On the ethics of engagement: health-related quality of life in terminally ill children and adolescents

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Abstract

Background— Pediatric cancer remains the leading cause of disease-related death in children and adolescents. Promoting excellence in the care of terminally ill children is socially dependent on recognizing the complex dimensions of death, dying and living that emerge from situating the child as an active social and moral agent in their healthcare. The continued underrepresentation of children's voices at the end of life, however, fails to ground modalities of care in the unique and evolving realities they face as palliative patients. Qualitative health research with terminally ill children has been proposed as a meaningful vehicle for engagement, to investigate the various dimensions of health-related quality of life and to augment their participatory agency in end of life care.

Objective—To explore the ethics of qualitative engagement in assessing health-related quality of life (HRQoL) among children and adolescents with cancer, and to identify areas where there is paucity of effective qualitative methods for such engagement in pediatric palliative care research.

Methods—This analysis was conducted as a critical assessment—combining policy and literature mapping from developmental child psychology, childhood sociology, jurisdictional codes of ethics for pediatric research and pediatric palliative care research—based on the framework for scoping review by Arksey and O'Malley (2005).

Conclusion—Qualitative HRQoL research with terminally ill children demands innovative methods that afford greater legitimacy to children's moral and social agency in palliative care settings. Because ensuring an optimal health-related quality of life (HRQoL) is the panacea of

pediatric palliative care, it is an ethical imperative that care practices become the province of childhood expertise and social epistemologies of terminal illness. What emerges from the critical assessment is that such methods are poised to respect children's participatory rights pursuant to the new sociology of the child and prevailing ethical norms governing pediatric research. Qualitative engagement in pediatric palliative care is both ethically defensible and a necessary element to delivering comprehensive patient care.

Résumé

Contexte –Le cancer pédiatrique est la principale cause de mortalité par maladie chez les enfants et les adolescents. Afin de favoriser l'excellence dans les soins de fin de vie chez les enfants en phase terminale, il est nécessaire de comprendre la perception sociale des dimensions complexes de la mort, des mourants et de la vie ainsi que de reconnaître les enfants comme des acteurs moraux et sociaux dans leurs soins de santé. Alors que la voix des enfants en fin de vie est sous-représentée, ces patients recevant des soins palliatifs font pourtant face à une réalité unique et en constante évolution. Une recherche qualitative auprès d'enfants en fin de vie a été proposée comme puissant véhicule pour engager cette population, pour étudier les diverses dimensions de la qualité de vie liée à la santé, ainsi que pour favoriser l'approche participative dans les soins de fin de vie.

Objectif—L'objectif est d'explorer l'éthique de l'engagement dans l'évaluation de la qualité de vie liée à la santé (QVLS) chez les enfants et les adolescents atteints de cancer, ainsi que

d'identifier les domaines où il y a une pénurie de méthodes qualitatives efficaces pour un tel engagement dans la recherche en soins palliatifs pédiatriques.

Méthodologie—Cette analyse est basée sur une évaluation critique, fondée sur une revue systématique telle que proposée par Arkey et O'Malley (2005). L'évaluation critique représente une cartographie des politiques et de la littérature portant sur la psychologie associée au développement de l'enfant, la sociologie de l'enfance et les codes de conduite en éthique de la recherche pédiatrique et en soins palliatifs pédiatriques.

Conclusion—La recherche qualitative pour l'évaluation de la QVLS chez les enfants et adolescents en soins palliatifs requière l'adoption de méthodes innovatrices, accordant une plus grande légitimité aux acteurs moraux et sociaux que représentent les enfants en soins palliatifs. Assurer une qualité de vie liée à la santé (QVLS) est la panacée pour les soins palliatifs pédiatriques. Pour y parvenir, il est impératif que l'éthique se soucie des pratiques et reconnaisse l'expertise des enfants et de l'épistémologie sociale de la maladie en phase terminale. À la lumière de l'évaluation critique qui a été réalisée, il ressort que ces méthodes sont disposées à respecter les droits de participation des enfants en vertu de la nouvelle sociologie de l'enfant et des normes régissant l'éthique de la recherche pédiatrique. L'engagement qualitatif dans les soins palliatifs pédiatriques est à la fois éthiquement défendable et un élément crucial à la prestation de soins complets aux patients.

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Chapter I

Qualitative Research, Palliative Care and Young People: An Introduction

"There can be no keener revelation of a society's soul, than the way it treats its children."

—Nelson Mandela, former president of South Africa

Qualitative methods are steadily becoming an indispensable component of health research, mostly fueled by the unparalleled outlooks they provide on how modern medicine impresses upon patient lives. Qualitative research effectively gives voice to the illness narratives of patients and their families (Bingley and Thomas 2008). It can, for example, better inform current and future health care delivery (Di Ciommo, Forcella, Cotugno 2012; Olds et al 2014) or expose deficiencies in care practices and/or healthcare infrastructures (Keers et al 2013; Walsh 2010). In an editorial on the significance of qualitative research to health science disciplines, Jones remarks, "When [T.S. Eliot] asked, 'Where is the understanding we have lost in knowledge? Where is the knowledge we have lost in information?' he anticipated by half a century the important role of qualitative methodologies in health services research" (Jones 1995, 2). Indeed such methods have made seminal contributions to palliative care services, elucidating and describing patients' experiences of death and dying. The World Health Organization (1990) defines palliative care as "an approach that improves the quality of life of patients and their families facing the problem 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." Palliative care research thus boasts a rich—though nascent—tradition of qualitative inquiry dedicated to exploring the

individually unique perspectives of terminal illness (Whitehead 2012; Walshe et al 2004) and guiding care practices that respect the plurality of end of life preferences and beliefs. Katz, Peace and Spurr (2012) write, "a study of patients' preference in palliative care may contribute to theories of ethics and humanity in medicine, thus suggesting relevance to other clinical situations…There are many who believe a key indicator of quality in qualitative research is its contribution to advancing theoretical understanding as well as useful knowledge" (428).

Further, Walshe et al (2004) conclude in an early assessment of palliative care research, "that the dynamic and complex nature of the dying requires robust methods which can examine and expose that complexity" (678). Palliative care research therefore "seeks to investigate the who, what, why, where, when, and how of dying, as well as approaches to improving quality of remaining life, although one could legitimately consider end-of-life research to include studies aimed at prolonging life and increasing longevity" (Phipps 2002, 106).

Froggart et al (2003) credit the enhanced social understanding of the death and dying process to a recent boom in qualitative, palliative care research. They report,

> The promise of qualitative research in palliative care to present the experiences of the users of services as the focus of research has rarely been fully realized. Professionals are most frequently researched, although patients, primarily cancer patients, form a large proportion of study foci. These patterns illustrate the challenges of researching this population. Interactions with people about palliative care issues is most easily facilitated in institutional care settings and siting research in these settings may offer the most pragmatic way of reaching people to explore their experiences. (103)

It has been noted, however, that "future work is needed to compare the relative merits" (Goodwin et al 2002, 81) of the differences in methodology among researchers in palliative care, and greater attention paid to the ethical considerations that qualitative research raises in palliative care generally (Raudonis et al 1992; Beaver et al 1999; Arraf, Cox and Oberle 2004)[i]. Among these are concerns pertaining to the rate of attrition in research protocols (Roberts et al 2014),

vulnerability of the terminally ill (Stevens et al 2003; Koffman et al 2009), and gatekeeping at the institutional, professional and familial level (Hudson et al 2005) of potential participants in palliative care studies.

Despite important progress in understanding adult terminal illness, there is a marked absence of qualitative engagement with children in pediatric palliative care research (Akard et al 2013; Carroll 2007), to say nothing of the concerns that major gaps in evidence-based practices within the pediatric palliative care community raise (Cooley et al 2000). This absence can be attributed in part to the relative rarity of terminal illnesses in pediatric populations (in comparison to adult populations)[ii] (Hutchinson, King and Hain 2003), the shortage of palliative care specialists (Baum et al 1997), and the rigid ethical-legal regulations governing pediatric participation in health research. Although increased pediatric engagement in palliative care research is emerging as a new priority (Ullrich and Morrison 2013; Steele et al 2008), commentators maintain merely the "bringing together of parental expertise and medical expertise is, generally speaking, the *sine qua non* of optimal care for pediatric patients [in pediatric palliative care]" (Browning 2010, 543). Considering the proposal that healthcare professionals have an ethical duty to palliate when a child is believed to be suffering at the end of life (Norton and Joos 2005; Wolfe 2000), the dearth of evidence-based best practices derived from qualitative research in pediatric palliative care settings is problematic. Cooley et al (2000) confirm this: "There is no place within a modern healthcare system for the adoption of unproven theories or outdated care. While no one would question the dedication and care delivered to children and their families by well-trained staff, the lack of research is a cause for concern" (346).

Both quantitative and qualitative research on health-related quality of life (HRQoL) is imperative to the discovery of child-centered care practices in most pediatric medical specialties, particularly in the care of children with advance stage or terminal cancers. Yet despite the

significance of HRQoL assessment at the end of life, few studies have attempted to investigate terminally ill children's views (Gaab 2013; Davies et al 2003) or have included children's perspectives of their illness experience in the quality improvement of palliative care services (Flavelle 2011; Davies 2005; Mongeau 2007).

What is HRQoL?

HRQoL is not an uncontested term. The International Society for Quality of Life Research proposes there is broad agreement that HRQoL refers to the "functional effect of a medical condition and/or its consequent therapy upon a patient…[and] is thus subjective and multidimensional, encompassing physical and occupational function, psychological state, social interaction and somatic sensation" (ISOQOL, What is Health-Related Quality of Life Research?). Armstrong (2009) chronicles the emergence of the HRQoL construct in medical research from 1970-2007, evolving from initial rhetorical use, periods of advocacy and methodological development and finally a "stabilized construction" with sophisticated assessment instruments used in health outcomes research. He maintains, "The process of establishing and organising this field of endeavour is continuing but the stages of development so far provide an insight into the way quality of life 'colonised' modern medicine. By turning a vague idea into a measurable 'fact' quality of life made the transition from rhetorical concept to hard end-point of clinical practice" (103-104). Armstrong further explains how clinical outcomes were traditionally reported based on binary measures, either cure or mortality. As such, the idea of HRQoL was presented in partial response to the "observation that the biological status of the patient might not reflect their subjective status, meaning that a patient might be helped biologically but report no improvement, or conversely, might achieve no biological improvement yet report considerable subjective betterment. At its most salient this was marked by

interventions that produced improvements in life expectancy counter-balanced by major decline in patients' subjective sense of well-being (Armstrong 2009, 103)." HRQoL research therefore attempts to provide a more holistic representation of health and illness as they are shaped by clinical experiences. In this way, HRQoL assessment is an invaluable tool to inform relevant care practices, not the least of which in pediatric palliative care.

The World Health Organization's definition of quality of life similarly reflects the multidimensionality of perceived health status that researchers in the early 1970's identified. It encompasses health-related factors affecting quality of life under an umbrella definition of quality of life, and makes important mention of relational aspects that can factor prominently in healthcare settings: "individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of their environment (1997)." The U.S. Center for Disease Control and Prevention (CDC) further speaks to the utility of HRQoL measures in national health standards and as a critical intersection between clinical and social determinants of reported health status:

> Focusing on HRQOL as a national health standard can bridge boundaries between disciplines and between social, mental, and medical services…Measuring HRQOL can help determine the burden of preventable disease, injuries, and disabilities, and it can provide valuable new insights into the relationships between HRQOL and risk factors…Analysis of HRQOL surveillance data can identify subgroups with relatively poor perceived health and help to guide interventions to improve their situations and avert more serious consequences. Interpretation and publication of these data can help identify needs for health policies and legislation, help to allocate resources based on unmet needs, guide the development of strategic plans, and monitor the effectiveness of broad community interventions. (CDC, Why is it Important to Track HRQoL?)

Later sections of this chapter will demonstrate the important contributions of HRQoL research in pediatric palliative care settings, and its pressing need in informing best practices in areas of terminal cancers, namely for pediatric brain tumors, that are witnessing the emergence of new standards of care. Indeed where empirical studies have investigated quality of life, symptom management (Friebert 2009; Houlahan et al 2006) or psychosocial and spiritual (Woodgate 2003) wellbeing of pediatric oncology patients, findings are overwhelmingly based on parental or health professional proxy (Blume et al 2014; Jones and Carter 2010; Sheetz and Bowman 2013; Huang et al 2011). Certainly proxy reporting is appropriate, even necessary in certain circumstances—for example if the child is nonverbal or suffers from severe cognitive deficits. The reality, however, that children's perspectives are rarely solicited directly in HRQoL research is problematic, particularly when best practices that ensure optimal HRQoL is central to prioritizing the "richness of life and the dignity of self-determination" for terminally ill children and adolescents (Freyer 2004, 381). As Berlinger, Barfield and Fleischman assert,

> Even very young children can hold and express preferences about what they like or try to avoid, especially in the chronic care context in which children gain experiential knowledge about living with disease and being exposed to interventions. Discussing patient preferences matters immensely in decision-making even if preferences are not explicitly about treatment, because they help all parties understand who the child is and how the child could be helped or harmed by the experience of treatment. Professionals should strive to help children and parents recognize these preferences and should talk concretely and compassionately about the impact of a treatment on the child's experience of living. (Berlinger, Barfield and Fleischman 2013, 790)

These trends are not conducive (and remain in stark contrast) to the mandate of the American Academy of Pediatrics: "The goal of pediatric palliative care is to add life to the child's years, not simply add years to the child's life" (2000). To this end, qualitative health research offers the most promising approach to ground palliative care (Candy et al 2014; Clark

2001: Pope and Mays 1995) in the unique realities of childhood terminal illness. Moreover, qualitative engagement further strengthens the relationships of trust between clinical teams and families through fostering platforms of shared decision-making (Schmidt 2011; Field and Behrman 2003).

Despite its anticipated benefits (Gans et al 2012), more recent studies of pediatric palliative care interventions by Schmidt et al (2013) and Moody et al (2011) discover there is still significant work to be done in easing child suffering at the end of life. There is reason to believe that recent initiatives to better integrate palliative care and cancer therapy are promising (Tadmor et al 2003). It is ultimately because terminal cancer in children is rare—and that children are not merely small adults—that engaging them in qualitative research expressly meant to better understand how they conceptualize their illness experience is fundamental to providing comprehensive healthcare at the end of life (Carnevale et al 2013). Greater utilization of pediatric palliative care services among children with life-threatening/limiting conditions (Crane 2011) enhances their position as critical stakeholder communities for whom effective service delivery should be designed.

Therefore through ethical and methodological lenses, this thesis explores the ways in which researchers might approach pediatric engagement in qualitative research to assess HRQoL and of end-of-life preferences among children and older adolescents with cancer. This critical assessment based on scoping review brings to the fore important ethical considerations of affording children the opportunity to meaningfully impact care delivery at the end of life. It justifies doing so using dominant principles of research ethics, theoretical tenets of the new sociology of the child(hood), and human rights codified in the United Nations Convention on the Rights of the Child. This thesis further defends that best practices in pediatric palliative care becomes the province of child expertise and social epistemologies of terminal illness, which best

emerge from engaging with pediatric patients themselves on their HRQoL.

In order to effectively capture the multidisciplinary themes reflected in the literature on pediatric research ethics and palliative care, a critical assessment based on the Arksey and O'Malley (2005)[iii] framework for scoping review was conducted. According to this proposed framework, article searches were carried out to identify all relevant literature related to the thesis topic, and intended to achieve "in depth and broad results" (2005, 8). As such, four overarching domains were identified to guide and organize the results of the policy and literature search on ethical considerations for pediatric participation in qualitative palliative care research. These domains included: i) ethics and social theory of children and childhood, ii) pediatric palliative care, iii) participatory rights of children, and iv) qualitative methodology with children.

An individual literature search was performed for each domain using McGill University access to the Worldcat search engine and PubMed. Prior to preparing the thesis manuscript, a comprehensive annotated bibliography detailed the preliminary literature search results. With greater familiarity and content saturation of the literature results under each domain, searches were conducted iteratively using search terms of greater sensitivity and specificity to the emerging themes. The increased sensitivity and specificity of these subsequent searches allowed for more nuanced analyses of such themes as childhood vulnerability, participation and citizenship, as well as social constructions of the child and childhood. In support of this research framework, Arksey and O'Malley propose, "the researcher may not wish to place strict limitations on search terms, identification of relevant studies, or study selection at the outset. The process is not linear but iterative, requiring researchers to engage with each stage in a reflexive way and, where necessary, repeat steps to ensure that the literature is covered in a comprehensive way" (2005, 8). Therefore because HRQoL research is a relatively nascent research area in

palliative care (Armstrong 2009) dating back to the early 1970's[iv], literature published between 1968-2014 were selected.

This critical assessment combines policy and literature mapping—including research ethics guidelines, developmental child psychology, child sociology and pediatric palliative medicine—to identify areas where there is paucity of effective qualitative engagement with children concerning their HRQoL. A literature review of existing HRQoL tools for use in pediatric populations is also provided. It's purpose is twofold. First the review substantiates the development and wider application of HRQoL assessment by exploring the theoretical underpinnings of its utility. Second, it synthesizes the available evidence to support the improved palliative care outcomes in children with terminal cancer when HRQoL assessment is utilized.

The literature review appears in Chapters I-II, and offers a detailed overview of the sociological shifts in conceptualizing the child, childhood and development theory. It is the collective effort to realize the rights-based notions of participation and agency the new sociology of the child espouses that engagement with terminally ill children in pediatric palliative care is hitherto premised. The chapter identifies the conceptual and theoretical foundations of the aforementioned shifts—based primarily in sociology, anthropology and the developmental psychology of children—and the importance of mirroring it in social science research of child health and healthcare. Until children's rights were officially codified in the UN Convention on the Rights of the Child (UNCRC), children were largely considered passive beings (Balen 2006) lacking the cognitive capacity to exercise agency in decisions affecting their lives. It is under the auspices of the UNCRC that the effort to improve pediatric palliative care delivery through a qualitative research vehicle is chiefly embedded and calls on for future pediatric research protocols to reflect evolving views on the moral status of the child(hood). As children's contributions to understanding the social world are afforded greater legitimacy, so too will their

participation in qualitative research become an instrumental component of quality assurance and service delivery in pediatric healthcare generally, and palliative care specifically.

An in-depth analysis of children's participatory rights is also provided as ethical support for children's inclusion in health research that purports to better understand how they navigate their illness experience(s) and improve the healthcare they receive. Recognizing that many, if not most, great medical advances in pediatric medicine are attributed to empirical research with these populations (Ochinsky 2005)—there is a strong argument for extending greater participatory rights to them in this regard. Scholars maintain the classical tension in pediatric research participation—that children should enjoy the benefits of research through their participation but must also be protected from the associated risks—is outdated and insufficient to justify their exclusion from efforts to improve services for children (Powell and Smith 2009). Moreover, stringent measures to protect children in human subjects research have become disproportionately overprotective and, in fact, counterproductive to advances in the field (Macklin 2005; Spriggs and Hy 2011). The research and clinical community alike must therefore regard children's participation in health research as essential to innovating child-centered therapies and tailoring care modalities to their evolving cognitive and social development.

Chapter II is dedicated to reviewing effective methods, as well as discussing their conceptual and theoretical bases, for engaging children in qualitative HRQoL research in palliative care. It provides empirical evidence for how qualitative methods commonly used in adult research fare when used in the pediatric setting. It also addresses methods of communication and the strengths of qualitative design for representing children's voices authentically. Through an analysis of researchers' first hand experiences, methodological issues and innovative techniques to engage children through a variety of dialogical and graphical mediums (such as deliberative focus groups, photography, drawing and interactive games) are

discussed. The summary provided of what is known about effective pediatric qualitative research methods further demonstrates gaps in the literature on the subject of qualitative engagement with terminally ill children.

The research population of interest—namely, terminally ill pediatric cancer patients—can be distinguished from most other pediatric populations who opt to participate in qualitative research due to the severity of the illnesses they face. As the case study in high-grade Astrocytomas will illustrate, the panacea of pediatric palliative care research (Committee on Palliative and End of Life Care for Children, 2003) is to better assess, from a child perspective, HRQoL elements that factor prominently during the death and dying process. This thesis therefore contains a broad collection of empirical, literary and ethnographic work on the unique lives of dying or hospitalized children in attempt to map these narratives against the backdrop of existing pediatric palliative care research and clinical modalities.

Health-Related Quality of Life in Pediatric Oncology and Palliative Care

According to the World Health Organization, "palliative care for children is the active total care of the child's body, mind and spirit, and also involves giving support to the family" (1990). Palliative care is not reserved for children who suffer from terminal or life-threatening illnesses, but rather encompasses the care of children with life limiting conditions as well[v]:

> Palliative care for children and young people with life-limiting conditions is as an active and total approach to care, from the point of diagnosis or recognition, throughout the child's life, death and beyond. It embraces physical, emotional, social and spiritual elements and focuses on enhancement of quality of life for the child/young person and support for the family. It includes the management of distressing symptoms, provision of short breaks and care through death and bereavement. (ACT 2009)

Bergstraesser (2013) summarizes the core concept of pediatric palliative care as being "defined by the child suffering from, but also living with and living despite of a life-limiting illness" (142). She goes on to note, "To provide high-quality care that strives to enhance the quality of life of these children and their families, the full range of clinical and educational resources of PPC must be made available" (142).

