attendance at LTFU clinics, cancer screening and health behavior practices, in the assessment and optimization of CCS' HRQL and health outcomes, and how they intersect with the concept of precision health.

Big data science and the immense amount of genomic/genetic data available have yet to be realized are other fortuitous ventures proposed for nursing engagement. The US federal government is conducting a precision health research program called "*All of Us*" that is in the process of enrolling a million or more volunteers. The program will have the statistical power to detect associations between environmental and/or biological exposures and health outcomes, and a wide variety of scientific opportunities will become available to nurse scientists [218, 219].

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Footnotes

1 Readers interested in more comprehensive descriptions of late effects may wish to consult https://www.cancer.gov/types/childhood-cancers/late-effects-hp-pdq.

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15. Pediatric Oncology Nursing Research in Low- and Middle-Income Countries

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Abstract

Cancer and other non-communicable diseases are a growing public health issue now that infectious disease control (e.g., HIV/AIDS, malaria, and tuberculosis) has made great strides across low- and middle-income countries (L&MIC). The large majority (85%) of children and adolescents with cancer reside in L&MIC where children represent up to 50% of a country's population, and resources are severely limited for the comprehensive cancer care these patients require. Nursing care of these patients and families must be based on research performed in country to account for challenges in access to care and limited resources and opportunities for nursing specialization. Examples of these challenges include cancer stigma, poverty, traditional medicine practices, cultural norms and decision-making hierarchies, limited education opportunities, lack of universal healthcare, and poor transportation infrastructure to access tertiary care. This chapter summarizes the 137 articles in five languages from 2008 to 2018 that communicate *nursing* research findings pertaining to pediatric oncology issues from L&MIC across all six World Health Organization (WHO) regions. Despite little or no funding, nurses in academic and clinical settings are actively exploring care priorities in their settings, most often (but not limited to) addressing parent coping, nurse and nursing care issues including symptom management (pain and fatigue, especially), and children's quality of life. The nursing research evidence presented here will begin to inform personalized and precision health in L&MIC to ensure that care is culturally acceptable and considers the environment, nursing practice, nursing science, family, lifestyle behaviors, and response to disease and treatment of this large patient population.

Keywords Low- and middle-income income countries – Childhood cancer – Nursing – Research

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15.1 Introduction

Until the mid-1970s, children and adolescents with cancer across the world had limited chances for survival [1]. Following the discovery of methotrexate by Sidney Farber in 1948 and its use in childhood cancer in the 1960s and 1970s [2], multiple drug therapy, radiotherapy, protocols, as well as improved supportive care including nursing specialization have contributed to overall survival rates today in high-income countries (HIC) that approach 80% [3]. For some diagnostic groups, including acute lymphoblastic leukemia (ALL) and Hodgkin lymphoma, survival rates can reach >90% [4]. Unfortunately, this success has not translated across the world in low- and middle-income countries (L&MIC) where >85% of the world's children reside [5]. Here, survival can be as low as 10%, and many children die before even reaching a tertiary care center and pediatric oncology care [6]. With a lack of universal health care, treatment abandonment is a major obstacle to survival [7, 8]. Specialized training for nurses caring for children and adolescents in L&MIC is often limited or not available [9]. The relatively limited research conducted by nurses in L&MIC means that HIC standards of practice (SOP) are often used to guide practice. This creates practice-related challenges because the conditions on the unit or outpatient facility do not align with those in HIC. As a result, practice guidelines based on evidence from nursing studies in HIC can be of limited value in L&MIC settings and should be used with caution. Nursing research in L&MIC is nascent, but a review of the last 10 years presented in this chapter highlights the work of nurses caring for children and adolescents with cancer across the world in settings with limited resources.

The text's framework of precision health with attention to the ill child's biology and genetics, growth and development, behavior, sense of self, family connection, and social and treating environments [10], environment, nursing practice, nursing science, family, lifestyle behaviors, and response to disease and treatment, provides the guiding structure. This chapter first outlines the current status of childhood cancer care in the context of L&MIC including nursing care to provide a description of the environment in which the care of the child and family is occurring as well as key influences on nursing practice and the conduct of nursing research. The chapter then summarizes pediatric oncology nursing research from 2008 to 2018 in Portuguese, French, English, Spanish, Persian, and Chinese, and provides a synthesis of knowledge that is ready for translation into practice and recommendations for the future of nursing science in L&MIC.

15.1.1 Definition of L&MIC

The World Bank classifies countries of the world into four major brackets according to Gross National Income (GNI) per capita: low-income countries (LIC), lower-middle-income countries, upper-middle-income countries, and HIC [11]. The classification is guided by predetermined thresholds for GNI per capita, which is modified with changing economic situations across the countries. The most recent threshold levels for this classification were designated in July 2018 (Table 15.1) [12].

Table 15.1 World Bank threshold for country classification by income level [12]

Threshold	Total countries (*n*)	GNI/capita (current US$)
Low-income	34	<995
Lower-middle income	47	996–3895
Upper-middle income	56	3896–12,055
High-income	79	>12,055

Source: https://blogs.worldbank.org/opendata/new-country-classifications-income-level-2018-2019

15.1.2 Caring for Children with Cancer in L&MIC

With advances in the prevention and management of infectious disease leading to an increase in population and aging, the global cancer burden is 18.1 million new cases, with 9.6 million deaths from cancer in 2018 [13]. Despite the lack of cancer registries, approximately 85% of children with cancer in the world each year live in L&MIC, meaning that these children are living with suboptimal, limited, or no childhood cancer care [14, 15]. Based on current population growth and decreases in infant mortality, the number of children diagnosed with cancer in these countries is expected to increase by 30% before the next decade [16]. The past Director of the World Health Organization (WHO), Margaret Chan, warned about an impending disaster in the rising incidence of cancer in L&MIC in 2008 [17]. Although childhood cancer represents only a fraction of the worldwide cancer burden (1.2% according to the American Cancer Society [18]), childhood cancer survival rates far surpass those of adults with cancer. Given the young populations in L&MIC, childhood cancer survival has a long-lasting effect on the development of these countries (see Fig. 15.1).

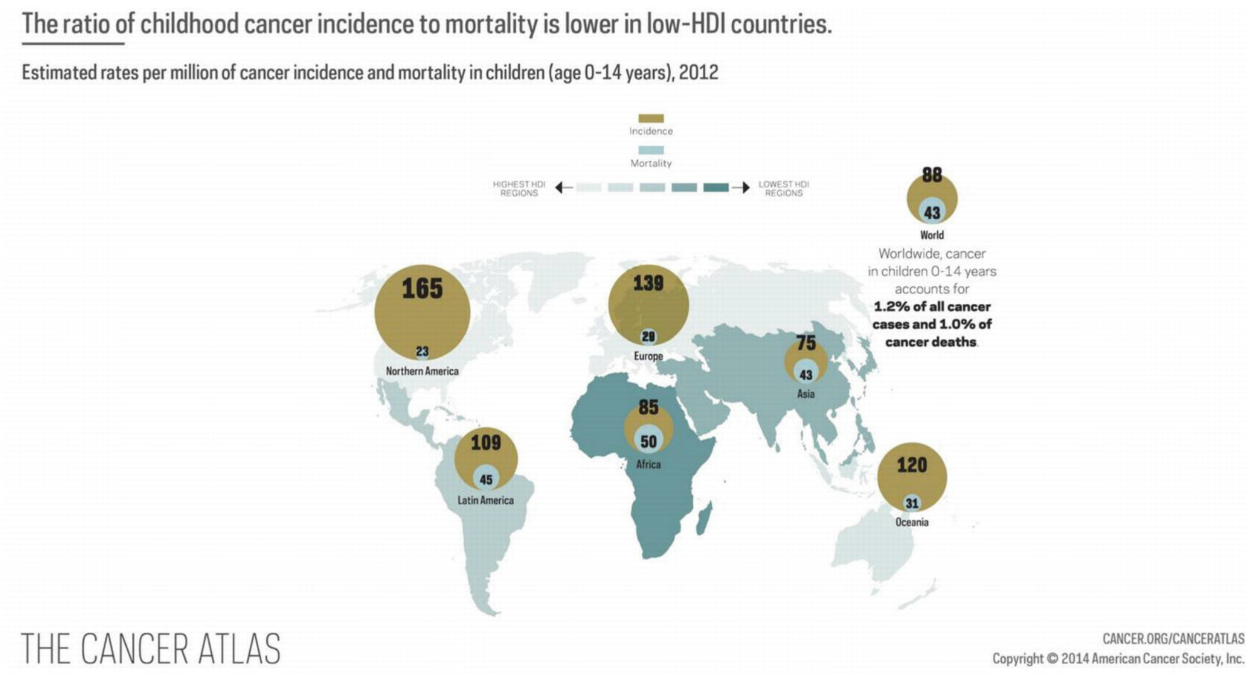

Fig. 15.1 Graphic representation of the number of children/million population diagnosed with cancer annually and the number who die each year by region. Reprinted with permission from American Cancer Society, Inc. (www.canceratlas.cancer.org/the-burden/cancer-in-children). All rights reserved

15.1.2.1 Biology and Genetics

Cancer incidence varies among racial/ethnic groups both within a single country and across countries with similar ethnic groups, particularly for indigenous populations [19]. For example, the incidence of childhood cancer in South Africa based on race/ethnicity was three times greater among whites = 116/million vs. blacks = 37/million. Among diagnostic groups, the incidence of Kaposi sarcoma (KS) was highest in blacks, retinoblastoma and hepatic tumors were more common in “coloreds,” and diagnoses of germ cell tumors were more frequent among children with Asian/Indian ethnicity [20]. The incidence of cancer is related to genetic predisposition, exposure to infectious diseases, as well as other factors in the various environments where children live [21]. Studies from the International Agency for Research on Cancer (IARC) indicate that the incidence of leukemias is up to tenfold higher in HIC than in L&MIC, while lymphomas and solid tumors have higher incidences among children living in L&MIC [22].

15.1.2.2 *Environment*

Some cancers with higher incidence among children in L&MIC are linked to infectious diseases [23], thereby highlighting the double burden on health care systems in settings faced with a rising cancer incidence while still striving to control infectious diseases. Two examples are Burkitt lymphoma, which is associated with Epstein Barr virus, and Kaposi sarcoma associated with HIV. A study on the distribution of childhood cancer in Africa between 1985 and 2011 [24] showed that Kaposi sarcoma was most prevalent in southern African countries like Mozambique, Zambia, and Malawi. In Eastern Africa, Kaposi sarcoma was actually the most common cancer of all for children in Uganda (22.03%), while in Kenya the most common cancer for children in two hospitals was Burkitt lymphoma [24].

Environmental differences related to the incidence of childhood leukemia have been recently studied. A study from Brazil noted, "in cities with high incidence rates of childhood leukemia in early age (Goiânia, Curitiba and Manaus), the major economic activities force is based on industrial plants as a proxy of an environmental exposures that deserves further ecological studies" [25]. A recent WHO report indicates that many cancers in children under 5 years can be "attributed to environmental causes" such as ionizing radiation, second-hand smoke, and pesticides [26]. Overall, widespread environmental toxicities in L&MIC with low rates of environmental protection from, for example, pesticides used in agriculture [27] and local tobacco sales (India is ranked second in the world for tobacco production and consumption [28]) put children at risk for potential transplacental exposure to carcinogens from said environment [29].

15.1.2.3 *Nursing Practice and Nursing Science*

Limited specialized nursing training and inadequate staffing result in longer hospital stays and more complications amongst patients in general [30–32]. L&MIC nurses face distinct challenges including a limited number of nurses in pediatric oncology units and mandatory rotation among specialties. In a recent survey of pediatric oncology nurses, the majority of L&MIC nurses cared for more than five patients each shift and 33% rotated to other hospital units compared with 4% of nurses in HIC [33]. Nurses in L&MIC often enjoy little physician communication and support [34]. Staffing shortages are made more acute by the lack of essential allied health care providers, e.g., nutritionists, pharmacists, and palliative care providers, which can lead to nurse burnout [35]. Nurses in pediatric oncology units in L&MIC receive little specialized education and training in the care for children and adolescents with cancer [36]. Equipment and supplies to support safe and efficient care, such as personal protective equipment and chemotherapy-tested gloves, are rare for nurses in these settings, thus posing health risks to nurses caring for children with cancer. Consequences of these conditions are highlighted in a study in Egypt of nurse and pharmacist exposure to hazardous drugs for cancer treatment and in a study of Iranian nurses who developed changes in mitochondrial parameters and in the cytotoxicity of lymphocytes following exposure to chemotherapy through inhalation [37, 38].

15.1.2.4 Family, Lifestyles, and Behaviors

Cultural misconceptions of cancer within L&MIC can be stigmatizing and lead to patients' and families' concealing cancer cases within communities [39]. Public awareness activities have been successful in promoting early diagnosis and better survival in L&MIC, including Botswana [40]. In general, individuals in L&MIC go to local health care providers when they have signs of cancer; however, many individuals experience health system delays for adequate diagnoses and prompt treatment, such as those reported in Indonesia and Kenya [41, 42].

Late presentation of childhood cancer patients in L&MIC is attributable to two key facets, patient delay and health system delay, as has been described in Nicaragua, Nigeria, and Colombia [43–45]. Approximately 90% of children with retinoblastoma worldwide live in L&MIC, and 95% of them already have metastatic disease at the time of diagnosis [46]. Patient delay is attributed to low levels of community awareness, difficult access to medical care, and cultural/spiritual beliefs [14, 47, 48]. L&MIC healthcare personnel frequently lack the training and clinical experience to diagnose childhood cancer, which is rare in their practice, and referral systems to specialized care are generally poor [49]. Education programs aimed at increasing childhood cancer knowledge amongst healthcare workers have been successful in increasing the number of patients diagnosed [50] and reducing the delay from onset of disease to diagnosis [40].

15.1.2.5 Response to Disease and Treatment

Greater than 90% of global childhood cancer deaths occur in L&MIC [51, 52], and survival rates are still as low as 10–30% [53, 54]. Five-year survival for children with cancer is directly proportional to health indicators including ratios of physicians and nurses per 1000 population and the proportion of government healthcare expenditure per capita [55, 56]. Other challenges plaguing pediatric oncology care in L&MIC include difficult access to essential medicines; limited capacity for supportive care; treatment abandonment; underdevelopment of palliative care services; late presentation, under-diagnosis and underreporting; lack of childhood cancer registries; and inadequate government investment in pediatric oncology [16].

Treatment refusal or abandonment is the failure to start or complete treatment aimed at cure in pediatric oncology [57], and L&MIC bear 99% of the global burden of treatment abandonment. Although rare in HICs, this problem has been and continues to be of high significance in L&MIC, sometimes exceeding other causes of treatment failure [58, 59]. At a tertiary center in India, 30% of patients with acute lymphoblastic leukemia (ALL) refused treatment and 15% abandoned [60]. In western Kenya, a 54% abandonment rate was reported from a cohort of 180 childhood cancer patients between 2007 and 2009 [61]. Reported causes of treatment abandonment include poverty, inadequate counseling on disease and treatment, length of treatment, fear of side effects, religious beliefs, stigma, lack of health insurance schemes, transportation difficulties, hospital detention policies, and inadequate social support systems [53, 61–63].

Even in countries with health insurance systems, like Colombia (a middle-income country), children from families without insurance or with lesser insurance have dismal cancer treatment outcomes compared to those with insurance: no insurance 23% (95% CI: 13, 35), public insurance 43% (95% CI: 39, 46), and private insurance 62% (95% CI: 58, 66) [64]. Despite universal healthcare systems, survival inequalities persist, highlighting the complexity of cancer treatment in L&MIC and not simply a lack of insurance coverage [64].

Direct application of treatment protocols that are effective in HICs is not possible in L&MIC due to the inability to provide commensurate levels of supportive care including infection control practices, laboratory and imaging monitoring, and transfusion support [16]. Death rates from neutropenic sepsis in the course of treatment are greater in L&MIC, and these settings usually have a distinct variety and virulence of microbial infections compared to HIC [65, 66]. Malnutrition, sometimes severe, is common amongst children with cancer in L&MIC and results in reduced tolerance and higher treatment toxicity, including severe neutropenia and resultant infections [44, 67].

Essential medicines for cancer care are usually not accessible in L&MIC. In a survey on access to essential medicines in nine L&MIC, these medications were often reported to be in short supply or completely unavailable, despite their inclusion on the WHO essential medicines list for children [68]. The report noted concerns with the quality of imported medications, and insufficient government attention to pediatric oncology drug procurement with pharmacists sometimes erroneously or deliberately not renewing drug licenses or even not procuring medications they deemed not financially lucrative [68]. The WHO essential medicines list for children was launched in 2007 and is updated every 2 years [69]. This resource provides a reference for advocacy with governments to support the availability and accessibility of pediatric oncology medications.

