

Quality of life of pediatric oncology patients: Do patient-reported outcome instruments measure what matters to patients?

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Abstract

Purpose The assessment of quality of life (QOL) is key within pediatric oncology and requires a clearly defined construct of QOL. The purpose of our study was: (1) to conduct a qualitative study to inform the theoretical underpinnings of QOL and (2) to determine the appropriateness of patient-reported outcome (PRO) instruments to assess and evaluate QOL in pediatric cancer patients and survivors.

Methods The study used an interpretative description approach. Children diagnosed with childhood cancer, aged 8–18 years, were recruited from four Canadian hospitals. Semi-structured interviews were completed, transcribed verbatim and coded through methods of constant comparison. In-depth analysis facilitated a comparison between emerging themes and the content of commonly used PRO instruments.

Results Thirty-seven children (19 females; 51 %) participated. The mean age was 13 years, and 19 (51 %) participants were post-treatment. Participant experiences reflected notions of positive and negative duality, including: maintaining physical functioning but longing for the

ability to participate in activities; experiencing a new level of intimacy with family and friends amidst isolation; and developing positivity amidst anger, sadness and lingering worry. Analysis showed that existing PRO instruments are missing concerns specific to this population and contain content not reflective of the QOL experiences of childhood cancer patients and survivors.

Conclusions Our research highlights important problems with content validity of existing PRO scales, indicating that the tools we have to date have limited utility in research and clinical practice. The development of a new PRO instrument should be considered to ensure that content validity is achieved.

Keywords Cancer · Patient outcome assessment · Pediatrics · Quality of life

Background

The assessment of quality of life (QOL) within pediatric oncology represents a topic of growing interest and importance. Yet, research initiatives require a clearly defined construct of QOL to support theoretical frameworks, and QOL proponents argue that both construct clarity and theoretical frameworks are lacking [1, 2]. Specific to pediatric oncology, the QOL domains and concepts that are most important to children with cancer remain unexplored and undefined [3–5]. This uncertainty permeates research in the field and invites debate regarding the most appropriate patient-reported outcome (PRO) instrument to examine QOL in a pediatric cancer population.

Our team explored QOL as an outcome variable in previously published work, based on systematic review data that identified 148 publications using PRO instruments

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to measure QOL, health-related QOL and/or health status in pediatric oncology research [6]. A total of 10 generic and 10 cancer-specific PRO instruments were identified (Table 1), and a content analysis was conducted [6]. All instrument items (879) were coded into four major domains of QOL and categorized within 11 subdomains and 98 identifying concepts that reflected item specificity (Fig. 1).

The purpose of the current study was to validate the conceptual basis of our proposed model and included: (1) conducting a qualitative study to inform the theoretical underpinnings of QOL, from the perspective of cancer patients and survivors and (2) mapping these findings onto our conceptual model of QOL, allowing comparisons between proposed domains and concepts. By eliciting the perspectives of children with cancer, as well as performing the described mapping exercise, we sought to determine the appropriateness of PRO instruments to assess and evaluate QOL in a pediatric cancer population. Thus, this study will allow for the transference of improved theoretical and construct clarity in QOL research to influence best practice regarding the use of PRO instruments in the clinical care of children with cancer.

Table 1 PRO instruments [2]