It is well recognized, therefore, that HRQoL ranks among the foremost priorities in pediatric palliative care delivery (Meyer et al 2006; American Academy of Pediatrics 2000), and individualized care plans the mechanism by which to improve quality of life (Baker et al 2008). Varni et al demonstrate, however, the continued under-identification of psychosocial problems related to care experiences, including what the authors term the "new hidden morbidity" in routine pediatric practice. Given the marked under-detection of these problems, HRQoL measures can serve as "standardized screening instruments for identifying physical and psychosocial health concerns from the perspectives of both the child and parent at the point of service that pediatricians might otherwise overlook" (Varni et al 2005, 36). Clinicians and researchers alike corroborate the need to develop HRQoL assessment tools based on the experiences of pediatric palliative patients themselves (Foster et al 2012; Hinds et al 2007) as will be made evident in later sections of Chapter I. These arguments set the stage for broader ethical considerations of building a stronger qualitative research foundation with children in pediatric palliative care.

Qualitative Research: A Palliative Care Tradition

Modern epistemological inquiry of death and dying has been a focus of social theorists, medical anthropologists and psychologists since the early 1960's (Glaser and Strauss 2005;

Sudnow 1967; Clark 1993). Glaser and Strauss were first to characterize a number of distinct trajectories of the dying process:

> Since dying patients enter hospitals at varying distances from death, and are defined in terms of when and how they will die, various types of trajectories are commonly recognized…For instance, there is the abrupt, surprise trajectory: a patient who is expected to recover suddenly dies. A trajectory frequently found on emergency wards is the expected swift death: many patients are brought in because of fatal accidents and nothing can be done to prevent their deaths. Expected lingering while dying is another type of trajectory; it is characteristic, for example, of cancer (1968, 6).

It is the latter trajectory within a pediatric context that will be discussed in depth in this thesis.

The relevance of using qualitative research in pediatric terminal illness stems from its ability to assess the nuances of patient needs (Chenail 2010; PLos Medicine 2007), inform policy and practice (Kearney 2001; Flemming, Adamson and Atkin 2008), and identify the sociocultural underpinnings dictating medical decision-making at the end of life (Tomlinson et al 2006). Jubb (2002) affirms a paucity of good evidence, qualitative or otherwise, still pervades the palliative care research community and attributes these circumstances "to perceived ethical challenges that allegedly distinguish dying patients as a special client class" (342). Pediatric palliative care research offers a unique example to illustrate this point.

A Field of Unmet Needs

Liben, Papadotou and Wolfe argue that little outcome data about the needs and effectiveness of many palliative interventions impede effective care delivery for seriously ill children (2008). Along with others, they contend the limited number of eligible research participants and dearth of standardized measurement tools for pain and quality of life (Varni, Seid and Kurtin 2001) comprise the primary reasons for why such data remain absent.

Himelstein et al (2004) argue while considerable strides have been made in adult palliative care with respect to defining the "good death" (1760), these factors are still largely indeterminate in children (Welch 2008; Contro et al 2002) in part because pain and other symptoms are not well managed (Friedrichsdorf and Postier 2014; Thompson et al 2013; Wilder Smith et al 2013; McCallum et al 2000; Wolfe et al 2000). Unsurprisingly, unequal and/or sparse access to adequate palliative care services poses additional challenges for families caring for children with life-threatening or life limiting conditions (Jones 2011; Knapp et al 2011; Rogers et al 2011), and only recently has greater attention been paid to social determinants of health and its influence on such access (Beaune et al 2013).

HRQoL Assessments for Children, By Children

Health-related quality of life (HRQoL) assessments have long been championed in palliative care research (Detmar et al 2002) as they attempt to provide insight into the psychosocial, emotional and mental wellbeing of a patient. Quality of life is moreover implicated in the World Health Organization's concept of 'health,' as a "state of complete physical, mental and social wellbeing; not merely the absence of disease" (WHO 1948). Like palliative care research, HRQoL measures have only recently garnered more attention in pediatric patients, after first introduced in oncology in the late 1980's (Heyn 1986). Like in adult palliative care, HRQoL assessment in pediatric populations is on the rise in response to increasing demands for critical care medical specialties for children (Hilden et el 2001), and its demonstrated usefulness in cataloging and better managing adverse symptoms at the end of life (Hunt 2003; Drake, Frost and Collins 2003).

The reality, however, is that many pediatric HRQoL assessments tools are inappropriately extrapolated from adult tools or populations of well children (Field and Behrman 2003). Field and Behrman assert, "To identify practices that affect the quality of life experienced by a child with a life-threatening medical problem requires measurement tools that can reliably and validly reflect the child's experiences, particularly when the problem has reached an advanced stage and death is expected or possible in the foreseeable future" (359). Eiser and Morse (2003) likewise suggest inappropriate assessment tools fail to capture the nuances of HRQoL children deem important. Tools specifically designed for pediatric patients, in contrast, have shown to improve early detection of psychosocial distress among children and their families following a poor prognosis (Vodermaier, Linden and Siu 2009; Kazak et al 2012) and support integrated family-centered care approaches which actively seek children's views on HRQoL in a collaborative way (Lindenfelser, Hense and McFerran 2012; Feudtner 2007; Feldman, Ploor and Cohen 1999).

Because improving HRQoL is a multifaceted goal of pediatric palliative care (Considine 2013), it requires a multidisciplinary team of health professionals (Remke and Schermer 2012). In order to coordinate the activities of a multidisciplinary team in this capacity, a working group from the American Cancer Society (ACS) recognized a need to first agree on a preliminary definition of quality of life itself: "Quality of life (QOL) in paediatric oncology is multidimensional. It includes, but is not limited to, the social, physical and emotional functioning of the child and adolescent, and when indicated, his/her family. Measurement of QOL must be from the perspective of the child, adolescent and family, and it must be sensitive to the changes that occur throughout development (Bradlyn, Richey and Harris 1995, 1333-34)."

In line with the views of the ACS, proxy only measurement of pediatric HRQoL is "antithetical to the purpose and utility of HRQoL instruments," (Bradlyn, Richey and Harris

1995, 1335). In addition, research indicates parent approximations of HRQoL are poorly reflective of children's experiences (Mahon et al 1996; Miller 2000; Cremeens, Eiser and Blades 2006). Field and Behrman (2003) highlight the consequences of this: "If parents or other proxies tend to overestimate, underestimate, or otherwise misperceive the quality of life experienced by their children, their reports may misdirect efforts to improve care" (361). One reason for a discrepancy between child self-reports and proxies may be the introduction of response biases as a result of parental psychological distress and anxiety surrounding their child's health status (Knapp et al 2010; Sato et al 2013). In a study by Eiser and Morse (2001), researchers set out to explicate the factors responsible for the inconsistency between self-reported HRQoL and parental proxy (from both mothers and fathers). They confirmed a number of methodological and contextual differences in the literature when defending the claim that parents are inaccurate evaluators of their child's HRQoL. The authors conclude, "There is a need to determine more satisfactorily how far [parent-child] agreement [in proxy reporting] is affected by the child's health. Parent-child agreement is likely to be moderated by the extent to which parents are responsible for giving treatment, the child's willingness or compliance with treatment and whether or not a condition is perceived to be life-threatening (356)."

Eiser and Morse further report on the complementarity between parent proxy rating in HRQoL and that of severely ill children: "This might suggest that parents are more able to rate the child's HRQoL in relation to domains of physical functioning or physical symptoms compared with less visible domains such as social or emotional functioning" (348). Terminal diagnoses for some pediatric cancer patients further heighten the need to better understand the scope and impact of cancer care on their life (Fraser et al 2011; Guyatt 1999). **Table 1** summarizes findings from a review of survey instruments used to assess HRQoL in critically ill pediatric patients (Bartlett et al 2014). The tools indicated were reviewed based on whether they

have been validated in a pediatric oncology population, and content analysis conducted to distinguish tools that are age-dependent.

Despite a wide array of assessment tools, and the multidimensionality of HRQoL factors they attempt to measure, moving away from parental proxy remains a relatively new concept (Rajmil L et al 2004). Using these existing frameworks as guides for further development of HRQoL assessment tools, specific criteria emerge as being particularly useful for evaluating HRQoL in terminally ill pediatric cancer patients, and for those with brain tumors specifically (Sato et al 2014). According to the empirical evidence that gave rise to the tools summarized in **Table 1**, future HRQoL assessment tool can be tailored to specific age groups to account for variations in cognitive understanding and ability to articulate responses.

To date, there is no available tool explicitly to assess HRQoL in terminally ill children and adolescents with cancer. Both the Pediatric Cancer Quality of Life Inventory (PCQL) and Pediatric Quality of Life in Pediatric Cancer (PedsQL4.0), however, come closest to describing the terminally ill cancer population discussed in this thesis. Moreover, many of the existing tools are developed from qualitative data in child cancer survivors, a similar albeit separate population of interest. One notable exception is the TACQOL, which was validated for use in recently diagnosed pediatric patients whose cancers are potentially life threatening, though amenable to treatment.

The near absence of children's voices and perspectives in developing these HRQoL assessment tools (Arbuckle and Abetz-Webb 2013) and those intended for use in palliative care is undisputed (Solans, Pane and Estrada 2008). Hinds, Gattuso and Fletcher (2004) underline the significance of children's ability to define HRQoL, and how meaning making—an integral component of defining HRQoL—is lacking in the existing assessment tools:

A qualitatively induced definition of quality of life for children and adolescents with

> cancer includes the definitional attribute of finding meaning in the illness experience. It is this attribute that is missing from seven quality-of-life instruments previously used to assess pediatric oncology patients. For established measures to accurately and completely measure the quality of life of children and adolescents with cancer, items reflecting the meaning of being ill need to be added. (771)

While palliative care research concerning HRQoL in children is growing in scope (Straatman et l 2008), much of the solicited perspectives are from parents (Tomlinson et al 2011; Zelcer, Cataudella and Cairney 2010; Hechler et al 2008; Knapp and Komatz 2011) and/or healthcare professionals (Davies, Sehrin and Partridge 2008; Burns Mitchell and Griffith 2001; Czarnecki et al 2011; Docherty, Miles and Brandon 2007; Tubbs-Cooley et al 2011; Kassam, Skiaderesis and Alexander 2013; Kassam, Skiaderesis and Habib 2013). To base standards of practice primarily on the views of parents and health professionals is to igore, as this thesis will argue, the essence of what and for whom pediatric palliative medicine (and research) aspires to do. In line with this thesis' objective, to explore the ethics of engaging terminally ill children in HRQoL research, the International Bioethics Committee declares, "It is clear...that the engagement of people as participants in clinical research is key in providing solutions to, and understanding of, medical problems affecting humankind" (2009, 4).

Chapter II

Literature Review: Social Constructions of the Child(hood) and Qualitative Methods of Engagement

Critics who treat 'adult' as a term of approval, instead of as a merely descriptive term, cannot be adult themselves. To be concerned about being grown up, to admire the grown up because it is grown up, to blush at the suspicion of being childish; these things are the marks of childhood and adolescence. And in childhood and adolescence they are, in moderation, healthy symptoms. Young things ought to want to grow. But to carry on into middle life or even into early manhood this concern about being adult is a mark of really arrested development. When I was ten, I read fairy tales in secret and would have been ashamed if I had been found doing so. Now that I am fifty I read them openly. When I became a man I put away childish things, including the fear of childishness and the desire to be very grown up.

— C.S. Lewis, author

"A person's a person, no matter how small."

—Dr. Seuss, author

Child Development and Its Historical Roots

Children have been the subjects of concentrated scholarship for millennia. Philosophers, psychologists, physicians and educators are but a few representatives of the disciplines which have made children a focal point. In social science research, children can provide insight into the longitudinal unfolding of social relationships, how behaviors are conditioned and/or reinforced, and how the diversification of childhood experiences shape individuals throughout the lifecourse. Social theories on the boundaries of 'childhood,' transitions to 'adulthood,' and the inherent characteristics of each are equally diverse. But as Desai (2010) writes, "children have been

perceived as immature and imperfect by thinkers from ancient to modern times" (10). She situates contemporary social theories of the child(hood) against a historical backdrop beginning with some of the first documented scholarship on the subject. Desai explains, "According to Aristotle, a human child is an immature specimen of the organism type human who, by nature, has the potentiality to develop into a mature specimen with the structure, form and function of a normal or standard adult" (11). Aristotle regarded children as property of the father, who even if considered an immoral being himself, warrants deliberative control over the social rearing of his child(ren). Desai further adds, "John Locke viewed the child neither as inherently bad nor good but rather as a 'tabula rasa'…This idea implied that children could be shaped by all kinds of experiences during their life. Locke added that the power that parents have over their children, arises from the duty, which is incumbent on them to take care of their off-spring, during the 'imperfect' state of childhood (Matthews 2004)" (11).

Rousseau, in his theories on early childhood education, rejected Locke's view that the blank slate is colored by social expectations, experiences and conditioning. He instead promoted the idea that independent of institutional forces, freedom of thought and behavior in children can flourish through "naturalistic education." Using a growing plant to demonstrate the difference between directed behavior that social conditioning governs and natural tendency, Rousseau posits,

> The only habit the child should be allowed to contract is that of having no habits; let him be carried on either arm, let him be accustomed to offer either hand, to use one or other indifferently; let him not want to eat, sleep, or do anything at fixed hours, nor be unable to be left alone by day or night. Prepare the way for his control of his liberty and the use of his strength by leaving his body its natural habit, by making him capable of lasting self-control, of doing all that he wills when his will is formed. (67)

Child(hood) theory and construction in the 20th Century was primarily the work of development psychologists, including Piaget and Erikson, who envisioned cognitive maturity

and the emergence into adulthood as a linear process with distinct biological and social hallmarks. Erik Erikson was first to suggest in 1968 that three interacting systems both produce and influence human development throughout the life course: i) the biological, (ii) physiological and iii) societal. Newman and Newman (2006) clarify that the biological consists of "all the processes necessary for the physical functioning of the system," and which change in response to environmental stimuli and genetically guided maturation. The physiological includes "all mental processes central to a person's ability to make meaning of experiences and take action" (6). Finally, the societal system "includes those processes through which a person becomes integrated into society" (6). This triad of developmental systems comprises what is known as the biopsychosocial theory of human development, and in turn mediates children's experiences with the physical and social world. For the purposes of this analysis, the chapters that follow will focus mainly on the interactions between the physiological—inasmuch as age and cognitive maturity are important characteristics underpinning the ethics of health research participation—and societal systems.

James, Jenks and Prout (1998) briefly, though no less critically, summarize the work of theorists who have brought to light the sociohistorical currents which they argue led to the production of contemporary conceptions of the child and childhood:

> Childhood is not a new phenomenon. It was, of course, the historical Philipe Aries (1962) who began the archaeology of childhood images with his breathtaking assertion that childhood has not always been the same thing. This established what Sennet (1993) referred to as 'the study of the family as a historical form, rather than as a fixed biological form in history' (1993: 92). Aries…records the launching of childhood in Europe in the mid-eighteenth century. Adults in particular social classes, he told us, were steadily beginning to think of themselves as of not quite the same order of being as their children. An age-based hierarchy and eventual dichotomy as becoming institutionalized in the relationship between adults and children and the defining characteristics of these differences were, by and large, oppositional. The obvious strengths of Aries's approach lay in the relativizing of the concept of childhood. It provided the grounds for its analysis in terms of its social context, rather than abandoning childhood to a naturalistic reduction. On the other hand, the poverty of

> such historicism, Archard notes, lies in its 'presentism,' that is, in the way that it appears to lock childhood in the realm of modernity. (4)

In her discussion of Boyden and Levison's theories, Desai (2010) identifies the "overall trend in development sciences accepts transformation from an immature child to mature adult, simple to complex, irrational to rational behaviours and dependent childhood to autonomous adulthood… The concept of 'developing' children into adults by 'teaching them implies that children are not developed or are incomplete" (11). Ryan (2008) regards this view as inherently flawed: "The often simplistic deployment of stage theories in institutional policies and their diametric relationship with the view of children as competent agents creates a stark opposition between positive developmental science and the contemporary sociology of childhood" (561). As the case study presented later in this thesis will illustrate, endorsing a lack of agency prescribed by children's presumed underdevelopment is especially problematic when terminal illness shape the trajectory of children's development.

The assumption that 'children' and 'childhood' are typified by a set of common (read stereotypical) set of characteristics proves damaging to a pediatric palliative care research agenda where potential participants may be viewed as "an undifferentiated category of all those under 16 or 18 years old" (Morrow 1995, 221). These age generalizations also have implications for the family-centered approach often promoted in palliative care delivery (Knapp et al 2010). Makrinotti's concept of "familism" illustrates this point (1994). He opposes the subsuming of children under the familial institution such that "their needs cannot be defined independently of those of the family, nor can their needs be realised without the family" (283). Certainly children facing terminal illness not only have needs that differ considerably from those of the family, but their perception on HRQoL can be expressly unique in comparison to siblings and other family members.

This brief exploration of different constructions does well to confirm the notion of child and childhood as chiefly influenced by sociocultural themes. In line with this idea, Mason and Steadman (1996) citing Dencik point out "while childhood as a concept may be defined and bounded by age, it is otherwise nebulous, changing over time and across cultures and also according to ideological perspectives" (35). Further, James and Prout's new paradigm in the sociology of childhood deems "no longer can children be the passing output of child-rearing practices, nor their social development envisaged as the simple product of biological determinism, but as social agents in shaping their own childhood experiences" (Desai 2010, 13).

Towards a New Sociology of the Child

Recently, the call for greater inclusion of children's voices in health research has been marked by modern re-conceptualizations of the child and child development itself (Balen 2006). Among the most vocal interlocutors, James and Prout (1997) outline the central tenets of this emerging paradigm. First, they argue 'childhood' must be conceived of as a social construction. Second, a study of childhoods cannot be divorced from analyzing social dimensions of class, gender and ethnicity. Third, "childhood and children's social relationships and cultures are worthy of study in their own right, and not just in respect of their social construction by adults" (James and Prout 1997, 4). A number of these themes overlap with what Lavalette and Cunningham (2002) outline as the ideological underpinnings of this paradigmatic shift:

- Childhood is not merely a biological phenomenon, but a social construction, affected and shaped by wider social and cultural elements, within concrete, historical circumstances.
- Children occupy and conduct themselves in worlds that are full of meaning for them, but about which adults are, at least partially, ignorant. It has led to an emphasis on listening to children's voices.
- Politically children are powerless and disadvantaged. The new sociology is a theory of advocacy, sociology for children rather than sociology of children. This approach has

closely tied into children's rights agenda.

- Children are an identifiable social group, with a common [basic] set of needs and rights.

In turn, these shifts have motivated concerted efforts to lend primacy to the status, ideas and rights of children in society, not least of which in the clinical research community. The 1989 adoption of the UN Convention of the Rights of Child (UNCRC) embodied this aforementioned shift. It created the first international and legally binding instrument to universally incorporate a human rights framework specifically for children. The product of decade-long negotiations, the UNCRC commits State Parties to promote laws that fully adhere to the values and principles outlined in the document. As a result, "the Convention has inspired a process of national legal implementation and social change in all regions of the world" (UNICEF. Frequently Asked Questions). Moreover, "the articles of the Convention, in addition to laying the foundational principles from which all rights must be achieved, call for the provision of specific resources, skills and contributions necessary to ensure the survival and development of children to their maximum capability" (UNICEF. Understanding the Convention). In effect, the UNCRC rendered the development and wellbeing of a child as being protected under the auspices of human rights doctrine. In her astute commentary on the early drafting and significance of the Convention, Mason writes,

> Defining human rights for children was not an easy task for the framers of the Convention, who labored at their task for ten years. Historically, children's rights, when they were considered at all, focused on protection from abuse and neglect and provision for basic maintenance. In most countries, parents and ultimately the state bore some legally defined obligations to provide protection and provision. Participation rights, where children assert claims to adult liberties, surfaced only recently in conjunction with the human rights movement of the second half of the twentieth century. The Convention on the Rights of the Child was unique in bringing together all three of these rights—protection, provision and participation—into one document. (955)

Mason points out the most important characteristic of the UNCRC, that it is first and

foremost a human rights document. As such, it outlines the most basic rights afforded to people in society. Lundy (2014) underscores this notion: "The use of the word 'basic' here is no accident since human rights are often modest standards whose dominant focus is said to be protecting minimally good lives for all people" (Nickel, 2006). Shue (1996) suggests human rights "define the lower limits on tolerable human conduct rather than great aspirations and exalted ideals" (2440). In effect, the qualitative research defended in this thesis does not merely achieve a greater understanding of the terminal illness experience of children and adolescents, but also offers a vehicle for meeting basic human rights attributed to children under the UNCRC.

United Nations Convention on the Rights of the Child

The four guiding principles of the UNCRC include non-discrimination; devotion to the best interests of the child; the right to life, survival and development; and respect for the views of the child (UNICEF Convention on the Rights of the Childs). The latter principle, in particular, sparked reconsideration in the research community concerning the ways in which children contribute meaningfully to understanding of the social world. As such, a focus on children's role in informing quality assurance and care delivery—including in palliative care—can be achieved in conversation with relevant articles outlined in the UNCRC. Of those, Article 12 lends the strongest support of children's inclusion and participatory rights in pediatric health research:

> States Parties shall assure to the child who is capable of forming his or her own views the right to express those views freely in all matters affecting the child, the views of the child being given due weight in accordance with the age and maturity of the child.
>
> For this purpose, the child shall in particular be provided the opportunity to be heard in any judicial and administrative proceedings affecting the child, either directly, or through a representative or an appropriate body, in a manner consistent with the procedural rules of national law.

