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Original Paper

Health-related Quality of Life in Survivors of Tumours of the Central Nervous System in Childhood—a Preference-based Approach to Measurement in a Cross-sectional Study*

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There is an evident need to measure the comprehensive burden of morbidity experienced by survivors of brain tumours in childhood. To this end, a questionnaire based on the Health Utilities Index mark 2 (HUI2) and mark 3 (HUI3) systems was completed independently for a cohort of such children by their parents, by a nurse, by physicians and by a selected group of the children themselves. Each of the HUI2 and HUI3 systems consists of a multi-attribute health status classification scheme linked to a preference function which provides utility scores for levels within single attributes (domains of health) and for global health states. All eligible families ($n = 44$) participated. Even cognitively impaired children of at least 9.5 years of age could complete the questionnaire. The greatest burden of morbidity, occurring in two-thirds of children, was in the attribute of cognition. Surprisingly, almost one-third of children experienced pain. Global health status was lowest in children who underwent radiotherapy before the age of 5 years and the corresponding utility scores were related inversely to the volume irradiated. Children with demonstrable disease had lower scores than those in whom disease was not evident. There was a high level of agreement (intraclass correlation coefficients > 0.5) on formal assessment of inter-rater reliability for global health-related quality of life utility scores. The usefulness of measures of health status and health-related quality of life, in children surviving brain tumours, has been demonstrated by this study.

Key words: quality of life, children, brain tumours
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INTRODUCTION

BRAIN TUMOURS are the commonest group of solid tumours in children in industrialised societies, and the incidence of these neoplasms is rising [1]. Furthermore, within some parts of the developing world, in which most children reside, there appears to be a serious problem of under-diagnosis [2]. As the prospects for long-term survival from neoplasms of the central nervous system continue to increase [1], at least for children in industrialised countries, there is growing recognition of the need to address the sequelae of these diseases and of their treatment [1]. The neuropsychological consequences of 'successful' therapy for brain tumours of childhood have been well summarised [3], but the comprehensive burden of morbidity that these survivors bear has been less well examined [4].

We have developed and applied instruments, based on Health Utilities Index systems (HUI) [5], for the measurement of morbidity burden. The HUI can capture multiple sequelae and describe varying levels of severity. A pilot study of a small case series of children surviving brain tumours has been reported [4]. The primary purpose of the present study was to investigate the comprehensive (global) health status of a larger group of such children, using a nurse as the primary assessor, and to use a preference-based approach to

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measurement in order to quantify their health-related quality of life (HRQL). Patrick and Erikson [6] defined HRQL as 'the value assigned to the duration of life as modified by the impairments, functional states, precautions and social opportunities that are influenced by disease, injury, treatment or policy'. Secondary objectives were an assessment of the proportion of children surviving brain tumours who could complete, by self-report, a questionnaire on their health status; and an assessment of inter-rater agreement (reliability) in health status measurements.

This paper is paired with that of Glaser and colleagues [7] as these are complementary contributions and the repetition of descriptions about several components (such as the HUI classification systems) is thereby avoided. Furthermore, although there are some differences in the survey methods, the populations being sampled are very similar.

PATIENTS AND METHODS

All children who had completed therapy for tumours of the central nervous system, and who were attending the neuro-oncology follow-up clinic in the Children's Hospital at Chedoke–McMaster (Hamilton, Ontario, Canada) during the interval February 1993 to February 1995, were eligible for the study. The sex, ages at diagnosis and time of study, and intervals from diagnosis and completion of therapy to time of study were recorded. Information was obtained on tumour histology, operative intervention, radiotherapy and chemotherapy. The status of disease at the time of study was categorised as none evident, residual or recurrent.

A 15-item self-administered questionnaire was completed with respect to each child independently by the nurse, a parent, one of four physicians and, when possible, by the child. As determined by the software package Right Writer (RightSoft Inc., Sarasota, Florida, U.S.A.), the readability index of the questions is approximately grade 6 (an average 11-year-old child). Information from the questionnaires was converted to health status classification system attribute levels of the HUI mark 2 (HUI2) [5] and the HUI mark 3 (HUI3) [5] by an established algorithm [8]. Health status in the HUI2 system comprises seven attributes (sensation, mobility, emotion, cognition, self-care, pain and fertility) with three to five levels of function per attribute. Many applications, including this one, do not assess levels of fertility. The HUI2 system describes 24 000 unique health states or 8000 unique states when fertility is not assessed. Health status in the HUI3 system comprises of eight attributes (vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain) with five or six levels of function per attribute. The HUI3 system describes 972 000 unique health states. The constructs for the shared attributes of emotion, cognition and pain differ between HUI2 and HUI3 [5]. HUI2 and HUI3 measurements have been shown to be reliable, valid and responsive, as well as acceptable and useful [9–12]. These are coarse, generic measures that are subject to 'ceiling effects'; although this last issue is not relevant to the present study.