Access to palliative care for children/adolescents with cancer in L&MIC is challenged by a lack of trained palliative care providers, limited government support, and restrictions on morphine import and use. A 2010 survey of 58 countries showed that lower-income countries had less availability of palliative care specialist services, pain management, and bereavement support [70]. The low survival rates in these countries emphasize the imperative to develop quality palliative care programs. In an outreach palliative care program in Cameroon, a trained nurse providing symptom control and emotional support at home using a motorbike for transportation improved the quality of life for terminal patients in rural settings, demonstrating that improvements in palliative care for children and adolescents with cancer are possible even in L&MIC [71].

15.1.2.6 Summary

The current situation for nurses caring for children and adolescents with cancer in L&MIC is challenging due to families living in poverty, cancer stigma, lack of universal health care, limited specialty training, limited resources including essential medicines and occupational protection for preparing and administering hazardous drugs, lack of ancillary professional support, high patient to nurse ratios, and limited support from physicians. Opportunities for nursing research to guide nursing practice are rare and generally unfunded in L&MIC settings. That said, this chapter presents the results of nursing research on topics of pediatric oncology from all six WHO regions. Despite the challenges that nurses caring for children and adolescents with cancer encounter in L&MIC, research is being conducted and led by nurses, particularly in Brazil and China. This work is laying the ground for improved nursing practice and care.

15.2 Methodology

A literature search of the following databases was conducted in Chinese, English, French, Arabic, and Portuguese: CINAHL, PubMed, Google Scholar, and Science Direct for publications from 2008 to 2018. Search terms included nurse/nursing, pediatric, cancer, and oncology. Articles deemed eligible for inclusion had to have at least one author who was a nurse from a low- or middle-income country by World Bank 2018 ranking, and the topic had to be about pediatric oncology. Articles were identified by title and abstract. If an article appeared to be appropriate for inclusion, the full-text was retrieved for further scrutiny. Reference lists in selected articles were reviewed as well for other potentially eligible publications. Grey literature was sought, but no research findings were located. A master list of eligible studies was created. With the exception of the Chinese publications, eligibility was verified by two authors of this chapter. Examples of rejected articles included those written by psychologists or other non-nursing specialists, those with samples of adult oncology nurses, and opinion articles.

15.3 Article Selection Results

15.3.1 Selection Process and Geographic Representation

A total of 5680 articles from L&MIC were screened. One-hundred-and-thirty-nine studies were identified by title and abstracts as meeting inclusion criteria, and full-text articles were located. After verifying that the publications were written by nurses (e.g., checking author affiliations or online search for author biographies) and that samples in studies of oncology nurses included pediatric oncology nurses, a total of 137 articles were included for analysis (see Table 15.2).

Table 15.2 Number of included and excluded nursing publications on pediatric oncology from low- and middle-income countries (2008–2018) according to the language of publication

Language	# of records	Included
Arabic	809	0
French	1246	0
Persian	1	1
Spanish	1718	5
Chinese	414	25
Portuguese	85	25
English	1407	81
Total	5680	137

Articles from 20 L&MIC from the six WHO regions included: the Americas (*n* = 51), Western Pacific (*n* = 37), Eastern Mediterranean (*n* = 24), European (*n* = 17), Africa (*n* = 6), and South-East Asia (*n* = 2). (Figure 15.2 shows the geographic distribution of articles.)

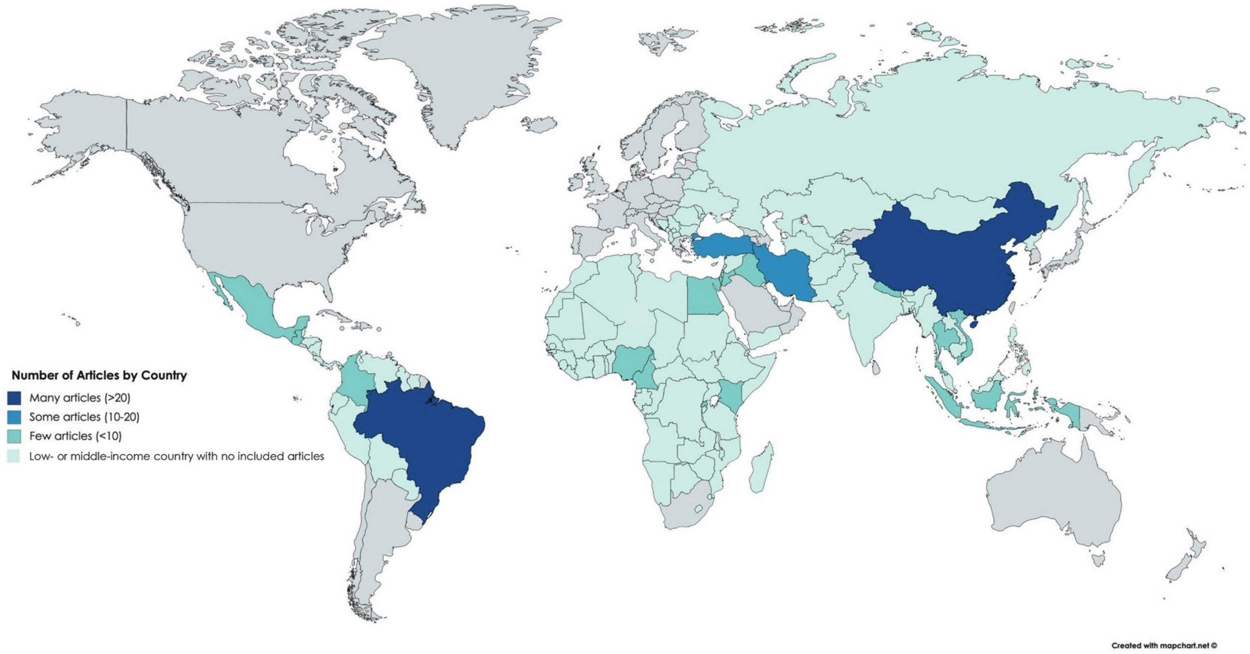

Fig. 15.2 Geographic distribution of the included nursing publications on pediatric oncology from low- and middle-income countries 2008–2018 (countries in gray are low- and middle-income countries without eligible articles for inclusion in this review)

15.3.2 Research Design, Quality Rating, and Strength of Evidence

The quality and strength of evidence of the selected studies were determined by using the Johns Hopkins Nursing Evidence-Based Practice Research Evidence Appraisal ranking [72]. Strength of evidence was determined as Level I (Strong) for RCT or meta-analyses of RCTs; Level II for quasi-experimental studies; Level III non- experimental, qualitative, or meta-synthesis studies; Level IV expert opinion; and Level V literature reviews [72]. The quality of evidence was graded as A (High), B (Good), or C (Low/Major Flaw).

The strength of evidence for the majority of studies (99/137) was level III, indicating that studies used a quantitative non-experimental design or were a systematic review of any study design. Most studies (105/137) were rated as good quality (i.e., B). Only, ten studies were rated as high quality (i.e., A) and 22 studies as low quality (i.e., C). Figure 15.3 summarizes the publications included in this review based on study design and geographic location.

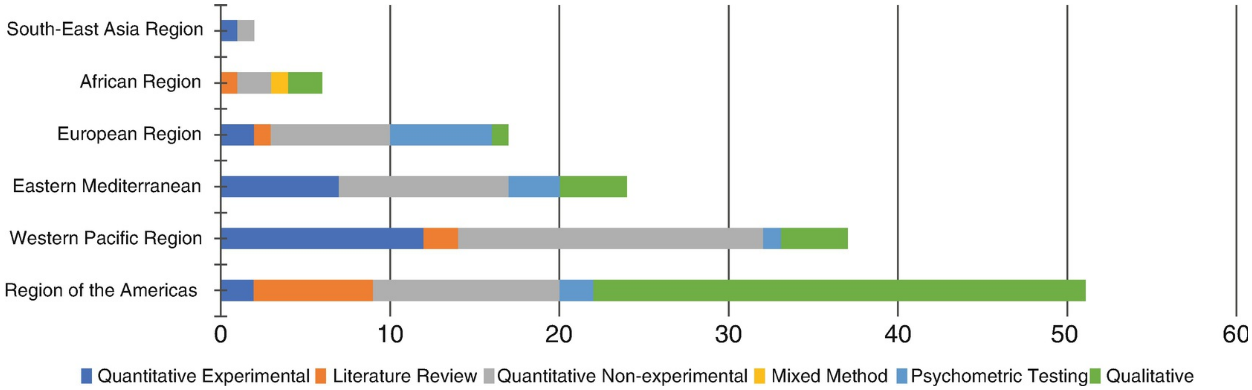

Fig. 15.3 Nursing publications on pediatric oncology from low- and middle-income countries (2008–2018) meeting inclusion criteria based on study design and geographical location

15.3.3 Study Sample Populations

Sample sizes and composition varied across studies ranging from 24 to 2093 children, 17–1588 parents/caregivers, and 4–661 nurses and/or health care providers. Figure 15.4 summarizes the composition of study samples of included studies based on geographic location.

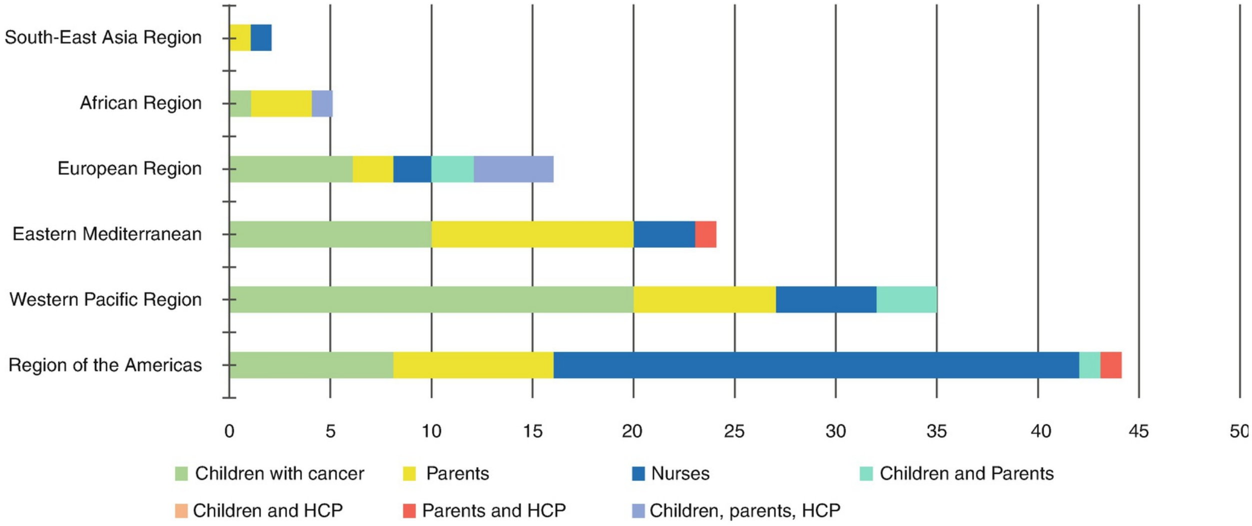

Fig. 15.4 Sample of the included nursing publications on pediatric oncology from low- and middle-income countries (2008–2018) according to the geographical locations

15.4 Summary of Nursing Research in L&MIC

The following section presents a summary of nursing research in L&MIC.

Studies are organized around their larger focus, including those that were primarily descriptive, addressed instrument development, emphasized nursing practice, intervention-based, and literature reviews. Studies are further described according to the WHO region where the study was conducted, with exemplars highlighted to provide a additional detail on the scope of research occurring in L&MIC. A complete summary of articles is provided in Table 15.3.

Table 15.3 List of included articles of pediatric oncology nursing research in low- and middle-income countries (2008-2018) categorized by topic focus

Citation	Country	Strength of evidence/quality	Sample	Methodolog
Descriptive studies—symptoms				
O manejo da dor em crianças com câncer: contribuições Para a enfermagem [Pain management in children with cancer: Contributions to nursing] [73]	Brazil	III/B	55 children 0–12 treated for cancer at one hospital in 2006	Qualitative t description notes
Dimensions of vulnerability for the family of the child with oncologic pain in the hospital environment [74]	Brazil	III/B	Nine family members of children with cancer(7 mothers, 1 father, and 1 grandmother)	Games and a expression u interview gui two sessions

Symptom experience among children with cancer: A cross-sectional study [75]	China	III/B	125 pediatric patients with cancer	[Full text not available]
Factores de riesgo asociados con complicaciones que obligaron al Retiro de catéteres venosos centrales de	Mexico	III/B	225 children with PICC lines (88 oncology patients) (2 months to 18 years)	Prospective c study, resear created data

inserción periférica en un hospital pediátrico de tercer nivel [Risk factors associated with complications that forced the removal of peripheral central venous catheters in a third-level pediatric hospital] [76]					
Pain and its impact on the functional ability in children treated at the Children's Cancer Center of Lebanon [77]	Lebanon	III/C		62 children with cancer (8–17 years; at least 1 month post diagnosis; outpatient and inpatient; 48.4% leukemia)	Adolescent P Pain Tool (fo report by chi 17); Functior Disability Inv and medical review

Fatigue and health-related quality of life in children and adolescents with cancer [78]	Brazil	V/B	38 children (8–12 years) and adolescents (13–18 years)	PedsQL Multidimensi Fatigue Scale PedsQL Inver Quality of Lif
Spiritual and religious coping and depression among family caregivers of pediatric cancer patients in Latin America [79]	Brazil	III/B	77 caregivers of pediatric oncology patients (68 female; mean age 37.3)	Beck Depress Inventory (B reported hea (one item fro WHOQOL-BR Brazilian ver and the Brazi SRC scale ada from the Nor American Re Coping (RCO
Investigation of the effects of planned mouth care education on	Turkey	III/C	16 children (8–18 years) hospitalized in the pediatric oncology	Child and Pa Information (researcher for demogra

the degree of oral mucositis in pediatric oncology patients [80]			and hematology clinics at a university hospital	disease and t information) World Healt Organization Mucositis Inc the Children' International Mucositis Ev Scale (ChIME
Descriptive studies—parent experiences				
Depression and	Iran	III/B	480 parents of	Hospital Anx

anxiety among parents of children with blood disease in Ahvaz, South West of Iran [81]			children with hematologic disorders (15 male)	Depression s
Cotidiano de mães-acompanhantes-de-filhos-que-foram-a-óbito: contribuições para a enfermagem oncológica [Daily of mothers-companions-of-	Brazil	III/B	14 mothers of children with cancer	Qualitative i

children-that-were-to-death: Contributions for the oncologic nursing] [82]				
O cotidiano dos pais de crianças com câncer e hospitalizadas [The daily routine of parents of children hospitalized with cancer] [83]	Brazil	III/B	13 caregivers (9 mothers, 2 fathers, and a couple) of children with cancer (5–10 years)	Interviews
Knowledge and home practices of caregivers having children with leukemia attending National Cancer	Egypt	I/B	192 caregivers of children with leukemia (6–12 years) receiving chemotherapy	24-item kno questionnair item caregiv practices

Institute Cairo University [84]				
Assessment of parents' perception of quality of pediatric oncology inpatient care at Kenyatta National Hospital [85]	Kenya	II/B	107 parents of children with cancer (0–12 years)	Mixed metho approach (questionnai focus group discussion)
Investigating the relationship between the quality of life and religious coping in mothers of children with recurrence leukemia [86]	Iran	III/B	200 mothers with children with leukemia (1–15 years)	Caregiver Qu Life Index-Ca (Persian vers RCOPE in Per

Qualitative research on the problem of the care of children with cancer in the other perspective [87]	China	III/B	8 caregivers of pediatric patients with cancer	[Full text not available]
Unmet family needs concerning healthcare services in the setting of childhood hospitalization for cancer treatment in mainland China: A	China	III/B	5 fathers and 14 mothers purposively sampled from four pediatric oncology departments mainland China from September 2013 to March 2014	Interviews

qualitative study [88]				
The information needs of South African parents of children with cancer [89]	South Africa	III/B	13 caregivers of children with cancer (8 mothers, 2 fathers, 1 grandmother, and 1 an aunt)	Qualitative i
Assisted therapy with dogs in pediatric oncology: Relatives' and nurses' perceptions [90]	Brazil	III/B	10 relatives/guardians of children with cancer and 6 health professionals	Participant observation depth intervi

Emociones del cuidador primario ante su enfermo con diagnóstico de cáncer [Emotions of the primary caregiver in front of his patient with cancer diagnosis] [91]	Mexico	III/B	2 parents of a child with cancer	Qualitative st
Coping with the diagnosis and hospitalization of a child with childhood cancer [92]	Brazil	V/B	9 mothers and 1 father (range 20–52 years) of children with cancer (multiple diagnoses 23 months to 14 years)	Semi-structu interviews
Cuidando da criança com câncer: Avaliaçâo da sobrecarga e qualidade de vida dos cuidadores [Taking care of children with cancer: Evaluation of the caregivers' burden and quality of life] [93]	Brazil	III/B	32 caregivers (28 females and 4 males) of children or adolescents with cancer on treatment for at least 2 months	22-item Care Burden Scale 36-item shor health surve the 21-item Depression I (BDI)