PRO instruments
<i>Cancer-specific</i>
<i>AQOL</i> Adolescent Quality of Life Questionnaire
<i>MMQL</i> Minneapolis-Manchester Quality of Life Instrument
<i>MPQOLQ</i> Miami Pediatric Quality of Life Questionnaire
<i>PEDQOL</i> Quality of Life in Children and Adolescents with Cancer
<i>Peds-FACT-Brs</i> Pediatric Functional Assessment of Cancer Therapy Childhood Brain Tumor Survivor
<i>PedsQL</i> Brain Pediatric Quality of Life Inventory—Brain Tumor Module
<i>PedsQL</i> Cancer Pediatric Quality of Life Inventory—Cancer Module
<i>POQOLS</i> Pediatric Oncology Quality of Life Scale
<i>QOLCC</i> Quality of Life for Cancer Children
<i>RMH-PQLQ</i> Royal Marsden Hospital Pediatric Oncology Quality of Life Questionnaire
<i>Generic</i>
<i>CHIP</i> Child Health and Illness Profile
<i>CHQ</i> Child Health Questionnaire
<i>DISABKIDS</i> Instrument
<i>DISQUOL</i> Questionnaire
<i>HUI</i> Health Utilities Index
<i>ITQOL</i> Infant Toddler Quality of Life Inventory
<i>Kidscreen</i> Questionnaire
<i>KINDL</i> Questionnaire
<i>PedsQL</i> Pediatric Quality of Life Inventory
<i>TACQOL/TAPQOL</i> TNO-AZL Child Quality of Life

Methods

Recruitment

Participants were recruited from four Canadian hospitals that treat approximately 40 percent of all children with cancer in Canada. Eligibility criteria included children between the ages of 8–18 years, diagnosed with childhood cancer of any type. A purposive sampling strategy was used to encourage maximum variation in age, gender, age at diagnosis, type of cancer and phase of treatment. A familiar health care provider contacted potential participants. Exclusion criteria included the inability to speak English and the presence of severe cognitive impairment, as both would limit interview participation. The number of interviews was dependent on theoretical saturation of collected data.

Research ethics board approval was received from participating institutions, and consent or assent was obtained from study participants.

Study design and methodology

An interpretive description (ID) qualitative approach [7] was used that presupposes that a study is informed by scientific, theoretical and clinical knowledge. ID was appropriate to our proposed research as it is driven by a purpose grounded in a practice goal and a desire to understand the current state of knowledge [7]. An interview guide was developed, based on the experience of the research team and the available literature, that included open-ended questions (e.g., “Can you tell me about what your life was like before you had cancer?”) and prompts to elicit further detail of emerging topics and themes. Each study participant completed a semi-structured interview that was audio tape-recorded and transcribed verbatim by a professional transcriptionist. Data collection was concurrent to data analysis, which included line-by-line coding of common meaning units, themes and patterns and multiple coders for a subset of transcripts to establish trustworthiness [8]. An iterative process guided further data collection and analysis as new ideas, themes and patterns emerged. NVivo 10 software [9] was used for data management.

Following thematic coding, qualitative codes were labeled to represent the domain of physical, psychological or social health and were associated with a subdomain from our proposed conceptual model of QOL. This process allowed us to map the themes and concepts that emerged from the participant interviews to our original proposed model of QOL. We then compared the relative distribution of PRO instrument items within each domain to the relative distribution of codes labeled within each domain as