The HUI2 and HUI3 multi-attribute health status classification systems are linked to preference functions which provide single-attribute utility scores and global health status utility scores [13]. Utility scores have interval scale properties. The utility scale for the functional levels of a single attribute is defined as the range having level 1 (normal) = 1.00 and the lowest level for the attribute (most highly impaired) = 0.00. The utility scale for global health status is anchored by perfect health = 1.00 and death = 0.00. The utility functions for the HUI2 system are based on preference measurements obtained from a random sample of 194 parents of school-age children in the general population [14]. In this study, fertility was not assessed directly (in view of the patients' ages) and, for the purposes of calculating global utility scores, fertility was assumed to be level 1 (i.e. representing no burden of morbidity). HUI3 single- and multi-attribute utility scoring functions have been developed using preference measurements from a random sample of 504 adults in the general population [13]. Preference scores, for both HUI2 and HUI3 utility functions, were obtained using the visual analogue scale (Feeling Thermometer) and the standard gamble (Chance Board) [14].

Mean community-based utility scores can be used for estimating morbidity and HRQL for various groups [13]. Furlong [15] analysed the variability of utility scores collected from three general population surveys in southern Ontario, Canada. The scores were for a wide variety of health state descriptions. In general, he found little or no association between utility scores and sociodemographic characteristics. Although a few studies have detected some effects due to age or gender [16, 17], in general there is little evidence of systematic or consistent effects [18–20]. With respect to the HUI2 scoring function, there were virtually no differences observed between the scoring functions based on preference scores from a random sample of parents in the general population and from a sample of convenience of parents of children with cancer [14].

Frequency distributions were used to summarise categorical health status classification data. Interval scale utility score data were summarised using mean and median estimates of central tendency, and related measures of variability. Analysis of variance and *t*-tests for independent groups were used to assess the statistical significance of differences in mean utility scores among subgroups of irradiated patients, and between those children with and without demonstrable disease.

Agreement between pairs of assessors (inter-rater reliability) was determined for levels of morbidity within individual attributes by per cent agreement and kappa statistics [21], and for global health state utility scores by intraclass correlation coefficients (ICC) [22]. Although kappa and ICC statistics are the appropriate statistical techniques, the per cent agreements are also displayed for descriptive purposes and because of common familiarity with these techniques. Weighted kappa point estimates were used for tables greater than 2×2 dimensions and unweighted kappa point estimates for 2×2 tables (i.e. when each assessor used only levels 1 and 2). Both quadratic and Cichetti weights were employed for calculations [23, 24]. Each of these weighting approaches penalises large discrepancies more than small ones. The strength of agreement, based on the kappa statistic [25], has been defined as poor (< 0.00), slight (0.00–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80) and almost perfect (0.81–1.00).

RESULTS

All eligible families ($n = 44$) agreed to participate and did so during clinic attendance. The patients were divided equally between boys ($n = 22$) and girls ($n = 22$). The ages at diagnosis were < 0.1–14.2 years, mean 6.2 years; and at the time of the study were 1.7–17.9 years, mean 9.5 years. The intervals

Table 1. Proportion (%) of children (n = 41) *by number of attributes affected**

	Number of attributes affected								
	0	1	2	3	4	5	6	7	8
HUI2	17	29	27	10	7	7	2	N/A	N/A
HUI3	22†	15	20	27	2	7	5	2	0

*Defined as a HUI level > 1 (other than normal). †In the 1991 Canadian General Social Survey, which used the HUI3 system, 'perfect health' (no attributes affected) was enjoyed by 44% of the youngest age group—15–19 years. N/A, not applicable, HUI, Health Utilities Index.

from diagnosis to the time of the study ranged from 0.2 to 8.6 years, mean 3.3 years; and from completion of therapy to the time of the study ranged from < 0.1 to 8.6 years, mean 2.6 years. The tumour types were astrocytoma/glioma ($n = 24$), primitive neuro-ectodermal tumour/medulloblastoma ($n = 7$), ependymoma ($n = 3$) and others ($n = 10$). Craniotomy was undertaken in 43/44 (98%) children, 27 (61%) received radiotherapy and 11 (25%) received chemotherapy.