Prevalence and predictors of post-traumatic stress symptoms in parents of children with ongoing treatment for cancer in South China: A multi-centered cross-sectional study [94]	China	III/B	192 mothers and 87 fathers of children with cancer participated from 4 general hospitals	Post-Trauma Checklist-Civ (PTSCC) (Chi version), Con Davidson res scale (CD-RIS (Chinese vers patient healt depression s (PHQ-9) (Chi version), and general funct subscale of M Assessment I (Chinese vers
Parents' needs of early diagnosed	China	III/A	14 children with acute	[Full text not available]

children with acute lymphoblastic leukemia: A qualitative study [95]			lymphoblastic leukemia	
An analysis on benefit finding level of parents with kids suffering from various cancer and its influencing factors [96]	China	III/C	170 parents of pediatric patients with cancer	[Full text not available]
Resilience and psychosocial function among mainland Chinese parents of children with cancer [97]	China	III/B	125 parents of children with cancer in southeast China from September 2013 to February 2014	Demographic Connor-Davi Resilience Sc (Chinese vers Coping Healt Inventory for (CHIP); Socia Questionnair (created by H Medical Univ Zarit Burent Interview; an rating anxiety depression sc
Descriptive studies—child experiences				
Quality of life and symptom prevalence as reported by children with	Lebanon	III/B	85 children with cancer (7–18 years; 44% leukemia)	Lebanese Ara “Quality of Pa Care Questio Pediatrics”— combination

cancer in Lebanon [98]					Pediatric Qua Life Inventor (PedsQL) can module and N Symptom Ass Scale (MSAS) items from E Organization Research and Treatment of Quality of Lif Questionnair (EORTC QLQ- that represen Global Health (GHS)/QoL su
The psychosocial experience of adolescents with hematological malignancies in Jordan: An interpretive phenomenological analysis study [99]	Jordan	III/B		14 adolescents (13–14 years; leukemia or lymphoma diagnosed within 3 months of study)	Semi-structu interviews
Quality of care and relationships as reported by children with cancer and their parents [100]	Lebanon	III/B		Convenience sample of 85 children and adolescents (7–18 years) and 85 parents or caregivers	Needs at End Screening To (NEST) tool t to Arabic, bac translated, an piloted

Quality of life and chemotherapy-related symptoms of Turkish cancer children undergoing chemotherapy [101]	Turkey	III/B	93 children (10–18 years) receiving chemotherapy in 4 children's hospitals	Patient form PedsQL 4.0 (12 years and 18 years) an Memorial Sy Assessment 18 years)
O brincar de faz de conta de crianças com câncer que se submetem ao processo de quimioterapia [The pretend play of children with cancer who	Brazil	III/B	5 children with cancer (aged 4–12) who had received at least 1 round of chemotherapy	Filmed childr playing using Dramatic The Toys

undergo chemotherapeutic treatment] [102]				
Children and adolescents with cancer: Experiences with chemotherapy [103]	Brazil	III/B	Children and adolescents receiving chemotherapy (8–18)	Semi-structu interviews
The correlation between post-traumatic stress disorder and life quality of children and adolescents with cancer [104]	China	III/A	100 pediatric patients with cancer and 100 pediatric patients with common non-cancer diseases	[Full text not available]
Health-related quality of life and its related factors in children and	China	II/C	149 children and adolescents with leukemia	PedsQL 4.0 (Core Scales) PedsQL 3.0 (module)

adolescent with leukemia during chemotherapy [105]				
The experience of informing and palliative care for 6 children with terminal cancer [106]	China	III/B	6 end-of-life stage pediatric patients	[Full text not available]
Children's lived experiences of hematopoietic stem cell transplantation [107]	Iran	III/C	Children receiving stem cell transplant (6–17 years)	In-depth and structured in

A comparison of quality of life, anxiety, and depression in cancer and non-cancer children in Kermanshah, Iran [108]	Iran	III/C		Convenience sample 30 children with cancer and 30 healthy children (10–16 years) (15 male/15 female both groups)	WHO Quality BREF; Childr Depression S (CDS); Revise Children's Ma Anxiety Scale
A presença de familiares na sala de quimioterapia pediátrica [The presence of family members in the pediatric	Brazil	III/B		7 children with cancer (6–12 years) receiving outpatient chemotherapy and screened for physical health to	Picture draw storytelling, a interviews if to elicit addit information

chemotherapy room] [109]			participate	
Calidad de vida en niños con cáncer mediante PedsQL Cancer module© [Quality of life in children with cancer through PedsQL Cancer module©] [110]	Mexico	II/A	199 children with cancer (7–18 years) and 197 caregivers	PedsQL canc modules (chi adolescent, a parent forms
Bereaved parental evaluation of the quality of a palliative care program in Lebanon [111]	Lebanon	V/C	29 bereaved parents of children who died of cancer from 2002 to 2007	Pediatric Qua Life and Eval Symptoms Technology S (PediQUEST) some parts o Parents Pers Questionnair as open-ende questions. Th was translate validated, an with 2 paren revised

Coping strategies used by hospitalized children with cancer undergoing chemotherapy [112]	Brazil	III/B	10 children with cancer (7–12 years)	Demographi info and one interview wit puppets
Realizing being a leukemic patient: The starting point of returning to normality in Thai adolescents [113]	Thailand	III/B	20 adolescents (12–19 years) with leukemia	One to two i interviews a observation chemothera administrati

Transfusion reactions profile in oncology pediatrics patients [114]	Brazil	III/B		162 records about transfusion incidents of pediatric oncology patients; September 2010–2013	Chart review

Study on the quality of life of school-age children with malignant tumors and the influential factors [115]	China	III/B	240 school-age children with malignant tumors	Surveys [full available]
The impact of hematologic cancer and its treatment on physical activity level and quality	China	I/B	125 children receiving treatment for hematologic cancer and 243 healthy children matched by age	Therapy-Rel Symptom Ch for Children (Cp); Chinese University of Kong: Physic

of life among children in mainland China: A descriptive study [116]					Activity Rati Children and (CUHK-PARC PedsQL Gene Module 4.0 a Cancer Modu
Determination of school-related problems in children treated for cancer [117]	Turkey	I/B		56 children (7–18 years) in remission and attending school; their parents; a control group of patients without cancer; and their teachers	2 researcher life evaluatio questionnair capture acad success of su and controls. child health questionnair PF50) measu

				physical, men social well-be the children. Teacher's rep (TRF/6–18) children's em and behavior symptoms
The level and influence factors of the health-related quality of life in children with bone tumors [118]	China	III/C	73 children with bone tumors	[Full text not available]
Descriptive studies—traditional and complementary medicine				
The role of traditional healers in the diagnosis and management of Burkitt lymphoma in Cameroon:	Cameroon	III/B	387 parents of children with cancer	Locally desig questionnair

Understanding the challenges and moving forward [119]				
Family strategies for managing childhood cancer: Using complementary and alternative medicine in Jordan [120]	Jordan	III/B	69 parents of children with cancer (0–18 years)	Questionnair
Complementary and alternative medicine used by pediatric patients with cancer in western Turkey [121]	Turkey	I/B	112 parents of children (1–18 years) treated for cancer	Researcher c questionnair
Descriptive studies—nutrition				
Assessment of nutritional problems in pediatric patients with cancer and the information needs of their parents: A parental perspective [122]	Turkey	III/B	69 parents of children (3–18 years) with cancer (85.7% mothers)	Face-to-face interviews

Descriptive studies—epidemiology					
Initiating childhood cancer treatment in rural Rwanda: A partnership-based approach [123]	Rwanda 2/6 and the USA 4/6	III/B		24 children (0–18 years) receiving cancer therapy	Retrospectiv review

Nursing practice					
Concepção dos enfereiros acerca da capacitção no cuidado à criança com cáncer [Nurses' conceptions about pediatric oncology care training] [124]	Brazil	III/B		Six nurses with experience working in pediatric oncology at study hospital	Semi-structu interviews ar participant observation
Cuidados paliativos à criança oncológica na situação do viver/morrer; A ótica do cuidar em enfermagem [Palliative care to the oncologic child in the situation of live/die: The	Brazil	III/B		5 pediatric nurses in one hospital in Rio de Janeiro	Qualitative interviews, tl analysis

optics of the care in nursing] [125]				
Nursing adherence to ethical codes in pediatric oncology wards [126]	Iran	III/B	200 mothers and 60 nurses in pediatric oncology wards of five major hospitals in Tehran, Iran	Descriptive comparative questionnair
Lived experiences of pediatric oncology nurses in Iran [127]	Iran	III/C	7 pediatric oncology nurses	Interviews

Evaluation of empathetic skills of nurses working in oncology units in Samsun, Turkey [128]	Turkey	III/C	50 nurses working in oncology units in two hospitals in Turkey	Demographi information “empathic ab form”
Chemotherapy-knowledge and handling practice of nurses working in a medical university of Nepal [129]	Nepal	III/B	125 nurses who work with cytotoxic drugs (CDs), random sampling	Structured a unstructured questionnair

Non-pharmacological approaches to control pediatric cancer pain: Nursing team view [130]	Brazil	III/B	35 pediatric oncology nurses (inpatient and PICU)	36-item ques
Fatigue in children and adolescents with cancer from the perspective of health professionals [131]	Brazil	III/B	53 health professionals (10 nurses, 33 assistant nurses, 3 physicians, 3 nutritionists, 2 psychologists, and 2 physical therapists	Semi-structu interviews

A sustainable model for pediatric oncology nursing education in low-income countries [132]	Guatemala	II/B	49 full-time professional pediatric oncology nurses from January 1, 2007 to September 30, 2009	Evaluation of nurse educat program
Criança com câncer em processo de morrer e sua família: Enfrentamento da equipe de enfermagem [Children with cancer in the process of dying and their families:	Brazil	III/B	1 nurse, 4 technicians, and 1 nursing assistant who had cared for a dying child in the last year	Non-directiv interviews

Confrontation of nursing team] [133]				
Educación Continua: construcción del conocimiento y estrategias educativas para las enfermeras de oncología [Continuing education: Construction of knowledge and educational strategies by oncology nurses] [134]	Brazil	III/B	30 oncology nurses (12 pediatric)	Semi-structu interviews
Desvelando o cuidado humanizado: percepções de enfermeiros em oncologia pediátrica [Unveiling humanized care: Nurses' perceptions in pediatric oncology] [135]	Brazil	III/B	9 pediatric oncology nurses (1 male; 24–28 years)	Semi-structu interviews
Humanização: Uma leitura a partir da compreensão dos profissionais da enfermagem [Humanization: A	Brazil	II/B	3 nurses and 8 nursing technicians in pediatric oncology unit	Semi-structu interviews

reading from the understanding of nursing professionals] [136]					
Vivência de enfermeiros no cuidado à criança em fase terminal: Estudo à luz da teoria humanística de enfermagem [Nurses' experience in caring for a terminally ill child: Study in the light of the humanistic nursing theory] [137]	Brazil	III/B		10 nurses who had cared for a child at end-of-life	Interviews
Usos y actitudes del personal de enfermería acerca de las terapias alternativas en un hospital pediátrico [Uses and attitudes of nursing staff about alternative therapies in a	Mexico	II/B		268 nurses (aides, general, and specialized)	Questionnair

pediatric hospital] [138]				
Palliative care in pediatric oncology in nursing students' perception [139]	Brazil	III/B	20 undergraduate nursing students in their senior year	Qualitative i
Assessment of mothers' attitude toward chemotherapy treatment for pediatric in oncology units Hospital Margin in Babylon City [140]	Iraq	III/A	100 purposely selected mothers of children with cancer receiving chemotherapy	Researcher c questionnair

Relationship between nurse working environment and nurse-reported quality of care in the department of pediatric hematology and oncology [141]	China	III/B		606 pediatric oncology nurses	Survey
Preliminary establishment of quality indicator system for pediatric hematology and oncology nursing [142]	China	III/B		15 pediatric oncology experts from 8 provinces	Instrument development

Estratégias de enfrentamento de enfermeiros frente ao paciente oncológico pediátrico [Coping strategies of nurses toward patients in pediatric oncology] [143]	Brazil	III/C	12 nurses working (or had worked) in pediatric oncology	Coping Strate Inventory administered
Lúdico no cuidado à criancṃa e ao adolescente com câncer: perspectivas da equipe de de enfermagem	Brazil	III/B	29 pediatric oncology nurses	Semi-structu interviews

[Playful activities in health care for children and adolescents with cancer: The perspectives of the nursing staff] [144]				
Nursing students: Undergraduate nursing students and self-reflective accounts of first clinical rotation in pediatric oncology [145]	Iran	III/B	Convenience sample of 25 senior undergraduate students (19 women, 6 men) in the final year of BSc nursing program	Interviews a journals
O enfermeiro e o cuidar da criança com câncer sem possibilidade de cura atual [The nurse and the care provided for child with cancer without the possibility of cure at the moment] [146]	Brazil	III/B	12 pediatric oncology nurses	Interviews
Cuidado de enfermagem à criança que tem doença oncológica avançada: Ser-com no cotidiano assistencial [Nursing care to children who have an advanced oncologic disease: Being-with on	Brazil	III/B	15 pediatric oncology nurses	Qualitative i

daily assistance] [147]				
Vulnerabilidades socioeconômicas e o cotidiano da assistência de enfermagem pediátrica: Relato de enfermeiras [Socioeconomic vulnerability and pediatric nursing care routine: Nurses report] [148]	Brazil	I/B	9 nurses with at least 1 year of caring for children with cancer	Semi-structu interviews
Influence of PFCC nursing model on quality of life of children with neuroblastoma [149]	China	III/B	53 children with neuroblastoma	PedsQLTM 4. PedsQLTM 3. surveys
A família da criança oncológica em cuidados paliativos: O olhar da equipe de emfermagem [The family of the	Brazil	III/B	15 nursing pediatric oncology nurses	Interviews

oncologic child under palliative care: The view of the nursing team] [150]				
O uso do brincar pela equipe de enfermagem no cuidado paliativo de criancṃas com câncer [The use of playing by the nursing staff on palliative care for children with cancer] [151]	Brazil	III/B	4 nurses and 7 technicians with at least 1-year experience caring for children with cancer	Semi-structu interviews
Morte digna da criança: percepção de enfermeiros de uma unidade de oncologia [Dignified death for children:	Brazil	III/B	8 nurses in the pediatric oncology unit of a public hospital	Semi-structu interviews

Perceptions of nurses from an oncology unit] [152]				
An evaluation of a palliative care outreach program for children with Burkitt lymphoma in rural Cameroon [71]	Cameroon	III/B	3 patients, 7 caregivers, and 2 nurses	Semi-structu interviews
A família da criança com câncer: Percepções de profissionais de enfermagem atuantes em oncologia pediátrica [The family of the child with cancer: Perceptions of nursing professionals working in pediatric oncology] [153]	Brazil	III/B	12 pediatric oncology nurses with at least 3 months experience	Interviews
Assistência de enfermagem na oncologia pediátrica [Nursing care in pediatric oncology] [154]	Brazil	V/C	Publications on nursing care in Portuguese from 1997 to 2015	Literature re

Pediatric oncology nursing workers: The use of defensive strategies at work [155]	Brazil	III/B	20 pediatric oncology nurses at a teaching hospital	Non-particip observation a group
Current status analysis of PICC maintenance in outpatient children with solid tumors	China	III/C	34 pediatric patients with solid tumors	[Full text not available]

[156]				
Health professionals’ estimation of cancer-related fatigue in children [157]	Turkey	III/B	44 nurses and 12 doctors	Researcher-c questionnair open-ended a closed questi
Evaluating the cancer-related fatigue by children, mothers, and nurses in Turkish pediatric oncology patients [158]	Turkey	II/B	26 children (7–12 years) recently diagnosed with cancer, their mothers, and their nurses	Child Fatigue 24 h, Parent I Scale-24 h an Fatigue Scale Scales were completed tw three groups 24-h periods second and tl weeks of first of chemother

Instrument development/psychometrics					
Developing scales for the assessment of fatigue in Turkish pediatric oncology patients aged 13–18 and their parents [159]	Turkey	III/A		184 adolescents (13–18 years; median 14.6 ± 1.4) with cancer and their parents (74.5% mothers) and 14 healthcare professionals	Child and par information f visual fatigu scale for the assessment o in pediatric o patients age and the scale assessment o in pediatric o patients age for parents
Developing the	Turkey	III/B		N/A	Child and Pa

scale for quality of life in pediatric oncology patients aged 13–18: Adolescent form and parent form [160]			instrumentation study	Information (created in-h based on lite Visual Quality Scale; in-hou developed sc QOL in pedia oncology pat aged 13–18: Adolescent a forms
Antineoplastic agents extravasation from peripheral intravenous line in children: A simple strategy for a safer nursing care [161]	Brazil	III/B	7 pediatric oncology nurses from the USA and 7 from Brazil	Two Delphi s conducted (o Portuguese a English)