The UNCRC further establishes in Article 13:

> The child shall have the right to freedom of expression; this right shall include freedom to seek, receive and impart information and ideas of all kinds, regardless of frontiers, either orally, in writing or in print, in the form of art, or through any other media of the child's choice.

One of the most celebrated achievements of the Convention has also been, paradoxically, one of the most controversial. Article 12 explicitly safeguards participatory rights granted to children, underscoring the prioritization and inclusion of youth voice never before recognized with any real legal legitimacy. It is groundbreaking, according to Freeman (1996) "not only for what it says, but because it recognizes the child as a *full* human being with integrity, personality and the ability to participate freely in society" (37, emphasis added). Member States at the time—namely Somalia and the United States—considered the rights to child expression to undermine adult proxy decisions and threaten parental authority (The Economist). While it is one challenge to ratify (meaning the treaty becomes legally binding in the national jurisdiction), establishing federal laws which adhere to the UNCRC principles is quite another (CBS News).

Article 14 and 24.3 illustrate this difficulty. Article 14 identifies the role of parents as facilitators, as opposed to arbiters, of children's views where exercising their participatory rights.

1. States Parties shall respect the right of the child to freedom of thought, conscience and religion.
2. States Parties shall respect the rights and duties of the parents and, when applicable, legal guardians, to provide direction to the child in the exercise of his or her right in a manner consistent with the evolving capacities of the child.
3. Freedom to manifest one's religion or beliefs may be subject only to such limitations as are prescribed by law and are necessary to protect public safety, order, health or morals, or the fundamental rights and freedoms of others.

And Article 24.3 can be interpreted to take a decisive stance on health practices, which, over time, have proven detrimental to and/or leave wanting the advancement of child health.

1. States Parties shall take all effective and appropriate measures with a view to abolishing traditional practices prejudicial to the health of children.

Smolin—then an American opponent of ratifying the UNCRC—argues Article 14 "is couched in language which seems to reduce the parental role to that of giving advice" (2006, 90). He asserts it "purports to define the respect that States Parties must accord to parental rights and responsibilities, its awkward and ambiguous language can be viewed as distorting the Convention's entire treatment of children's rights. If the Convention mischaracterizes parental rights and responsibilities, it can be argued that it similarly mischaracterizes the interrelated set of children's rights" (91-92). Smolin's argument is useful. First, it demonstrates the ways in which children, even in rights-based rhetoric, are frequently seen as agents who delimit, infringe upon and threaten the rights of parents and their authorities. Moreover, it offers a stark example of how these assumptions are the product of an adult-centered outlook that maintains an otherwise arbitrary division between 'child' and 'adult,' both of whose designations are used to underpin the ethics of permissible research participation.

The consequences of positions like Smolin's is "the position of children has evolved from a strong social participation with minimal protection during the eighteenth and nineteenth centuries, to a strong protection with minimal participation during the twentieth century. As a result, children spend most of their time among themselves, secluded from the rest of society, in a psychosocial moratorium (Dasberg 1965, cited from Jans 2004)" (Desai 2010, 13). The more recent history of children's participation in health research lends credence to this view, and is discussed in further detail in the subsequent section.

The motivation for Article 12 was to serve as a powerful force meant to bring the children of the 21st Century out of the "psychosocial moratorium" Desai describes. It was meant to ensure children are granted respectful means to exercise their social citizenship, and facilitate—rather

than merely granting recognition of—their important contributions to our understanding of the social world. Though not intended to supersede the rights and responsibilities of parents to care for their children, nor entirely divorce children's interests from those of the parents or extended family, "[Article 12] is in many ways the barometer for children's rights since, when it is implemented effectively, other rights fall into place naturally" (Lundy 2007, 940).

Children as Social Actors

In the wake of a new sociology of child(hood), the "key task, then, is to develop further substantive studies which situate children's agency in specific settings" (James and Prout 1997, xii). Further, "if children are to be seen as social actors, they first have to be seen as being capable of social action" (Hendrick 2000, 55). One avenue for exercising social action is through voice. By ensuring the child's voice is heard in clinical decision-making—and considered integral to informing modalities of their palliative care—we are also confirming the child's social importance. In conversation with Berger, Schilling (1993) elaborates on social importance during the death and dying process: "If we take seriously Berger's point that death is an essential feature of the human condition that requires people to develop means of coping with it, then to neglect death is to ignore one of the few universal parameters which impinge upon the body in social systems. Indeed, it is only in the context of the body's inevitable death that we can understand its full social importance" (187). Though Schilling does not explicitly refer to children, they are an ideal example in demonstrating how their participation in conversations of HRQoL is an important method for attributing social importance in palliative care.

Sartain et al (2000) delineate between respecting their voices as children and as patients with a chronic illness. The authors maintain the "application of qualitative research to the

experience of childhood chronic illness is essential if we are to understand both the commonalities and diversities of childhood as one phenomenon and chronic illness as another and how they both interact at different stages in the child and family biography" (920). Because the study population is faced with the reality of a fatal illness, it is distinguished from other studies engaging children with chronic illness. This specificity heightens the importance of the illness narrative to care delivery. Researchers should, as a result, carefully consider the implications of discussing the death and dying process with patients whose family may not be able to relate personally to the impending encounter with death the child faces. Moreover, preconceptions of children with chronic illness tend to situate the disease as central to the child's identity. Therefore in engaging children through dialogue or other interactive activities, researchers' language should not reflect the misguided view Sartain et al caution against in which the disease takes center stage in participants' sense of identity or HRQoL.

Qualitative Methods to Recognize Voice in Death and Dying

Alongside acknowledging the significance of voice, open recognition of the prospect of death can also lend social importance to both the child as well as the terminal illness experience itself. Goldman and Christie's study (1993) exploring communication patterns on a pediatric oncology ward confirm this. They describe how children come to learn of the severity of their illnesses and how this information affects their relationships with family and clinicians. Their findings illustrate how healthcare professionals in oncology are gradually adopting more open and honest communication approaches with children concerning severe illness. One reason supporting these emerging trends is, they argue, from "direct observation of children in oncology wards that demonstrated [children] acquire information about their disease, including how

serious it is, the practical details of treatment and the possibility of death, without being told specifically. This includes those children cared for by staff and parents who believe that by not discussing their disease with them the children remain naive and protected" (229).

Bluebond-Langner observed an identical phenomenon in her ethnography, *The Private Worlds of Dying Children*, still considered one of the most provocative demonstrations of children's acuity and agency in terminal illness. She first presents a five-act play to animate the ways children discern the severity of their illness, and how to manage the information they implicitly absorb from their environmental and personal interactions with healthcare professionals and family during their stay on a pediatric oncology ward. Employing Mead and Blumer's process of child socialization, Bluebond-Langner not only confirms children's acute understanding of their place within the social order of being diagnosed with a severe illness; she describes the ease with which children actively participate in, and sustain the norms and etiquettes that construct it. Children recognize this 'mutual pretense', to use Mead and Blumer's term, effectively fostering a culture of prognostic ignorance that intends to protect children—through exclusion—from the realities of their illness. For instance,

> A more obvious example [of the mutual pretense] was the time Mary was able to talk about her prognosis, the most dangerous topic, and maintain mutual pretense by focusing on the doll rather than on herself. When Mary died, and I questioned her mother about the incident, she stated that Mary was trying to tell her 'something,' but 'she knew I didn't want to hear that kind of talk.' She also admitted to crying about it later that day when she looked at Mary's paper dolls." (202).

Ryan (2008) summarizes, Bluebond-Langner "laid bare the politics of childhood innocence and exposed the weakness of the centuries-old assumption that adults could orchestrate childhood without children perceiving it as such" (574). Weir and Peters (1997) make an important connection between childhood innocence and the maturity that terminal illness

inevitably fosters among young people. The level of maturity witnessed in young terminally ill patients complicates the chronological distinctions between 'adult' and 'child' that preclude participation in pediatric research, including in palliative care:

> Having experienced years of physical and psychological suffering, gone through multiple hospitalizations and numerous treatments, probably experienced depression and probably observed the suffering and dying of several hospitalized friends with similar medical problems, [that] these adolescent patients are frequently mature beyond their chronological years. They have had, at the very least, multiple opportunities to think about the inescapable suffering that characterizes their lives, the features of life that make it worth continuing, the benefits and burdens that accompany medical treatment and the prospect of death. (Weir and Peters 1997, 34)

Using qualitative research designs like those Bluebond-Langner employ, it is possible that engaging children in the orchestration of their own childhoods—where terminal illness is a daily reality—could transform what Browning terms the "microethics" of physician-patient relationships and interactions with young children (Browning 2010). From a methodological standpoint, Prout and Christensen (2002) put forth the notion of 'ethical symmetry' in responding to the contemporary shift in theoretical perspectives of viewing children as social actors. They argue new ethical challenges emerge, and greater responsibilities placed on researchers to both embrace and safeguard this theme in social science studies with children. Researchers who employ 'ethical symmetry'—the idea that a researcher "takes as his or her *starting* point the view that the ethical relationship between researcher and informant is the same whether he or she conducts research with adults or with children"(484)—need not work with a different set of ethical standards when engaging with children. Alanen reiterates the importance of recognizing one's inherent subjectivity no matter the methodological approach: "There is no Archimedean perspective, or God's eye view that is disinterested, impartial, value-free or detached from the particularly historical situations in which everyone participates…knowledge

always contains a perspective from one or another location, a standpoint from which the world is known" (cited in Hendriks 2000, 54). Rather, the research methods employed must be in line with children's experiences, interests, values and everyday routines.

The complexity in adopting 'ethical symmetry' lies in evaluating the variations of children's experiences and competencies. This is achieved through identifying their commonalties and differences in particular contexts, and by understanding the ways they engage with and respond to the research itself. In order to meet these challenges, Christensen and Prout propose "complementary dialogue first between the community of social science researchers of childhood, and second between researchers and the children who take part in their research" (494). Deciding from the broader methodological 'toolbox' in palliative care to elicit children's valuable perspectives, demands special consideration of the diverse contextual elements shaping the child's social environment. Social theory, therefore, plays a critical role in directing and substantiating qualitative research methodology (Willis et al 2007). As Jenks notes, "indeed [social theory] aspires to reveal the essential unification of theory and method in the study of childhood, and importantly, to militate against the outmoded view that there are methods (in the form of techniques), free from theoretical disposition…" (In: Research with Children 2000, p. 63).

This begs questioning whether constructing the taxonomy of a pediatric qualitative research ethic, markedly distinct from other research ethics norms, is guilty of reinforcing 'Otherness.' As Dixon-Woods, Young and Ross (2006) contend, "It is widely accepted that maturational and developmental features of childhood usually demand the use of unique or special research instruments and paradigms, particularly for work with very young children and infants. By contrast, some sociologists argue that using 'special' techniques risks reinforcing the

notion of children as 'other', and that the assumption that methods should be based on the age of children is flawed" (167).

"Power is Everywhere"—Foucault

Despite their evolving cognitive, physiological and moral development, children are afforded a set of basic human rights outlined in the UNCRC. Furthermore, the new sociology of child(hood) promotes the idea that children should be seen as individuals under the protection, rather than possession, of more powerful social actors, including the family, the state etc. From this distinction emerges a particular power structure, which serves to explicate a number of the relational dimensions of children in research and the ethical tensions that arise. Though he refrains from a singular definition of the phenomenon, Foucault theorizes power as "a mode of action which does not act directly and immediately on others. Instead, it acts upon their actions: an action upon an action, on existing actions or on those which may arise in the present or the future…it incites, it seduces, it makes easier or more difficult; in the extreme it constrains or forbids absolutely" (Dreyfus and Rabinow 1983, 219-220). Because power is relational, according to Foucault, unequal distributions of power in the triangulation of medical decision-making does not originate from one "repository of power, but merely a particular set of networks through which power is exercised over other power relations within the social body" (Dreyfus and Rabinow 1983, 220).

Envisioning power as an abstraction of capacity or action puts into sharp relief the severity of children's exclusion from clinical decision-making, especially at the end of life. In a liberal democratic society, governments are charged with contributing to and augmenting human flourishing among its constituents. This might include providing for children when families are

rendered incapable for lack of resources, capacity or other reasons. Such a responsibility exists as children are born entirely dependent beings that rely on the care and guidance of adults (presumably parents or guardians) towards personal independence. Thus the actions—or inactions—of governments in areas such as education and health factor strongly in how children chart their path towards achieving such independence, particularly because children's views are categorically marginalized in the political process. Children do not vote, for example, and therefore cannot exercise—with good reason in some cases—one of the most obvious forms of political agency that democracies afford citizens at the age of majority.

Lending primacy to children's voices is therefore one avenue for respecting their participatory agency. Hart is perhaps best known for his work in this field, describing how child participation can be viewed as a ladder towards an ideal empowerment model. Hart loosely defines participation as referring to "the process of sharing decisions which affect one's life and the life of the community in which one lives. It is the means by which a democracy is built and it is a standard against which democracies should be measured. Participation is the fundamental right of citizenship" (1992, 5). Similarly, Roche supports the idea that "envisioning citizenship as something of greater horizontal, as opposed to vertical, dimension, a society in which children are recognized as important contributors to social structure and organization is possible" (485). Through chronicling a history of citizenship in both political and social theory, Roche presents an argument for a rights-based approach to broadening children's participatory role in commentaries on social and political life.

However just as Foucault maintains the intentionality of power cannot be divorced from its effects, "researchers investigating children's participation might gain important insights by looking at the effects of participatory initiatives, rather than at the professed intentions of the people involved in designing and implementing those initiatives. It might therefore be useful to

make a distinction between discourse – what is *said* or written about participation – and practice what is *done* under the auspices of participation" (Gallagher 2008, 408). Dixon-Woods, Young and Ross (2006) raise similar issues in evaluating the integrity of genuine participation in pediatric chronic illness, namely cancer. Of the limited academic literature that does interrogate the nature of participation in pediatric research, the authors contend that questions have been "debated as ethical or normative principles largely in an empirical vacuum" (175) and can preclude interdisciplinary commentary.

Gallager eloquently weaves co-dependence and negotiated power dynamics within institutions to construct a fitting metaphor for enhancing sociopolitical agency through greater participation:

> If…social structures and the agency of individuals are co-dependent, then participatory initiatives could be seen as an explicit acknowledgement of this co-dependency. To use a spatial metaphor, we could say that participation is the frontier on which the wills of individuals and the wills of institutions directly confront one another, and are forced to acknowledge their mutual dependence. For an institution, the recognition that involving its subjects in decision-making will improve the efficiency of its governance is a tacit admission of that institution's dependence upon the agency of its subjects. For the subjects, the very act of taking part in institutional decision-making likewise constitutes a tacit recognition of the limits of their individual agency, and their need to link into institutional networks to exercise power more effectively. Participation is thus the locus of an ongoing struggle, where the will of an organisation and the will of its subjects engage with and attempt to influence and re-align one another." (15-16).

Qualitative researchers in various child-oriented disciplines (Sumsion et al 2014; Phelan and Kinsella 2013; Willig 2013) propose that a continuous process of reflexivity is critical (Berger 2013) to fostering meaningful engagement in research environments prone to stark power differentials, such as with children and young adolescents. Sumsion et al (2014) give precedence to reflexivity and mindfulness in qualitative research with young children in their assertion that,

> "Being critically reflexive and mindful requires us to interrogate our epistemological and ontological assumptions, the theoretical and methodological resources that we use, the practices in which we engage and the meanings that we assign. It involves looking beneath the surface, going beyond the commonly accepted, being wary of theoretical and methodological fads and attending to power relations and their effects. It also means recognising that our desires to formulate revolutionary ways of seeing (Agbenyega) may blind us to the limitations of those ways of seeing and lead us, inadvertently, to reproduce the social, theoretical and methodological status quo and in doing so possibly exacerbate the inequities that we may have set out to address." (169).

Reflexivity is likewise an important component in an ethical analysis of pediatric research participation as well, insofar as it highlights a researcher's responsibility to be attuned to the context in which their own life and those of their participants are situated: "A consideration of whether special guidelines are needed [in palliative care research] is important because it draws attention to the life circumstances of research participants and our obligations as researchers to them" (Phipps 2002, 102). It would thus be useful to develop unique reflexive tools, like those found in clinical settings (McNeilly and Price 2007), especially for researchers working in the field of pediatric palliative care.

The Ethics of Participation

Many commentators argue children's participation in research raises no ethical issues that are not considered within other realms of research with vulnerable populations (Elliot 1997; Fulford and Howse 1993; High and Doole 1995). While many would equate the 'otherness' of children with those of minority groups or women, Jordonova (1989) insists children are unique: "where children are involved, however, the 'otherness' we assign… is paradoxical in that we have all experienced childhood—hence to make the child other to our adult selves we must split off a part of our past, a piece of ourselves" (6).

While children surely benefit from the scrutiny adult researchers exercise in preventing abuses or unsound scientific methodologies, it should not be assumed that protectionist policies are free of danger. An assumption like this "can be most potent when adults are most convinced of their own disinterested beneficence and of children's dependence" (Alderson and Goodey 1996, 114). Nor do over protectionist stances treat young research participants justly. The Tri-Council Policy Statement: Ethical Conduct For Research Involving Humans 2 (TCPS2), the Canadian federal guidelines on the ethical conduct of human subject research, reads:

> Over-protectionist attitudes or practices of researchers or REBs, whether intentional or inadvertent, can exclude some members of society from participating in research. The exclusion of individuals, groups or communities may constitute a failure to treat them justly. For example, age has been used to exclude individuals from participation in research, particularly health research (e.g., studies that only accept participants between the ages of 18 to 35). As a result, sufficient research may not be done on groups that fall outside of narrow age criteria. The inclusion of the young and the elderly in research, for example, ensures that treatments frequently given to these populations are effective and safe.

Children warrant protection not solely because they are incapable of appreciating the risk dimensions accompanying their decisions, nor because they lack a certain moral compass of their own. In fact, empirical evidence reveals some children as young as nine years old exhibit understanding of projected risks and benefits associated with clinical research participation that meets required competency thresholds outlined in the TCPS and its American equivalent (Ondrusek 2000; Zwiers and Morrissette 1999). Instead, power differentials and implicit assumptions regarding the social, biological and psychological superiority of adults over children (misguidedly) influences the protective instruments used to satisfy ethical mandates for pediatric research, particularly surrounding competency. Alderson and Goodey share this view:

> Competence is not something that lies within individuals, to be assessed in terms of their psychological rationality, so that [childrens'] ethical status can only be predicated upon

> this. That approach sets an agenda about control, and an equality that belongs to rational beings and excludes non-rational ones; children then have to struggle to make this grade. However, children can rearrange the agenda. The rearrangements are neither anarchic nor egotistical in a 'child-centred' sense. They seem to stem from a profound difference, which nevertheless does not belong in biological or psychological (developmental) nature and indeed seems to refute such concepts. The difference lies not 'within' the child or 'between' some adult world and themselves, but in the philosophical positions of all of us." (115).

Moreover, competence cannot be conflated with chronological age[vi]. The chronologisation of development using biological markers (i.e. teething, walking, puberty etc.) "Negates variations in movements through childhood" (Desai 2010, 14) that often characterize moral and social competency. Hart agrees it can be "misguided to use simple developmental stages or age-related norms to determine what children are capable of" (1992, 31). Children's ability to exhibit mature understanding of their terminal illnesses exposes the mischaracterization of children that results from using strict physiological or age normalized markers to define competency (Bluebond-Langer 1978; Kendrick et al 1987).

The notion of child assent—legally and socially distinct from 'consent'—takes into consideration the "variations" Desai identifies by ensuring children's evolving autonomy, their preferences and experiences morally count in decision-making and ought to be respected. These assent processes matter when considering what influences the child's decision to undertake research at all. In an analysis on parental involvement in home-school relations, Edwards and Alldred (1999) maintain children conceptualize their social status—and perhaps the relevance of their participation in research—through three distinct social processes: institutionalization, familialization and individualization. The authors describe the home and school as two institutional spaces whereby children are compartmentalized, and implicitly communicated their social roles. Children's familial dependency is "anchored in their assuming roles as daughters, brothers and sisters, and falling with the social and financial responsibilities of their parents"

(262). Finally, Edwards and Alldred describe the process of individualization, supporting the notion that children "can (and should) be informants on their own lives in social research concerning them" (263). In a palliative care setting, institutionalization and familialization of pediatric patients are both tangible. Children's spaces are compartmentalized, confined to hospital rooms and, in some cases, entire hospitals dedicated solely to the care of children. They can be assigned distinct social roles, typically the vulnerable, sickly child whose needs precede all others within the family. It is the latter social process, individualization, that pediatric palliative care research can be well placed to enhance with more opportunities for targeted engagement of terminally ill patients.