The nurse was designated as the primary assessor to provide consistency among subjects for she was the only participant who assessed almost all of the patients ($n = 41$). The descriptive statistics for this subsample of 19 males and 22 females are very similar to those of the entire sample. Data using the assessments of the nurse are displayed in Tables 1–5. The frequency distributions for the number of attributes affected are presented in Table 1 and the frequency distributions of the attribute levels are presented in Table 2. More than 50% of the children had disabilities in two or more attributes. As may be predicted from clinical experience, the greatest burden of morbidity was in the attribute of cognition, but pain was also surprisingly prevalent. Only 17% of children ($n = 7$) had no morbidity at all, according to HUI2, and only 22% ($n = 9$) according to HUI3. The median utility scores for global HRQL (based on the reports of the nurse) were 0.92 (mean = 0.85, range = 0.12–1.00) for HUI2; and 0.77 (mean = 0.69, range – 0.27–1.00) for HUI3.

Table 2. Frequency distributions of attribute levels. Proportion (%) of children (n = 41) *affected*

Level	Sensation	Mobility	Emotion	HUI2 Cognition	Self-care	Pain		
1	61	80	73	34	85	73		
2	17	10	24	56	7	24		
3	17	2	2	7	0	2		
4	5	5	0	2	7	0		
5	N/A	2	0	N/A	N/A	0		
Level	**Vision**	**Hearing**	**Speech**	**HUI3 Ambulation**	**Dexterity**	**Emotion**	**Cognition**	**Pain**
1	68	98	85	80	66	73	34	68
1*	74	100	98	100	100	79	76	88
2	17	0	12	10	22	24	10	27
3	2	0	0	0	7	2	10	5
4	2	2	0	2	2	0	37	0
5	7	0	2	2	0	0	7	0
6	2	0	N/A	5	2	N/A	2	N/A

*In the 1991 Canadian General Social Survey, which used the HUI3 system, the proportions (%) of the youngest age group—15–19 years—enjoying level 1 (no morbidity) in each attribute are listed. N/A, not applicable; HUI, Health Utilities Index.

Table 3. Impact of age at diagnosis on global health-related quality of life (utility) scores (n = 41)

Age (years)	*n*	Mean	S.D.	Median	Minimum	Maximum
HUI2—non-irradiated patients						
0–5	7	0.88	0.14	0.92	0.60	1.00
5.1–10	4	0.92	0.06	0.92	0.85	1.00
10.1 +	5	0.91	0.11	0.95	0.72	1.00
HUI2—irradiated patients						
0–5	13	0.70	0.26	0.73	0.12	1.00
5.1–10	10	0.91	0.04	0.92	0.85	1.00
10.1 +	2	0.97	0.04	0.97	0.95	1.00
HUI3—non-irradiated patients						
0–5	7	0.78	0.24	0.71	0.37	1.00
5.1–10	4	0.86	0.16	0.89	0.66	1.00
10.1 +	5	0.85	0.18	0.88	0.58	1.00
HUI3—irradiated patients						
0–5	13	0.44	0.40	0.35	– 0.27	1.00
5.1–10	10	0.77	0.14	0.79	0.56	1.00
10.1 +	2	0.91	0.12	0.91	0.83	1.00

S.D., Standard deviation; HUI, Health Utilities Index.

The association between age at diagnosis and global HRQL in these survivors (as reflected in the utility scores) is illustrated in Table 3 for non-irradiated and irradiated children. In general, children who were irradiated before the age of 5 years had a significantly lower ($P=0.007$) mean HUI2 utility score than those in all the other categories. Of the possible pairs of cells defined by the HUI2 section of this table, only one pair of mean utility scores were significantly different ($P<0.05$), due, at least in part, to small sample sizes and low testing power: irradiated patients age 0–5 years versus irradiated patients age 5.1–10 years.

Table 4. Impact of extent of radiotherapy on global health-related quality of life (utility) scores (n = 41)

	Utility score					
Site of radiotherapy	*n*	Mean	S.D.	Median	Minimum	Maximum
HUI2						
None	16	0.90	0.11	0.94	0.60	1.00
Posterior fossa	9	0.92	0.06	0.95	0.80	1.00
Supratentorium	5	0.82	0.25	0.90	0.38	1.00
Craniospinal	11	0.71	0.25	0.73	0.12	0.93
HUI3						
None	16	0.82	0.19	0.84	0.37	1.00
Posterior fossa	9	0.79	0.15	0.77	0.56	1.00
Supratentorium	5	0.71	0.36	0.83	0.08	1.00
Craniospinal	11	0.42	0.38	0.35	− 0.27	0.93

S.D., Standard deviation; HUI, Health Utilities Index.