Reliability and validity of Turkish versions of the child, parent, and staff cancer fatigue scales [162]	Turkey	I/B	52 children (7–12 years) with cancer, 86 parents and 43 nurses from clinics and polyclinics of 3 pediatric oncology hospitals	The Turkish of Child Fatig 24 h, Parent Scale-24 h an Fatigue Scale tested for rel and validity. validity estab translation to and back-tra
Post-traumatic stress symptoms among Iranian parents of children during cancer treatment [163]	Iran	I/B	100 mothers and 100 fathers of children with cancer (0–18 years; 73% leukemia) admitted November 2013 to February 2014	Impact of eve —revised (IE (translated a validated)
Developing a scale	Turkey	III/B	204 children (7–	Psychometri

for quality of life in pediatric oncology patients aged 7–12—children and parent forms [164]			12 years) with cancer and their parents	of the scale f of life in pedi oncology pat aged 7–12 ch parents form two addition instruments expert opini nursing acad professional validity)
Developing a scale for the assessment of fatigue in pediatric oncology patients aged 7–12 for children and parents [165]	Turkey	III/A	204 children with cancer and their parents at a university hospital in Turkey and 14 healthcare professionals	“Child and pa information Visual Fatigu Scale for the Assessment in Pediatric Patients Age and the Scale Assessment in Pediatric Patients Age for Parents”
Comparability of the patient-reported outcomes measurement information system pediatric short form symptom measures across culture: Examination between Chinese and American children with cancer [166]	China	III/A	Chinese ($n = 232$) children in treatment for cancer and American ($n = 200$) children and adolescents (8–17 years) in treatment for cancer or survivors	Patient-repo outcomes measuremen information (PROMIS) pe forms (C-Ped PROMIS) in and English
Psychometric	China	II/B	253 families with	Instrument v

validation of an instrument to measure family coping during a child's hospitalization for cancer [167]			children hospitalized in pediatric oncology departments in 4 hospitals mainland China	using the Co Health Inven Parents (CH (Chinese vers
Creating and validating an instrument to identify the workload at an Oncology and Hematology Outpatient Service [168]	Brazil	III/B	N/A instrumentation study	Instrument c with 32 inter from the Nur Intervention Classificatio relevant for hematology/ Delphi proce for validatio
Turkish validity	Turkey	III/B	146 children (8–	The PedsQL

and reliability of a pediatric quality of life cancer module for children aged 8–12 and parents [169]			12 years) with cancer and 146 parents from hematology-oncology polyclinics of two university hospitals	Generic Core and a demog questionnair
Construction of a Chinese version of combined patients' self-report pain assessment system for children with cancer [170]	China	III/A	87 pediatric patients with cancer	Instrument development not available
Developing a tool for nurses to assess risk of infection in pediatric oncology patients in China: A modified Delphi study [171]	China	III/B	24 experts from 8 hospitals in 6 provinces of China	Delphi (three

Intervention studies

Comparison of different modes of patient-controlled analgesia for pediatric patients with non-surgical, cancer pain [172]	China	II/C	36 pediatric patients with cancer	[Full text not available]
Efecto del programa de habilidad de cuidado para cuidadores familiares de niños con cáncer [Effect of the care skill program for family caregivers of children with cancer] [173]	Colombia	II/B	106 family caregivers of children with cancer	Caring Ability Inventory too
Effects of massage therapy on pain and anxiety arising from intrathecal therapy or bone marrow aspiration in children with cancer [174]	Turkey	II/B	25 children (4–15 years) with cancer (12 in experimental and 13 in control groups)	Pain and anx measured by analog scale and after ma the child if o the child's m below five
Use of Joint Commission International standards to	Guatemala	III/B	N/A	Evaluation u selected Join Commission International

evaluate and improve pediatric oncology nursing care in Guatemala [175]				standards rel nursing, com before and af implementat on reviews o policies, and interviews
The effect of aerobics on mild depression in children with cancer [176]	Iran	V/B	Convenience sample 31 children with cancer (7–12 years)	Children dep inventory
The impact of an interactive computer game on the quality of life of children undergoing chemotherapy [177]	Iran	III/B	Convenience sample 64 children with cancer (8–12 years)	Randomized trial
Acupressure for nausea vomiting and fatigue management in acute lymphoblastic leukemia children [178]	Iran	III/B	120 hospitalized school-age children with ALL	RCT using ad Rhodes index nausea and v for Pediatrics Fatigue Scale

Effect of education on quality of life of family caregivers of children with leukemia referred to the Oncology Clinic at Kerman’s Afzali-Poor Hospital (Iran) [179]	Iran	III/B	80 parents of children with leukemia (7–10 years)	Quality of lif scale (a speci for first-degr caregivers of with leukemi (Ferrell and
Enhancing a specialized nursing care guidelines improves acute lymphoblastic leukemia patients outcome during induction phase; a developing country experience [180]	Egypt	III/A	74 oncology nurses received education for designed a nursing care plan. 132 children with ALL in induction phase	Intervention control grou
The effectiveness of resilience training on the condition of coping and stress of mothers with children with leukemia [181]	Iran	III/B	60 mothers of children with leukemia	Case-control using Conno Davidson Re Questionnair of Coping an Parental Stre short form w noted; howe body of the t coping quest (Folkman an 1980) and a questionnair Abidin (1995 described as instruments

Application of 113 cases of implanted venous port in children with tumor and treatment of its complications [182]	China	II/B	113 pediatric patients with cancer	Full text not a
The effect of fatigue-related education on pediatric oncology patients' fatigue and quality of life [183]	Turkey	II/B	80 children (7–12 years) with cancer and their parents admitted to oncology unit in university hospital	Fatigue-copi education intervention min modules fatigue mana Data were co baseline and months post

					intervention
Music therapy to reduce pain and anxiety in children with cancer undergoing lumbar puncture [184]	Vietnam	III/B		40 children (7–12 years) with leukemia (25 male)	The children randomized i groups to rec music therap (listening to they preferre earphones) o wearing earp with no musi (control grou
The effect of spiritual care on mental health in mothers of children with cancer [185]	Iran	II/B		25 purposively selected mothers of children (6–18 years) on therapy at least 8 months	Intervention sessions face for 90 min ov 9 months
The effect of educational intervention on	Indonesia	III/B		24 parents (66.7% male) of pediatric inpatients (2–	One group pr posttest desi PedsQL 4.0 (

the quality of life of acute lymphocytic leukemia who [are] undergoing chemotherapy [125]			14.4 years)	Core Scale) a PedsQL 3.0 (module)
Musical dynamics in the sensitization of nursing students in the face of palliative care in pediatric oncology [186]	Brazil	V/C	11 nursing students in their last year	Group discus participant observation, artistic produ
The application and nursing care of PICC among patients with chemotherapy in pediatric oncology department [187]	China	II/C	60 pediatric patients with cancer	[Full text not available]

The clinical value of knowing, believing, and doing health education in postoperative PICC catheterization of neuroblastoma [188]	China	II/B	100 pediatric patients with neuroblastoma	Intervention
The effects of spiritual care on anxiety in adolescents with cancer [189]	Iran	II/B	32 purposely selected hospitalized adolescents (12–18 years; at least 8 months post-diagnosis)	Intervention measured by Speilberger S Trait Anxiety Inventory
Development of questionnaire to assess infection risk after chemotherapy in children with malignant tumors [190]	China	III/C	9 doctors, 9 nurses, 6 infection control experts from 9 hospitals located in 6 provinces	Instrument development not available
Effect of whole environment protection nursing on nosocomial infection and quality of life of children with leukemia [191]	China	I/B	60 pediatric patients with leukemia and their parents	Full text not
Extravasation	China	III/C	16 pediatric	Full text not

management in the pediatric oncology ward of Children’s Hospital of Fudan University: a best practice implementation project [192]			oncology nurses Shanghai	
The practice and effects of establishment of kindergarten in leukemia pediatric wards [193]	China	II/B	60 pediatric patients with leukemia	Full text not a
Effect of cognitive behavioral therapy on resilience and negative moods in children with malignant tumor	China	I/A	106 pediatric patients with cancer	Full text not a

during chemotherapy [194]				
Effects of patient- and family-centered care on the quality of life of children with leukemia [195]	China	I/B	78 pediatric patients with leukemia	Full text not
Retrospective analysis of the effect of comfortable care on the survival time of children with medulloblastoma [196]	China	II/B	78 pediatric patients with medulloblastoma	Retrospectiv of the effect comfortable the survival t children wit medulloblast
Literature reviews				
The effectiveness of distraction as procedural pain management technique in pediatric oncology patients: A meta-analysis and systematic review [197]	Nigeria and UK	I/B	N/A	Meta-analysi

Perspectives of children, family caregivers, and health professionals about pediatric oncology symptoms: a systematic review [198]	China	III/B	33 studies (no start date to May 2017)	Literature re

A enfermagem nos cuidados paliativos à criança e adolescente com câncer: Revisão integrativa da literatura [Nursing in palliative care to children and adolescents with cancer: Integrative literature review] [199]	Brazil	V/C	Articles published on palliative care of children with cancer from January 2004 till May 2009	Literature se
Cuidados de enfermagem à criança com câncer: Uma revisão integrativa da literatura [Nursing care to the child with cancer: An integrative review of the literature] [200]	Brazil	V/C	Published articles on nursing care of the child with cancer in English, Portuguese, or Spanish (no date range noted)	Literature re
Estresse e burnout no trabalho em oncologia	Brazil	III/B	Literature on stress and burnout published in 1998–2012	Literature re

pediátrica: Revisão integrativa da literatura [Stress and Burnout at Work in Pediatric Oncology: an Integrative Literature Review] [201]

Quality of life of children and adolescents with cancer: revision of studies literature that used the pediatric Quality of life inventory^{TM} [202]	Brazil	III/C	Publications in Spanish, English, or Portuguese (1998–2013) using Pediatric Quality of life Inventory 3.0 Cancer Module	Literature re
Children’s experiences of cancer care: A systematic review and thematic synthesis of	China	III/B	Qualitative publications from January 2000 to January 2016 on experience of children with	Literature re

qualitative studies [203]			cancer (0–18 years) (no proxy data)	
Processes of care for children with cancer: a documentary research [204]	Brazil	III/B	Dissertations and theses on nursing care of children with cancer; 2003–2012	Literature re
Measurement of fatigue in children and adolescents with cancer: An integrative review [205]	Brazil	III/B	Publications in Spanish, English, or Portuguese on fatigue in children with cancer (no time limit)	Literature re

Complementary and alternative medicine in pediatrics in Turkey [206]	Turkey	III/B	N/A	Literature re (2002–2012

Assistência de enfermagem na oncologia pediátrica [Nursing care in pediatric oncology] [154]	Brazil	V/C	Publications on nursing care in Portuguese from 1997 to 2015	Literature re

15.4.1 Descriptive Studies

Descriptive studies investigated symptoms, parent/caregiver experience, child experience, traditional and complementary medicine, epidemiology, and nutrition.

Studies addressing children's symptoms most frequently investigated pain, fatigue, and issues related to peripherally inserted central catheters (PICCs). Symptoms were reported as problematic by both children and adolescents and/or their parents. The patient's level of pain was often related to the stage of treatment. Perceptions of symptoms were sometimes culturally influenced (e.g., boys trying to be brave) and managed. Non-pharmacological interventions were not common.

Studies investigating the parent/caregiver experience studies included measurement of aspects of quality of life (e.g., stress, anxiety), need for education and/or information, and satisfaction with the child's care. Study results reflected distinct challenges faced by parents and caregivers. In particular, end-of-life care was seen by parents in a study from the Region of the Americas to be "impersonal." In a study in Africa, the parents wanted information on how to discuss impending death with their child and family.

Description of the child or adolescent's experience with cancer included quality of life, school, play, isolation, prejudice/stigma, friendship, and social function. Studies across WHO regions found that children/adolescents reported negative experiences including loss of friends and problems in their community due to their alopecia.

Studies on traditional and complementary medicine (T&CM) use for childhood cancer were based on parental questionnaires. In all cases, parents were using traditional and complementary medicine, but specific ingredients and approaches differed among regions.

Only one study reported the epidemiology of childhood cancer in the local region, and that was from Rwanda. Nutritional problems and parental concerns were explored by one group of researchers in an L&MIC in Europe.

15.4.1.1 Descriptive Study Exemplars from the African Region

Parent/Caregiver Experience

Keiza et al. [85] employed a mixed method approach (questionnaire and focus group discussion) to explore parents' satisfaction with their child's cancer care. The majority of parents were mothers (82.2%) and more than half (55.1%) lived in rural areas. Chemotherapy was not available when needed according to 14.9% of the respondents whose children were receiving chemotherapy. Doctors were noted as being available as needed by 64.5% of the respondents, but nursing availability was reported by 75.7%. Only 55.9% of the respondents were satisfied with radiotherapy treatments. More than half of the parents (59.8%) reported receiving no information about their child's disease or treatment. Results of this study were shared with staff, the pediatric department, and the hospital administration. Additional psychosocial support and parent education were recommended.

Traditional and Complementary Medicine (T&CM)

In Cameroon, 55% of the parents (*n* = 387) of children with Burkitt lymphoma had consulted a traditional healer, and three-quarters of these parents had done so before accessing biomedical care. T&CM included "…massage, cuts, concoctions and incantations" (p. 1). The choice of T&CM was seen to be determined by family beliefs and accessibility [119].

Epidemiology

Stulac et al. [123] from Butaro, Rwanda conducted a retrospective chart review of children treated with cancer from 2006 to 2011 in a partnership between Partners in Health, a non-governmental organization in Boston, Massachusetts, USA and Rwinkwavu Hospital. Of the 24 children who were treated for multiple diagnoses, 13 were in remission (1 still receiving therapy), 2 died from treatment complications, 7 died from their disease, and 2 were alive but receiving end-of-life care. None of these 24 patients abandoned their therapy. This review demonstrated the feasibility of treating children with cancer in a rural low-income setting.

15.4.1.2 Descriptive Study Exemplars from the Region of the Americas

Symptoms

A Brazilian study by Bueno et al. [73] conducted in the state of Rio Grande do Sul reported a qualitative thematic description of nursing notes for 55 children under 12 in one pediatric oncology center. Findings revealed that almost half (47.27%) the children reported having pain and their pain was generally addressed by pharmacological intervention 75% of the time (paracetamol 42.24%, morphine 25%, and codeine 6.9%). Non-pharmacological pain management was uncommon, and sometimes a specific pain intervention was not noted, nor was the outcome. The authors recommended that nurses be trained in developmentally appropriate pain assessment (taking a history and physical exam) and systematize this practice with consistent nursing documentation.

Parent/Caregiver Experience

In Brazil, Carneiro et al. interviewed 14 mothers of children with cancer at the child's end-of-life [82]. The mothers described being lost in "impersonal" treatment by the healthcare team when they perceived being treated just like anyone else on the unit. This overall attitude did not allow individual specifics about the mothers' feelings about their child to emerge such as sadness, doubts, and fears. For the mothers, this meant an emergence of the threat of their child's "not-being." The authors advised the nurse caring for a dying child and their mother to have "[an] opening attitude of nursing to listen to the mother, in an empathic encounter and intersubjectivity, makes it possible to say something to the other (mother) and to her (nurse), contributing to a learning of support and shared care" as an existential moment (p. 62). In this way, once established, this approach can be sustained even after the child's death when the mother will continue to need support.

Child Experience

Cicogna and colleagues [103] in São Paolo, Brazil, investigated the experience of 10 children and adolescents with cancer (8–18 years old) receiving chemotherapy with semi-structured interviews. Children and adolescents reported experiencing prejudice from family members because of alopecia, suffering with pain during treatment, being left by friends. Some respondents also believed that the chemotherapy side effects were indicative of its power to heal, and so they continued with the treatment, while others saw chemotherapy side effects as discouraging and causing "concern, anxiety and depression" due to the lack of control over the effects (p. 871). The researchers recommend that nurses understand the complexity of childhood cancer treatment and have continuous training in how to address their “physical, emotional, social and cultural” needs as well as those of their families (p. 871).

15.4.1.3 Descriptive Study Exemplars from the Eastern Mediterranean Region

Symptoms

Nurse researchers [77] in Lebanon used The Adolescent Pediatric Pain Tool, Functional Disability Inventory, and medical record review to investigate pain and function of 62 adolescents with cancer (mean age 12.3; SD 2.9) [77]. The majority had leukemia (48.4%) and most were receiving chemotherapy (93.5%). The authors noted cultural norms for boys to be brave and not complain about pain and for girls to “express their pain and emotional distress” (p. e12). Just over half of the adolescents (57.4%) reported having pain on occasion and moderate dysfunction. The most common areas of pain included forehead, abdomen, and lower back and intensity was highest for tumors with metastasis. The highest scores for dysfunction were for running, gym class, and walking. Predictors of pain intensity included “time since diagnosis, treatment-related pain, previous surgical treatment, radiotherapy” (p. e16). The authors note that their findings differed from other studies for higher rates of moderate to severe pain, and the frequency and duration of pain (as assessed in this study) were not reported in most literature. This study’s findings on pain location, descriptors and sources, factors associated with intensity, and pain predictors were in line with literature from other countries, including high-income settings. Recommendations include noting continued unrelieved pain in adolescents with cancer and a call for continued research on pain and functioning as well as national policies and legislation to address pain in this population.