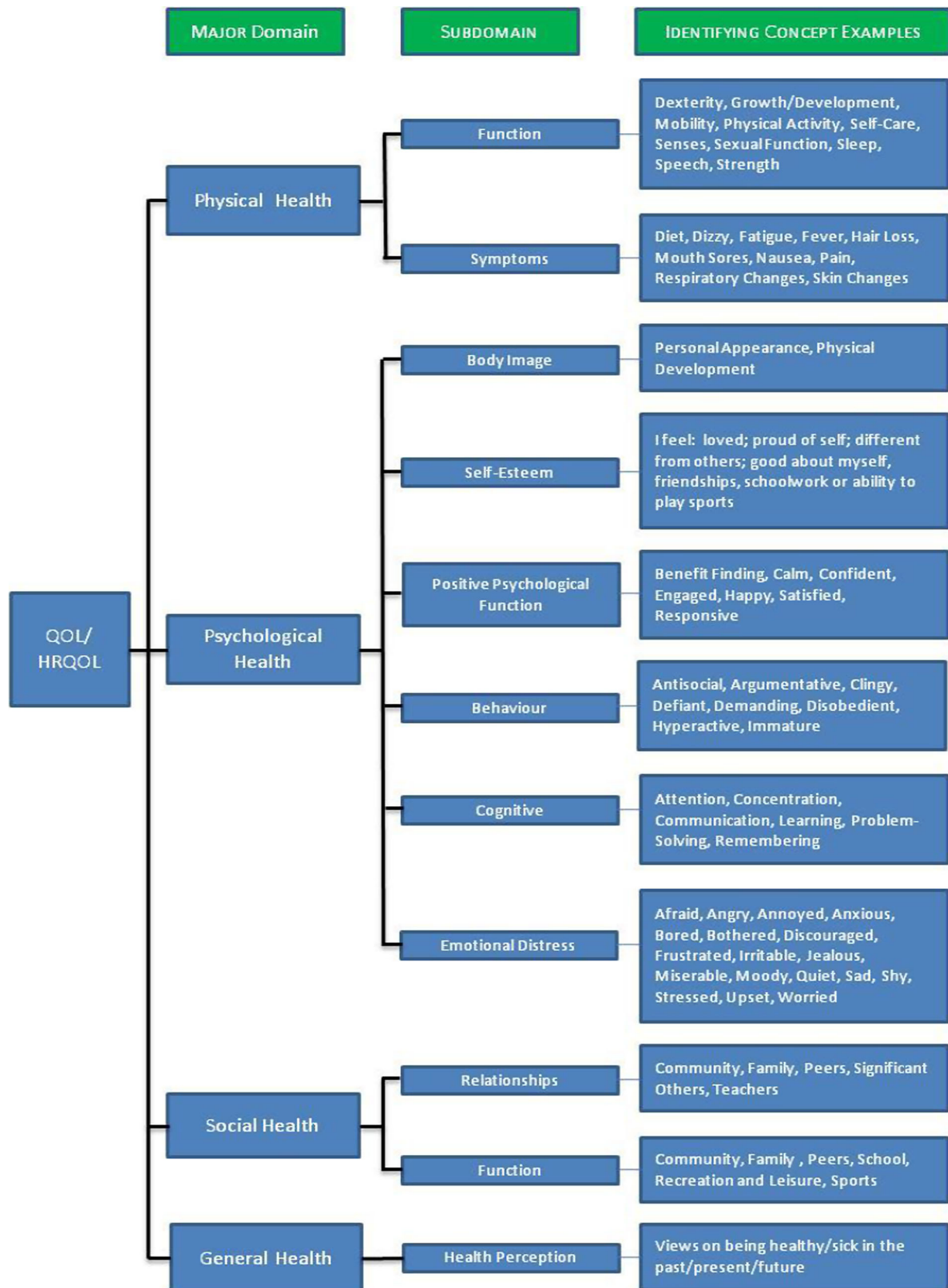


Fig. 1 Working model of QOL/HRQOL domains, subdomains and concepts most commonly assessed in PRO instruments for Pediatric Oncology (reproduced from [6])

identified by research participants as key to their QOL experience. This also allowed us to identify data that were unique to the participant experience and not addressed by PRO instruments.

Specific means to ensure the trustworthiness of the study included the use of a code–recode strategy and double-coding (dependability); member checking and reflexivity (credibility); regular coding process meetings; maintaining an audit trail (confirmability); and thick description of the research process, participants and setting (transferability) [10, 11]. Verification strategies to ensure rigor were incorporated into our methodological processes, including: (1) ensuring that our sample was appropriate to the research question and (2) ensuring that an iterative process of analysis was maintained to facilitate consistency of code and theme generation between stages of data collection.

Results

A total of thirty-seven children (19 females; 51 %) participated. Mean age was 13 years (range 8–18) at the time of interview. A total of 19 (51 %) participants were post-treatment, and 17 had completed their treatment protocol within the past five years. Diagnoses included: acute lymphoblastic leukemia ($n = 12$, 32 %); acute myeloid leukemia ($n = 4$; 11 %); lymphoma ($n = 9$, 24 %); and other solid tumors ($n = 12$, 33 %), including central nervous system tumors ($n = 6$, 16 %), sarcoma ($n = 3$; 8 %), embryonal tumors ($n = 1$; 3 %), testicular cancer ($n = 1$, 3 %) and ovarian choriocarcinoma ($n = 1$, 3 %). Participants came from diverse ethnic and racial backgrounds.