In attempt to parallel theory and practice, Christenson et al (2010) use a case study approach to evaluate the efficacy of the Comfort Care Communication Tool (CCCT), modeled after a similar tool used in end of life decision-making among HIV-positive youth (Lyon et al 2009). Meant to facilitate communication on sensitive topics and to purposefully incorporate adolescent patient perspectives in palliative care decision-making,

> The CCCT uses a four-quadrant design to document the (a) medical, (b) quality of life, (c) contextual, and (d) preferences of the adolescent. The medical quadrant includes information about the disease, its expected trajectory, treatment, and anticipated effects. It also includes the adolescent's and family's understanding of the medical situation. The quality of life quadrant documents activities stated by the adolescent as enhancing his or her life, such as significant relationships, activities, hopes and dreams, and fears and concerns about the future. It is here that the adolescent defines his or her short-term and long-term goals realistically. The contextual quadrant provides health care providers with psychosocial information about this adolescent and his or her life outside of the hospital. This quadrant also includes beliefs and values about life and spirituality, insurance coverage, and use of resources for additional income (e.g., Supplemental Security Income, food stamps, low-income housing, and other eligible assistance). The preference quadrant documents choices with respect to the use of life support measures, transplant options, comfort care, and thoughts of preferred location at end of life. The use of the CCCT provides a forum to discuss difficult topics using open-ended questions and a nonjudgmental approach. Conversations gradually become more in-depth and reflective of personal goals and desires. (Christenson

et al 2010, 288)

The explicit inclusion of adolescent patients (as young as 14) in discussions on matters of quality of life, and greater description of the contextual features that individualize the illness experience, makes the CCCT particularly conducive to the level of engagement advocated in this thesis. The presence of clinicians as well as parents and social workers during these discussions with the patient appears to be one of the only caveats of the model, and which the authors duly acknowledge: "…parents and adolescents together decide who will be present for the discussion. It is not uncommon for adolescents to try to protect parents, and vice versa, from difficult issues that can be highly emotional" (288).

In similar fashion, Wiener et al (2012) reinforce the positive outcomes that can result from involving adolescents (16 years and over) in advance care planning. The study assesses and compares previously adapted advance care planning guide, My Thoughts, My Wishes, My Voice (MYMWMV) to the adult counterpart Five Wishes. The researchers report,

> Terminal illness presents adolescents and young adults (AYAs) with an exceedingly difficult and contradictory challenge: they are dying yet it is their nature ad developmental need to want to live. They are concerned about their lack of achievements and although they believe they should be immortal, they wonder if they will be remembered. The avoidance or lack of conversation about impending death by adults around them creates a sense of isolation, fear and anxiety. AYAs are unclear how to say goodbye or how to communicate how they wish to be remembered. Ultimately, it places AYAs at risk for dying in emotional isolation. The endorsement of the wishes presented in both Five Wishes and MTMWMV as both appropriate and helpful confirms what AYAs living with serious illness contemplate specific end of life issues and want to part in decisions pertaining to their care. (902)

Interrogating 'Participation'

As Hart posits, "While the child's freedom of expression and participation in community issues may often be contrary to the child-rearing attitudes of the child's parents or caretakers, it is ultimately in the best interest of all children to have a voice" (7). Hart implies that for a child to be a social actor or informant in their life is to recognize their participatory agency. Participation, according to McNeish, can have both positive and negative implications for pediatric research participants and the subsequent health policies that affect them (1999). Although it may be intuitive that participation is always welcome, researchers must ensure that children do not feel shame in opting to refrain from participating (in research), or that young participants will be disadvantaged because of their decision. Since willingness to participate in a research study, for example, can be a proxy for self-confidence and self-assurance to discuss personal ideas openly, researchers must also be prepared to accommodate reluctance among some. Furthermore, McNeish cautions against regarding participation primarily as a means to an end—improving palliative delivery in this case. He claims while our "processes might be participatory, the outcomes and knowledge translation remain defined by us, the 'experts'" (202).

Moreover, McNeish claims young people who have had difficult life experiences are "less likely to have the confidence and self-esteem to participate. If their views have not been taken into account in the past they are less likely to be motivated to participate in the present" (200). The negative consequences of qualitative protocols that purport to use more participatory methods must be considered carefully, as they may wrongfully claim participation will not result in any harm; justify any exclusions of young people or their voices; guarantee consent has been obtained without coercion or pressure; and that young people sufficiently understand the dimensions and the scope of their role as a research participant.

Graham and Fitzgerald similarly describe participatory interactions with children as a

unique "dialogic encounter." Using evidence from qualitative studies, they also present a number of factors that children identify as being key to achieving authentic participation (i.e. respect, access to information, and decision-making capabilities though not necessarily full responsibility for the decision itself, to name a few). A useful corollary to the discussion on child assent presented earlier, is Graham and Fitzgerald's idea that recognition be inherent to the goal of achieving authentic participation:

> Neale (2004) suggests, recognition should be viewed as a precondition of children's participation, precisely because it is as crucial to children's well-being as well as their need for care and protection. In terms of translating the conditions and elements for recognition and resilience into possibilities for progressing children's participation, it then becomes obvious that *relationships* with important others (adults and children) potentially feature as a key locus of self-discovery and self-affirmation. Such opportunities are not simply social courtesies but instead constitute a 'vital human need' (Taylor, 1995: 226). At the same time, one hardly needs to add that children do not enjoy a priori recognition nor do relationships with adults necessarily afford them this. Indeed, as Lister (2008b: 13) puts it, 'a common theme in the literature is the lack of recognition and respect for the responsibilities that children exercise'. When participation is postured as intimately connected to the recognition of children and the development of their self- identity, we must therefore also acknowledge that recognition has to be won through an exchange or struggle (Taylor, 1995). This is consistent with Hill et al.'s view that 'almost all discourse about young people's participation refers back at least implicitly to notions of power; less often, however, does that involve explicit identification, clarification and deconstruction of what is meant by power and how power operates' (Hill et al., 2004: 89)." (349)

In addition, the authors offer commentary on ways in which researchers can avoid exploitation of children's voices. They argue to strive toward integrating these perspectives implies drawing attention to a number of issues that impede clarity and resolution of childhood participation. First, the authors assert the characteristic ambiguity that constitutes children's participation as governed by mainstream social and political life. They emphasize there is a "complex interplay between the possibilities and limits of participation that should ultimately stem from the voices of child participants themselves" (343). Finally, the focus on recognition further substantiates the critical role of the dialogic encounter. When used as an approach to augment child participation

based in relationships, it "orient[s] towards children's self-understanding and individual agency, as well as to the self-understanding of the adults involved" (356).

As research methodologies attempt to operationalize the new sociology of the child(hood), Stein argues our notion of 'participation' must too encompass a more rigorous commitment to social citizenship:

> The inclusion of young people implies far more than just giving them the opportunity to "have a say" or "be listened to". These forms of participation, often used in international settings, have been rightly criticized. Participation needs to move beyond a decorative element and the occasional display of good will. Inclusion of young people implies a widening of the concept of participation to a concept of active citizenship…The concept of citizenship indicates a collection of rights and responsibilities that all members of a community have, and all members of this community are enabled to exercise these rights through democratic action (Smith et al). Such a truly democratic approach, or radically democratic as some refer to it, is a logical consequence of the new childhood paradigm if the notion of agency is to be strived for in practice. (9)

Roche similarly cautions against the rosy depictions of greater pediatric engagement and participation, and implies a firm approach to ensuring its implementation in practice. With proper attention to the context in which pediatric involvement is being recommended, Roche maintains,

> An increasingly inclusive politics for children will require only the proper resourcing of practices which are supportive of children's citizenship claims and those of institutions which contribute to such claims. We need to think through the terms on which participation is being offered, to be aware of the context in which children are being 'invited in' and risk of responsibility for making a decision being thrust upon children in circumstances not of their choosing. The languages of participation and empowerment are cosy but we need to be more critical of the circumstances of inclusion and the kinds of adult support (i.e. advocacy and representation) that children might need. In this sense the children's rights project and emerging demands for 'inclusion' as citizens involves a redrawing of what it is to be an adult and a child (487).

In Chapter III, this thesis applies—and indeed redraws—an inclusive politic of engagement with terminally ill children and adolescents. It will explore the ethics of qualitative research that

engages children and older adolescent in assessing HRQoL during the course of palliative care.

Chapter III

The Ethics of Engagement: Pediatric Health Research in Oncology and Palliative Care

"To die will be an awfully big adventure."

—J. M. Barrie, *Peter Pan*

It is fitting to precede the ethical analysis of pediatric qualitative engagement with a modern historical account of pediatric research abuses in the last half century. Discovery of such widespread abuse triggered reform to subsume pediatric populations under the remit of existing research ethics guidelines, and heightened awareness of the characteristics that predispose children to situations of special vulnerability in research. This chapter will consider the Ethics of Engagement (EoE), a case study analyzing the ethical permissibility of a qualitative research protocol on HRQoL among newly diagnosed children with brain cancer. The case study will interrogate the study-specific notions of minimal risk, vulnerability and differentiation between therapeutic and non-therapeutic research procedures in accordance with the ethical frameworks outlined in the Tri Council Policy Statement 2: Ethical Conduct for Research Involving Humans (TCPS2). Finally, this chapter analyzes the ethical challenges and questions that arise in pediatric oncology, where both research and therapy are frequently combined under the auspices of patient care. Regulatory guidelines from jurisdictions in North America (United States, Canada and the province of Quebec), as well as international declarations from the United Nations Educational, Scientific and Cultural Organization and the International Bioethics Council, are provided as

ethical justification for research with pediatric palliative care participants.

Pediatric Research: A History of Abuse

Until well into the 1950's and 60's, institutionalized children were disproportionately recruited for clinical research (Lederer and Grodin 1994). In 1966, Henry Beecher effectively exposed the inhumane ways in which the clinical research enterprise was built on the involuntary participation of vulnerable populations, including children (Beecher 1966). In the wake of reported human subjects violations like those at Willowbrook and the Fenald School, the regulatory landscape of clinical research changed dramatically (Kahn, Mastroianni, Sugarman 1998). The spirit of pediatric research ethics and social attitudes towards the permissibility of children in research has been likened to a swinging pendulum (Carroll and Guttman 2011). The pendulum metaphor describes the degree of protectionism in pediatric research, which oscillates between over protectionism at one extreme, to overt coercion and exploitation on the other.[vii]

Earlier work of the United States National Commission for the Protection of Human Subjects codified three basic principles for human subjects participation: respect for persons, beneficence and justice. Caroll and Guttman provide one of the only historical chronicles of the discussions and debates concerning the issue of pediatric research participation. The resultant set of guidelines produced from those negotiations was eventually featured in the Belmont Report in 1978. Caroll and Guttman note, "The National Commission's discussion of research on children took place in an era when attitudes about children and adolescents were changing, and when notable transformations in how young people were treated came about as a result" (2011, 85). The Commissioners were charged with striking an appropriate balance between facilitating the necessary research poised to benefit pediatric populations, while prohibiting a repeat of historical

abuses. Many of the most pressing ethical concerns at the time remain foremost issues currently, namely children's inability to consent, their burgeoning autonomy and acceptable levels of risk. Caroll and Guttman further discuss the historical backdrop against which discussions of pediatric research participation took place, and the inevitable significance this had on the moral theories invoked to defend the Belmont Report:

> All this debate took place in another context, this one a scholarly discussion of what was then a newly discovered history of childhood that was reformulating notions of childhood and children's autonomy vis-à-vis parents and the state. During one of the Commission's meetings, biomedical ethicist Albert Jonsen cautioned his fellow members, noting that: One of the most important things that we have to do as we proceed in these studies is to begin to consider the nature of the child as a moral being, as a person as it were. It seems to me it is a very peculiar thing that in our culture really very little explicit attention is paid to the ethics of dealing with children. We live with the kind of an ethical tradition where discussions of ethics always presume that the other is an autonomous being capable of responding with freedom and intelligence to actions made toward them, and therefore the child is a kind of an ethical anomaly in our culture . . . Is the child an autonomous being? Are our obligations toward the child primarily protective or primarily fostering and do children have moral obligations . . . (2011, 85)

With that, Jonsen sparked what would become an important theme in contemporary research ethics discourse from which children have emerged as a population worthy of special reflection and continued interest.

Is Palliative Care Research Ethical?

Integrating palliative care only once a child's prognosis is considered extremely poor is to ignore the many children who could benefit from identifying palliative needs at an earlier stage in their care (Flint and Weidner 2012; Glare, Eychmueller and McMahon 2004; Ripamonti, Farina and Garassino 2009). Indeed, Viallard sheds light on the significance of this: "It is not on the verge of death, during the last moments of life, that we can take the measures that could have meaning and comfort. Rather, it is early on in life, as part of the treatment approach, precisely in

order to preserve a sense of life and deliver the right kind of shared care that an invaluable tool should be offered to patients, parents and professionals alike" (31).

The tendency to delay palliative care until the final stages of life renders immediate the qualitative, as well as quantitative clinical research initiatives aimed at expanding the provision of these care services to optimize HRQoL for children with both life limiting and life threatening conditions. According to some investigators, qualitative methods present the best methods for embarking on in-depth study of palliative care (Wilkie 1997), though must still undergo methodological evaluation for reliability and validity (Strang 2000). Unlike most scientific research, however, the use of qualitative methods "comprises a particular way of seeing and a framework for a certain kind of research ethics in which subjective experience is acknowledged and harnessed" (Clark 1997, 159). Accordingly, it presents researchers with a wide range of challenges, many practical (Morse 2012), political (Thompson et al 2009), and some that do not arise within other realms of clinical research.

For many, such research initiatives raise unresolved ethical concerns. Perhaps one of the most vocal opponents to palliative care research generally, De Raeve (1994), asserts,

> We are going to have to think of some compelling justifications to permit research on dying people, and perhaps for some no justifications will do. To research at all into the needs and experiences of this client group could be said to be an affront to the dignity of those people who are terminally ill and expression of profound disrespect for the emotional and physical state of such patients. (301)

Employing a strictly deontological ethics framework, Raeve rejects the objectification of the terminally ill patient in palliative care research, whom Raeve posits is inappropriately used as merely the means to a research end. Others, however, consider "this strictly dichotomous view does not give due regard to the heterogeneity of the patient population, the dynamic nature of dying, and the relative risks and benefits of different modes of investigation" (Jubb 2002, 345;

see Mount 1995). In their attempt to clarify the problematic ethical questions in palliative care research ethics, Casarett and Karlawish (2000) opine:

> At the heart of this debate is the question of whether palliative care research creates new or unique ethical challenges. The answer to this question will have important implications for the design and conduct of palliative care research. If palliative care research does raise unique ethical issues, then special restrictions, protections, and guidelines should be considered. If it does not, then the strategies devised by investigators in other fields will suffice to protect subjects and special guidelines are not necessary. (130-131)

In line with the authors' latter view, a deontological ethic of participation should not uniquely apply to the terminally ill patient or to palliative care research alone. Nor should it be taken as universal—and can be considered disrespectful even—that terminally ill pediatric patients are categorically fragile, incapable of decision-making and warrant the paternalistic gaze of a healthcare team or incumbent researcher (Ross 1997). Rather this thesis argues, as Ling, Reed and Hardy (2000) do, that "Good quality quantitative research in palliative care is difficult, but not impossible. To be successful, it is essential that studies are designed to suit the particular characteristics of the patient population under study" (626). Bluebond-Langner et al (2010) likewise endorses research authenticity achieved through involving child patient-participants in a clinical setting: "The value of a requirement to involve children in decision making about their care and treatment underscores the importance of talking to and listening to a child at a time when it can be extraordinarily difficult to do so" (338).

Indeed, many researchers defend that some research participation in studies at the end of life may offer particular emotional and therapeutic benefit (Skinner and Bosley 1995; Davies 1998; Gysels, Shipman and Higginson 2008). While Ulrich (2005) points to a limited knowledge based that such benefit exists, Beaver et al (1999) maintain "The potential benefits to vulnerable persons of being involved in [qualitative research] may not be immediately obvious although

altruism, in wanting to help others in a similar situation in the future, and the therapeutic effect of telling one's story may have indirect benefit for some. However, it may not be possible for the researcher to ever fully ascertain the actual benefit and harm incurred in carrying out such work" (13).

The rest of this chapter will explore ethical tensions implicit in qualitative engagement with children and adolescents with terminal cancer, including exposing them to risks, assessing potential benefits and other research considerations. Such tensions arise in identifying how best resolve two ethical imperatives in pediatric research: that children should not be excluded from research endeavored to benefit them directly, but they nevertheless warrant special measures to protect them from risks associated with research participation. The subsequent sections will discuss how despite these underlying tensions, pediatric research has been imperative to the discovery of child-specific therapies in pediatric oncology and, with greater advocacy, palliative care. The theoretical and evidence-based overlap between research and therapy in the pediatric oncology context is provided as an example.

The Clinical Research Imperative in Pediatric Oncology

Few clinical specialties reside at the interface between research and care like in pediatric oncology (de Vries et al 2011). Clinical investigations combining research and therapy create a unique nexus that augments (Caldwell et al 2004) innovation in child-specific cancer therapies and standards of care (Unfuru 2011). Hence "pediatric oncology professionals have both a duty and an opportunity to take a leadership role in applying ethical principles and practices to the conduct of clinical research" (Joffe et al 2006). The past fifty years in coordinated research activities within pediatric oncology have witnessed increases in five-year cancer survival rates

that now exceed 80 percent (National Cancer Institute; O'Leary et al 2008). Medical progress in this context can be partially attributed to the increased enrollment in ongoing clinical trials (Pui et al 2011) where an overwhelming number of American pediatric oncologists consider access to state of the art treatment the primary reason for enrollment (Joffe and Weeks 2002). While only a small percent of adult cancer patients opt to enroll, nearly 70 percent of child cancer patients participate in clinical research. Insofar as clinical trials potentiate the only possible therapeutic benefits in cases of rare pediatric and adolescent cancers, the ethical policies invoked to govern research and clinical care separately can be blurred. In a discussion of the intended benefits of participating in pediatric oncology research, Caldwell et al (2004) write,

> The benefits for the participants of paediatric cancer clinical research are numerous and include the rigorous process of protocol development, incorporating review at many levels and incorporating best practices, commonly centralising pathology review and radiation therapy planning, and mandating close adherence through audits and review of performance. Response and toxicity are closely monitored and pooled through a unified database, and investigators develop long-term research relationships, often undertaking a series of clinical trials. This creates a powerful empirical force for adjusting treatment regimens and improving outcomes in each subsequent trial, which, together with widespread participation in trials, has created a culture in which there is almost a fusion between clinical research and clinical practice in paediatric oncology. (808)

The nexus forces reconsideration of the ethical principles that distinguish each, and how it integrates—rather than compartmentalizes—activities that produce generalizable knowledge and the delivery of high quality, innovative care to young people. For, "Where there are only unwelcome options, prohibiting participation in well-conceived clinical trials can be an injustice" (Kipnis 2003, 108). The following case study will explore the nuances of these ethical considerations in depth.

Ethics of Engagement in Practice

Between 2005 and 2009, Canadian Cancer Statistics identified the leading cause of childhood cancer-related deaths were cancers (including glial tumors) of the central nervous system (34%) (Canadian Cancer Statistics, 2013), surpassing leukemias (Fontebasso, Bechet and Jabado 2013). Among these, high-grade astrocytomas (HGA) and glioblastomas (GBM) continue to be responsible for the majority of brain tumor cases, and affect approximately 300 children and young adults in Canada annually (Canadian Cancer Statistics 2013). There is currently no cure for pediatric HGA, and 10% of newly diagnosed patients survive 2 years past diagnosis (Dolcek et al 2012; Jansen et al 2012). As such, CNS brain tumors, including HGA, carry the highest rate of mortality among all childhood brain cancers. Limited research on child morbidity using HRQoL assessment indicates this patient population consistently reports low on HRQoL measures (Sato et al 2013; Penn et al 2010). Despite allocating approximately $150,000,000 CAD in tertiary care resources, ninety percent of patients die within three years of diagnosis. To date, HGA tumors remain incurable largely due the unresponsiveness of certain types to radiation therapy (Geyer et al 1995), invasive surgical procedures or toxic anti-tumor drugs. Not surprisingly, these ineffective interventions levy substantial financial and emotional burdens on young patients, their families and the healthcare system. Such burdens are exacerbated by the hastened death of children with progressive HGA, paucity of therapeutic options and the limited availability of pediatric palliative care services.

Until recently, the genetic architecture of HGA tumors was unknown. In 2012, a team of clinical researchers and oncologists aggregated tissue samples and international expertise to establish the **I**nternational **CH**ildhood **A**strocytoma **IN**tegrated **G**enomic and **E**pigenomic (iCHANGE) Consortium, a revolutionary initiative to better understand the mechanism and clinical profile of HGA in children and adolescents. One major research development has been

the identification of recurrent somatic mutations in histone 3 variants (H3.1 and H3.3) in a significant fraction of children and young adults with HGA (80% of midline HGA including diffuse intrinsic pontine gliomas (DIPG and up to 30-40% of cortical pediatric HGA). According to iCHANGE investigators, these histone genes are involved in regulating all body processes and biological functions are they are part of the chromatin core. Importantly, H3.3, a replacement histone, is actively loaded in the developing brain and seemingly involved in brain development n. It is thought these mutations partly explain why certain diagnosed HGA patients are unresponsive to conventional cancer treatments, despite relative homogeneity of the tumors under a microscope and other imaging techniques.

The iCHANGE consortium has since discovered four primary mutations intrinsic to pediatric HGA. Findings indicate recurrent mutations in brain tissue result in major changes to the chromatin architecture that affect lysine K27 and 36, two critical residues in the histone 3 variant 3 (H3.3) (Schwartzentruber et al 2012). They further proved H3.3 mutations exhibit high correlation with specific patient age ranges and neuroanatomical localization (Sturm et al 2012). That is, certain tumors appear more frequently in children of a specific age, likely paralleling various stages of brain development in children (Khuong-Quang et al 2012). Importantly, 40% of children with HGA harbor the K27 mutation that remains resistant to all known therapies, and are subsequently identified as early candidates for palliative care (Khuong-Quang et al 2012; Sturm et al 2012).