Parent/Caregiver Experience

Khanjari et al. [86] also explored religion in Tehran, Iran, in relation to quality of life of 200 mothers of children (mean age 6.65 ± 3.82 years) with leukemia (89.5% had had at least one recurrence) using the Caregiver Quality of Life Index-Cancer (Persian version Cronbach’s alpha

0.91) and RCOPE in Persian as instruments (Cronbach’s alpha 0.91 and 0.86 for positive domain and 0.87 for negative domain). Results indicated that in general the mothers had a low quality of life (61.3 ± 14.98 of a total possible score of 140 on the CGQOL-P scale). Higher education level, income, and having an occupation all had a significant association with higher quality of life ($p < 0.05$, $p < 0,001$, $p < 0.001$, respectively). Religious coping as measured by the RCOPE was only correlated with positive coping dimension of quality of life since mothers engaged in negative religious behavior when stressed. A high negative RCOPE score predicted quality of life better than the positive RCOPE score. The authors recommended consideration of parental religious life as a mechanism to improve quality of life.

Child Experience

A qualitative study by Al Omari and Wynaden [99] was performed in Jordan with 14 adolescents (13–17 years old) diagnosed with leukemia or lymphomas. Semi-structured interviews on two separate occasions were conducted and after analysis by two researchers, three themes were identified: “being in hospital, the changing self, and fearing the unknown” (p. 2). The respondents commented on the negative aspects of hospitalization including having to stop their normal activities, which they found stressful. They also began to have negative experiences with developmental growth such as peer group interactions (fearing rejection), identity, in particular with physical changes, and stigma leading to isolation. The authors call for further studies to address “culturally sensitive quality nursing care” for these adolescents (p. 6).

Traditional and Complementary Medicine

The majority of 69 Jordanian parents (65%) described by Al Qudimat [120] used T&CM during their child’s treatment. Treatments categorized as “biologic and nutritional” (70.5%)…and “body and soul” (22.2%) were most common. Most parents reported not discussing T&CM use with the healthcare providers.

15.4.1.4 Descriptive Study Exemplars from the European Region

Symptoms

Cancer fatigue was measured in 26 Turkish children with cancer in Izmir (newly diagnosed, mean age 10.0 ± 2.0; 69.2% did not know their diagnosis), their mothers (*n* = 26; mean age 36.4 ± 5.6), and their day shift nurses (*n* = 26; mean age 27.6 ± 4.0; none had received education about fatigue) [158]. The groups were tested with the CFS-24 h, PFS-24 h, and SFS-24 h. Validity and reliability testing for the Turkish versions of these scales were reported above. Scales were completed twice by all three groups for two 24-h periods in second and third weeks of first round of chemotherapy. The children's level of fatigue was described by all three respondent groups as moderate. The mothers and children rated the child's fatigue as higher on the second day ($p < 0.05$), but nurses did not ($p > 0.05$). The authors state that fatigue is subjective and levels can change in 24 h, thus highlighting the need for daily assessment, particularly by nurses. Parents' participation in fatigue assessment is empowering. The early timing of the study was deliberate to avoid additional symptoms from clouding results. Further research using these tools and individualized interventions to prevent fatigue as well as nurse education are encouraged.

Child Experience

Yilmaz et al. [117] compared 56 childhood cancer survivors aged between 7 and 18 years attending school full time to 56 controls with similar sociodemographic characteristics. Two academic life evaluation questionnaires were developed by the researchers and used to capture information on academic success for the survivors and controls. The child health questionnaire (CHQ–PF50) was administered to parents to measure the physical, mental, and social well-being of their children while the teacher's report form (TRF/6–18) was administered to teachers to obtain information on the emotional and behavioral symptoms of the children in both groups. The authors recommend the use of hospital schools during treatment to prevent back-to-school anxiety amongst children with cancer. They also highlight the essence of the school nurse to counsel survivors on risk factors for anxiety such as amputation, alopecia, and scars and their role in helping these survivors establish peer relationships.

Traditional and Complementary Medicine

In Izmir, Turkey, a convenience sample of parents of children with cancer (*n* = 112) reported by researcher-designed questionnaire that three-quarters of them were using T&CM for their child with cancer. The most frequently mentioned was herbs and nutritional supplements, but the majority of parents had not informed the medical team about this use [121].

Nutrition

One study in Ankara, Turkey by Arpaci et al. [122] investigated the nutritional problems of children and nutritional concerns of their parents. Over a period of 18 months, face-to-face interviews were conducted with 68 parents of children aged 3–19 years (median 9.71 ± 4.94) who were hospitalized for cancer treatment for 1–120 days (median 16.97 ± 26.16). The diagnoses of the children were mainly leukemia (44.9%); solid tumors (26.1%), CNS tumors (15.9%), and lymphomas (11.6%). Over two-thirds of children (69.9%) had received only chemotherapy. Sixty-one percent were receiving a normal diet, and 39.1% were receiving a neutropenic diet. The most common nutritional problems of the children as perceived by their parents were appetite loss (85.5%), nausea (84.1%), vomiting (81.2%), fatigue (79.7%), and mucositis (66.7%). According to the parents, the nutritional problems of their children were due to physiological factors (100%), factors related to hospital food like taste and portion size (65.1%), factors related to hospital environment like hygiene (31.9%), and emotional factors like home sickness (13.0%). The major information needs expressed by the parents were about food/drugs interactions (58.0%), food/illness interactions (52.2%), the type of nutrients that should be eaten or avoided (46.4%), and the frequency of meals (36.2%). The parents who received education about nutrition education at the time of their child's diagnosis reported that this was insufficient. The authors recommend provision of information about nutritional concerns to children and their parents at the beginning of treatment and provision of oral and written educational support to parents in the hospital and at home.

15.4.1.5 Descriptive Study Exemplars from the Southeast Asian Region

Child Experience

In a qualitative study conducted in Pathum Thani, Thailand (just north of Bangkok), Treenai and colleagues [113] used grounded theory to investigate 20 adolescents' (mean age 16.4 year; range 12–19) experience with leukemia. One to two in-depth interviews and observation during chemotherapy administration were performed. The adolescents mentioned "realization being a leukemic patient," as their starting point for "returning to normality," which the researcher called a social process. Three additional subcategories included "having alarming symptoms," "knowing the diagnosis," and "accepting the leukemic patients' role" (p. 7). The adolescents believed they had to endure chemotherapy, but they had chosen this path for the opportunity to be cured. Some had sought information about their disease and treatment from medical textbooks and wanted to learn more. The researchers noted that adolescents require "direct explanation [of their disease and treatment] with appropriate timing" (p. 12–13).

15.4.1.6 Descriptive Study Exemplars from the Western Pacific Region

Parent/Caregiver Experience

Ye et al. [97] conducted a cross-sectional study to explore the resilience and psychosocial functioning of 111 parents (37 fathers and 74 mothers) of children (6.85 ± 4.37 years) with cancer (multiple diagnoses) in southeast China compared to population norms across China. Tools included demographic survey, Connor-Davidson Resilience Scale (Chinese version), Coping Health Inventory for Parents (CHIP), Social Support Questionnaire (created by Hunan Medical University), Zarit Burent Interview, and Self-rating Anxiety and Depression Scales. The parents had fewer resilience resources, and higher anxiety and depression than the general Chinese population ($p < 0.001$); however, they also had greater social support ($p < 0.001$). Multivariate analysis conducted on six variables identified that depression was an independent predictor of level of resilience. The parents selected "keep the family united, cooperated and optimistic" as the most effective action item on the CHIP. The authors recommended improved communication between the healthcare team and parents and for evidence-based resilience building strategies to be offered to parents.

Child Experience

Wang et al. [115] explored the QoL of 240 school-aged children with a malignant tumor. Results showed that 6–8-year-old children's scores for physiological function (37.82 ± 11.67), role function (51.72 ± 11.43), operational anxiety (40.24 ± 11.51), and communication (42.32 ± 10.57) were below the scores of children 9–11 years old (for all $p < 0.05$). The scores for the younger children for emotional function (59.43 ± 14.53), social function (54.69 ± 12.61), treatment anxiety (51.11 ± 11.41), fear (64.19 ± 12.49), and evaluation of appearance (70.14 ± 11.67) were higher than the older children (all $p < 0.05$). Multivariate stepwise regression analysis showed that child's age, disease duration (>2 years), and hospitalization (≥3 times) were significant ($p < 0.05$). The authors concluded that 6–8-year-old children need more care for physiological function than 9–11-year-olds, who need more emotional support. More frequent hospitalizations of children with malignant tumor reduced their quality of life.

15.4.2 Instrument Development Studies

Twelve studies described instrument development and psychometric testing, including translation of existing instruments to local languages and evaluation of cultural expectations and validation testing.

15.4.2.1 Instrument Development Study Exemplar from the Region of the Americas

Martin and Gaidzinski [168] developed and validated an instrument to measure the workload of nurses and also determine the time spent on each patient care activity at an outpatient oncology and hematology facility. The instrument was validated by experienced nurses using the Delphi process. The authors noted that the next step will include testing the instrument's reliability in practice.

15.4.2.2 Instrument Development Study Exemplar from the Eastern Mediterranean Region

An Iranian study by Iranmanesh, Shamsi, and Dehghan [163] adapted and validated the Impact of Event Scale—Revised (IES-R) to measure post-traumatic stress disorder (PTSD) in parents of children with cancer. Translation and back-translation were done by two nurse educators with experience in oncology and the final draft piloted with 20 parents. Content validity by 20 nursing faculty was deemed to be adequate. Using the adapted IES-R instrument, 100 fathers and 100 mothers of children with cancer were assessed for PTSD. Mothers had higher post-traumatic stress symptoms compared with fathers ($p < 0.05$). Adjusted odds ratio showed that the prevalence of post-traumatic stress symptoms among mothers was 2.49 times more than that among fathers ($p = 0.01$). There was no association between sociodemographic data and post-traumatic stress symptoms. The authors recommended more research to elucidate the Iranian parents' experience of having children with cancer.

15.4.2.3 Instrument Development Study Exemplar from the European Region

A study by Bektas and Kudubes [159] to develop a tool to measure fatigue in adolescents with cancer had a sample of 184 adolescents with cancer (13–18 years; median 14.6 ± 1.4) and 184 parents (74.5% mothers). Four tools were designed by the researchers based on the literature and one existing tool was selected. Fourteen healthcare experts, including three academic nurses, assessed the content validity of the researcher-created tools. A pilot was conducted with children and parents with equivalent characteristics to the proposed study sample, using the final scale (32 items). Results were satisfactory; therefore, no changes were made. Content validity coherence was 0.803 and deemed acceptable. Factor analyses, cutoff point, known group comparison, internal consistency, item-total score correlations, test-retest, and reliability over time were found to be acceptable. The authors stated that this fatigue scale was "convenient and comprehensive…also is peculiar to our country [Turkey]" (p. 9897). The recommendations are for the two scales to be used in clinical practice so interventions can be designed to address fatigue in adolescents with cancer in Turkey.

15.4.2.4 Instrument Development Study Exemplar from the Western Pacific Region

Zhou et al. [171], in Nanjing, created a tool to measure infection risk in children with cancer. After three rounds of consultation using Delphi methodology, a two-part tool was developed, Immune Status Scale (ISS) with 5 items and a Checklist of Risk Factors of Infection (CRFI) with 14 items. Based on the ISS score, nurses could stratify children into the low-risk and high-risk groups. For high-risk children, the authors recommended nurses screen risk factors of infection every day by the CRFI, and twice weekly for low-risk children. The tool was specifically designed to address Chinese cultural norms and resource realities and so was deliberately nursing work-based, and Chinese-specific. Further studies are needed to verify the instrument's efficacy.

15.4.3 Nursing Practice Studies

15.4.3.1 Nursing Practice Study Exemplar from the African Region

A qualitative study from Cameroon researchers [71] explored palliative care (PC) for children with cancer based on semi-structured interviews in 12 patients' homes with the children with cancer, parents, and healthcare providers. The majority of caregivers and children spoke about God having the final word on survival. Changes in daily life and dependence on extended family were also mentioned by the caregivers and children. The nurses wanted additional PC and counseling training, which the researchers also recommended. More counseling for family caregivers (especially females) and increased family open communication with the child, in particular about near-death status as well as expanding community support, were also recommended.

15.4.3.2 Nursing Practice Study Exemplars from the Region of the Americas

A study explored Brazilian healthcare professionals' perceptions of fatigue in children with cancer [131]. Participants included 10 nurses, 33 nursing assistants, 3 physicians, 3 nutritionists, 2 psychologists, and 2 physical therapists from one hospital's pediatric oncology department. Results from semi-structured interviews showed no consensus on the definition of fatigue. Assessment of fatigue was generally by observation, although some respondents could not identify fatigue. Some participants mentioned fatigue in combination with depression and children missing normal life activities like school and being with friends as contributory. The authors noted the lack of training on fatigue management and conceptual knowledge about this common symptom in children being treated for cancer, as well as the lack of Brazilian literature on the topic. They believed addressing fatigue for pediatric oncology patients is a fundamental role of the healthcare team and should be considered in Brazil.

A study, from Guatemala [132], involved establishing a full-time nurse educator position within the National Pediatric Oncology Unit. A nurse dedicated exclusively to staff education for a specific unit within a hospital was a new concept for a public hospital in a low-income country. Prior to implementing the educator position, no organized nursing education was provided within the oncology unit. The nurse educator's primary responsibilities included providing pediatric oncology education for newly hired nurses, teaching courses in chemotherapy administration and central-venous line care, and providing continuing education. Two years post implementation of the educator position, of the nurses employed, 86% participated in the chemotherapy course, and 93% achieved competency; 57% participated in the central line course, and 79% achieved competency. The nurses completed a mean of 26 hours of continuing education yearly. The annual direct cost of the educator ($244/nurse) was markedly less than other models. A study from Mexico reported findings on the use of complementary and alternative medicine (CAM) by nurses and its impact on nursing care. Gómez-Martínez et al. [138] surveyed 268 nurses about their use of CAM. The majority of nurses (68%) reported using CAM themselves and about one-quarter (27%) recommended its use to patients. The researchers recommended having open and non-biased conversations with parents about CAM given its widespread use in Mexico.

15.4.3.3 Nursing Practice Study Exemplar from the Eastern Mediterranean Region

A study by Borhani et al. [127] examined the lived experiences of Iraqi undergraduate nursing students and self-reflective accounts of first clinical rotation in pediatric oncology. A total of seven interviews were performed and transcribed. After analysis, five main themes of experiences of pediatric oncology nurses were extracted: attachment, supportive care, trying to repress feelings, feeling of helplessness, and the need to be supported. The authors concluded that nursing students who provide care for children with cancer require support and the experiences deeply affect their professional, individual, and even family life. The findings of this study can be useful in planning interventional programs to support nurses.

15.4.3.4 Nursing Practice Study Exemplar from the European Region

In Izmir, Turkey, 44 nurses and 12 doctors working in four pediatric oncology clinics participated in a study to evaluate health care professionals' estimation of cancer-related fatigue [157]. All responded that fatigue was a significant issue for children with cancer, although none used a tool to assess a child for fatigue, but rather depended on visual or laboratory assessments of anemia. The authors noted that fatigue as a side effect of childhood cancer treatment is a new concept in Turkey, although measures to address fatigue had been tried including nutrition, discussions, or pharmacologic support. Most participants said they would benefit from education on fatigue since they considered themselves under-informed. The researchers recommended use of an assessment tool in clinical practice and evaluation of same.

15.4.3.5 Nursing Practice Study Exemplar from the South-East Asian Region

A study from Nepal by Chaudhary and Karn [129] explored chemotherapy knowledge and handling using a structured and unstructured questionnaire given to 125 randomly selected nurses who prepare cytotoxic drugs (14 pediatric nurses). A total of 83% of the nurses prepared cytotoxic drugs in the nurses' station and 17% in the treatment room both without biosafety cabinets. Almost all nurses (92%) reported using gloves; however, only 5% wore surgical masks while preparing cytotoxic drugs. No nurse reported using all protective equipment, although 62% did wear gloves and surgical masks simultaneously. Information about handling cytotoxic drugs came from textbooks and the internet (for 86.3% of the nurses), while only a small percent came from nursing administration (for 5.2% of the nurses). The authors recommend inservice training and current guidelines for cytotoxic drug preparation be shared with the hospital administration and practice settings. They noted that the hospital needed a safety committee with appropriate policies to provide continual staff support.

15.4.3.6 Nursing Practice Study Exemplar from the Western Pacific Region

In a study by He et al. [142], the investigators created a preliminary quality indicator system for nurses caring for children with cancer. They conducted three rounds of expert consultation with 15 experts from eight provinces on the tool and authority coefficients were 0.93, 0.93, and 0.96. For concordance, the coefficients were 0.209, 0.166, and 0.332 ($p < 0.01$). There were three indicators at the first level, eight at the second level, and 29 at the third level. An analytical hierarchy process was employed to determine weight. The authors concluded that their system was a reasonable tool that considered the specialty's characteristics and could support the development of pediatric hematology oncology programs.