Table 5. Impact of disease status on global health-related quality of life (utility) scores* (n = 41)

	Utility score					
Status of disease	*n*	Mean	S.D.	Median	Minimum	Maximum
HUI2						
None evident	28	0.89	0.13	0.93	0.46	1.00
Residual	10	0.81	0.19	0.89	0.38	0.95
Recurrent	3	0.56	0.41	0.65	0.12	0.92
HUI3						
None evident	28	0.78	0.26	0.82	− 0.13	1.00
Residual	10	0.56	0.26	0.66	0.08	0.89
Recurrent	3	0.32	0.57	0.35	− 0.27	0.88

S.D., Standard deviation; HUI, Health Utilities Index.*At the time of assessment.

The association between extent of radiotherapy and global health status utility scores is shown in Table 4. Craniospinal irradiation had a significant ($P=0.021$) deleterious effect on the HUI2 utility score (as a measure of HRQL) than less extensive irradiation. Mean HUI2 utility scores were statistically significantly different between two pairs of groups: none versus craniospinal ($P<0.02$); and posterior fossa versus craniospinal ($P<0.05$). Frequency distributions of global health states, ranked by utility scores and grouped by category of radiotherapy, are displayed in the Appendix. These reveal that increasing volume of radiation is associated with a diminishing proportion of children with little or no morbidity and an increasing proportion of children with multiple morbidities (on three or more attributes). The considerable burden of sensory morbidity (HUI2) evident in children who received craniospinal irradiation is in the attributes of vision and speech (HUI3).

The association between status of disease at the time of the study and global utility score is revealed in Table 5. Children with demonstrable disease (residual or recurrent) had a significantly poorer HRQL than those whose disease appeared to be in complete remission ($P=0.027$ for HUI2). The mean HUI2 utility score for patients with non-evident disease was significantly different ($P<0.001$) than that for patients with recurrent disease. We recognise that these results are potentially confounded by possible interactions between disease status and exposure to radiotherapy.

A total of 15 children, aged 9.5–17.9 years, mean 13.5 years, completed the self-administered questionnaire independently. Assessments by children and their parents were typically mutually exclusive (i.e. only six pairs of child/parent assessments were collected) and, therefore, these results were not analysed. Comparisons of the levels of function within each attribute, based on responses from various pairs of assessors, are listed in Table 6. The kappa point estimates were similar whether quadratic or Cichetti weights were used, so only the quadratic weighted results are displayed. Low kappa statistics in association with high values for per cent agreement indicate a lack of variability in the underlying data, and these results provide little, if any, evidence about reliabilty. Inter-rater reliability was higher for the more observable attributes of mobility and self-care than for the others, but higher for pain than for the remaining subjective attributes, such as emotion. Agreement between raters was lowest (and ‘fair’ at best according to the interpretative guidelines for kappa statistics by Landis and Koch [25]) for assessments of

Table 6. Measures of agreement about HUI2 single attribute levels by pairs of raters (total sample n = 44*)*

		Attribute					
Rater pair (number of pairs)		Sensation	Mobility	Emotion	Cognition	Self-care	Pain
Nurse versus parents (23)	P.A.	69	92	59	65	77	77
	K	0.70	0.82	0.15	0.60	0.44	0.50
Nurse versus children (15)	P.A.	73	93	67	73	93	87
	K	0.05	N/A	0.13	0.57	N/A	0.71
Nurse versus physicians (12)	P.A.	65	86	69	67	81	72
	K	0.43	0.78	0.30	0.54	0.50	0.41
Parents versus physicians (12)	P.A.	64	86	70	65	83	78
	K	0.37	0.84	0.28	0.22	0.37	0.43
Children versus physicians (12)	P.A.	67	87	58	65	88	75
	K	0.42	N/A	0.13	0.37	N/A	0.73

P.A. per cent agreement; K, kappa statistic; N/A, not available (one rater used only level 1); HUI, Health Utilities Index.

