

## Health-related Quality of Life in Children with Cancer Undergoing Treatment: A First Look at the Singapore Experience

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### Abstract

**Introduction:** With intensive chemotherapy and increased survival, quality of life in our paediatric population is of increasing concern. The aim of this study was to assess the children's quality of life during the treatment process. **Materials and Methods:** Patients between the ages of 7 and 18 years old who are undergoing cancer treatment in the Division of Paediatric Haematology-Oncology, Department of Paediatrics, National University Health System, were identified. The child self-reported his/her health-related quality of life (HRQOL) using the PedsQL Paediatric Quality of Life Inventory and Cancer module as a validated assessment tool. **Results:** Thirty-two patients were enrolled over a 3-week period in November 2007. The median age was 11 years (range, 7 to 17). There was 1 non-responder (3%). Fourteen (45%) boys and 17 (55%) girls were interviewed. There were 8 (26%) and 23 (74%) patients with solid and haematologic malignancies, respectively. For the Cognitive Problem Dimension score, 86% of patients with haematologic malignancy and 50% of those with solid malignancy scored below the 75<sup>th</sup> percentile (82), [OR 0.72 (0.01-0.8),  $P = 0.03$ ]. For the Physical Health Summary score, patients with solid malignancy scored worse, 25% below the 10<sup>th</sup> percentile, as compared to 4.3% of patients with haematologic malignancy. This is reflected by a worse Pain and Hurt Dimension score for patients with solid malignancy. For the Perceived Appearance Dimension score, patients with solid malignancy (75%) scored lower than the median score (67) compared to those with haematologic malignancy (44%). **Conclusions:** The domains of HRQOL are affected to different extents for the patients with solid and those with haematologic malignancy. This is most likely to be due to the differences in treatment strategies and clinical course. Healthcare professionals should be aware of the effects of treatment on HRQOL and take practical steps to address these issues.

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**Key words:** Childhood cancer, Self-reported health and well-being

### Introduction

Health-related quality of life (HRQOL) has been progressively acknowledged as an essential health outcome measure in clinical trials and health services research and evaluation.<sup>1-3</sup> HRQOL, compared to QOL, is a more defined conceptual term which encompasses only health-related aspects of life directly amenable to healthcare services and medical products.<sup>4</sup> Hence, HRQOL is a more appropriate term to represent the patient's perception of the impact of an illness and its treatment which are within the scope of healthcare services and products. A HRQOL instrument must be multi-dimensional, consisting at the minimum

of the physical, psychological (including emotional and cognitive), and social health dimensions delineated by the World Health Organisation.<sup>5</sup>

With better treatment strategies in place, these have led to an increased survival.<sup>6,7</sup> However, current treatment strategies still remain intensive and aggressive.<sup>8,9</sup> As such, concerns about quality of life for children with cancer have been raised for those undergoing treatment. Treatment protocols can cause children to be frequently unwell and fatigued. These children are also more vulnerable to infections with a constant need to attend the hospital on a regular basis, resulting in long absences from school.

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Family and social activities are also limited.<sup>10</sup>

The objective of this study was to take a first look at the HRQOL in children with cancer undergoing treatment in Singapore. The secondary objective was to identify areas of HRQOL that were adversely affected by treatment protocols and thus any necessary measures could be set in place to improve these domains of HRQOL.

## Materials and Methods

### *Study Population and Study Design*

The Singapore Childhood Cancer Registry (SCCR), a hospital-based cancer registry of children under 15 years of age, initiated by the Paediatric Oncology Group-Singapore (POGS), reported their first monograph from 1997 to 2005. National University Hospital System (NUHS), Division of Paediatric Haematology/Oncology is a main referral centre for new and relapsed Paediatric Oncology cases locally within the island state and from the Southeast Asian region such as Malaysia, Indonesia, Philippines, Brunei, Vietnam, Myanmar, India and Sri Lanka. According to the SCCR, approximately 100 new cases of childhood cancer are seen in Singapore with up to 50% of them being referred and treated in NUHS. From the year 1997 to 2005, SCCR reported 197 cases of childhood cancer seen and treated at NUHS.<sup>11</sup> Eligible children were between 7 and 18 years of age and were presently undergoing treatment for their cancer at NUHS. The minimum age of 7 years old was selected as the investigators wanted to determine the effect of cancer treatment on school-going children. The children were randomly selected by a random sequence generator by the Department of Biostatistics.