15.4.4 Intervention Studies

Interventions were diverse and included interventions to improve the quality of nursing care, supportive care for patients and families, parental coping, family education to increase the child's quality of life, pain control, intravenous access, extravasation, family-centered care, and cognitive behavioral therapy for child depression, anxiety, and stress.

15.4.4.1 Intervention Study Exemplar from the Region of the Americas

Carrillo et al. [173] measured the impact of Caring for Caregivers program for parents of children with cancer in Colombia. The Caring Ability Inventory tool was used to measure knowledge, courage, and patience. The intervention group who participated in the Caring for Caregivers program showed significantly higher scores for overall caregiving ability, knowledge, and patience compared to the control group. The authors recommended that further research be conducted on the program's feasibility and costs and factors that might impact caregivers' ability to manage their child's care such as housing, previous caregiving experiences, and treatment phase.

15.4.4.2 Intervention Study Exemplar from the Eastern Mediterranean Region

Nikseresht et al. [185], in Tehran, Iran, studied the impact of a spiritual program provided to mothers of children with cancer. The program comprised six sessions and included a discussion of current problems and religious practices, treatment and side effects, expressions of hopefulness and spiritual support, and exploration of the mother's spirituality and sources of strength. Compared to pre-program findings, a significant improvement in physical problems, anxiety, social dysfunction, depression, and overall mental health as measured by questionnaires was found. The authors state that because interventions related to spirituality have no side effects and spirituality is culturally acceptable and encouraged in Iran, nurses should deliver this care to parents to improve their health and well-being while their child is on treatment for cancer.

15.4.4.3 Intervention Study Exemplar from the European Region

Çelebioğlu et al. [174] examined the effects of massage therapy (10–15 min by a certified nurse massage therapist) for procedural pain and anxiety due to intrathecal chemotherapy or bone marrow aspiration. Measurements of pain and anxiety were done by a visual analog scale before and after massage by the child if over five or the child's mother. Pain and anxiety scores decreased among the experimental group. Scores for the control group did not significantly change. The researchers found that massage was effective in reducing children's pain and anxiety related to procedures and recommend it for use in multiple invasive procedures.

15.4.4.4 Intervention Study Exemplar from the Southeast Asian Region

In a study from Indonesia, Novrianda, and Khairina [207] used a single group pretest-posttest design to evaluate an educational intervention delivered to 24 parents (67% male) of children with leukemia (mean age 6.9 ± 3.52). Educational topics included leukemia, chemotherapy, side effects, and nutrition. Baseline and 1 week after the intervention data were collected using the PedsQL 4.0 (Generic Core Scale) and PedsQL 3.0 (Cancer Module). Baseline mean scores were PedsQL 4.0, 64.28 ± 15.88 (range 57.57–70.98) and PedsQL, 3.0 65.95 ± 14.87 (range 59.66–72.23). The mean scores after receiving the educational intervention were PedsQL 4.0, 69.65 ± 14.49 (range 33.28–95.95) and PedsQL 3.0, 69.72 ± 13.85 (range 47.70–97.20) with a significant difference for each instrument ($p = 0.012$ for the PedsQL 4.0 and $p = 0.000$ for the PedsQL 3.0). The authors endorsed providing educational interventions to improve the QoL of children with leukemia receiving chemotherapy.

15.4.4.5 Intervention Study Exemplar from the Western Pacific Region

Nguyen and colleagues [184], in Hanoi, Vietnam, conducted a study to determine if music therapy could decrease pain and anxiety during lumbar punctures. The children were randomized to receive music therapy (listening to music they preferred on earphones) or wearing earphones with no music. The children’s pain ratings were significantly lower for the intervention group both during and after the procedure. The intervention group’s anxiety scores were significantly lower at baseline and after the procedure. The researchers recommended music therapy for children undergoing lumbar punctures as a non-pharmacologic intervention. This study is particularly important since in Vietnam, the study site, analgesics are not offered during the procedure.

15.4.5 Literature Reviews

Most literature reviews included articles from high-income countries as well as L&MIC; however, most authors made recommendations for local practice in the L&MIC setting. The predominance of Brazilian and

Chinese authorship for these literature reviews reflects a higher level of nursing education at a university level with high quality research being performed by postgraduate nurses for academic purposes [208, 209].

15.4.5.1 Literature Review Exemplar from the African Region

Distraction for Pain Control

Bukola and Paula [197], first author from Nigeria and second from the UK, conducted a meta-analysis of RCTs (quasi-experimental or quasi-randomized trial) for distraction to manage procedural pain in children with cancer (port access, lumbar punctures, intrathecal injections, and needle procedures). The authors included seven articles (US $n = 4$, Sweden $n = 1$, Vietnam $n = 1$, Iran $n = 1$) that met inclusion criteria (including ages 0–19, any cancer diagnosis, and use of a control group) from eight databases (start dates varied by ranged from 1806 to 2016). Outcome measures included self- and observer reports and physiological assessments. Results showed that multiple tools were being used to assess procedural pain including: self-report—Visual Analogue Scale (VAS), Numerical Rating Scale, Wong Baker Faces Scale, and Color Analogue Scale, observer report—VAS, and the Children's Hospital of Eastern Ontario Pain Scale. Unfortunately, standard deviations and means were not reported for all self or observer reports, so several studies had to be excluded from the analysis. There was a significant effect of distraction for reducing pain during procedures according to self-report (standardized mean difference [SMD]—0.64 95% CI [1.10–0.17]), but no consistent findings for observer reports (nurse, parent, or researcher). For physiological assessment, all studies recorded the children's pulses, which were found to significantly decrease during distraction ($p < 0.001$). The authors recommended further studies, particularly in sub-Saharan Africa, where they noted distraction to reduce pain is not common practice, and inpatient populations under 2 years of age. They also noted that when reporting the results of RCTs, authors should include important statistical findings and procedures conducted so as to be eligible for meta-analyses. Poor nurse staffing in low-income settings was also highlighted as an obstacle to distraction interventions for pain as well as attention needed to control distraction tools as potential vectors for infection.

15.4.5.2 Literature Review Exemplars from the Region of the Americas

Nursing Care

da Silva et al. [200] summarized literature in Spanish or Portuguese pertaining to pediatric oncology nursing care. Ten eligible studies were identified and the majority were qualitative descriptive and exploratory. Nurses struggled with pain assessment in infants and to include families in care plans. In addition, findings indicate that nurses can be worn out, suffering, and sad when providing care to children with cancer. Overall, the studies recommended offering nurses psychological support to manage their emotions suffering and more training to increase their appreciation of subjective aspects of care.

Nursing Stress and Burnout

dos Santos and dos Santos [201], from Brazil, performed a literature review of nursing stress and burnout in pediatric oncology from 1998 to 2012 in English, Spanish, or Portuguese. A total of 18 articles were eligible articles for analysis (15 in English and 3 in Portuguese, of which 10 were descriptive, 3 experimental, and 5 theoretical or review). The authors found 10 themes and subthemes: (1) conception of stress, (2) conception of burnout, causes, and prevention, (3) impact of childhood cancer and aspects involved in caring for the affected child, (4) identification of the area of pediatric oncology as highly stressful and discrimination of the most common stressors reported by professionals of the area (most reported), (5) evaluation of the level of burnout, (6) impact of stress and burnout and coping strategies used, (7) proposals for intervention with professionals (second most reported), (8) stress-response sequence model, (9) positive aspects of stress, and (10) demands/exigencies and rewards of work. The authors note the paucity of research on nursing burnout and stress in pediatric oncology, although nurses were the most frequently studied for this topic among health professionals. Therefore, it was not possible to compare nursing stress and burnout to other professionals caring for children with cancer. It is worth noting that only 5/18 articles were from low- or middle-income countries: four from Brazil and one from China. The authors recommend further research on strategies to address pediatric oncology nursing stress and burnout rather than simply describing these phenomena.

Quality of Life of Children/Adolescents with Cancer

Farias Queiroz et al. in Brazil [202] conducted a literature review of studies published from 1998 to 2013 on the QoL of children and adolescents with cancer that used the PedsQL 3.0 cancer module as an instrument. Twenty-one studies in English were identified with sample sizes that varied from 26 to 420. Just over half (13/21) of the studies had both child and parent respondents, while the rest had only parents. The authors note that self-report is an important voice from the patients themselves. There was substantial missing data (e.g., not described, not assessed, or scores only by groups). For parent reports, a general score was described in six articles and dimensions in only seven articles. The authors note that some articles had given the questionnaire to parents with children below 2 years of age and above 18 years of age despite those ages being the limits for the tool. They also note small sample sizes limiting the power of the analysis. A standard for dimensions could not be achieved in general across studies for either respondent group; however, anxiety by child/adolescent report had the highest score indicating it was the least troublesome. Thirteen of these studies were from HICs and just under half were from the Americas, with the majority (61.9%) of all the studies dated between 2011 and 2013. Recommendations were for nurses to "demistifies [sic] and clarify" issues related to quality of life for the children/adolescents and families during treatment (p. 353).

Fatigue

A group of Brazilian nurse researchers from São Paolo performed a literature review for childhood cancer fatigue [205]. Fifty-two full-texts were identified in English, Portuguese, and Spanish that measured fatigue in this population. Data were grouped by Instrument development and validation or measurement. After exclusion of ineligible articles, 21 publications (2002–2011) were included in the review (2 USA, 2 Brazil, 2 Greece, 2 Canada, 1 Turkey, and 7 multiple countries) authored by nurses (*n* = 7) or medical professionals (*n* = 6) or others. Instruments included in the sample included: "PedsQL Multidimensional Fatigue Scale (5), Fatigue Scale-Child, Fatigue Scale-Adolescent, Fatigue Scale-Parent e Fatigue Scale-Staff, separately or in combination (14), Fatigue Visual Analogue Scale in combination with the Fatigue Scale-Adolescent and Fatigue Scale–Parent (1), Pediatric Functional Assessment of Chronic Illness Therapy-Fatigue, in combination with the Multidimensional Fatigue Scale (1)" (p. 494). The authors noted that no Brazilian instrument had been validated. Findings were that age ranges varied widely (2–18 year) as did diagnoses (leukemias, brain, and solid tumors) and sample sizes (children alone 40–100, children and adolescents together 22–100, and parents 53–258), although it was noted that conducting fatigue studies on a single diagnostic group would be difficult despite the fact that chemotherapy protocols vary and may impact fatigue. The authors noted the lacuna of instruments to measure fatigue in children, in contrast to adults; lack of validated instrumentation for fatigue in Brazilian children/adolescents with cancer as only one instrument had been translated into Brazilian Portuguese; and highlighted the importance of nursing research on this significant component of QoL.

Palliative Care

Pediatric oncology nurse researchers in São Paolo, Brazil [199], conducted a literature search on pediatric palliative care for children and adolescents with cancer. They found 29 references published between 2004 and 2009 in Portuguese, Spanish, or English (online abstracts or full-text) of which six met inclusion criteria. In summary, the authors found that nurses should consider and give attention to the "biopsychosocial" needs and QoL of the child at end-of-life. Although only one article was from an L&MIC (Brazil), cultural taboos about death and the child's being near death were seen to cause much suffering and distress. The authors recommend, "Ensuring dignity as well as promoting quality of life at this time is to respect individuality and provide serenity before death in view of the humanization of care" (p. 783).

Brazilian Theses and Dissertations

Nunes de Lima and Santos from Brazil conducted a literature search dissertations and theses on childhood cancer in the *Coordenação de*

Aperfeiçoamento de Pessoal de Nível Superior [Coordination of Improvement of Higher Level Personnel]/CAPES database from 1987 to 2012 [204]. The authors found seven qualitative studies: six master's theses and one dissertation generally from Brazil's southeastern and midwestern regions. Only four of the seven studies were about nursing (two on nursing performance and one on nursing theory and one not described), and the others were on psychology and language. The authors decried the lack of research on childhood cancer in Brazil and little in the area of graduate education. They recommend additional attention be directed to research that explores the children's "feelings and anxieties and vision on care" to deliver "multidisciplinary humanized assistance" in pediatric oncology (p. 3303).

15.4.5.3 Literature Review Exemplar from the European Region

Traditional and Complementary Medicine

A review of 11 T&CM studies on children with various diseases (including childhood cancer) in Turkey following an unrestricted internet literature search in March 2012 for literature in the previous 10 years included three studies of children with cancer [206]. Eighty-seven percent of the Turkish pediatric patient populations in these studies used T&CM, and most often herbs (92%), prayer (55%), or vitamins/supplements (28%). Almost half (41%) of the children were reported to use religious interventions "religious-man prayer, votive offering and tomb visit" (p. 302). Most had learned about T&CM from their extended family as well as friends, although two families of children with cancer had heard about it from other patients (10.2%) or the media (14% and 22%). For families of children with cancer, in one study almost all (92%) had not spoken to the healthcare team about T&CM use; however, in the other two studies, only 27.9% and 26% had not done so. The authors recommended educating healthcare staff about T&CM, encouraging respect towards parents who use T&CM, and integrating this topic in discussions with parents and children with a focus on safety. The high rate of use of T&CM in this study resonates with the suggestion of Diorio et al. [210] for L&MIC with rates of disclosure very low in in L&MIC compared to HICs.

15.4.5.4 Literature Review Exemplars from the Western Pacific Region

Children's Lived Experiences

Two nurses in Shanghai, China participated in a nursing research team [203] that conducted a literature search of articles on children's (2–18 years of age) lived experiences with childhood cancer using interviews (open-ended, semi- and structured) with the children themselves (no proxies). Five themes were identified across 51 studies from 16 countries, only five of which were L&MIC: "suffering because of cancer, fluctuating realities, coping strategies, new roles and responsibilities of the child, practical resources to enable managing cancer" (p. 533). The children noted that nurses were important for their social support and enhanced their cancer experience. The researchers note that the findings of this study inform health professionals caring for children with cancer and can guide their practice to address issues of concern identified by the children themselves.

Symptoms During Cancer Treatment

Cheng et al. [198] identified 33 articles on symptoms reported by (at least two-third groups) children with cancer (6–18 years with multiple cancer diagnoses), their family caregivers, and health professional in a literature review with no start date for publications, but through May 2017. The largest number of articles (17) were from the USA, quantitative (26) or included children and caregivers as respondents (24). Only nine studies included all three respondent groups. Most studies were descriptive and of low quality. Results demonstrated that there are incongruent findings across respondent groups probably due to the complexity of measuring symptoms, variety of tools used, and parent proxy reports. Most publications suggested allowing the child to self-report and the authors here name several instruments that would allow for this approach (e.g., PROMIS® or Symptoms Screening in Pediatrics Tool [SSPedi]). Children's self-report was more aligned with caregiver report than the healthcare professionals report. The authors note it is important to consider "particularly the impact of pediatric cancer to and interactions of the symptoms with the various aspects of children, family members, family dynamics, and social behaviors" (p.

2969) and recommend further investigation of various perspectives and influencing factors on the symptoms of children and adolescents with cancer receiving treatment.

15.5 Discussion

15.5.1 Quality and Strength of Evidence

As previously described, the quality and strength of evidence of the selected studies were determined by using the Johns Hopkins Nursing Evidence-Based Practice Research Evidence Appraisal ranking [72]. Overall, we found a small number of Level I studies. Most studies were descriptive or literature reviews that identify challenges in nursing care, child/adolescent coping, and parent stress and coping during their child's treatment. Although recommendations for future research tended to be vague with limited follow-up of existing findings and interventions to address gaps in nursing care, nursing research in these countries is providing guidance to local issues of childhood cancer treatment and how these might be addressed locally to improve nursing care.

15.5.2 Recommendations

Several research findings in the areas of nursing education, parent education and support, nursing support, and nursing practice are ready for translation into practice in low-and middle-income countries. Nursing education priorities included non-pharmacological pain interventions, end of life care, red blood cell and platelet transfusion safety, prevention strategies for extravasation, safe handling of chemotherapy, use of complementary and alternative therapies, and symptom assessment and management. Parent education and support priorities included establishing language preferences for receiving education whether written or spoken, incorporating a holistic approach to care, and providing patient and family centered care. Recommendations for nursing support included psychological support and strategies for coping with death and dying and use of self-reflective journaling. Priorities for practice included using valid and reliable instruments in research and practice when available, implementing holistic/patient and family centered approach to care to address psychological needs of child and family, use of nurse educator model as a cost effective and reliable method to improve clinical skills, and implementing non-pharmacological intervention for children with cancer such as aerobics to decrease depression, computer games as a tool to improve QoL, and distraction techniques, massage, and music therapy for pain management.

15.5.3 Precision Health Framework

Precision health, the framework used for this text, represents all available knowledge that spans the child's biology and genetics, growth and development, behavior, sense of self, family connection, and social and treatment environments [10]. Precision health recognizes each person is unique and thus focuses on customizing care.