Perceptions of QOL interwove positive and negative accounts of the illness experience—“so it’s the good with the bad. You can’t have good without bad, you can’t have bad without good”—as highlighted by the following three themes.

Maintaining physical functioning but longing for ability to participate in activities

While participants reported that many aspects of their physical functioning (e.g., mobility, self-care, etc.) were not limited, they expressed the importance of being able to maintain their physical ability to do “the things that they liked doing the most”. For most participants, this was an important QOL concern, as highlighted in the following passage:

...definitely someone’s life being good would really just [mean] ... being able to do what you love, whether it’s sports or school or whatever. (*Female, age 15, on treatment*)

Unfortunately, activities of choice were not often congruent with the activities that one was physically able to participate in. Participants described wanting to engage in activities with family and friends, as well as activities that were favored prior to a cancer diagnosis, such as competitive sports, running or dancing. Being off-treatment did not necessarily guarantee an increase in QOL, as some participants experienced lasting, long-term, physical effects from treatment, resulting in restrictions from participating in favorite activities:

I can’t dance as much... I just can’t do any of the stuff. And I feel useless sometimes because of my knees...I do cry. (*Female, age 15, off treatment*)

Overall, participants’ levels of satisfaction with their physical abilities seemed relative to the degree of participation achieved in desired activities. In turn, this level of satisfaction had a large influence on one’s perception of QOL. However, a few participants acknowledged that a positive effect on QOL was experienced at any level of activity participation. For these individuals, “just being able” to participate for the benefit of social inclusion was enough:

Because there are limitations...I can’t participate. I don’t need the running and everything to have fun - I just need to participate with them [friends]. (*Male, age 12, on treatment*)

Experiencing a new level of intimacy with family and friends amidst isolation

Participants talked about feelings of isolation and loneliness as being particularly distressing to their QOL. Such feelings were most prevalent at the time of active treatment, when participants reported restrictions to freedom due to hospitalization or confinement precautions. The pervasiveness of these feelings may account for the extensiveness in which isolation was described, particularly in the essence of being trapped and/or bored.

It was just like me kind of like trapped in a room and being sick all the time. Not being able to go anywhere or do anything that I wanted to do. (*Female, age 18, off treatment*)

Feelings of isolation persisted when participants returned home since they faced additional stresses of confinement to avoid the risk of potential infection. As one interviewee described:

...because my counts were down and I couldn’t go outside. I couldn’t really see people unless they were wearing masks...and then they didn’t really know

when to visit me and when to not ...it sucked...I was alone a lot. (*Female, age 18, on treatment*)

Yet, despite feeling isolated during various stages of cancer, almost all participants simultaneously described how their experience with cancer brought them emotionally closer to family.

I felt like, ‘wow, this is my family’. They were there for me. They took care of me...After getting out, I appreciated that they were there...[it] made me closer to them. (*Male, age 15, off treatment*)

Participants also talked about growing closer to friends and discovering their “real” friends. One participant expressed, “I realized I know who my real friends are now...Those are the people I grew closer to.”

Developing positivity amidst anger, sadness and lingering worry

Interviewees frequently spoke of feelings related to emotional distress: sadness and feelings associated with anger were talked about most often. In particular, these feelings of distress were most prevalent at the time of diagnosis and during the initial stages of treatment. One participant described this emotionally turbulent time: “...it kind of hit me that I had cancer...it was kind of sad. I was angry. It was almost as if I didn’t think it was fair. Why me?” Another interviewee shared: “I’d be really sad most of the time because I felt like it was unfair when people get cancer—people shouldn’t get it at all.”