Identified children were approached when attending a routine outpatient clinic appointment at the Division of Paediatric Haematology/Oncology, NUHS. They were given verbal and written information by the investigators. After obtaining consent from the parent(s) and child, the child then self-reported his/her HRQOL using the PedsQL Paediatric Quality of Life Inventory and Cancer module as a validated assessment tool. Permission for use was obtained from Mapi Research Trust. All data were collected at the particular clinic setting and the investigator was available to help those who experienced any difficulty. The study was conducted over a 3-week interval during November 2007. The study received ethical approval from the institutional review board.

### *PedsQL*

The PedsQL Paediatric Quality of Life Inventory and Cancer module were employed as assessment tools in this study. PedsQL has been validated to be feasible and reliable for use in studies which require children to self report their quality of life.<sup>12-14</sup> The PedsQL includes an 8-item physical

health summary score (physical functioning) and a 15-item psychosocial health summary score (school, social and emotional functioning). A total QOL score can also be calculated from these summary scores. A total of 8 Domain Scores can be calculated from PedsQL Cancer Module. They are Pain and Hurt Domain Score, Nausea Domain Score, Procedural Anxiety Domain Score, Treatment Anxiety Domain Score, Worry Domain Score, Perceived Appearance Domain Score, Communication Domain Score and Cognitive Problem Domain Score.

There are separate versions for those aged 7 (or less), 8-12 and 13-18 years old. Items for each form are essentially identical, differing only in developmentally appropriate language, or first or third person tense. Participants were then asked how much of a problem has been experienced over the last month. Items are rated on a 5-point Likert scale, from 0 (never a problem) to 4 (almost always a problem). The items are then reversed scored and linearly transformed to a 0-100 scale as follows: 0 = 100, 1 = 75, 2 = 50, 3 = 25 and 4 = 0. After transformation, scores range from 0 to 100, with higher scores representing better HRQOL. Scores would not be computed if 50% of the items in the scale are missing.

## Results

### *Characteristics of the Study Population*

Thirty-two patients, all currently undergoing treatment for their cancer, consented and participated in the study. There was 1 non-responder (3.0%). Eight (26.0%) patients were diagnosed with a solid malignancy, whilst 23 (74.0%) patients were diagnosed with a haematologic malignancy. The median age at enrollment was 11 years (range, 7 to 17). Fourteen (45.0%) boys and 17 (55.0%) girls were recruited for the study. Among those with a solid malignancy, primary diagnosis include osteosarcoma (n = 4, 50%), germ cell tumour (n = 3, 37.5%) and neuroblastoma (n = 1, 12.5%). As for those with a diagnosis of haematologic malignancy, majority are acute lymphoblastic leukaemia (ALL) with a total of 16 patients (69.6%). Other diagnoses include 2 (8.7%) patients with acute myeloblastic leukaemia (AML), 2 (8.7%) patients with non-Hogkin's lymphoma, 2 (8.7%) patients with other specified leukaemia and 1 (4.3%) patients with chronic myeloblastic leukaemia. All patients who consented for the study completed the assessment. General characteristics of the patients are listed in Table 1. Therapy for haematologic malignancies consists of systemic chemotherapy which may span over 6 months to 3 years depending upon the particular diagnosis. Some of the children who present with central nervous system disease (CNS) may receive radiation therapy to their brain as part of the treatment. Therapy is intensive in the first few months followed by the maintenance phase.