Together, these findings represent an unprecedented leap in characterizing HGA pathology, and a first step in the development of a laboratory test to personalize effective therapy based on the child's specific tumor type. The diagnostic test will eventually help stratify children based on their mutational status. It will enable scientists to further study the downstream targets of specific tumor mutations amenable to treatment—currently in experimental phases—that demonstrate the

greatest potential for improving survival rates in HGA patients. The hope is that with the help of next generation sequencing, diagnostic tools can be developed with greater sensitivity/specificity to isolate the genetic composition of tumor types, and direct treatment targets of greatest promise for patients. Next generation sequencing (NGS) will allow researchers to identify robust biomarkers and genetically subgroup HGA patients to optimal treatment strategies. NGS thus portends effective integration of personalized medicine in the pediatric oncology setting; changes to clinical best practices; and redirection of future clinical trial designs to make greater use of genome diagnostics.

Until curative therapies are developed and validated in clinical trials, pediatric palliative care will play an almost exclusive role in the care of HGA patients who are diagnosed with the K27 mutation. Improving palliative care modalities through qualitative research on HRQoL in children is therefore essential. In order to achieve this, knowledge translation (KT) researchers have also joined the iCHANGE consortium to better understand the unique illness experiences of young patients with HGA and their families. Through a qualitative research vehicle, they aim to i) identify salient factors that augment, as well as impede, HRQoL in children, ii) solicit the views of stakeholder communities on the theme of therapy de-escalation and its relation to HRQoL and iii) define the ways in which the proposed diagnostic test to determine the specific HGA variant will factor, or not, in clinical decision making pathways. These questions are motivated by the fact that it is currently unknown what parents and children value in HRQoL while receiving palliative care.

The translational aspects of the diagnostic test and its impact on the existing care practices for pediatric HGA and palliative care are still yet to be determined. As clinicians alter current standards of care to reflect the new therapeutic approaches to pediatric HGA—including

palliative care for the K27MH3.3 mutation—researchers will need to better understand how children's clinical experiences are affected in turn.

Pediatric patients—along with their parents and clinicians—represent crucial stakeholder groups in the evolution of new standards of care for HGA. Based on Fishkin's model for deliberative consultation[viii], iCHANGE researchers plan to engage terminal HGA patients aged 7-16 in qualitative discussions on their HRQoL post-diagnosis and tumour typing. Researchers ultimately hope to translate children's perspectives on optimal HRQoL into palliative best practices that reflect these views.

Fishkin's public engagement methods must satisfy two fundamental criteria: political equality and deliberation. Political equality refers to when the "public," in this context the pediatric HGA patients, have equal participatory involvement in the policy decision, or the new standards of care in treating HGA. One method for achieving political equality is to recruit all individuals in the target population of interest, in this case the pediatric HGA community in the greater Montreal area. It is estimated 6-10 children will be recruited to participate.

On the day of the deliberation, the participants will hear a presentation on the disease, the genomic test and the concepts of quality of life. A clinical child psychologist will then serve as the small group facilitator to encourage the participants to reflect, share and communicate their experiences and HRQoL perceptions. It is estimated this deliberation will last approximately 45 minutes. It is important to note, only children capable of verbal communication and who do not suffer from severe cognitive disabilities will be recruited. As a result, this exclusion criterion presents one notable study limitation in representing the widest stakeholder community possible of pediatric HGA patients.

While a defense of Fishkin's deliberative democratic theory is beyond the scope of this thesis, the participatory spirit of the deliberative consultation method will be a lens through

which to discuss the research ethics implications of engaging terminally ill children in oncology and palliative care research.[ix]

Risk and Benefit

An important consideration in any research ethics analysis, let alone involving children, is the evaluation of risks and benefits. The classic ethical tensions arising in pediatric research (that children should not be excluded from research endeavored to benefit them directly, but nevertheless warrant measures to address their situation(s) of vulnerability) have been published extensively in the academic literature, and are often centerpieces of ethical discourse surrounding permissible risk-benefit evaluations. Recognition of these tensions motivated a number of federated guidelines (World Medical Association; Directive 2001/20/EC; Royal Australian College of Physicians; National Institute of Health), establishing risk thresholds for pediatric research participation. These bodies determined some risks are justified—even necessary—to reap any benefits of the research itself. As the Belmont Report states, "[E]ven avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm…Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks" (The United States National Commission). Depending on the jurisdiction, a balanced evaluation of risk thresholds and anticipated benefit is performed using slightly different criteria. A cross-jurisdictional overview of the guidelines from the U.S., Canada and Quebec is presented in **Table 2**.

For example, the U.S. Department of Health and Human Services (DHHS) minimal risk classification permits certain research participation commensurate with potential therapeutic benefit (Department of Health and Human Services). In 1983, protections for children involved as subjects in scientific research were included in subpart D 45 CFR Part 46. The federal provisions categorize four levels of risks in which research with children are permissible. The notion of 'minimal risk,' however, spurred considerable debate within the medical and research communities, which challenged the universality of the proposed standards across such a wide range of childhood circumstances. These risk distinctions were later clarified in a report by a special Institute of Medicine (IOM) committee in 2004, where Field and Berman (2004) write,

> Consistent with the conclusions of a number of other groups, the committee rejected an interpretation of minimal risk that would allow greater research risk for children exposed to higher than average risk of harm in their personal lives (e.g., because they are ill or live in unsafe neighborhoods). This "relative" interpretation misinterprets the minimal risk standard and undercuts its moral and social purposes for pediatric studies, which are to guide judgments about when risks are low enough to safely and ethically enroll children in studies that are not designed to benefit them. The assessment of risk should be compared or indexed to the experiences of average, normal, healthy children. (5)

Most participation in pediatric oncology research in the U.S. is approved under the second provision of the DHHS (see **Table 2**), and involves studies that take the form of single-agent, nonrandomized trials (Berg 2011). Clinician-investigators justify exposing children to greater than minimal risks when there are anticipated therapeutic benefits and/or patient participation yields information that is crucial to elucidating novel therapeutic treatments for children, specifically. As such, the most promising treatment for rare childhood cancers is oftentimes delivered through a research vehicle, substantiating the research imperative in pediatric oncology discussed earlier.

A similar "threshold concept" of ethically permissible risks also appears in policies dictating children's participation in research in Canada, where the regulatory equivalent of the DHHS guidelines is the Tri Council Policy Statement 2: Ethical Conduct for Research Involving Humans 2 (TCPS2). A comparison of the different conceptualizations of minimal risk is provided in the ethical analysis later in the chapter. A 2010 revised version of its original release in 1998, the TCPS2 now includes an revised chapter on qualitative research-specific guidelines that are relevant to the proposed study designs discussed in this thesis to engage terminally ill children.

Moreover, a recent modification to Article 21 of the Civil Code of Quebec reduced the minimum age of consent to minimal risk research:

> Consent to research that could interfere with the integrity of a minor may be given by the person having parental authority or the tutor. A minor 14 years of age or over, however, may give consent alone if, in the opinion of the competent research ethics committee, the research involves only minimal risk and the circumstances justify it (Quebec Civil Code 2013, c. 17, s. 2.)

This clause specifically is timely and relevant to the EoE study, as it permits young, potential participants (14 years of age or older) to consent for themselves. As a result, they will be legally afforded the right to weigh the potential risks and benefits of their participation in the study. Because over-reporting of parental proxies in pediatric palliative care research has been cited as a barrier to studying HRQoL in children, modification to consent regulations may have a positive effect on participant recruitment and encourage further research in this area.

Classification and Justification

Component analysis, one risk-benefit classification framework proposed by Weijer (2000)

justifies certain risks incurred during the research process by differentiating between therapeutic and non-therapeutic research procedures. These procedures are individually governed by different ethical standards. Historically, the sum total of a research protocol was classified as either therapeutic or non-therapeutic research. This poses particular challenges, however, for protocols that combine both research and clinical care, as most protocols approved in pediatric oncology often do. Therefore, it better serves the ethical analysis to distinguish between therapeutic and non-therapeutic *interventions*, an approach the component analysis framework promotes.

According to Weijer (2000), the component analysis framework defines therapeutic research procedures as those in line with the standard of care the patient would receive regardless of their participation in a research protocol. These activities have a therapeutic intent and could include, for example, the administration of drugs or conducting imaging or surgical procedures. In contrast, non-therapeutic research procedures are those administered strictly to answer the research question at hand. Such interventions might include extended patient interviewing, extra blood draws or x-rays not included as part of the standard of care. That is, these interventions are performed strictly for research purposes. Both therapeutic and non-therapeutic procedures together ultimately support the production of generalizable knowledge in research. While not every protocol involves therapeutic procedures, it is a defining characteristic that all research protocols involve non-therapeutic procedures. This point will be taken up further in the corresponding analysis of children's engagement in qualitative research investigating self-reported HRQoL.

Component Analysis: Non-therapeutic vs. therapeutic

Using the component analysis framework, this section considers the ethical implications of involving terminally ill children's in a qualitative study on HRQoL in a pediatric palliative care context. For the purposes of this analysis, the study will be referred herein as the Ethics of Engagement (EoE). Furthermore, a glossary of terms adopted by the TCPS2 and Canadian Panel on Research Ethics is provided in **Table 3**. For reasons discussed in more detail below, providing ethical justification for qualitative inquiry of terminal illness in children requires addressing the vulnerability of the participant population, the sensitivity of the topic under investigation, and the clinical import of the inquiry itself to improving palliative medicine in children. Although the bioethical principles governing clinical trials, for example, are operationalized differently in qualitative research, the underlying themes are nevertheless salient. It is anticipated that respect for persons, beneficence/non-maleficence and justice trigger passionate responses, and often concern, about how pediatric research ethics guidelines are interpreted, and how populations should be treated in the context of research.

In the Quebec Civil Code, two requirements must be met in order to justify their children's participation in research: i) the risks associated with the protocol must not be disproportionate to the anticipated benefits and ii) in the case of research with vulnerable groups, there must be a potential benefit for each participant, or others in the same age category who have the same illness or disability as the participants. Justification hinges in part on not exceeding the established minimal risk thresholds for the therapeutic/non-therapeutic procedure classification.

The first element in Weijer's component analysis is determining which procedures are therapeutic, and which are non-therapeutic. Although a positive psychosocial improvement in children may be incident to participation in the EoE protocol, targeted discussions of self-reported HRQoL led by researchers and/or in the presence of other children are explicitly done for research purposes and are therefore considered non-therapeutic. While assessment of HRQoL

may certainly be in the scope of discussion topics with a palliative care clinician and perhaps as part of standard of care, the structure around, and conduct of, these discussions places them under the auspices of non-therapeutic procedures performed for the explicit purpose of answering the questions of the EoE protocol. As such, Weijer posits,

> By definition, risks associated with non-therapeutic procedures cannot be justified by the prospect of benefits to individual research subjects. Hence, a risk-benefit calculus is inappropriate to assessing the acceptability of these risks. The IRB must first ensure that the risks associated with non-therapeutic procedures are minimized…Second, the IRB must ascertain that the risks of such procedures are reasonable in relation to the knowledge to be gained…Thus, the ethical analysis of risks associated with non-therapeutic procedures involves a risk-knowledge calculus. The knowledge that may result from a study is essentially its scientific value. Freedman has argued that the proper assessment of the scientific value of a study requires not only the opinion of experts from relevant disciplines, but also the opinion of representatives from the community at large. (355)

Using Weijer's classification of non-therapeutic research procedures, ethical analysis of the EoE study centers on the anticipated utility of the knowledge generation and its associated risks.

Component Analysis: Determining Minimal Risk

Justification of the risks follows classification in Weijer's component analysis, obligating researchers to ensure the protocol minimizes all risks. Moreover, researchers and ethics committees alike must scrutinize, among others, the proposed methodology to determine whether the risks incurred are indeed as a result of a study that is scientifically sound in its ability to answer the proposed research question(s). With respect to the EoE protocol, will the non-therapeutic procedures outlined by the principle investigators in fact lead to an in-depth understanding of terminally ill children's perceptions of HRQoL? Is it possible to generate the same, or likewise useful knowledge by employing a methodology with lesser risks of harm? In order to answer these questions, the researcher(s) must counter balance the risks associated with

the methodology, and the benefits this patient population—and potentially future populations—might receive in the form of improved palliative care delivery.

In considering qualitative research, including the EoE protocol, it is important to note preventing *physical* risk of harm does not preclude the possibility of *psychosocial* risks that may result from research participation. The latter presents the most immediate type of risks participants in the EoE may experience. Qualitative research procedures that give rise to these risks may include, but are not limited to, in-depth interviewing about sensitive topics and extended interactions with unfamiliar (adult) personnel and/or environments. Young participants may feel overwhelmed or highly emotional reflecting on their illness experience, contemplating the implications of death and the dying process, and discussing their end-of-life preferences during the deliberative consultation. Since many of the discussions will be conducted outside familiar settings, the unfamiliar environment may exacerbate uncomfortable feelings. Additional risks may include those associated with the participant's mobility or fatigue. These are case-specific considerations that should be discussed in the consent/assent process with the participant and his/her proxy. To minimize these risks, appropriate services must be made available to participants. Clinicians should be readily accessible if research participation becomes too physically demanding for participants, and counselors prepared to accept referrals from the study investigators in the event the participant(s) are adversely affected as a result of their participation.

As presented earlier, minimal risk classification in the United States is determined by those general events or circumstances that an otherwise healthy child would endure in daily life. In contrast, the minimal risk threshold in Canada is contextualized based on the life circumstances of the proposed research population. Using the Canadian classification, a minimal risk threshold for terminally ill children might differ considerably from a threshold appropriate

for an otherwise healthy pediatric population. To illustrate this, consider a research protocol whereby children are recruited to a sleep study and in which they must be admitted to the hospital overnight. While this may pose a substantial risk, among others, of psychosocial distress on a child who is not familiarized with a nosocomial setting, this same procedure might pose a lesser risk for a chronically ill child who is frequently hospitalized. It can be argued, therefore, the EoE protocol that requests a child participant discuss their HRQoL in the context of their terminal illness might pose a lesser risk of psychosocial harm than asking healthy children to imagine the possibility of their death.

Perhaps surprisingly, empirical evidence suggests positive psychosocial benefit to openly discussing sensitive topics in the context of research (Scott et al 2002). In a retrospective, qualitative study of pediatric patients with Ewing's carcinoma, Scott et al endorse child participation in research that addresses potentially sensitive or distressing subject matter. Others too testify to the personal benefits of qualitative interviewing (Smith 1999; Hutchinson, Wilson and Wilson 1994), including its cathartic, meaningful and empowerment-inducing outcomes for participants.[x]

Component Analysis: Vulnerable Populations

Due to their age and prognosis, terminally ill children are considered individuals in situations of special vulnerability that warrant caution with respect to their participation in research. Nevertheless, the exclusion of groups with special vulnerabilities from research that could yield important benefits for the group is duly unjust, according to justice framework proposed in the TCPS2. According to jurisdiction, the risks imposed on vulnerable populations must not exceed a minor over minimal risk (see **Table 2** for specific regulatory guidelines).

Researchers who intend to recruit participants in situations of vulnerability must be mindful of additional ethical obligations that include, but are not limited to, recognizing the source of vulnerability, addressing this source, and employing special protections that attenuate it. In this regard, assessing the nuances of participant vulnerability as it relates to terminally ill children is necessary.

The International Bioethics Committee (IBC) of UNESCO released a thematic report on vulnerability following adoption of the Universal Declaration of Bioethics and Human Rights. It highlighted the significance of Article 8[xi] in responding to ethical issues surrounding research with participants in situations of vulnerability (UNESCO 2011). The IBC sought to reinforce the permanence of Article 8 in guiding the ethical conduct of research generally, but more importantly in bridging the concepts of vulnerability and personal integrity in special populations. The IBC report begins,

> The human condition implies vulnerability. Every human being is exposed to the permanent risk of suffering "wounds" to their physical and mental integrity. Vulnerability is an inescapable dimension of the life of individuals and the shaping of human relationships. To take into account human vulnerability acknowledges we all may lack at some point the ability or means to protect ourselves our health and our well-being. (2)

It is true that even patients who exemplify standards of physical and cognitive capacities for decision-making are vulnerable to the extent that they submit and expose their bodies to the professional expertise of a treating physician. In research, the absence of a prima facie duty to act in the best interest of the patient renders a different kind of vulnerability, for which other ethical guidelines apply. These guidelines are in part motivated by a fear that a "researcher's (or society's) understandably strong desire to pursue useful generalizable knowledge gives rise to the temptation to under protect or ignore the participants' wellbeing" (4).

Yet the IBC report goes further to note, "special vulnerability in the scope of Article 8 means that there are individuals and groups that are especially prone to violation of personal integrity, disrespect for autonomy, due to exploitation, deception coercion and disregard through the application and advancing of scientific knowledge medical practice and associated technologies" (13, Article 41). It is in this context that an assessment of terminally ill children's vulnerability should be situated. In order to provide a "more useful conceptual machinery to the pediatric medical research subject" (108), Kipnis (2003) outlines seven avenues by which vulnerability could manifest in conducting research with children and could affect the ethical permissibility of endorsing their participation:

1. **Incapacitational**: Does the [pediatric candidate-subject] C-S lack the capacity to deliberate about and decide whether to participate in the study?
2. **Juridic**: Is the C-S liable to the authority of others who may have an independent interest in that participation?
3. **Deferential**: Is the C-S given to patterns of deferential behavior that may mask an underlying unwillingness to participate?
4. **Social**: Does the C-S belong to a group whose rights and interests have been socially disvalued?
5. **Situational**: Is the C-S in a situation in which medical exigency prevents the education and deliberation needed to decide whether to participate in the study?
6. **Medical**: Has the C-S been selected, in part, because of the presence of a serious health-related condition for which there are no satisfactory remedies?
7. **Allocational**: Is the C-S or proxy lacking in subjectively important social goods that will be provided as a consequence of participation in research? (110)

Although not necessarily explicit to the terminally ill pediatric population, ethical and circumstantial reasoning can make a case for many of these vulnerabilities in the context of the EoE protocol. Like Kipnis, I will consider both incapacitational and juridic vulnerabilities together. Kipnis maintains that evaluating whether these vulnerabilities are relevant requires taking into considering the child's maturity in deciding to participate (or not) in the study, as well as the parental scope of authority to make this decision on behalf of the child. The dilemma

researchers face is therefore the possibility they "erroneously accord weight to the preferences of a minor who lacks pertinent adult capabilities, or can erroneously defer to a parental authority that importantly disregards a minor's interests and reasonable goals" (112). Certainly this threat is clear in considering EoE. It is possible the parents of younger patients may mischaracterize their children's ability to participate comfortably in HRQoL discussions, or conversely, impose overprotective limitations on their ability. In the case of the latter situation, the opportunity cost is the authenticity and value of the knowledge the child could contribute to pediatric palliative care. Kipnis claims the main populations of concern for incapacitational and juridic vulnerability are thus "uncaring or misguided parents, immature children, and enterprising researchers will subject minors to unwholesome research programs" (113).

Next, the issue of deferential vulnerability makes central a focus on the relationships between researcher, clinician, or a clinical-researcher, and the child. Regardless of the precautions a researcher, clinician or parent may take to ensure children know their participation in entirely voluntary, deferential vulnerability may render terminally ill children more susceptible to the social hierarchal pressures and power dynamics between them and the adults they encounter. Kipnis asserts, "The challenge is to devise a process that eliminates as much as possible the social pressures that a candidate-subject may feel even if, in reality, they are not being imposed" (114). One can imagine it might be difficult for a child to express unwillingness to participate in a study both his/her clinician and parent encourage. Further, children are not the only potential subjects of deferential vulnerability. Parents too could exhibit this vulnerability, especially if trusted clinicians are responsible for approaching and/or explaining to them the benefits of providing consent for their children to participate in the study. In general, however, clinicians are rarely permitted to do so. Clinical research coordinators or other administrative personnel are expected to maintain an impartial front precisely for such reasons. Therefore one

approach to minimizing this power differential and its potentially coercive impact on participant recruitment is for the clinician-investigator to distance him/herself as necessary from recruitment procedures, and enlist the support of third-party personnel like research coordinators or other educators.

Perhaps most relevant to previous chapters detailing the social construction of the child(hood) and its implications for recognizing participatory rights, Kipnis' notion of social vulnerability gets at the exclusions children endure "in our society, [where] knowledgeable beneficence toward children can be taken for granted" (114). In this way, ageism—prejudice or discrimination on the basis of age—in research can invite social vulnerability, albeit unintentionally and for protectionist purposes, just as gender or ethnic discrimination. Moreover, prevailing physiological, psychological or other age-related stereotypes can threaten researcher and ethics committee's willingness to conduct and review protocols involving children, respectively. Like other historically disenfranchised groups, the rights and needs of terminally ill children as a specific social group, though certainly individually unique, can be ignored or brought under the management of other social authorities. This prevents pediatric palliative care from becoming the province of children's expertise.

The responsibility to counteract the adverse effects of social vulnerability is likewise included in the IBC report. While the UNESCO Declaration implies a duty on the part of member states to prevent the exploitation of populations in vulnerable situations—as well as threats to their dignity—the IBC report adds, "We are compelled to act in a positive way to help people cope with the natural or social determinants of vulnerability" (2, Article 10). In its attempt to end terminally ill children's exclusion from HRQoL research in palliative care, the proposed research employs methods of engagement to diminish the social vulnerability this population routinely experiences.