Several studies reviewed in this chapter sought to better understand the child's and parents' response to the cancer diagnosis and certain aspects of the treatment experience. Because valid and reliable instruments used to understand these responses have generally been created in HIC, studies were necessary to adapt these instruments for use in specific L&MIC. Although most studies related to understanding the child's and parents' response involved instrument adaptation, this is an essential and often labor intense first step in the research process that will ultimately allow additional studies. Further research findings that reflect the realities of care within the settings of L&MIC are needed to translate evidence into a precision health approach to nursing care. Simply implementing evidence-based care gained from research conducted in a HIC setting in L&MIC would be completely contrary to a precision health model. For example, treatment protocols that are effective in HIC when implemented in L&MIC resulted in higher mortality rates due to neutropenic sepsis.

Full application of the framework of precision health will require more research across cultures. The child's response to cancer treatment varies according to the culture and environment within which it is received. The responses of a child and a child's family receiving cancer treatment in a HIC will be uniquely different from those of a child receiving treatment in an L&MIC. Nursing as a discipline and a science provides care based on the child's response to treatment at all levels from biological to psychological. Thus, it is essential that the nurses in

L&MIC identify and understand the child or adolescent's response to his/her disease and treatment and the impact on the family so as to direct their nursing care in a precise way. Unfortunately, without nursing specialization and local nursing research and evidence, this approach awaits implementation.

15.5.4 Comparison with Pediatric Oncology Nursing Research from High-Income Countries

A search of pediatric oncology nursing research published by authors in HIC from 2008 to 2018 was conducted in the following journals: *Journal of Pediatric Oncology Nursing* (JOPON) (official journal of the Association of Pediatric Hematology/Oncology Nurses, USA), *Cancer Nursing* (official journal of the International Society of Nurses in Cancer Care, USA), *European Journal of Oncology Nursing* (official journal of the European Oncology Nursing Society, Belgium), and the *Asian-Pacific Journal of Oncology Nursing* (official journal of the Asian Oncology Nursing Society, India). Results were as follows: *JOPON* (210 articles), *Cancer Nursing* (36 articles), *European Journal of Oncology Nursing* (30 articles), and the *Asian-Pacific Journal of Oncology Nursing* (three articles) (see Table 15.4).

Table 15.4 Comparison of top five topics researched in low- and middle-income countries (L&MIC) and high-income countries (HIC) and those only found in HIC publications based on studies from the *Journal of Pediatric Oncology Nursing* (JOPON), *Cancer Nursing* (CN), *European Journal of Oncology Nursing* (EJON), and *Asian-Pacific Journal of Oncology Nursing* (APJON), pediatric oncology nurse research articles (2008–2018)

Top 5 most frequent topics addressed in both L&MIC and HIC studies						**Top 5 topics add L&MIC studies**
	JOPON	**CN**	**EJON**	**APJON**	**Subtotal**	
Nursing practice	28		6	1	35	Brain tumors
Survivors	21	4	2		27	Sickle cell disease
Parent/mother/grandparent experience	18	2	3	1	24	Siblings
Adolescents/young adults	13	1	1		15	Bone marrow

					transplant/stem cell transplant
Parent/patient/family education	10	1		11	Clinical trial

The most frequent article topics from these four journals that were shared among publications from L&MIC included nursing practice, parent/caregiver experiences, adolescents/young adults, parent/patient/family education, literature reviews, child experience, psychometrics, and symptoms. Although the settings differed, these similarities reflected shared priorities to advance the nursing care of children with cancer on a worldwide basis. Examples of topics that were not included in nursing research in L&MIC (in order of highest frequency) reflect aspects of pediatric oncology care that are not widely available across L&MIC and included: brain tumors, sickle cell disease, siblings, bone marrow/stem cell transplant, clinical trials, research techniques, and radiotherapy.

Articles addressing nursing practice were most frequent among both HIC (*n* = 28) and L&MIC studies (*n* = 36). The specific aspects of nursing practice however differed across settings. Examples of nursing practice topics from L&MIC included palliative care, acknowledging child and parent autonomy in decision making, nurse self-care, and health professional perspectives on fatigue in children with cancer. From HIC, nursing practice topics included publications on topics such as quality of nursing care of children with cancer in France [211], developmental screening of very young children and infants in the USA [212], and prevention of tumor lysis syndrome in Hong Kong [213]. Other topics in common (in order of frequency) were parent/caregiver experiences during treatment, parent/patient/family education, and adolescent and young adults. Examples of nursing research in L&MIC focused on parent coping at the time of diagnosis in Mexico [91], parent needs while child is hospitalized in China [88], and living with the treatment in South Africa [89]. These topics contrasted to parent/caregiver experiences in HIC, which were exemplified by studies on cultural beliefs and strategies for coping of South Asian immigrants in Canada [214], parent's feelings of hope in the USA [215], and parental involvement in the child's pain management, also in Canada [216].

Although few RCT were published by nurses in L&MIC, this was also similar to relatively few RCTs from HIC reported in the four journals searched. Literature reviews in L&MIC included topics of distraction for pain control, nursing care, nursing stress/burnout, child/adolescent QoL, fatigue, palliative care, and Brazilian theses and dissertations. In contrast, in HIC literature reviews (all but one conducted by US-based nurses), examples of topics included nursing coping and resilience in Australia [217], immunizations after a bone marrow transplant in the USA [218], and skin cancer prevention in children/adolescents in the USA [219]. Topics addressed by one study in a HIC that were also addressed in L&MIC literature included music therapy, nutrition, and animal assistance for patients.

The HIC countries most frequently represented in the selected pediatric oncology nursing research articles were the USA, Canada, Sweden, and Australia (in order). Figure 15.5 shows all countries in the group of HIC articles.

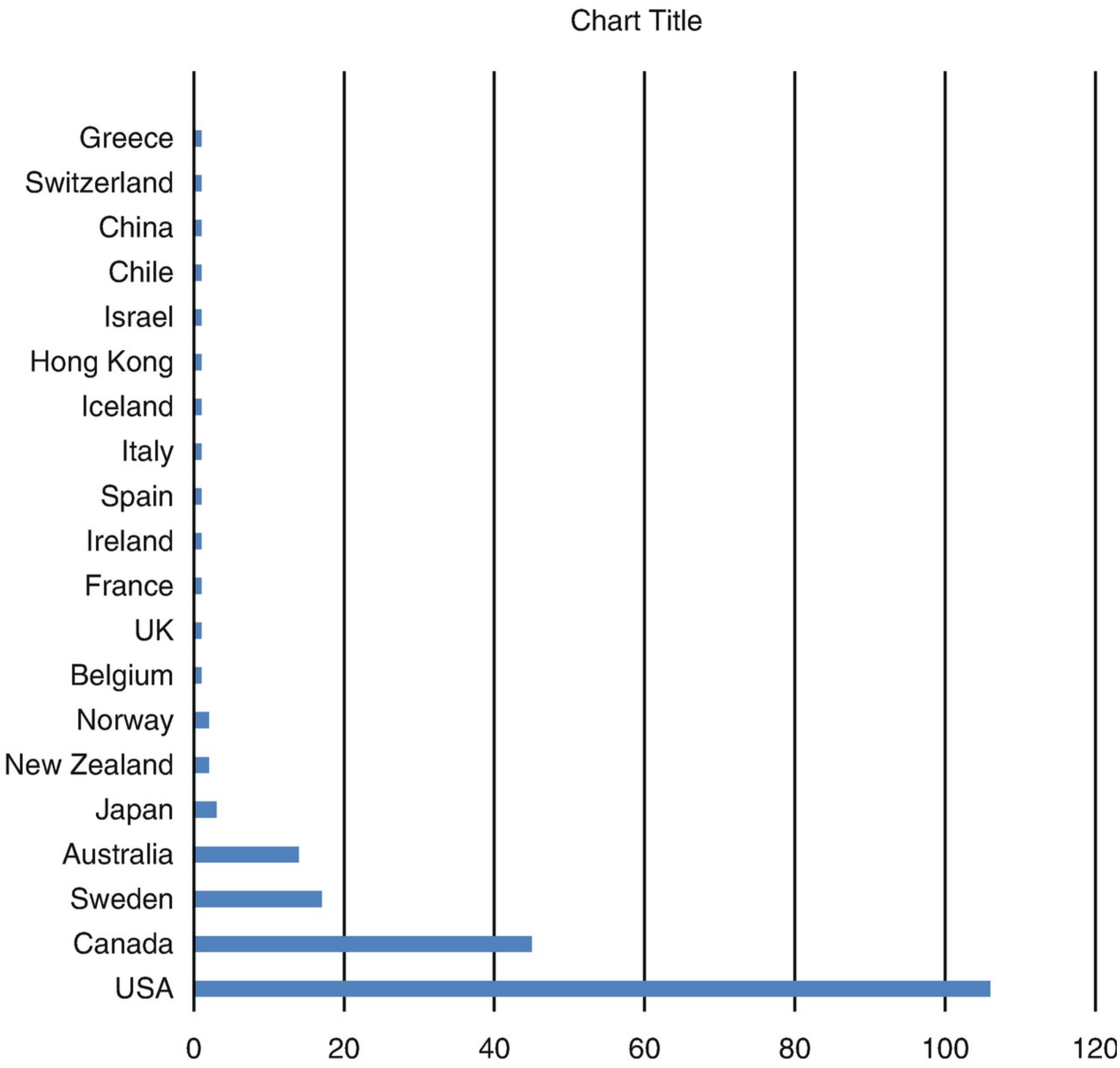

Fig. 15.5 Number of articles on pediatric oncology nursing research in high-income countries included from search of *Journal of Pediatric Oncology Nursing*, *Cancer Nursing*, *European Journal of Oncology Nursing*, and the *Asian-Pacific Journal of Oncology Nursing* publications from 2008 to 2018

Only two articles from pediatric oncology nurse researchers in L&MIC were published in the four journals mentioned above in the 10 years of included publications. This indicates that there is a division between easily accessible pediatric oncology nursing research in L&MIC and that which is available in commonly read nursing journals in HIC. This is unfortunate since many of the research topics are similar and so findings would be relevant in all regions of the world. The greater diversity of topics in HIC country research could inform nursing practice and inspire pediatric oncology nurse researchers in L&MIC to expand their investigations, especially since great strides are being made in childhood cancer care in those regions.

15.5.5 Limitations of Nursing Studies from L&MIC

Limitations of nursing studies from L&MIC included small sample sizes, non-experimental research designs, and lack of funding. A small sample size was the most frequently reported limitation (e.g. [120, 123, 127, 220]). Moreover, the samples for some studies were taken from a single site which limited the generalizability of the findings (e.g. [164]). Many studies also included patients who were heterogenous with regards to diagnosis which has implications in relation to different physiological effects as well as emotional consequences for the patient and family. This was a noted limitation among studies which examined at quality of life, fatigue, parent coping, and treatment.

A glaring lack of articles addressing adolescent experiences with childhood cancer was noted. This important group, traditionally ignored even in HIC, should be prioritized for additional investigation and support.

Many studies used quantitative non-experimental design (i.e., cross-sectional surveys) with a few case-control studies, which limit the establishment of causal relationships. In many studies, a convenience sampling technique was used, and others used a retrospective design, both of which create a risk of information bias and limits the generalizability of the findings (e.g. [79, 84, 119, 127]). Also, HIC authors of some studies were visiting researchers in L&MIC, which poses a potential risk for geographic bias.

Multiple articles that met the inclusion criteria were not included because of our inability to obtain the full texts. Twenty-five selected articles were published in Chinese and are included in this chapter. The authors of this chapter do not read Chinese and could not review the full-texts; however, brief translated summaries and an assessment of the quality of evidence of presented in these articles were provided by two Chinese PhD students working in Hong Kong. All efforts were made by an extended network of Portuguese- and Spanish-speaking colleagues and chapter authors (one is a native Arabic speaker, one speaks and reads French, and one speaks and reads Spanish) to locate publications. Despite a comprehensive search, in the end, no eligible articles had been published in Arabic or French, so results from Francophone Africa and parts of the Middle East are limited. Publications in Spanish were few and did not address pediatric oncology nursing issues across Latin America (excluding Brazil and Belize). No articles were found for the Caribbean, which is also a lacuna. For these reasons, generalizability of the findings of this study is limited and strong cultural distinctions worldwide discourage extrapolating findings beyond the country in which the research was conducted.

15.6 Conclusion

Progress in nursing research capacity among L&MIC is promising. This is reflected by the large number of pediatric oncology nursing studies that have been published over the past 10 years. Major barriers to pediatric oncology nursing research in L&MIC persist; however, and a clear strategy on how to best improve nursing practice by using the findings of those studies is required. Despite an evolution in conducting and publishing strong evidence (i.e., a few studies were rated as high level and quality of evidence), most of the published studies by pediatric oncology nurses in L&MIC are descriptive (i.e., quantitative non-experimental, literature reviews, and qualitative). Also, most of those studies have shared focuses on a few patient care-related aspects (e.g., fatigue, pain and supportive care, etc.) with vague recommendations for future research. These concerns raise the flag on how nurses at the point of care will utilize the findings of this large body of local research in L&MIC to improve their clinical practice and to address gaps in other areas of their nursing care. Therefore, more high quality, peer-reviewed open-access publications are needed to reflect the full range of gaps in clinical practice and to support the increased use of local (or regional) L&MIC evidence into practice by pediatric oncology nurses in these settings.

Nevertheless, collaboration between academia scholars and clinical professionals that highlights the need to foster investigations and publications by pediatric oncology nurse researchers in L&MIC was evident. This collaboration may have contributed to the enhanced level and quality of the currently published research evidence. Despite this important collaboration, most of the published studies are not funded, which limits the ability of the research teams to enhance the level and quality of the evidence and generate knowledge that can make an impact on nursing policy and practice.

A significant number of articles were available only in Chinese and Portuguese (although a small number of both were available in English as well). Due to language barriers, dissemination of findings is limited for these studies. Given the large number of children and adolescents in both countries and the ability of the nurse researchers to have larger sample sizes and collaborations regionally than afforded in most HIC, this is a particularly unfortunate circumstance. We also point out the lack of published research from pediatric oncology nurse researchers in India, Pakistan, and other Asian countries with large numbers of children and adolescents being treated for cancer, which is a serious lacuna in our findings. It would appear prudent to investigate a way for nursing research findings from China, Brazil, India, Pakistan, and other under-represented L&MIC to be shared in English, either in print, digitally, webinars or in person at international conferences.

Only 14 of the 82 studies published in English reported funding sources with support most frequently coming from a university or a foundation. This highlights an endemic situation across L&MIC, that of poor financial support for nursing research, which means nurses already caring for large numbers of children and adolescents with cancer (ratios up to 10–15 patients/shift [33]) must find not only the time, but their own resources for nursing investigations. This may explain the preponderance of qualitative and non-experimental research publications from these countries. Only a few quantitative and experimental studies were rated as high quality or with high strength of evidence. These studies might have the potential to be translated into nursing practice [221]. However, the majority of the studies were rated at lower quality and/or strength of evidence. This may indicate that most researchers are not prepared or mentored to conduct more sophisticated research studies and/or because of the lack of research funding.

Unfortunately, strategies on how to best improve practice by conducting clinical nursing research or applying local research findings in L&MIC are lacking. Recommendations for future research tend to be vague with poor follow-up of existing findings and interventions to address gaps in nursing care. Nursing research in L&MIC is, however, providing guidance to local issues of childhood cancer treatment that can be addressed locally to improve nursing care. However, how these local nursing research efforts will impact advances in precision health in childhood cancer remains to be seen. The exploration and documentation of the numerous components of precision health (e.g., biology, development, and social environment) are in early stages across L&MIC. Some regions are more active in pediatric oncology research than others (the severe lack of published research from the Southeast Asia Region is already noted). However, it is encouraging that despite limited resources, nurses caring for children and adolescents with cancer have begun to investigate child, parent, and guardian experiences during treatment, symptoms such as pain and fatigue, traditional and complementary medicine, and psychometric testing of instruments to measure coping and quality of life in local languages and in culturally appropriate ways. In fact, several intervention studies are noted, particularly from the Middle Eastern Region, China, and Brazil.

Finally, our findings indicate that many of the studies were published in closed-access journals and many with low impact factors. This has a significant effect on the dissemination and the accessibility of the study findings especially since the target audiences are nurses from L&MIC where funds to support purchasing articles are generally non-existent, which ultimately limits the usability of the findings of those studies in local L&MIC pediatric oncology nursing practice.

We call upon the international pediatric oncology nursing community as well as our physician colleagues and other stakeholders, e.g., global and regional parent groups, to increase their support of pediatric oncology nursing research dissemination in open access journals, international conference presentations, and cross border nursing as well as multidisciplinary research collaboration. Experienced pediatric oncology nurse researchers in HIC should consider reaching out to colleagues in L&MIC to engage in applying local research findings to practice and supporting research efforts to establish local evidence-based practice. It is no longer reasonable to apply evidence from HIC to practice in L&MIC without careful review of cultural appropriateness and consideration of local resources. The findings presented in this chapter indicate that pediatric oncology nurses in many L&MIC are conducting research that begins to create the evidence for stronger nursing care in their regions. Precision health requires data on multiple aspects of the child or adolescent with cancer (e.g., physiology, behavior, treatment response, family and community, nursing practice). The L&MIC nursing research presented here established the beginning database for precision health approaches in the future in these settings.