Table 1. General Characteristics of Study Population

Characteristics	Solid malignancy	Haematologic malignancy
Age (range), y	13 (7 to 17)	11 (7 to 17)
Female, n/N	4/8	13/23
Male, n/N	4/8	10/23
Duration since diagnosis, mean years (SD)	1.3 (1.5)	1 (1.3)
Total, N	8 (26%)	23 (74%)

*P* = NS

Therapy for solid malignancies consists of systemic chemotherapy with surgery and or radiation therapy depending upon the specific diagnosis. Therapy is intensive throughout which may span over 8 months to over a year. Surgery may also consist of limb-salvage surgery or amputation requiring intensive physical therapy sessions.

*PedsQL Scores*

Health Summary Scores

Health Summary Scores are obtained from PedsQL Quality of Life Inventory. Two different summary scores can be obtained – Physical and Psychosocial Health Summary Scores. Physical Health Summary Score is obtained from Physical Functioning Scale Score, whereas Psychosocial Health Summary Score is obtained from Emotional, Social

Table 2. Health Summary Scores

Summary score	Solid malignancy	Haematologic malignancy
Physical health Summary score, mean (range)	53.3 (18.8-87.5)	63.4 (9.4-100)
Psychosocial health Summary score, mean (range)	68.1 (53.3-86.7)	60.7 (35-86.7)

*P* = NS

Table 3. Domain Scores

Domain score	Solid malignancy	Haematologic malignancy
Pain and Hurt, mean (SD)	68.8 (24.1)	73.4 (21.4)
Nausea, mean (SD)	76.9 (23.3)	63.3 (21.2)
Procedural Anxiety, mean (SD)	57.3 (29.7)	53.3 (30.1)
Treatment Anxiety, mean (SD)	90.6 (12.1)	82.2 (26.3)
Worry, mean (SD)	52.1 (26.3)	61.6 (27.0)
Perceived Appearance, mean (SD)	63.5 (20.9)	71.4 (25.2)
Communication, mean (SD)	84.4 (18.6)	62.7 (27.0)
Cognitive Problem, mean (SD)	75.3 (21.2)	65.9 (17.8)

and School Functioning Scales. The Physical Health Summary Score has a mean of 60.8 (range, 9.4 to 100). Psychosocial Health Summary Score has a mean of 62.6 (range, 35 to 86.7) (Table 2).

*Domain Scores*

Domain Scores are obtained from the PedsQL Cancer Module. Our patients scored best for Treatment Anxiety Dimension score with a mean of 84.9 (range, 0 to 100), and worst for Procedural Anxiety Dimension Score with a mean of 54.2 (range, 0 to 100) (Table 3).

Differences in Scores

Several domain scores differed when compared between those with solid and those with haematologic malignancy. Looking across the percentiles (10<sup>th</sup>, 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup>), 86.4% of patients with haematologic malignancy and 50% of those with solid malignancy scored below the 75<sup>th</sup> percentile for Cognitive Problem Domain Score, [OR 0.2 (0.01-0.8), *P* = 0.03]. This means that among those with haematologic malignancy, a greater proportion of them would have a lower Cognitive Problem Domain Score, as compared to those with solid malignancy. Similarly, as we compare the Physical Health Summary Score between the 2 groups across the percentiles, patients with solid malignancy performed worse, with 25% scoring below the 10<sup>th</sup> percentile, as compared to 4.3% of patients with haematologic malignancy. This result is supported and reflected in the worse Pain and Hurt Domain Score for patients with solid malignancy (Table 3, Pain and Hurt Domain Score). Moving on, in the domain of Perceived Appearance, 75% of patients with solid malignancy scored lower than the median score of 67 when compared to 44% of those with haematologic malignancy. Also, for the Nausea Dimension Score, there is a higher proportion of patients with haematologic malignancy scoring below the 4 percentiles as compared to those with solid malignancy (Tables 4 to 7).