Because the EoE study does not involve matters of medical exigency that prevent an informed deliberation about the child's ability to participate, the situational vulnerability is less applicable in this case. Researchers involved in the EoE protocol will approach children soon after diagnosis, rather than at the final stages of terminal illness when they are often weak, or when symptoms prevent them from feasibly participating. Similarly, the medical vulnerability is not a prime consideration in this group either. Although pediatric palliative care patients suffer from an incurable infirmity, they are not motivated by cure. Rather the goal is improve delivery of comfort care in better understanding the factors that improve or impede HRQoL in palliative care. The purpose and aims of the research underpinning the EoE could also alleviate the possibility for the therapeutic misconception. If a researcher who is not the treating physician is charged with engaging the participant in HRQoL discussions, the child may more clearly differentiate between activities performed as part of their care, and those done for some other purpose (research in this case).

Finally, Kipnis argues, "Allocational vulnerability properly directs attention to the substance of the bargain. Is it fair to the party in the weaker position? Is there a just division of the benefits and burdens attached to the conjoint enterprise?" (118). It is worth noting that compensation is not a foremost consideration in this case. Indeed the notion of collective or individual benefit invariably is, and "While it can be easy to identify the allocational disadvantages in many cases, it is often harder to discern the difference between just and unjust compensation packages" (118). The recognition of allocational vulnerability in the EoE protocol first demands evaluation of the proposed benefits and burdens, which were presented in Component Analysis Part 2-3. Because the EoE protocol produces greater knowledge of HRQoL in terminally ill children, ensuring mechanisms of knowledge translation can go some way towards responding to their allocational vulnerability. Most often, clinical research findings are

disseminated through academic publication. This spawns subsequent research and reproduction of previous findings until (ideally) best practices reflect these now widely supported findings. This process can be especially slow, and the patient population may wait years to witness the allocational benefits in clinical practice.

In a series of practical examples, the IBC discusses a situation that invites a certain kind of allocational vulnerability Kipnis describes: vulnerability due to lack of research within a special population (10, IV.5). The lack of research is in essence the social good which terminally ill children are unable to access and continues to be a reality in the context of pediatric palliative care (see Chapter I). Applying the IBC's logic, the nature of this type of special vulnerability is the continued underrepresentation of terminally ill children in research on HRQoL. The cause of this marginalization may be the additional ethical safeguards (regulatory and/or institutional), methodological complexity or researcher expertise required to conduct studies into the factors that most prominently impact HRQoL for these patients. Because assessing HRQoL is integral to the delivery of comprehensive palliative care, terminally ill children's exclusion from research expressly meant to better understand HRQoL violates the "right of a human being to the highest attainable standard of health" (UNESCO 2011, 27).

Models of Consent and Assent

Vulnerability is certainly not the only reason why children's participation in research might be unethical, Kipnis (2003) rightly states; however, nor should vulnerability sanction pediatric medicine as a "forum" to perpetuate paternalism (Miller, R 2003). Weijer confirms through component analysis of non-therapeutic research procedures, the utility of the knowledge and vulnerability of the participants both have the most bearing on risk-benefit calculi. Because incapacitational vulnerability usually erodes with increasing age and maturity of the child, the

co-occurrence of research and therapy in pediatric oncology demands that clinician-investigators adapt traditional consent models to better reflect their participants' burgeoning autonomy.

Contrary to research involving participants in vulnerable situations—including adults in a persistent vegetative state or the mentally disabled—incapacitational vulnerability (Kipnis 2003) in children is not necessarily static. Merely the inability to provide 'fully' informed consent often defines vulnerability in the pediatric research context. Accordingly, children's chronological age is the prevailing benchmark to indicate decision-making capacity, and thus proxy consent is typically required to protect children from their "immature" clinical decisions. Leikin (1993) challenges these assumptions with regard to end-of-life decision-making. Rather he validates the importance of disease stage in an adolescent's ability to conceive of one's future *good*: "…adolescents with cancer will conceive of their good differently, depending not only on their cognitive capacity, but also on their experience with the illness, on their understanding of death and dying and its imminence, and on their sense of independence. These factors may change with a given adolescent and with the stage of cancer" (3343). The respect for persons principle—as a pillar in both research and clinical ethics—therefore validates a relationship between vulnerability, competence and need for special protections. That is, insofar as one metric of vulnerability is characterized by the inability to make fully informed decisions vis-à-vis participation in clinical research—certainly Kipinis and the IBC elucidate the many ways vulnerability can be constructed—special measures to protect child participants are warranted.

Indeed, there is at least some reason for concern in qualitative research as well. Considering that informed consent to any kind of research is a fundamental principle in bioethics, how might researchers provide children with sufficient information about a qualitative research protocol that is known to be subject to variability, and evolves as the research itself unfolds? Mishna et al (2004) speak to this: "Discerning how to adequately prepare children for

consenting or assenting to qualitative research is further complicated by emerging evidence that suggests that children and adults may have different frames of reference with respect to what might cause discomfort or harm (Woodhead and Faulkner 2005) (455)." Taken together with Kipnis' views, this demands a situational specific approach to determining a child's ability to participate in qualitative discussions on HRQoL. Certainly, a one-size-fits all determination could unethically exclude potential participants with valuable insights to contribute to the EoE study.

In their focus on the dimensions of patient autonomy, Walter and Friedman Ross (2014) point to the dismissal of emotional experiences, in favor of capacities for rational thought, as the implicit reason for denying children's decision-making ability in clinical care, but that could also be applied in decisions related to research participation. They argue exploring the social and relational layers of individual autonomy better contextualize the significance of experiences that ultimately underpin children's decisions (to participate in research). Appreciating relational autonomy is one of continual reflexivity and tolerance: "If children never have anyone validate their desires or emotional experiences, they may have difficulty developing or articulating their wishes and experiences…When adolescents are given opportunities to make choices about their lives, they gain important insights about who they are and who they are becoming. Finally, these relationships affect an individual's ability to bring his or her autonomous desires or choices to fruition" (Walter and Friedman Ross 2014, 319). For these reasons, Alldred and Burman (2005) do not promote "special" or "age-appropriate" methods in qualitative research (177). Kipnis agrees, noting, "Once we have teased apart the tangle of issues, we can drop the goal of developing special sets of standards for children and each of the other vulnerable groups…Though children are characteristically more vulnerable than adults, there is nothing special about their vulnerabilities and the accommodations researchers need to make for them (as

opposed to the rest of us)" (119).

There is some evidence to suggest that parents themselves often do not understand important elements of the research design and trial procedures (Kodish et al 2004). Likewise, HRQoL perceptions of their terminally ill children can be vague approximations at best (Eiser and Morse 2001; Wolfe et al 2000). Parental misunderstanding may therefore unnecessarily restrict children from participating in research that could benefit them significantly. As Richard Miller (2003) notes, "…[the] norm of parental autonomy is not absolute... Medical professionals may act with an eye to a child's interests with fewer restrictions on their decision-making authority than in cases involving adult patients" (52). The model and process for obtaining consent should vary in accordance with the perceived risks and competence of minors to appreciate the dimensions of their research participation. Hart (1992) reiterates the theoretical significance of developing autonomy through recognizing participatory agency:

> Piaget argued that if [children] are always subject to authority and do not have opportunities for establishing rules through relationships with mutual respect, they cannot develop as autonomous selves. The blooming of a personality through the development of autonomy depends then on these social relationships. Seen in this light, children's participation is not just an approach to developing more socially responsible and cooperative youth; it is the route to the development of a psychologically healthy person. (35)

Clinician-investigators are routinely faced with patients who have not yet reached the age of majority—generally set at 18 in most jurisdictions—and seek participation in research that can pose greater than minimal risks. There is added ethical complexity in determining vulnerability when the participant is an older adolescent who may exhibit a level of maturity that closely matches that of consenting adults. On this point, there is consensus in the adolescent psychology literature that maintains minors appeal to morality and logic in informing their decisions by middle adolescence (Mann, Hamoni and Power 1989). This finding questions whether it is

appropriate that parental consent should supersede the wishes of a mature minor if in conflict. Furthermore, it opens the possibility for conducting highly sensitive yet valuable research with similar adolescent populations that might otherwise be hindered by parental consent requirements, for example research on high-risk sexual behaviors or suicidal ideation. This was the primary motivation for reform in Quebec, lowering the requisite age of consent for some research to fourteen. Certainly, the protective function of "parental permission is combined with more strict regulations about acceptable risks, the supervision of research ethics committees (REC) and the responsibility of clinicians/researchers. As proxies could misjudge the impact or distress of a study on a child, there remains a role for the child to protect herself as well" (Giesbertz et al 2014, 267).

It has been established that where young children are concerned, parental consent is required for participation and the child's assent is strongly preferred (or required) in some jurisdictions. The regulatory architecture of conducting research with children is thus in part born from their inability to exercise full and informed consent. Morrow and Richards (1996), however, challenge the applicability of existing ethical guidelines from medical or psychology disciplines for social science research, namely those pertaining to competency. They contend the reason these guidelines "appear unlikely to provide specific, clear applications to the dilemmas that researchers face" is namely because researchers use two dominant approaches to ethical issues: the ethical absolutist and the ethical relativist" (Morrow and Richards citing Plumer, 1996, 96). Rather, social science researchers should instead regard these issues as being "co-terminus with everyday life, and ethics be produced creatively in the concrete situation at hand" (96). That is, the evaluation of competency in research with children should be context and situational-specific.

Balen also discusses the incongruity of consent requirements for research and notions of genuine competency required of children. An additional tension, therefore, is in both striving to treat children as 'active beings' and prime decision-makers in matters that affect their health, while conforming to normative ethical conventions of pediatric research ethics. Balen argues research gatekeeping that occurs as part of research ethics board approval demonstrates how social science research should highlight how classical issues of vulnerability and incompetence are produced and, ultimately, preclude further investigation into childhood and child health. Since the "view of childhood persists as a process where the acquisition of cognitive and social skills marks the development of mature adult rationality, children will continue to be 'marginalized beings awaiting temporal passage' and their voices 'muted'" (36) (see section on the *Ethics of Participation* in Chapter III).

Balen, Morrow and Richards effectively establish a no benefit scenario for pediatric palliative patients. Although qualitative research might have the greatest methodological promise in understanding their childhood, experiences and unique epistemologies, setting an adult-centered threshold for rationality to determine the ethics of participation will continue to restrict them from the very avenues of progress capable of helping them most. Potential palliative care participants do not have the luxury of "awaiting temporal passage." According to Balen's logic, their voices are at risk of being muted indefinitely. Preventing such an outcome requires that specific attention be paid to the special situations of vulnerability that can arise from research with pediatric palliative patients, not the least of which includes their capacity to consent/assent, the severity of their illness and its implications for decision-making, and the import of HRQoL studies in pediatric medicine itself.

The next section will focus on determining how qualitative methodologies can promote the meaningful engagement necessary to meet ethical standards in pediatric oncology research,

as well as extend children the participatory rights they deserve. The co-occurrence of research and therapy in pediatric oncology is discussed in relation to the unique ethical challenges it can pose for researchers, child participants and their families.

Qualitative Approaches to Pediatric Oncology Research

Argued earlier in this chapter is the ubiquitous nature of research and therapy coexisting as mechanisms of patient care in the pediatric oncology context. This theme will be taken up in closer discussions on how qualitative research can also contribute to the coproduction of knowledge with young people in palliative care. Like in oncology, HRQoL research and palliative care should be envisioned as a positive union. Certainly, evaluating minimal risk and recognizing special vulnerabilities are critical to maintaining this synergism between research and care in pediatric oncology. Any ethical analysis of risks, therefore, demands that one is clear about who are the researchers, caregivers and knowledge generators because different ethical obligations apply. As this section will demonstrate, clinician-investigators can serve both the roles as researchers and caregivers, parents can serve as care givers and knowledge generators, while children are the primary knowledge generators in HRQoL research in palliative care.

Ethical Implications of Rarity and the Clinician-Investigator Role

The rarity of childhood cancers underscores the need for an integrated ethics approach that better reflects and further cultivates a positive nexus between research and therapy in pediatric oncology. Rarity of pediatric cancers also constrains the provision of high quality care and innovative research. Despite great strides in diagnosis and treatment, childhood cancer

remains the leading cause of disease-related death among children in North America (American Childhood Cancer Association. Childhood Cancer Statistics). Challenges persist in understanding the biology of many pediatric tumor subtypes (Murphy 1995) and resolving disparities in outcomes among adolescents and young adults (Kent 2011, Desandes 2007). Yet precisely because childhood cancers are rare, effective therapies depend on multidisciplinary collaboration between clinicians, investigators and institutions that is "anchored in a strong clinical research infrastructure" (McGregor 2007). Like other rare disorders, targeted subject recruitment and referrals for clinical trials evaluating new therapies may do the work of matching the most promising regimens to individual patients. For this reason, and others, nearly 70 percent of pediatric cancer patients receive treatment under the auspices of a clinical trial (Cancer.gov).

Limited research investment in pediatric cancer (Boklan 2006; Fernandez and Barr 2006) however, further strains personnel available to investigate novel therapies while delivering care to patients, simultaneously. In his analysis on how to reconcile the ethical mandates of clinicians and investigators, Miller suggests this dual role is a source of conflict in research ethics and underlines why a distinction between research and care is necessary. His proposal, however, is at times hardly feasible—and may be exceedingly risky (Blake, Joffe and Kodish 2010)—where clinician-investigators' contributions to discovering future therapies are paramount to clinical progress such as in pediatric oncology and palliative care.

Of concern for research ethics generally is the potential for therapeutic misconception. Broadly defined as "inaccurately attributing primacy of therapeutic intent and individualized care typically seen in ordinary clinical settings to research procedures" (Lidz et al 2004, 1691), the nature of the therapeutic misconception and its prevalence among research participants have been the subject of longstanding controversy (Appelbaum et al 1987; Kimmelman 2007; Miller and Joffe 2006), especially involving severely ill populations. Furthermore, the dual clinician-

investigator often characteristic of research in pediatric oncology is seen to exacerbate the therapeutic misconception:

> Indeed, subjects have difficulty believing that physicians and other health care professionals would ever do anything that was not intended to be directly beneficial to them. Thus, many potential research subjects enter the consent transaction with a strong therapeutic bias. Investigators' disclosures may reinforce the predilection to view the therapeutic intent of clinical research as being equivalent to that of ordinary treatment. Investigators may fail to disclose aspects of research methods that limit personal care, perhaps because of their discomfort in deviating from the allegiance to patient well-being that undergirds normative medical practice. (Lidz and Appelbaum 2002, V58)

Yet this concern is not entirely applicable in pediatric palliative care, where the nature, aims and purpose of research is not centered on the possibility of cure. Insofar as the primary aim of palliative care is to comfort and improve HRQoL, concerns surrounding the therapeutic misconception and the consequences for informed consent become less qualified. Because patients and families are not necessarily motivated by the prospect of cure—and the research procedures participants undergo as part of the qualitative EoE study are unlike those performed in clinical trials research for example— their willingness to participate may be more altruistic and less cure-oriented. These contextual circumstances of pediatric palliative care research go some way to minimizing the common risks brought on by an inability to differentiate research from care and misinformed consent that so often threaten the prospect of ethical research participation in general.

It is moreover clear that participation in a qualitative study does not resemble clinical treatment in the way that some research procedures done as part of a clinical trial might seem. Since studies like the EoE do not involve administering drugs, conducting laboratory tests or demanding extended hospitalizations, patient-participants may more clearly differentiate what interventions constitute research and clinical care. Additionally, qualitative research is carried out by separate personnel altogether in some cases. This may alleviate potential confusion that

clinician-investigators might invite by virtue of their recognized role as a care provider. While conducting research with patient-participants, and especially with children, researchers who are not clinicians should be transparent about their professional role as such.

What should be the focus of ethical concern in qualitative research is to what extent intrusive burdens on young patients and their families could be classified as risks. Qualitative research in healthcare settings commonly uses methods such as in-depth interviews, focus groups or ethnography. These methods demand time and energy from both researchers and participants. Interfering with necessary patient care, such as scheduling qualitative interviews during daily clinical follow-up, or demanding that patients spend long hours in unfamiliar settings pose considerable risks to their well-being and should be avoided. Thus the logistical and practical arrangements are considerations of significant ethical import in both minimizing risks for young participants and ensuring sound qualitative research design. Research activities should therefore accommodate patients' daily lifestyle and clinical routines in effort to minimize the foreseeable, and attempt to anticipate the unforeseeable risks that participation in qualitative research might pose. An observation study that explores children's interactions with each other, for example, could conduct observations during scheduled times for play, resulting in a modest intrusion and minimizing additional risks outside the scope of children's daily activities.

Decisions regarding where and how participant interactions will be coordinated should be made carefully so as to ensure the research does not physically or emotionally overexert young participants or severely inconvenience their care providers. The immediate consequences of doing so include compromising the care and therefore the health of the child, tarnishing researcher-participant relationships cultivated among members of the community, and violating ethical codes of conduct. Failing to minimize these risks in the long term could threaten the

authenticity and richness of the qualitative data, among other things, unjustifiably exposing participants to risks that result in no tangible benefit to them or the population they represent.

Minimizing risks also depend on whether the proposed methods are the most appropriate for answering the research questions at hand. Put differently, are all procedures that require children's involvement necessary and sufficient to answer the proposed research question(s), or is it possible to gain the same knowledge using less intrusive means? Furthermore, the most ethically justifiable research method(s) distribute burdens fairly, and ensure the benefits are shared equally among participants and/or others within their community.

Frustrating the Fundamental Distinctions

Childhood cancers are not simple variations on adult cancers. In cases where the cancer subtype is exceedingly rare, patients and families may also opt to forgo curative therapies and transition to comfort and/or palliative care options. Demands in palliative care have witnessed an emergence in recent decades (Berger, Shuster and Von Roenn 2007), with greater resource allocation towards expanding palliative services to children with advanced disease including cancer (NIH Palliative Care: Conversations That Matter, 2014).

One commentator argues the ethical frameworks distinguishing between research and therapy stem from the primary goals that define them. Franklin Miller contends, "medical care has a personalized focus. It is directed to helping a particular person in need of expert medical attention. Clinical research essentially lacks this purpose of personalized help for particular individuals . . .The distinctive purpose of clinical research [is] to develop generalizable knowledge" (11). If Miller's proposal is to confirm research and treatment differ in their focus, it is possible to understand how his assertions are rarely, if ever, reflective of the reality for

pediatric oncology patients, specifically. Miller's statement implies that clinical research adopts an explicit group focus, concerned with gathering data generated from following uniform protocols across a select sample size. In contrast, clinical care makes the individual patient its focus, and is the unit of analysis from which clinicians devise tailored therapies.

Highly coordinated research partnerships in pediatric oncology, however, adopt a global pediatric research architecture that serves both group and individual interests. The Clinical Oncology Group (COG), for example, operates as a concerted research body aggregating over 7,500 scientists, clinicians and researchers across 220 institutions. The largest pediatric cancer research consortium in the world, COG institutions deliver care to more than 90 percent of the 13,500 children and adolescents diagnosed with cancer each year in the U.S. and Canada. Likewise, the Pediatric Oncology Experimental Therapeutics Investigators' Consortium (POETIC) operates in tandem with the COG. It declares as its mandate,

> To promote the early clinical development of promising therapies for the treatment of children, adolescents and young adults with cancer and related disorders…To develop intensive, biologically driven Phase I clinical studies in pediatric oncology with two goals in mind: to simultaneously offer patients new and different options for treatment; and to rigorously evaluate novel agents in order to identify their most appropriate use in cancer treatment" (Pediatric Oncology Experimental Therapeutics Investigators' Consortium).

Such organizations lend support to a culture of research-based medicine seldom witnessed to the same degree in other clinical specialties. In establishing highly collaborative research agendas, the COG and POETIC demonstrate how research occurs alongside clinical practice, and more importantly, informs it in the process. The practice of pediatric oncology—traditionally a forum for delivering patient care exclusively—is "constructed to bring the most pertinent forms of scientific understanding to bear on clinical care, as clinical care generates new scientific learning. Producing and using generalizable knowledge can thus be a deliberate and integrated aspect or part of practice, not a set of maneuvers logically distinct from it" (Kass et al 2013, S7).

Put simply, where the rationale for segregating the ethical frameworks is that the goals of research and care inevitably diverge, pediatric oncology problematizes this distinction when knowledge generation becomes an integral component of providing high quality patient care.

Moreover, the co-occurrence of research and care often shapes the professional domains within pediatric oncology itself. In support of this view, Cantrell (2007) explains "the art and science in the practice of pediatric oncology nursing inextricably combines the delivery of complex care interventions, such as implementing an intricate treatment chemotherapy protocol that requires a significant amount of scientific knowledge and critical thinking, with nurses' creativity, resourcefulness, and imagination" (135). Although Miller agrees the tension between ethical responsibilities of investigator and clinician in the pediatric oncology arena can be managed, the specialty is constructed such that it can also be encouraged. While an acknowledgement of how the two sets of responsibilities may entail different ethical duties might be a useful exercise, such a distinction presupposes that integrating the two frameworks abandons an individual patient's best interest. The documented success in pediatric oncology, a field epitomizing the research-therapy nexus, suggests otherwise.

It would be inaccurate to claim the nexus has not benefitted from the operational requirements of research-treatment distinctions, namely the role of responsible ethics review. Component analysis (discussed in greater depth earlier in this chapter) offers a systematic approach that REBs employ to evaluate the ethics and scientific merit of experimental protocols, including those that enroll pediatric subjects. This is not to suggest an integrated ethics approach justifies abandonment of the regulatory oversight for research outright; nor does it propose that clinical interventions subsumed under a duty to care should present for REB review. Rather, the core distinction between research activities and care need not preclude the possibility that the moral imperatives inherent to each can complement in pediatric oncology and palliative care

contexts. The notion of the child's best interest can be seen as one such point of convergence that brings together the aims of research and care.