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16. Conclusion and Future Perspective

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Abstract

This chapter revisits the organizing framework guiding the text. Through its chapters, this text has presented a summary of pediatric oncology nursing science in support of precision health for the child with cancer. While each chapter addressed a distinct aspect related to the care of the child with cancer, shared, cross-cutting themes pertinent to advancing a precision health approach to the care of the child and family were present across chapters. This concluding chapter summarizes and interprets these shared themes with attention to knowledge ready for translation into practice and directions for future research.

Keywords Precision health – Pediatric oncology – Nursing practice – Pediatric oncology nursing science – Child health – Family health

16.1 Contributions of Nursing Science to Precision Health for the Child with Cancer

In this closing chapter, we revisit the organizing framework of precision health. As depicted in the model and across the chapters of this text, precision health involves the use of multiple sources of information about the child with cancer individually and children with cancer as a population to provide targeted, predictive, and personalized care [1]. This text has explored a breadth of aspects of nursing science providing multiple sources of information, including genomic, biologic, behavioral, and environmental, which have already contributed to and are continuing to advance nursing care that positively influences precision health for the child with cancer. We begin this chapter by briefly summarizing content from the multiple chapters specific to the major components of the Pediatric Oncology Nursing Practice and Nursing Science Precision Health Model (Fig. 16.1).

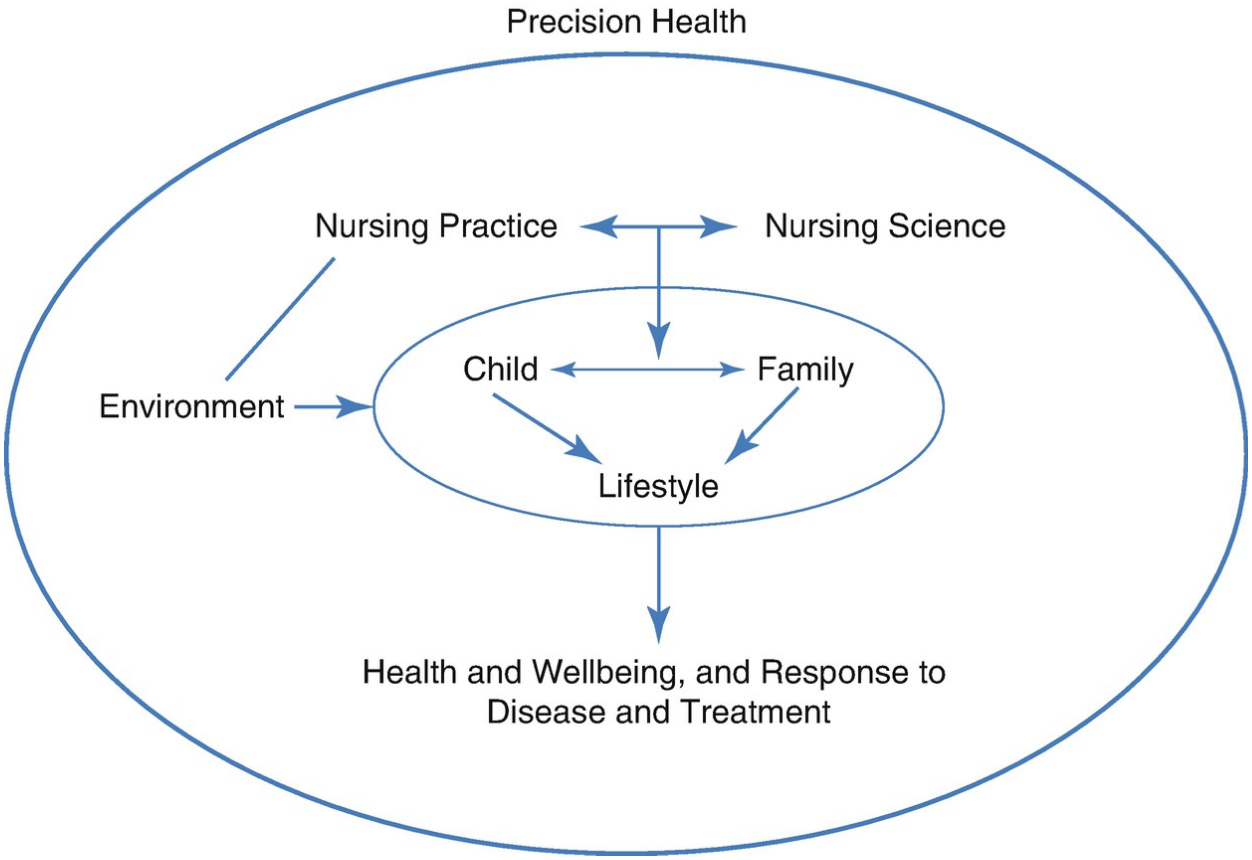

Fig. 16.1 Influence of nursing practice and nursing science on child and family health

and response to disease (cancer) and its treatment within the context of precision health

16.1.1 Nursing Care of the Child with Cancer

The chapters within this text emphasize each child's individual treatment experiences as the basis for precision health across the cancer continuum. This distinction is exemplified through the description of commonalities across children while giving attention to unique influences such as the child's development, previous health and well-being, biologic influences, including genetics, social support and family presence, and culture that further shape the individual child's cancer experience.

This growing understanding of the child's cancer experience is guiding nursing practice through an increasing availability of resources for assessment, particularly for symptoms and other patient-reported outcomes. Supporting a precision health-based approach to pediatric oncology nursing care also includes ensuring that the child's voice is represented across the treatment continuum beginning with age-appropriate input into symptom presence and intensity, strategies that help to respond to challenges inherent to the cancer treatment experience, and decisions regarding treatment. Nurses' efforts to elicit the child's perspective regarding the cancer experience constitute a clear commitment to listening to and honoring the child's preferences while collaborating with the child's family and clinical care team members to maximize the child's health and well-being. Chapters within this text have demonstrated children's capacity to engage in making their preferences known including in discussions pertaining to palliative and end-of-life care in a meaningful manner.

16.1.2 Nursing Care of the Family

This text has also given emphasis to the influence of the family and the necessity of supporting the family's well-being. Optimizing family support enhances the well-being of the entire family unit, which in turn, can positively influence the individual child's health, well-being, and response to disease and treatment. Likewise, the child's suffering as a consequence of his or her illness and treatment adversely influences the quality of life of the entire family. Implementing a family-centered approach to pediatric oncology nursing care is a component of fostering resilience among all family members. Attention to the family's physical and psychosocial needs across the treatment continuum creates a supportive environment for engaging family members in contributing to decisions related to their child's care. Nursing care of the family also extends to the provision of education, including teaching family members how to care for the child in the home setting, and education about other family members' genetic risk for cancer and actions that can be taken in response to that risk.

16.1.3 Nursing Care of the Environment

The chapters within this text have further explored the broad, multi-faceted aspects of the environment in which care is provided and how nursing practice can influence the environment of care to support precision-based care of the child and family. Many chapters attended to the influence of culture and the role of nursing practice to support cultural values and preferences to enhance the care environment. Communication from healthcare team members, including nurses, further shapes the environment of care for children and their families and can be perceived as supporting or hindering the child and family's experience across the care continuum.

Technology is having an ever-increasing influence on the lives of children and their families, including how both children and parents interface with the healthcare team. Examples of how emerging technology is influencing the care environment include the development of resources to support child-centric symptom reporting and the delivery of education and psychosocial support to children and their families. Technology is also shaping how nurses receive education and increasing opportunities for nursing education, which may positively influence the care environment.

Finally, the text addressed environment on a larger scale in terms of the global environment and resources that may or may not be available to offer the potential for cure. Despite limitations in resources in low- and middle-income countries, research conducted by nurses reflects shared priorities across all settings, including symptom management, the child and family experience, and patient/family education to advance towards precision health for the child with cancer.

16.2 Knowledge that Can Be Translated into Practice to Support a Precision Health-Based Approach to Nursing Care of the Child with Cancer

While additional work remains, nursing science has provided a rich foundation of descriptive knowledge for advancing precision health of children with cancer, their families, and the systems in which care is provided. Examples of knowledge ready for translation into practice are highlighted below.

- *Recognition of the individual child*. Perhaps most important to this text is the evidence supporting the basis of precision health—the distinct individuality of each child. Each child's experience across the cancer care continuum is shaped by his or her individual developmental stage; genetic and genomic variation (including that of the cancer) (Chap. 13); family (Chap. 2); prior physical (Chap. 9) and psychosocial (Chap. 4) health; as well as his/her experiences with treatment (Chap. 5). Children's preferences for and responses to a given intervention, including technology, are also individual (Chap. 8). Nurses need to recognize children's capacity to participate in decisions related to their care (Chap. 10) and to determine their individual preferences for engaging in decisions even in the context of palliative (Chap. 11) and end-of-life care (Chap. 12).
- *Recognition of each family unit as distinct*. Likewise, current knowledge supports the recognition of each individual family as distinct. Family-centered care (Chap. 2) is regarded as the center of pediatric oncology nursing. Nurses caring for families affected by childhood cancer must appreciate that each individual family varies in terms of access to support systems and in their type and extent of coping skills (Chap. 4) which will further shape how families receive education regarding the child's diagnosis and care (Chap. 6). Caring for the family also involves evaluation of inherited risk for cancer and consideration of how that risk might extend to other family members, including siblings (Chap. 13).
- *Role of assessment*. Performing a baseline assessment provides the foundation for precision health. Assessment may be directed toward the child, such as identifying the child's physical activity (Chap. 9); the

family, with attention to parental coping styles (Chap. 4); and the environment, including access to resources to support self-management behaviors (Chap. 3). Whenever possible, assessment should be tailored to the child's developmental level, recognizing that even young children can provide a meaningful self-report when actively offered the opportunity to do so (Chap. 7). Given the strength of this research-based knowledge, not having this child and family baseline assessment completed in these components of care risks providing care that is not best practice and is not tailored to the needs and values of the specific child and family.

- *Availability of evidence to guide assessment*. Rich, descriptive data provide a foundation to guide meaningful nursing assessments. Evidence regarding the distressing nature of symptoms and the prevalence of common symptoms while recognizing that each child's symptom experience is distinct (Chap. 5) can be implemented into practice. Validated age-specific patient-reported outcome measures (Chap. 7) are available to support assessment of symptoms and treatment-related toxicities. Evidence is also available to support assessment and screening as part of survivorship care (Chap. 14). Outcomes of nursing care in pediatric oncology should now routinely include the standard use of patient-reported outcomes for those children aged 7–20 years .
- *Appreciation of culture*. Supporting precision health also requires attention to cultural influences and practices that are important to the child and family regardless of the practice setting. Because cultural norms and values influence decisions regarding treatment and care across the cancer continuum, assessing children's and families' preferences for receiving information and making decisions should be a routine part of care (Chaps. 10, 12, and 15).
- *Consideration of the environment*. Whether on a local or global level, the environment in which care is provided influences the health and well-being of the child and family. Nursing practice can optimize the environment through adopting a family-centered approach to care (Chap. 2); provision of timely, effective education (Chap. 6); and supporting clear communication across the treatment continuum (Chap. 12) regardless of the setting in which care is provided (Chap. 15).

- *Development of policy*. Whether at the local, national, or even international level, current knowledge can be translated into policy to advance precision health of the child with cancer. The work of the Children's Oncology Group Nursing Discipline Committee to prioritize patient/family education needs at the time of diagnosis has resulted in the development of teaching materials that are available for adoption within individual institutions (Chap. 6). Other current priorities for policy development and implementation include ensuring children's access to palliative care services (Chap. 11) and policy around genetic testing and communicating results of testing (Chap. 13).

16.3 Recommendations for Future Research to Support a Precision Health-Based Approach to the Nursing Care of the Child with Cancer

Likewise, the chapters of this text have identified shared priorities for future research and provide key direction for nursing science to advance toward precision health for the child with cancer. Many of these priorities also align closely with those of other organizations seeking to promote precision health of individuals and families, including the strategic plan of the National Institute for Nursing Research [2]. These priorities include:

- *Use of conceptual or theoretical frameworks to guide future research*. Some areas of nursing science are well positioned to be guided by established conceptual frameworks, notably the Resilience in Illness Model (Chap. 4) and the Individual and Family Self-Management Theory (Chap. 3). For other areas of nursing science, conceptual frameworks require additional development. For example, although family-centered care is a recognized philosophical approach to care (Chap. 2), much of the research has not been guided by family-centered theories.
- *Clarity of concepts within studies*. Future studies need to ensure clarity of concepts to support meaningful comparisons across studies. An example is that of oral medication adherence (Chap. 3), in which studies have reported other adherence-related behaviors in addition to taking a given medication as prescribed.

- *Study design*. To date, many areas of nursing science have been largely guided by cross-sectional descriptive studies. Studies utilizing longitudinal designs are particularly needed. A noted current example is the work of Hockenberry and colleagues [3] which is evaluating symptom trajectories in children and adolescents receiving treatment for leukemia (Chap. 5). Longitudinal studies are also needed to evaluate children's decisional preferences (Chap. 11) across treatment. To continue efforts to support precision health, study designs that support analyses based on developmental stage, diagnostic group, or phase of survivorship are needed.
- *Methods*. Chapters also addressed a methodological need for future research to address intra- and inter-individual differences. Methods that facilitate the inclusion of typically excluded groups such as non-verbal and preverbal children as well as children and family members who do not speak the primary language of the healthcare setting are needed. Strategies to support inclusion of individuals with limited literacy regardless of their primary language also are needed.

Methods that enhance our understanding of underlying biologic mechanisms influencing the child's response to disease and treatment are needed. These include methods to enhance an understanding of the biologic basis of symptoms and their trajectory across treatment (Chap. 5) as well as late effects of treatment (Chap. 14).

- *Implementation studies*. Several chapters addressed a need for implementation studies. As consensus recommendations are developed and implemented, such as for patient and family education (Chap. 6), evaluation with attention to actual implementation of recommendations, as well as patient/family outcomes, heath care utilization, cost implications, and health outcomes are necessary.
- *Intervention studies*. Research is needed to both develop and evaluate interventions to support precision health for the child with cancer. Examples include the role of technology to enhance interventions (Chap. 8) and the need for effective interventions to increase physical activity (Chap. 9). Future research is also needed to evaluate the efficacy of interventions with studies designed to identify those most likely to benefit.
- *Ensure representation of the child's voice*. Priority should continue to be

given to ensuring representation of the child’s voice. Even in the context of providing family-centered care, care should be taken to allow the child to express his or her preferences (Chap. 2). Examples of priorities for future research to ensure representation of the child’s voice include attention to those who refuse to answer PRO measures (Chap. 7), developing strategies to incorporate experiences of children who are preverbal or nonverbal, and facilitating children’s participation in treatment decision-making (Chap. 10).

- *Measurement of outcomes*. As research priorities shift from descriptive to implementation and intervention studies, evaluation of outcomes becomes a larger focus. Outcomes may be behavioral in nature, such as outcomes of symptom or self-management interventions (Chaps. 3 and 5) or risk reduction behaviors among survivors (Chap. 14). Outcomes may also include health-related outcomes such as in response to physical activity (Chap. 9) or educational (Chap. 6) interventions. Analytic approaches such as those using “big data” may further support measurement of outcomes.
- *Environmental factors influencing the child and the family*. Using a broad definition of environment, priorities for future research include the influence of other individuals, such as peers and healthcare providers, on the child and family in relation to the symptom experience (Chap. 5), education delivery (Chap. 6), or supporting decision making across the care continuum (Chaps. 10, 11, and 14). Likewise, additional research is needed to evaluate the influence of other family members on the child’s experience as well as factors influencing the well-being of the family, including social determinants of health (Chap. 2).
- *Needs of the healthcare team*. Priorities for future research also include attention to the educational needs of members of the healthcare team, including nurses. Examples include identification of the most effective strategies, including technology-based strategies for nursing education (Chap. 8), as well as strategies to support nursing competence in palliative care (Chap. 11) and survivorship (Chap. 14) as the science of precision health for the child with cancer advances. Research addressing best practices for representation of data, including genomic data, within electronic health record systems to guide precision health is also needed (Chap. 13).

- *Advancing global healthcare of children with cancer*. Supporting precision health for the child with cancer extends globally and many of the above-named priorities for advancing precision health are shared across settings. Future research priorities include scaling interventions for implementation in resource-limited settings (Chap. 15). Other priorities include determining the clinical value of measures that have been developed in Western settings, including PRO measures (Chap. 7) and measures of resilience (Chap. 4) within and across other countries.

16.4 Conclusion

As demonstrated across the chapters of this text, pediatric oncology nursing science has generated a strong evidence base that is ready now to be translated into nursing practice to support precision health for the child with cancer. This evidence also provides direction for future research to advance the health and well-being of children, their families, and the nurses and other clinicians who care for them. As stated at the close of Chap. 1, this is the very reason for our work and for our specialty.

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