**Discussion**

Assessment of HRQOL during the treatment process is a way of allowing the children to voice their fears and concerns. It is also a way for the medical team to assess the impact of treatment on the HRQOL. The outcome of the assessment at various phases of diagnosis of treatment can then help guide the parents, the healthcare providers, the medical team and the social workers on how best to provide support and facilities necessary to help the child through this difficult period. However, there is limited data on how children in Singapore with a diagnosis of cancer are affected in the various domains in their HRQOL during the treatment. Thus, we have attempted to investigate this using a recognised and validated scale – PedsQL – in our population in Singapore.

Table 4. Cognitive Problem Domain Score across the Percentiles

Percentile (Score)	≤10% (45)	≤25% (55)	≤50% (70)	≤75% (82)
Solid	25.0%	25.0%	37.5%	50.0%
Liquid	9.1%	27.3%	63.6%	86.4%
OR (95% CI)	3.3 (0.4-29.0)	0.9 (0.1-5.7)	0.3 (0.06-1.8)	0.2 (0.03-1.0)
<i>P</i> value	0.275	0.901	0.210	0.05
Adjusted* OR (95% CI)	0.7 (0.03-13.6)	0.5 (0.06-4.2)	0.2 (0.03-1.5)	0.72 (0.01-0.8)
Adjusted* <i>P</i> value	0.785	0.506	0.122	0.03

\*Adjusted for type of malignancy, gender, duration and age

Table 5. Physical Health Summary Score Across the Percentiles

Percentile (Score)	≤10% (19)	≤25% (47)	≤50% (66)	≤75% (81)
Solid	25.0%	37.5%	50.0%	75.0%
Liquid	4.3%	26.1%	52.2%	60.9%
OR (95% CI)	7.3 (0.6-95.3)	1.7 (0.3-9.4)	0.9 (0.1-4.6)	1.9 (0.3-11.7)
<i>P</i> value	0.128	0.542	0.916	0.476
Adjusted* OR (95% CI)	100 (0.1-500)	1.3 (0.2-8.5)	0.7 (0.1-3.9)	1.6 (0.2-10.6)
Adjusted* <i>P</i> value	0.996	0.818	0.653	0.618

\*Adjusted for type of malignancy, gender, duration and age

Table 6. Perceived Appearance Domain Score Across the Percentiles

Percentile (Score)	≤10% (42)	≤25% (50)	≤50% (67)	≤75% (92)
Solid	12.5%	37.5%	75.0%	87.5%
Liquid	13.0%	30.4%	43.5%	87.0%
OR (95% CI)	1.0 (0.09-10.7)	1.4 (0.3-7.4)	3.9 (0.6-23.6)	1.1 (0.09-11.8)
<i>P</i> value	0.968	0.713	0.916	0.968
Adjusted* OR (95% CI)	0.3 (0.01-7.3)	1.2 (0.2-7.2)	4.4 (0.6-29.9)	1.0 (0.08-12.9)
Adjusted* <i>P</i> value	0.452	0.842	0.132	0.995

\*Adjusted for type of malignancy, gender, duration and age

### Cognitive Problem Issues

Patients with haematologic malignancy have a longer treatment process as compared to those with solid malignancy, as such, they are more likely to be absent from school for a longer period of time. This prolonged absence from school, when without other educational support at home or elsewhere, lead to an impact on these children coping with school work and cause them to fall behind the progress of their healthy schoolmates. This is especially true in Singapore where education is very

important and competitive amongst peers. Additionally, some patients who have haematologic malignancy may need radiation therapy to the brain for their CNS disease. This irradiation has been proven to affect the mental capacity of patients to a certain extent, making it more difficult for them to cope with school work as their memory and attention span are affected.<sup>15-18</sup> Additionally, side effects of medications such as corticosteroids may also affect mood and attention span, all proving to be a hindrance to learning.<sup>19,20</sup>