Best Interests of the Child: What Are They and Who Defines them?

Promoting a rhetoric of engagement should be accompanied by furthering research agendas that situate the child at the center of knowledge generation (Young et al 2010; Truon et al 2011; Lambert and Glacken 2011). It broadens the notion of best interest, a concept whose definition can subject to wide sociocultural interpretation and varies significantly depending on the context in which it is petitioned. For example, Beauchamp and Childress claim the best interest standard is useful in the clinical setting in order to "protect another's well being by assessing risks and benefits of various treatments and alternatives to treatment, by considering pain and suffering, and by evaluating restoration or loss of function. It is, therefore, inescapably a quality-of-life criterion" (102). In an updated report on pediatric decision-making, the American Medical Association opined best interests to be "determined by weighing many factors, including effectiveness of appropriate medical therapies, the patient's psychological and emotional welfare, and the family situation. When there is legitimate inability to reach consensus about what is in the best interest of the child, the wishes of the parents should generally receive preference" (American Medical Association).

These related yet distinct frameworks for evaluating the child's best interest have important consequences for the decisions deemed acceptable for minors to make in a palliative care setting, and for the future of predictive genetic testing as part of routine clinical care (Ross 2013).[xii] In his comparison of withdrawing life-sustaining interventions in France and Italy, Carnevale evidences the sociocultural embeddedness of best interests as they concern pediatric

patients. He writes,

> In France, it is argued that children have an interest to avoid life with disability even if this entails their death, whereas in Italy it is held that children have an interest in living as long a life as possible, even if this is sustained through prolonged resuscitative technologies. This contrast highlights two sharply distinctive forms of *hypergoods*: able-bodied-ness in France (commonly referred to as "quality of life") and "sanctity of life" in Italy. This does not mean that each societal setting does not value both goods. Rather, we have a clear indication that, in each of these countries, one good is clearly regarded on a higher ground; as a form of *hypergood*" (150).

Expanding on the theoretical underpinnings for Taylor's "modern malaises" of modernity, Carnevale challenges the 'objective' assumptions that couch notions of the "hypergood" in determining a child's best interests, particularly when compared across culture and space. The cross-cultural meeting of priorities and outlooks on the death and dying process can be incredibly stark. This is best illustrated in Fadiman's, *The Spirit Catches You and You Fall Down*. Through chronicling the story of Lia Lee, a young Hmong girl suffering from a rare form of epilepsy, Fadiman vividly details the consequences of cultural dissonance between a family and the healthcare system. Ultimately, this cultural impasse over Lia's best interests severely compromises her care and raise important questions as to how emerging pediatric palliative care modalities accommodate for the sociocultural plurality in death and dying.

Although some scholars admit the "judicial and administrative standard of 'the best interest of the child' has been so tragically abused by ideology and political agenda so as to have rendered it harmful to children," (Finley 2002, 629)—or outright reject the ethical applicability of the best interest standard insofar as it is ambiguously applied (Salter 2012)—others maintain a more optimistic outlook. Emily Logan—then Chairperson of the European Network of Ombudsmen for Children—remarked in a 2008 address to the Council of Europe,

> When considering the need for a clear articulation of the best interests principle, it is worth noting two related but distinct questions: why a best interests determination

> is needed in the first instance and how such a determination might be made. The first question relates more directly to the basic cultural assumptions which underpin our approach to children and young people, while the second question touches on the notion of determinacy…This potential difference in outcome arises from the fact that if children are not treated as individual rights holders, not only is it possible that a determination of what is in their best interests will not take into account all relevant rights, but the question may sometimes not be asked at all. That is where the need for a cultural shift regarding children and young people's rights is placed in stark relief. That is not to say that the change of emphasis to regarding children as individual rights holders means that the best interests principle always trumps other considerations. That is one of the enduring myths about children's rights which we work so hard to dispel. The issue is not about having a trump card but rather doing away with a blind spot. It is a question of redressing an imbalance rather than giving the best interests principle a disproportionate weight (Logan 2008, Janusz Korczak lecture).

Therefore from a health research perspective, direct engagement with terminally ill children in pediatric palliative care research facilitates the process of informing best clinical practices—and best interests by recognizing young patients' unique expertise in experiencing terminal illness. Ethicist Daniel Sokol supports this idea when he maintains "only by reading or conducting social science research may ethicists deviate from "armchair bioethics that so frequently fails to ground theory in the clinical realities of their chosen subject" (1226).

Respect for Autonomy and Research Participation

Echoing the findings of Chapter II on the ethics of participation, a study of self-reported HRQoL necessitates authentic representation of children's voices if it is to genuinely fulfill the respect for persons mandate from a bioethics standpoint. The right to exercise individual autonomy in clinical decision-making and research participation originates from the atrocities witnessed at Nuremberg, and was reinforced more stringently following the Tuskegee Syphilis study and others. The concept of individual autonomy is predicated on the ability to demonstrate competency and maturity in appreciating both long and short-term implications of a particular

decision. Evaluative measures exist to ascertain these skills in the clinical setting (Nasreddine 2005), although the age of majority serves as an implicit social designation for maturity and competence in many jurisdictions. As Shaw (2001) writes, "The law imposes a dichotomy (competent v. incompetent) on what, from a developmental perspective, is a spectrum of ability" (150). It is in determining where on the spectrum a child is positioned with respect to their burgeoning autonomy that extending clinical and research decision-making rights to children is problematized.[xiii] As well, decision-making capacity is decision-relative. That is, one is rarely wholly capable or incapable of making decisions, but meets capacity standards for certain decision situations. In some jurisdictions or for some decisions, this "right" to decide on one's own behalf requires the individual to be both capable and an adult; in others, one must only be capable.

In these respects, the social, legal and clinical determinations of decision-making capacity are thus frequently at odds. Such discrepancies are especially stark in the context of end of life pediatric care. The use of an (arbitrary) age of majority to determine decision-making capacity is complicated when prevailing consent models do not reflect the truncated autonomous development of children with terminal illnesses. In most consent/assent guidelines outlined for children, age is one of the determining factors for allowing potential research participants to make individual decisions. It has been argued in earlier chapters that age is often not an accurate proxy for maturity, rationality or competency, particularly in children facing end-of-life situations. Thus an age-dependent determination of ethical participation in research may be systematically more convenient, yet may also inappropriately deny some terminally ill children the ability to improve their situation(s) of vulnerability or exercise participatory agency in the (short) time they have left to live.

Protocol-based therapies have been the cornerstone of advancements in pediatric oncology, while cultivation of a research-therapy nexus has created the space for clinical partnerships between patients, practitioners and their families over the years. Because childhood cancers are rare, offering patients the opportunity to enroll in research—qualitative or otherwise—"might not only be a defensible option, but it might also be the most ethically sound course of action" (Pritchard-Jones 2008, 395). Ashcroft (cited in Chalmers 2007) agrees: "for ethical as well as scientific reasons [research] is the treatment, when there is uncertainty about the relative merits of alternative treatments" (401).

Despite "lingering claims to the contrary, qualitative methods are no 'soft' option'" (Clark 1997, 159). It has been a longstanding perception, largely promulgated by the natural science community that social science research succumbs to the biased, subjective and contaminated nature of its methodologies. Unsurprising, this is not a view social theorists, philosophers and anthropologists share. Jones (1995) speaks to this in the context of health services research: "Qualitative research has struggled to find its present position in health services research. One reason may be that clinical scientists have had difficulty in accepting the research methodologies of the social sciences, in which the generation of hypotheses often replaces the testing of hypotheses, explanation replaces measurement, and understanding replaces generalisability" (2).

In pediatric palliative care research, formidable challenges exist in defining ethics norms that both protect and address the needs of patient-participants during an especially vulnerable time in their lives. Establishing an appropriate framework to guide qualitative inquiry in pediatric end-of-life care faces compounded ethical challenges that include situations of special vulnerability; sensitivity of the topic under investigation; and the clinical import of the research itself to palliative care delivery.

Research ethics board review of all research protocols in pediatric oncology, regardless of whether they employ therapeutic, non-therapeutic or a combination of such procedures, should remain a requisite component of research in the field. Yet the maintenance of a hard theoretical distinction between research and therapy as a protective mechanism for patient-participants can instead impose excessive burdens. Lantos (2004) refers to this scenario as a "confused ethical analysis" (72). Until pediatric palliative care research can more inclusively engage with terminally ill children, their continued underrepresentation will continue to delay the improvement of care practices that are reflective of their terminal illness experience.

Justice

Distributive and social justice in a research context can be seen as pursuant to the goals of new paradigm shifts in the rights and sociologies of the child(hood). The ethical permissibility of sanctioning palliative care research with terminally ill children actualizes the UNCRC's demand for free expression and participatory rights; promotes the accessibility and availability of pediatric palliative services that are reflective of children's experiences during the end of life; expands modes of representation among this population in health research; and achieves direct stakeholder engagement with the primary users of pediatric palliative care.

In the section on Fairness and Equity in Research Participation, the TCPS2 outlines the circumstances of just participation in research: "The principle of Justice holds that particular individuals, groups or communities should neither bear an unfair share of the direct burdens of participating in research, nor should they be unfairly excluded from the potential benefits of research participation. Issues of fair and equitable treatment arise in deciding whether and how to include individuals, groups or communities in research, and the basis for the exclusion of some."

Recruiting participants for clinical trials and subsequently preventing them access to the beneficial drugs once approved is one practical example demonstrating an unfair share of direct burdens with no tangible benefit. Equally unjust is the categorical exclusion of patient groups in clinical trials research, particularly those who suffer from conditions the drug specifically purports to treat. The EoE study is poised to address both justice concerns. Since researchers are exploring HRQoL in terminally ill children specifically, then the disproportionate recruitment of terminally ill children to the EoE study is both methodologically necessary and ethically justified. In contrast, the exclusion of this important stakeholder group from research on HRQoL in pediatric palliative care is ineffective for meeting the study objectives and (more disadvantageous) denies them the benefits of improved palliative care services. As such, the EoE prioritizes engagement of this stakeholder group in making quality improvements to pediatric palliative care.

The TCPS2 definition of justice therefore implies that young participants in the EoE study should not be excluded, nor overused for research purposes. Both a just distribution of research benefits and promoting the social justice agendas of the new sociology of the child(hood) begins with participation. As an identifiable patient group, terminally ill children deserve to participate in, and reap the benefits of, clinical research conducted with participants from their own patient population.

Consider the following discussion of distributive justice that appears in the President's Commission Report (2014) on children in biomedical countermeasure research:

> Ethical distribution of research burdens and benefits generally prevents the possibility of asking participants and families to consider bearing too heavy a burden on behalf of society. More specifically, in the conduct of research, justice requires that research participants not be denied a benefit to which they are entitled and that no individual participant be burdened with undue risk of harm or hardship… Just distribution of research risks applies not only to the design and conduct of research, but also to subject selection. Even when they are treated equitably once enrolled in research,

> children and families might be selected unjustly if they are chosen from certain subgroups of the population that are already excessively burdened by conditions of socioeconomic disadvantage, that have made uncommon sacrifices in the course of public service, or that have been subject to repeated recruitment for research enrollment. (33)

The Report points to the ideal proportionality of benefits and burdens in a small population from which researchers are able to recruit for a given study. In addition to ensuring children are included in research posed to benefit them directly, researchers must also ensure this population is not unduly burdened by their participation. It is possible that because the potential recruitment pool of children undergoing palliative care for terminal cancer is small, they could be at risk for over recruitment in such studies. Ensuring local feasibility of protocols is one approach to minimize this overuse. That is, departmental heads, research ethics boards or other personnel in administrative leadership positions have the responsibility to gatekeep the volume of research conducted within specific populations.

Such coordination between research and clinical teams, as well as research ethics boards, are practical examples of how distributive justice issues can be managed in situations where issues of distributive justice are accentuated. Making knowledge translation a priority research objective is yet another example. Including knowledge translation as part of the overall study incorporates an internal "check" to ensure research benefits are reaching the intended communities; and if not, can help researchers to redirect such efforts or propose feasible methods for translation given the study specifics. In the proposed EoE study, effective knowledge translation would ensure the findings from deliberative consultations with children indeed shaped new care practices in palliative care and help healthcare professionals in developing them.

Terminally Ill Children and HGA Care

The engagement of terminally ill children with HGA in HRQoL research, using the deliberative consultation model described above, can be successfully defended from both bioethical and methodological standpoints. The purposeful inclusion and targeted exploration of children's illness experiences in terminal care delivery fulfills both the respect for persons mandate and Article 12 of the UNCRC (Southall et al 2000). Their rights to participate in research and open the door for greater clinical decision-making opportunities are accentuated by virtue of the limited number of decisions they are in fact able to make as a result of their terminal illness.

The near absence of direct engagement and overwhelming proxy reporting of children's HRQoL in pediatric palliative care research neither benefits care delivery nor acknowledges the paradigmatic shifts in conceptualizations of the child(hood). Given the central focus of HRQoL to palliative care, this thesis argues overrepresentation of proxy accounts and underrepresentation of young patients themselves in such discussions is problematic. Yet still, the generalization of children and childhoods implied in normative thresholds of minimal risk (like those reflected in the DHHS regulations) can invite paternalism or prevent potentially beneficial research involving children with life-threatening illnesses. Although terminally ill children face daily risks exponentially greater than those of a healthy child, healthy childhoods serve as the basis for evaluating risk and benefit in the DHHS guidelines.

In response to ethical concerns surrounding maturity and capacity of palliative research participants, it is insufficient to speak of these children's *burgeoning* autonomy. Their poor prognoses and limited life expectancies make certain that most HGA patients will not live to reach the age of majority (18 in most jurisdictions) to legally consent to research, qualitative or

otherwise. Other factors, (e.g. their well-being and the well-being of other HGA patients, the minimal risk of the EoE research procedures etc.) outweigh this concern. Their exclusion from research participation can hardly be considered ethical if based solely on a legal, albeit arbitrary, age benchmarking the end of childhood and beginning of adulthood—a transition argued elsewhere in this thesis as a social construct.

It is important to also note the relative risks involved in children's participation, and how they will be addressed during the course of this study. Although inaccurate to homogenize all 'children' under age 18, and their presupposed reactions, it is not implausible to consider the possible psychosocial harms that may accompany the deliberative consultations. The sensitive nature of the topic under discussion and some children's inability to emotionally cope with the gravity of their diagnosis are but a few of the risks that have been documented (Docherty and Sandelowski 1999) and hence are duly considered by EoE researchers.

The deliberative consultation presents one qualitative technique that engages participants in "rationalization through conversational exchange." The primary goal for utilizing deliberative consultation is to demonstrate what stakeholders genuinely think of an issue or topic. Its projected aim is to identify a set of recommendations that are of critical importance to filling a gap or responding to inadequacies concerning the issue at hand. In addition, deliberative consultation methodologists underscore the strength in soliciting a multiplicity of participant perspectives while straying away from (over) representation of investigator views that often accompany mediated focus groups. Thus in contrast to other qualitative data collection methods, deliberative consultation minimizes the role of the moderator and does *not* require a representative proxy for young participants.

Chapter IV

Discussion and Conclusion

"Our lives begin to end the day we become silent about things that matter."

—Martin Luther King Jr., Nobel Peace Prize Winner and Activist

Meeting Theorized Goals

If children's participation is important, and indeed this thesis corroborates the idea that it is essential to good pediatric palliative care, then the qualitative methods employed as part of the iCHANGE project meet many of the theorized goals of engaging children that are explored in this thesis. First, the deliberative consultations elicit the views of the main stakeholder group directly, (terminally ill children undergoing or transitioning to palliative care in this case) and furthermore offer a platform for capturing the nuances of those views. More importantly, the study is designed to yield new, clinically useful knowledge to enable modalities of care to be informed and grounded in the sociocultural realities of children in a palliative care context.

Second, the level of community development anticipated with iCHANGE is particularly important given this stakeholder community is comparably small. Improvements in the built environment, care practices among health professionals and insights into HRQoL are but a few

characteristic elements of the pediatric palliative care community in which young patients can help to further develop and strengthen. iCHANGE, specifically the EoE study, contribute to this development through aggregating all actors within the palliative care community and facilitating dialogue around the ways in which it can be best served. Lastly, as is the underlying purpose for all research broadly, iCHANGE seeks the contribution of new generalizable knowledge in the field of HGA. At its core, iCHANGE is improving the ability to *cure* HGA, while elucidating practices that optimize HRQoL and *heal* children and their families facing this devastating condition.

Certainly, the implications for the future of qualitative health research with children in the wake of initiatives like iCHANGE are far-reaching. Although not sufficient, promoting a rhetoric of engagement and citizenship in palliative care research is a starting point in lending the necessary primacy to the meaning and lived experiences that terminally ill children derive from their HRQoL. It further opens the door for recognizing their legitimacy and capacity in other traditionally exclusive social structures. Stein confirms this: "If participation could be conceived of as not only consisting of speaking and being heard, but also of active and routine inclusion in vital social processes, new prospects could be opened up for the situating of children in society."

Situating the voice of the child as an ethical centerpiece in innovating HGA care practices represents how iCHANGE is augmenting pediatric participation in investigating health issues that directly affect them. As a result, it sets a modern, though not novel, precedence that exclusion of children is no longer conducive to scientifically sound or representative research in pediatric medicine. Rather, children's inclusion is "reverting from a tendency to see children as future adults, referring to who they will become, not who they are now" (Moules 2009, 323). The EoE study thus abandons child 'Otherness' through deliberative engagement, implying that young patients play a central role—rather than a peripheral one—in shaping pediatric palliative

care practices and modalities for improving HRQoL.

Conclusion

Methodologies that promote research *with* children, as opposed to *on* them, remind us of the sociopolitical embeddedness of research and research agendas in healthcare. They call upon researchers and clinicians alike to embark on a "thick" (Carnevale 2005) bioethical analysis of their rights to decision-making as well as research participation. Social and democratic theory of children's participation is manifest in these methodologies, and underpins the meaningfulness of collaborative partnerships among patients, clinicians and healthcare institutions. As well, the degree of inclusion and consideration of children's voices at various stages of the research process should, where applicable, be interrogated with equal rigor as methodology and/or data analysis during the peer review process.

The EoE case study presented here is perhaps a perfect culmination of the central pediatric research tensions discussed in this thesis. It puts into sharp relief a number of both classical and contemporary ethical themes that have now become ubiquitous in the 'genome era,' and are placed at the forefront of debate on the progress of pediatric healthcare vis-à-vis genome medicine. These themes include, but are not limited to, the ethics of engaging terminally ill children as partners in important health research, and their participatory rights; the recognized shift in medicine toward treating and conceptualizing disease on a strictly molecular basis; and the prowess of Western medicine juxtaposed with its marked cultural aversion to death and dying (Meyer 2014; Leclerc et al 2014), particularly for children and adolescents (Himelstein et al 2004; Browning and Solomon 2005).

The unjust suffering of young people and the incomprehensible loss to follow from the death of a child are emotions of incomprehensible measure, and are certainly beyond the scope

of rational understanding. Under these circumstances, one can begin to imagine the multifaceted dimensions of pediatric palliative care, its deeply humanistic aims and celebratory tribute to the life of a child. Thus to promote excellence in pediatric palliative care, ensuring that we add "life to a child's years," is to embark on an exploration of the unique dimensions of death, dying and living, one that can only be truly guided by children themselves. Researchers are therefore charged with unifying i) the opportunity to better situate children's illness experiences at the center of palliative care delivery, and ii) the methodological soundness required of such an endeavor. It is in strengthening the methodology that the ethics of engagement contributes to this unification, and does so by using the immediacy of research like the EoE and others to underpin its justification.

The need for more targeted engagement is also demonstrated by the dearth of assessment tools used to measure HRQoL in pediatric palliative patients. In earlier chapters, a summary of the existing tools drew attention to this need. The overwhelming inclusion of parental or health professional proxy—and notable exclusion of reporting from children directly in many cases—is notably problematic. The limited tools available, along with their questionable utility in children specifically, is a sample of the barriers to informative HRQoL research in pediatric oncology and palliative care. Nevertheless, it is true that adult palliative and critical care medicine boasts a rich qualitative research tradition. It can therefore serve as the platform upon which similar work within the pediatric population can build. Though some methodological techniques such as deliberative consultation are clearly inappropriate for use with some children—namely those with severe intellectual disability or infants who are nonverbal—the specialization or significant modification of these techniques for use in qualitative engagement with children is not necessarily warranted. Doing so, many scholars argue, implicitly uses research methodology to reinforce, and perhaps widen, the divide between 'child' and 'adult,' inviting the notion that

research is an acceptable forum in which the 'othering' of children is acceptable. As a result, it is the responsibility of researchers, health professionals, scholars and child advocates to recognize both the covert as well as overt ways in which children's rights can become peripheral in healthcare or other established social venues. Reflexivity, as discussed, is a critical process to this end.

Due to implicit power differentials, children can be defenseless in preventing their marginalization in research and elsewhere. The lack of power and agency of those below the age of majority is largely the work of legal delineations that restrict children from taking part in social activities reserved for adults, for example voting or consenting to research participation. This is not to say that such restrictions are obsolete and should necessarily be done away with. Rather, research must not use the fact that children are denied such rights under the law as a justification for perpetuating their exclusion from activities that could help them exercise these rights. In line with this view, Ryan (2000) eloquently avows, "One of modernity's cardinal features is the special importance that it has granted to childhood in the discourses on being human" (553).