Yet, despite the feeling that being diagnosed with cancer is “not fair”, as well as feeling sad and/or angry when trying to determine, “why me?”, study participants found strength in the adoption of new life perspectives. This included participants as young as age ten and those in the early stages of treatment. One participant stated simply, “The best thing is if you can survive it, you come out such a stronger person”.

Participants talked extensively about how their outlook on life changed as they established new perspectives and priorities as a result of their illness experience. As one participant explained:

I don’t get upset over most things because I realize that it’s life. Life is supposed to put you down. It’s supposed to challenge you and test you and the easiest way to go through it is to be happy. So why be sad when there’s so much good that’s going on? (*Male, age 14, off treatment*)

However, despite developing enhanced positivity, participants lived with lingering worries about the possibility of death and whether or not the cancer would return. One

participant explained: “You know, having doubts... thinking, oh, I still have a risk of my cancer coming back.” These were fears that participants carried with them, even for years post-treatment, despite the inherent positive growth that took place.

Children with cancer and childhood cancer survivors—stories lived differently?

The participant sample included children with cancer and childhood cancer survivors. This introduces the element of temporality and invites one to question whether the participant experiences of QOL differed across the temporal trajectory of living with cancer and its aftermath. While QOL was described differently by children with cancer and by childhood cancer survivors depending on their current lived experience, the emergent themes identified provided an overlay across the trajectory of QOL, regardless of current illness status. Participants described lower QOL at the time of diagnosis and spoke about the psychological distress and isolation experienced during the initial treatment and hospitalization. Our findings suggested that QOL typically improved over the course of the oncology journey, yet participants continued to speak about various biopsychosocial phenomena that affected their QOL. These phenomena included the long-term physical effects from treatment and lingering worries and fears about the future. Although specific references and examples varied given the current status of participants, each theme identified within our findings was reflected across the temporal trajectory of living with cancer, thus creating a common experience across both children living with cancer and childhood cancer survivors.

Relationship between PRO instrument content and patient experiences

Figures 2 and 3 show the distribution of items within PRO instruments, and the qualitative codes labeled across the primary QOL domains and subdomains, considered by treatment phase (on or off), and stemming from the framework of our conceptual model.

Physical domain Content items from the PRO instruments concentrated on the physical domain; the subdomains of function and/or symptoms were heavily-populated and captured by all 20 PRO instruments identified within our systematic review. Although study participants reported many physical health concerns, these concerns were not perceived as burdensome compared to other domains of QOL. Within the subdomain of physical function, mobility (e.g., walk, bend, lift) was the most prevalent concept

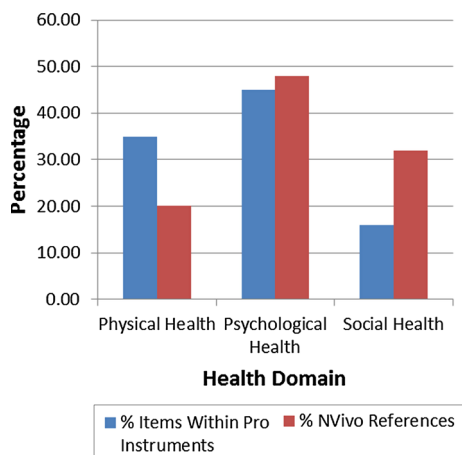
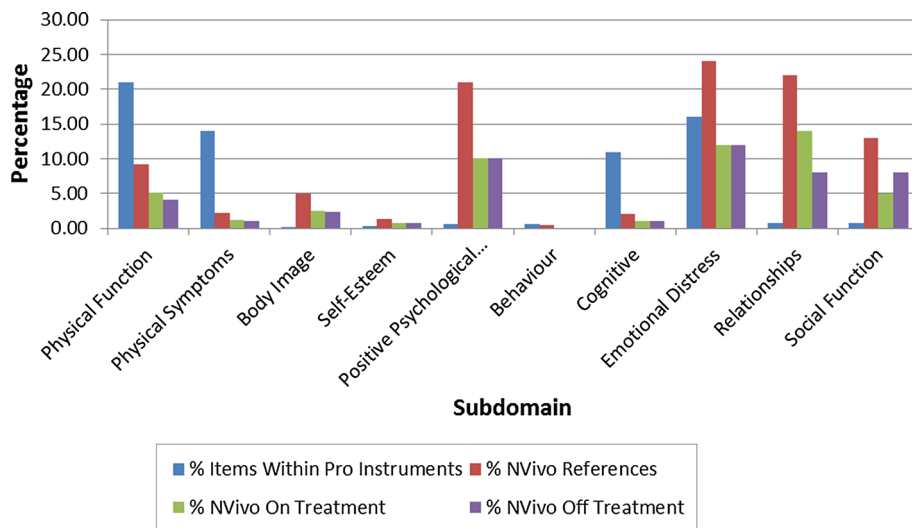