Table 7. Nausea Domain Score across the Percentiles

Percentile (Score)	≤10% (40)	≤25% (50)	≤50% (70)	≤75% (85)
Solid	12.5%	25.0%	25.0%	62.5%
Liquid	21.7%	30.4%	69.6%	87.0%
OR (95% CI)	0.5 (0.1-5.2)	0.8 (0.1-4.8)	0.1 (0.02-0.9)	0.3 (0.04-1.6)
<i>P</i> value	0.574	0.771	0.039	0.148
Adjusted* OR (95% CI)	0.486 (0.03-7.2)	0.7 (0.1-7.6)	0 (0-500)	0.2 (0.02-1.9)
Adjusted* <i>P</i> value	0.601	0.765	0.998	0.155

\*Adjusted for type of malignancy, gender, duration and age

### Physical Health and Nausea Issues

It is well known that chemotherapy drugs have significant side effects, especially in those of a tender age. Toxicities such as nausea, vomiting, severe pancytopenia, the need for transfusions, and high infection risks have always been an issue in many studies involving paediatric oncology treatment regimens.<sup>21,22</sup> Among the 2 groups, drugs used for the treatment of solid malignancy tend to be more emetogenic with more severe toxicities, thus having a greater side effect on the young child. As such, patients with solid malignancy reported a worse Physical Health Summary Score, reflecting the child's effort tolerance, the ability to do sports, house chores and other activities of daily living. Although the drugs used in the treatment of solid malignancy have greater side effects, nausea and vomiting remain a side effect which was reported more commonly in patients with haematologic malignancy in our cohort.

### Perceived Appearance Issues

Patients with solid malignancy fared lower in the domain of perceived appearance. This is as expected as the treatment for some of the solid malignancies often involves surgical extirpation of the tumour such as limb-salvage or amputation.<sup>23,24</sup> Very often, many larger scars are left behind by the procedure. As such, those children with haematologic malignancy reported a better self-image, thus a higher self-esteem to deal with situations surrounding them.

### Limitations

One limitation of this study is that the assessment of HRQOL of these patients is done at a single time point. Hence, their HRQOL before treatment could not be established. Any 'poor' HRQOL reflected in this assessment might be due to other reasons, and not the treatment process itself. For instance, a child with co-existent asthma may have a low HRQOL even before the treatment for his/her cancer is initiated. Furthermore, assessing the HRQOL at various points of treatment would be helpful. The intensity

of treatment for both haematologic and solid malignancies varies with the phase of treatment, such as the Induction phase followed by the Maintenance phase. Therefore, the side effects of medications, duration of absence from school, emotional strain and other factors would affect HRQOL to varying degrees at each phase.

The second limitation of our study is that our sample size is rather small to indicate statistically significant differences between those with solid and haematologic malignancies and make a definitive conclusion. Also, as our study aims to take a first look at the HRQOL of these patients in Singapore, the number of eligible patients who fit the inclusion and exclusion criteria is relatively small, making it difficult to have statistically significant differences between those with solid and haematologic malignancy. As such, there are patients with differing tumour types and stages included in this study.

The third limitation is that our patients come from different countries of origin. These children may thus have different perception and mindset as a result of their previous experiences. As we have a significant number of children from overseas seeking treatment here in Singapore, we felt it was not justified to simply analyse the Singaporean children alone.

### Conclusions

Our study is the first randomised study on the Singapore experience in HRQOL of children with cancer undergoing treatment. We have shown that treatment protocols could potentially have a significant impact on the HRQOL of these children. With the highly commendable and continued efforts by the medical professionals to develop new regimens leading to better survival rates and lower toxicity, it is imperative to incorporate the assessment of HRQOL into their clinical studies. In this way, children, during their treatment process, can voice out their concerns and fears. This in turn allows the various domains of HRQOL which have been affected by the treatment process to be

addressed earlier by the healthcare team, the parents and many support facilities. Future plans include prospective multi-institutional studies assessing HRQOL at various time points during the treatment of childhood cancer in Singapore.

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*The authors declare that there is no conflict of interest.*

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