As the case study involving children and adolescents with high-grade astrocytomas exemplifies, the prevailing notion that children will eventually burgeon into the adults worthy and capable of exercising these rights freely is thwarted by their terminal illness. Reference to a future autonomy is negated when the possibility of the future itself is nonexistent. That there is yet so much to learn from children *during* the death and dying process in order to better care for future children *through* the death and dying process, is only a partial ethical justification for permitting terminally ill children to participate in HRQoL research. Conceiving of this research as a vehicle for children to participate in determining their own best care practices, and as an opportunity to partner with those closest to them in making meaning of their life however short,

can perhaps in itself be considered a form of healing or as contributing to healing.

How discussions on HRQoL with young patients will be affected by new sociological shifts in conceptions of the child and childhood remain to be seen. Researchers can be optimistic, however, that efforts to expand engagement and participatory rights for terminally ill children are both fruitful and well guided. As Roche avers, "Ultimately the children's rights project is not just about making a better world for children (King 1997), it is about making a better world for all of us" (489). Part of granting greater legitimacy to children's moral and social agency during end stage illness is rendering the continued absence of their voices in palliative care research, and others, an antiquated protectionist argument of the past. Doing so can make way for more creative and inclusive methods. This year marks the 25th anniversary of the UNCRC's adoption, giving us pause to reflect on the victories and spotlight areas for improvement. In many ways, healthcare is an ideal setting in which to strive towards actualizing the theoretical ideals of participation, protection and provision the UNCRC embraces, according to Mason (2005). The emergence of an international initiative in pediatric palliative care research, and identification of its pressing need in the clinical community is arguably a large victory. A more concerted research agenda that prioritizes the engagement of children in these efforts is one area for improvement.

Finally, the underepresentation of children's voices on the fringes of major technological and clinical innovation in pediatric oncology and palliative care is unjust at best, and unethical at worst. Full-fledged in the age of genomics and amidst vast changes in the landscape of clinical practice, now more than ever necessitates a return the most basic principles of participatory rights and citizenship. The pediatric engagement in qualitative palliative care research advocated in this thesis, calls for a corollary paradigm shift observed in recent decades within child development and sociology of the child(hood). In order to achieve this, Western medicine must

temper its obsession for curative rigor with a greater respect for human values both through appreciating the sui generis aspects of children's realities and their unique epistemologies of terminal illness.

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[i] For comprehensive review of the debates surrounding the ethics of participation, methodological integrity and utility in palliative care research, see Duke and Bennet 2010.

[ii] It is estimated there are approximately 4,000 children living with a life-limiting or life-threatening conditions who may benefit significantly from pediatric palliative care services in Canada alone (see Widger et al 2007).

[iii] Citing Mays, the authors consider "At a general level, scoping studies might 'aim to map *rapidly* the key concepts underpinning a research area and the main sources and types of evidence available, and can be undertaken as stand- alone projects in their own right, especially where an area is complex or has not been reviewed comprehensively before' (Mays *et al*. 2001)" (Arksey and O'Malley 2005, 5). Furthermore, Arksey and O'Malley identify four primary purposes for conducting a scoping review, as opposed to traditional systematic reviews. The review presented here is motivated by both the third and fourth purposes, to "summarise and disseminate research findings," and to "identify research gaps in the existing literature," respectively.

[iv] empirical studies and academic scholarship began appearing in medical and methodology journals only in the early 1960's, and pediatric palliative care only in the last 20 years.

[v] Bergstraesser clarifies the distinction between the two terms: "In the context of pediatric palliative care, two additional terms need to be defined, i.e., "life-threatening" and "life-limiting" disease. The former describes a disease for which a cure is realistic but may fail, and the latter describes a disorder for which there is no hope of cure. Pediatric palliative care has its focus on life-limiting diseases and thus on a limited lifespan even if it may be applied earlier on, or in serious illnesses with prognostic uncertainty" (139).

[vi] See Alderson PA. Children Ethics and Social Research. Illford: Barnardos, 1995.

[vii] Fine (2003 argues policies governing end of life research with children are more akin to the former, and invite paternalism to the point of inaction.

[viii] Longo and Bartlett (2014) summarize Fishkin's theory:

> According to James S. Fishkin, deliberative democracy can only be successfully achieved if two fundamental values, namely *political equality* and *deliberation,* are fulfilled. While political equality aims at providing citizens with the equal opportunity to express their diverse perspectives on the policy issue at hand, deliberation is the communicative process by which these diverging opinions are exchanged and discussed in a mutually respectful environment. More precisely, deliberations and, thus, deliberative research methods, involve "face-to-face discussion[s] by which participants conscientiously raise, and respond to, competing arguments so as to arrive at considered judgments about solutions to public problems[12]." In simpler terms, deliberative democracy ensures that the public's perspectives on a given policy issue are considered and counted equally under conditions where participants are effectively motivated to engage in an informative and mutually respectful debate while remaining reflective, open-minded and understanding about contrasting arguments or opinions (3).

[ix] In their critical methods assessment, Longo and Bartlett describe the utility and applicability of Fishkin's model for the EoE study.

> This approach to stakeholder/public engagement is a modified version of deliberative polling in that it does not aim to recruit a large statistically representative sample of the public as the health policy topics affect only a small proportion of the general population. As such, participants will be recruited based

> on epistemic diversity while minimizing selection biases to allow for an equal opportunity of all stakeholders to participate in the deliberations. Thus, recruitment aims to engage participants with viewpoints representative of their specific stakeholder groups. This recruitment approach is particularly applicable to genetic research projects having a public engagement component with a small target population and a limited budget. (Longo and Bartlett 2014, 9)

Young people's inclusion as an equal partner in the deliberative consultations serves as a formal recognition of their participatory agency in the palliative healthcare context, and fulfills the 'political equality' Fishkin's model prioritizes. Moreover, a comparison of the "public" defined in Fishkin's model and the one defined in the EoE study reveals how a difference in scope changes the democratic representativeness of the stakeholder groups. Put simply, the EoE study could be more representative of general pediatric cancer HRQoL if KT researchers did not discriminate based on diagnosis. But doing so ensures the improvements in treatment and care practices are tailored to pediatric HGA *specifically*. It therefore justifies extending the deliberative invitation to HGA patients only. To this end, Fishkin offers an important perspective on targeted deliberation and engagement the EoE study proposes:

> Some approaches to deliberations interested not in discussions representing the general population but rather in those that are restricted to activist groups engaged in what Cass Sustein has called "enclave deliberation." It is undoubtedly valuable for groups that wish to change society (the civic rights movement, the environmental movement, the women's rights movement) to deliberate among themselves. Contributions to deliberative advocacy by various subgroups enrich the broader discourse in the society at large. But they are not themselves manifestations of deliberative democracy in the sense defined here. It is a representation of what the public would think. Deliberation among activist groups could in principle be studied or provide consultation if the population of advocates were well defined. (Fishkin 2009)

The iCHANGE deliberations with pediatric HGA patients thus satisfy the two fundamental principles of Fishkin's deliberative democratic theory, political equality and deliberation. It likewise ensures the democratization of public engagement with the relevant, albeit it small, stakeholder group of pediatric HGA patients is achieved. Despite a more narrowed definition of the "public" with whom engagement is intended to take place, the deliberative democratic processes still commence.

[x] It should be noted, however, that not all participants will view the research experience in the same ways, underscoring the importance of researcher acuity when employing qualitative methods. There is some debate concerning the risk of psychosocial harm, and the approaches undertaken to alleviate it. Orb, Eisenhaur and Wynaden recommend: "…searching for possible solutions for the participants' distress indicates that researchers are aware of the vulnerability of participants and their rights. The moral obligation of researchers is to refer participants to counseling or ensure that they have regained control of the situation by talking. In some cases, a follow- up phone call or visit may be appropriate" (94). Others maintain counseling interventions could exacerbate some of these affects, stigmatizing participating or generating more than harm than good (see Kyte, Draper and Calvert 2013.)

[xi] Article 8 of the UNESCO Universal Declaration on Bioethics and Human Rights states: "In applying and advancing scientific knowledge, medical practice and associated technologies, human vulnerability should be taken into account. Individuals and special groups of special vulnerability should be protected and the personal integrity of such individuals respected."
[xii] To the latter point, parental consent to undergo genetic testing impinges on a child's right to what Dena Davis refers to as an "open future." That is, predictive testing for adult-onset conditions should be delayed until the child is able to consent on his or her own behalf. For children diagnosed with a terminal High-Grade Astrocytoma (HGA), the right to an open future calls for further interrogation of what 'future' means in this context. Surely for many patients, their future constitutes only a few weeks or months. Since the routinization of the laboratory genetic test in the diagnosis of HGA mutation type will soon become a standard of care, it is questionable whether a child or their parent will be able to exercise a "right not to know" in forgoing the test.

[xiii] Supreme Courts in both Canada and the United States grappled with these issues in numerous precedent-setting cases. See *Gillick v. West Norfolk and Wisbech Area Health Authority,* 1986 AC 112; *Jehovah's Witnesses versus King County Hospital*, 1967. *Federal Supplement* 278, 309 U.S. 598, 278 F. Suppl. 488, 1967, 488–508; *Prince vs. Commonwealth of Massachusetts*. Jan. 31, 1944. 321 U.S. 804, 64 S. Ct. 784; *Re I.D.K.*, 48 R.F.L. 2d 164, Ontario Province Court Family Division, 1985.

Table 1*:* Summary of *HRQoL Assessment tools developed for terminally ill children with cancer*[1]

Instrument	Validation Population	Respondent	Targeted Ages	Items and Scale	Validity	Scores	Advantages and Limitations
Not tailored to Specific Ages							
Miami Pediatric Quality of Life Questionnaire (MPQOLQ)	U.S.	Parent Proxy Physician	< 18	56-item questionnaire assessing 3 principal factors in parents of children with cancer: social competence, emotional stability and self-competence. Each item assessed using a 5-point Likert Scale. Additional forms gather information regarding the diagnosis and treatment plan, and physician's evaluation of the child's HRQoL on the Likert Scale.	A factor-based analysis confirms the internal consistency and validity of the tool in 132 children and their parents	Scores are used as a means of comparison, though unknown how scores are calculated from the Likert scales.	**Advantages**—Developed explicitly for pediatric cancer patients; Second questionnaire given to child's physician **Limitations**— Not focused on, nor validated for terminally ill patients; no self-reporting of the child
Pediatric Oncology Quality of Life Scale (POQOLS)	U.S.	Parent Proxy	1-18	21-item questionnaire that gauges symptom-related factors and behavioral indications of HRQoL measured on a 3-factor scale. Examples include: "My child has anger outbursts", "My child has expressed fear about the disease and its treatment", "My child has been sad" etc.	Internal consistency and inter-rater reliability validated based on pilot study of 107 parents of children with cancer	Positive responses to questions translated into high final score, indicative of poor HRQoL, while low final scores interpreted as an excellent quality of life.	**Advantages**: Scale validated for parents. **Limitations**: Only one 'blanket' questionnaire applies to all ages and uses parent proxies
Decision Conflict Scale (DCS) & COMRADE	U.S.	Parent Proxy	1-18	16-item survey that measures 5 domains relevant to decision making: uncertainty, informed feeling, values clarity, support and effective decision-making. A 5-point Likert scale is used to evaluate responses. The COMRADE tool measures the concepts of risk communication and decision-making effectiveness; it was originally	Internally validity and consistency demonstrated in 266 parents of children with cancer.	The DCS score is calculated by transforming scores from a specific domain into a 0-100 scale using a developer-supplied algorithm; 0	**Advantages**: Tools are satisfactory in evaluating the decision-making process for terminally ill children **Limitations**: Fails to evaluate the child's perspective, and applicability of the tool within diverse socioeconomic contexts not yet validated.

[1] Bartlett G, Longo C, Rahimzadeh V, Crimi L. iChange: Ethics and Methods for Engagement in Genomic Research with Vulnerable Populations. Preliminary GE^{3}LS Report submitted to the Research Oversight Committee for the Genome Canada Project: Study of Biomarkers for Pediatric Glioblastoma through Genomics and Epigenomics. 2014

				developed for a broad range of clinical conditions but has been adapted for pediatric cancer research. The survey consists of 20 items measuring two domains: satisfaction with communication and confidence in the decision using also a 5-point Likert scale to evaluate responses.		indicates lowest rates of conflict and 100 the highest.	
Tailored to Specific Ages							
Pediatric Cancer Quality of Life Inventory (PCQL)	U.S.	Parent Child or Teen	8-12, 13-18	Five domains evaluated: physical functioning, disease-related and treatment-related symptoms, psychological functioning, social functioning and cognitive functioning. A 4-point Likert scale is used, 0-if the specific factor is never a problem, 1-if it is sometimes a problem, 2-if it is often a problem and 3-if it is always a problem.	Statistically valid scaling range using a study of 291 pediatric cancer patients and their parents; Demonstrated acceptable internal consistency and reliability in both patient and parent-proxy forms.	The 4-point Likert scale is translated into scores, which are then converted to z-scores and transformed. Higher scores represent more symptoms and health related problems.	**Advantages**: Survey a valuable tool based on both patient-self report and parent-proxy form. **Limitations**: Only only evaluates children older than 8 years of age.
KIDSCREEN Questionnaire	Europe (Austria, France, Germany, Spain, Switzerland, Netherlands)	Parent Child or Teen	8-11, 12-18	52 item questionnaire exploring 10 dimensions: physical well-being, psychological well being, moods and emotions, social support and peers relation, parents relation and home life, self-perception and body image, autonomy, cognitive and school functioning, bullying and social rejection and perceived financial opportunities. Each item is measured using a 5-point Likert scale.	The item-internal consistency and reliability evaluated in a pediatric population of 1194; self-report and proxy instruments statistically valid.	Scores calculated as the mean of the ratings for 10 dimensions; Score from each dimension is transformed into a linear 0 – 100 point scale, 100 being the best and 0 being the worst.	**Advantages**: comprehensive assessment dimensions that consider factors external to clinical environment. **Limitations**: general survey questionnaire not aimed to evaluate HRQoL for terminally ill children with cancer specifically
Pediatric Quality of Life (PedsQL) in Pediatric Cancer	U.S.	Parent Child or Teen	6-15	4 core functioning domains include: physical (8 items), emotional (5 items), social (5 items) and educational (5 items). A 5-point Likert response scale is utilized for both the self-report and parent proxy report (0 = never a	Internal validity and reliability determined for group comparisons; validated for	Scores are generated by reverse-scoring Likert scale; a higher PedsQL score is indicative	**Advantages**: Module designed specifically for HRQoL in pediatric cancer patients. The PedsQL for pediatric cancer has all of the components of the general PCQL tool, in addition

				problem, 1 = almost never a problem, 2 = sometimes a problem, 3 = often a problem and 4 = always a problem). The young child self-report is further simplified and uses a 3-point Likert scale illustrated using happy and sad faces (0 = not at all a problem, 2 = sometimes a problem and 4 = a lot of a problem).	specific use in pediatric cancer populations using 220 child self-reports and 337 parent-proxy reports.	of higher HRQoL.	to the newly developed PedsQL Multidimensional Fatigue Scale, designed to measure child and parent perceptions of fatigue. Tool can also be administered by an interviewer, which can accommodate children who have motor or sensory disabilities as a result of their tumor. **Limitations**: Not specific to terminally ill patients.
TACQOL	Netherlands	Parent Child or Teen	8-18	7 dimensions measured: physical functioning, concerning motor functioning, independent daily functioning, cognitive functioning, social contacts, and both positive and negative moods.	Validity demonstrated using analyses from a study of 2520 pediatric cancer patients	Scores are generated using multiple correspondence analyses (HOMALS)	**Advantages**: Applicability for children who have just received a diagnosis versus child survivors. A recent study validated the use of the TACQOL questionnaire in conducting a prospective assessment of children during their first year of diagnosis (Validated in 52 patients)[2]. **Limitations**: Does not explicitly evaluate terminally ill children.

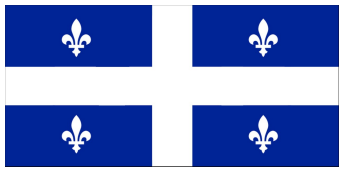
[2] Landolt MA, Vollrath M, Niggli FK, Gnehm HE, Sennhauser FH. Health-related quality of life in children with newly diagnosed cancer: a one year follow-up study. *Health and Quality of Life Outcomes* 2006; **4**: 1-8.

Table 2: *Federal and provincial regulations governing human subjects research in the United States, Canada and Quebec.*

 **45 CFR 46 Health and Human Services Special Protections for Children As Research Subjects[1]**	i) Research not involving greater than minimal risk to the children ii) Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child subject iii) Research involving greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research, but likely to yield generalizable knowledge about the subject's disorder or condition iv) Research that the IRB believes does not meet the other conditions but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.
 **Tri Council Policy Statement 2[2]**	*For research involving individuals who lack the capacity, either permanently or temporarily, to decide for themselves whether to participate, the REB shall ensure that, as a minimum, the following conditions are met:* (i) The researcher involves participants who lack the capacity to consent on their own behalf to the greatest extent possible in the decision-making process; (ii) The researcher seeks and maintains consent from authorized third parties in accordance with the best interests of the persons concerned; (iii) The authorized third party is not the researcher or any other member of the research team; (iv) The researcher demonstrates that the research is being carried out for the participant's direct benefit, or for the benefit of other persons in the same category. If the research does not have the potential for direct benefit to the participant but only for the benefit of the other persons in the same category, the researcher shall demonstrate that the research will expose the participant to only a minimal risk and minimal burden, and demonstrate how the participant's welfare will be protected throughout the participation in research; and (v) When authorization for participation was granted by an authorized third party, and a participant acquires or regains capacity during the course of the research, the researcher shall promptly seek the participant's consent as a condition of continuing participation.

[1] Department of Health and Human Services. Protection of Human Subjects Code of Federal Regulations. 45 CFR 46 Subpart D-Additional Protections for Children Involved as Subjects in Research, 2009.

[2] Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada, Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, December 2010.



Quebec Civil Code[3]

Division I: Care

Article 21. A minor or a person of full age who is incapable of giving consent may participate in research that could interfere with the integrity of his person only if the risk incurred, taking into account his state of health and personal condition, is not disproportionate to the benefit that may reasonably be anticipated.

Moreover, a minor or a person of full age incapable of giving consent may participate in such research only if, where he is the only subject of the research, it has the potential to produce benefit to his health or only if, in the case of research on a group, it has the potential to produce results capable of conferring benefit to other persons in the same age category or having the same disease or handicap.

In all cases, a minor or a person of full age incapable of giving consent may not participate in such research where he understands the nature and consequences of the research and objects to participating in it.

The research project must be approved and monitored by a competent research ethics committee. Such a committee is formed by the Minister of Health and Social Services or designated by that Minister from among existing research ethics committees; the composition and operating conditions of such a committee are determined by the Minister and published in the *Gazette officielle du Québec*.

Consent to research that could interfere with the integrity of a minor may be given by the person having parental authority or the tutor. **A minor 14 years of age or over, however, may give consent alone if, in the opinion of the competent research ethics committee, the research involves only minimal risk and the circumstances justify it.**

Consent to research that could interfere with the integrity of a person of full age incapable of giving consent may be given by the mandatory, tutor or curator. However, where such a person of full age is not so represented and the research involves only minimal risk, consent may be given by the person qualified to consent to any care required by the state of health of the person of full age. Consent may also be given by such a qualified person where a person of full age suddenly becomes incapable of giving consent and the research, insofar as it must be undertaken promptly after the appearance of the condition giving rise to it, does not permit, for lack of time, the designation of a legal representative for the person of full age. In both cases, it is incumbent upon the competent research ethics committee to determine, when evaluating the research project, whether it meets the prescribed requirements.

1991, c. 64, a. 21; 1992, c. 57, s. 716; 1998, c. 32, s. 1; 2013, c. 17, s. 2.

[3] Civil Code Of Québec: *Preliminary Provision*. Updated to Feb 1 2014, available online at http://www2.publicationsduquebec.gouv.qc.ca/dynamicSearch/telecharge.php?type=2&file=/CCQ_1991/CCQ1991_A.html [Accessed 22 Feb 2014].

Table 3 *Glossary of Terms: TCPS 2* (available online at http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/glossary-glossaire/#r)

Risk	The possibility of the occurrence of harm. The level of foreseeable risk posed to participants by their involvement in research is assessed by considering the magnitude or seriousness of the harm and the probability that it will occur, whether to participants or to third parties.
Minimal Risk Research	Research in which the probability and magnitude of possible harms implied by participation in the research is no greater than those encountered by participants in the aspects of their everyday life that relate to the research.
Consent	An indication of agreement by an individual to become a participant in a research project. Throughout this Policy, the term "consent" means "free (also referred to as voluntary), informed and ongoing consent."
Harms	Anything that has a negative effect on participants' welfare, broadly construed. The nature of the harm may be social, behavioural, psychological, physical or economic.
Coercion	An extreme form of undue influence, involving a threat of harm or punishment for failure to participate in research.
Justice	A core principle of this Policy that refers to the obligation to treat people fairly and equitably. Fairness entails treating all people with equal respect and concern. Equity requires distributing the benefits and burdens of research participation in such a way that no segment of the population is unduly burdened by the harms of research or denied the benefits of the knowledge generated from it.
Research	An undertaking intended to extend knowledge through a disciplined inquiry or systematic investigation.
Welfare	The quality of a person's experience of life in all its aspects. Welfare consists of the impact on individuals and/or groups of factors such as their physical, mental and spiritual health, as well as their physical, economic and social circumstances.