Fig. 2 Domain items within PRO instruments versus % of NVivo references within domains of physical, psychological and social health

identified within PRO instruments and was accompanied by concepts, such as self-care, sleep, sexuality, dexterity, growth and development. In contrast, study participants emphasized the importance of physical activities and their ability to participate in sports and recreational activities. There was considerable overlap for the concept of physical activity, which was addressed by 16 of the 20 PRO instruments. While disease and treatment symptom-related concepts, such as pain, fatigue, and nausea, were highly populated throughout the PRO instruments, study participants did not emphasize their importance as key contributors to overall QOL. For example, children identified physical discomfort but acknowledged that there was medication or local anesthetic that could help to alleviate pain.

Fig. 3 Subdomain Items within PRO instruments versus % of NVivo references



Psychological domain While Fig. 2 shows a similar proportion of content between study participant experiences and PRO instruments within the realm of psychological health, we found incongruences, particularly within the areas of cognitive functioning and positive psychological functioning. While cognition was one of the most populated subdomains within the PRO instruments, this concept was seldom mentioned by study participants. When participants did address cognitive concerns, such as learning, attention and problem-solving, they often identified the difficulty in differentiating limitations attributable to cancer and its treatment and those attributable to one’s actual cognitive ability, irrespective of cancer. Positive psychological health represented one of the widest discrepancies between the emergent QOL themes of study participants and PRO instrument content. Participants spoke extensively about developing new life perspectives, shifting priorities and gaining a stronger sense of self. However, only 50 (0.6 %) of the 879 PRO instrument items addressed elements of positivity (e.g., happy, calm), with only two items pertaining specifically to benefit finding: e.g., “The illness experience has taught me to appreciate life” and “The illness experience makes me a stronger person”.

Social domain The social domain represented the greatest divergence between PRO instrument content and patient experiences. Seventeen of the 20 PRO instruments included items pertaining to social health. The three exceptions included: (1) the Health Utilities Index, the second most common generic PRO instrument used in pediatric childhood cancer QOL studies; (2) the Pediatric Quality of Life Inventory—Cancer Module, the most commonly utilized cancer-specific PRO instrument; and (3) the Pediatric

Quality of Life Inventory—Brain Module. Our content analysis revealed that 139/879 (16 %) of the PRO instrument items had social health content and included the subdomains of function (e.g., involvement in and satisfaction with one’s usual roles in life situations and activities) and relationships (e.g., with family, teachers, peers etc.). The concepts of loneliness and isolation were prioritized by study participants as key to QOL, yet were captured by only 12 of the PRO instruments. Further, the PRO instruments failed to capture the essence of being trapped and/or bored as a result of hospitalization or confinement precautions, with only one PRO instrument item addressing boredom. Within the social domain, the theme of enhanced relationships with family and friends was also paramount to participant experiences; almost every PRO instrument contained items addressing relationships with family and friends. A noteworthy exception was the PedsQL: It is the most widely used PRO instrument, yet did not contain a single item concerning family functioning or family relations.

Conclusions

Our study found that the effects of cancer on children had a substantial impact on physical, psychological and social well-being. Participant experiences yielded themes of QOL, including: (1) maintaining physical functioning, but longing for the ability to participate in activities; (2) experiencing a new level of intimacy with family and friends amidst isolation; and (3) developing positivity amidst anger, sadness and lingering worry. These findings support a continuum of negative and positive experiences within the illness journey of children with cancer and childhood cancer survivors [12–21]. Children and adolescents acknowledge negative aspects of their illness journey, describing that they often: (1) are physically limited from participating in desired activities and (2) feel isolated and lonely, and experience emotional distress, particularly, sadness, anger, fear and worry [12, 15–17, 19, 21, 22]. Positive events reported include experiences of improved relationships with others and altered attitudes about self and life [13–15, 17, 20, 21]. This interplay between negative and positive consequences has been referred to as a “dialectic phenomenon” [19] and provides important insights into the response of children to the cancer experience.

Our findings suggest that existing PRO instruments are missing content that reflects the QOL experiences and perspectives of childhood cancer patients and survivors. Although our findings do show some similarity of content in existing PRO instruments, our team opined that these measurements only weakly address some important and

unique concerns. PRO instruments tend to focus more on the physical health domain, including function and symptoms, while qualitative results suggest that study participants emphasized the importance of social health, including function and relationships. Within the domain of psychological health, positive psychological well-being was one of the key themes present throughout the experiences of study participants; however, this subdomain and the concept of personal growth are poorly represented in the PRO instruments. Our findings confer with those of Hinds et al. [3], who found that several established PRO instruments used in pediatric oncology were conceptually incomplete and failed to accurately measure the QOL of children and adolescents with cancer.

Our findings support the development of new PRO instruments to improve upon the best measures available and to ensure that content validity is achieved. It is crucial that PRO tools capture the key concerns of childhood cancer patients, and survivors to effectively facilitate research in this field. While developing a new tool may be criticized as unnecessary or redundant, due to the proliferation of valid and reliable measures available, our research highlights a need given concerns of content validity in existing scales. If a new PRO scale is developed for this population, we advise that internationally accepted guidelines are followed for the development of PRO instruments [23–26]. This process involves rigorous qualitative research with the target population [23, 25, 26], a design element not addressed by many QOL scales used in pediatric oncology [27]. PRO instruments developed using modern psychometric methods (e.g., Rasch Measurement Theory) would provide end users with scales that are sufficiently valid and reliable to allow their use in clinical practice for patient monitoring and management [28, 29].

Although our sample is diverse across demographic, illness and treatment variables, we acknowledge that our findings emerged from a purposively selected sample of children; an alternative selection of participants may have expressed different QOL experiences. Participants were from diverse ethnic and racial backgrounds across participating sites; however, all participants were Canadian residents. Cultural experiences and perceptions of QOL may vary among other countries, and our findings may not be representative of this possibility. Further, our research did not include perceptions of parents, siblings, teachers, or other key individuals with reflective insights on the participant’s QOL. However, it is recognized that children’s perspectives of illness should be at the center of research concerning their own health and well-being [30, 31].

Childhood cancer is a complex, multi-layered process of difficulty, adjustment and growth. Our findings suggest that existing PRO instruments contain content that does not

reflect the QOL experiences and perspectives of childhood cancer patients and survivors. Further, these measurements weakly address important concerns unique to this population, indicating that the current PRO instruments have limited utility in research and clinical practice. If current PRO instruments continue to be utilized, important aspects critical to understanding the QOL of pediatric oncology patients will not be captured, and the validity of the assessment will be questioned. Our findings support that the perspectives (i.e., health status vs QOL) and content characteristics of PRO instruments need careful consideration when selecting instruments for research and clinical evaluation purposes [32]. Future research initiatives may propose to develop a new PRO instrument to ensure content validity of assessing QOL in childhood cancer patients and survivors.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval All procedures performed in this study were in accordance with the ethical standards of all participating institutional research committees and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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

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