Table 7. Inter-rater agreement using HUI2 utility scores of global health-related quality of life (total sample n = 44*)*

Raters	*n*	ICC
Nurse versus parents	23	0.75
Nurse versus children	15	0.85
Nurse versus physicians	12	0.57
Parents versus physicians	12	0.54
Children versus physicians	12	0.95

HUI, Health Utilities Index; *n*, number of paired assessments on individual children; ICC, intraclass correlation coefficient; ICC > 0.5 is indicative of a strong correlation (high level of agreement).

emotion; but 'fair' or better (kappa > 0.20) for most assessments of the other attributes. The notable exception was agreement between the nurse and the children for sensation, which is 'slight' at best. These results should be interpreted while keeping in mind that there is not one 'gold standard' point of view. The opinions of all types of assessors are legitimate. The correlations of HRQL scores for global health status, based on reports by pairs of assessors, are given in Table 7. In general, the ICCs indicate that there is strong agreement between global HRQL utility scores reported for health status assessments by various types of raters.

DISCUSSION

A simple system for ranking the global health status of children surviving brain tumours was devised by Bloom and colleagues more than 25 years ago [26]. Despite its limitations, especially in the property of sensitivity [4], this approach has remained in use [27–29]. Not surprisingly, such systems seriously underestimate global and specific morbidity burdens [4, 30]. The need for a more comprehensive and detailed strategy for health status measurement in these children has been recognised for more than a decade [30–32]. Lansky's Play Performance rating [33], based on the Karnofsy scale [34], was followed by others [30, 35] with a variety of shortcomings [36, 37]. More recently, Johnson and associates [38] and Goodwin and colleagues [39] presented more comprehensive and detailed strategies for health status measurement in children with cancer, the former focusing on those with medulloblastoma.

We have previously applied the HUI instruments to children surviving brain tumours [4], as have colleagues in the U.K. [7, 40, 41]. The present study highlights the multiplicity of sequelae experienced by individual patients and identifies a wide range of severity in morbidity within single attributes, as well as morbidity of global health status and overall HRQL. Approximately 80% of children who have had brain tumours experienced some subsequent morbidity, with more than one attribute affected in the great majority. Overall HRQL was negatively associated with radiotherapy in children 5 years of age or less at the time of treatment. In part, this may reflect the fact that more than 50% (7/13) in this group had the most extensive (craniospinal) irradiation. Craniospinal irradiation was associated with significantly more damage (in terms of subsequent health status) than other, lesser volumes. In further support of clinical experience, HRQL was related inversely to the extent of disease at the time of health status assessment.

Assessing the prevalence and severity of morbidity, attribute by attribute, is often informative for issues related to clinical management, but it is also important to remember that this type of data does not provide much information about the overall health status experienced by the children. Overall health status is complex but very important to patients and their families, and is important also for efficient management of patients with complex comorbidities. Efficient tools for assessing overall health status and HRQL, such as the HUI, have become available only recently. The techniques for analysing and interpreting the results are, however, still under development. In general, the interpretation of HUI data is facilitated by exploiting the relationship between health state descriptions and utility scores associated with each of the states, as illustrated by the results in the Appendix. For HUI2 nurse assessments, the most prevalent ($n = 7$) overall health states are perfect health (vector 111111 having a utility score of 1.00), and the state having level 2 cognition, with all other attributes at full capacity (vector 111211 having a utility score of 0.95). However, it is important to note that none of the patients who received craniospinal radiotherapy was living in these two states, or for that matter in any other states having utility scores equal to or greater than the scores for these two states. Furthermore, it can be seen that none of the unique health states was used to describe the health status of children in all four radiotherapy groups. Perfect health (vector 111111) was the most prevalent state among children who received no radiotherapy; level 2 cognition (i.e. learns and remembers school work more slowly than classmates) with no other disabilities (vector 111211) was the most prevalent state among children in the posterior fossa group; level 2 sensation (i.e. requires equipment to see or hear or speak) and level 2 cognition with no other disabilities was the most prevalent state in the supratentorium group; and level 2 cognition and level 2 pain (i.e. occasional pain relieved by non-prescription drugs or self-control activity without disruption of normal activities) with no other disabilities was the most prevalent state in the craniospinal group. It appears also that the shapes of the frequency distributions are different among the groups. The frequency distributions of health states reported for the children receiving no radiotherapy or radiotherapy to the posterior fossa are skewed towards states having relatively high utility scores. The frequency distribution of patients treated with craniospinal radiation is almost uniform. Most of these patterns are very similar, but generally more striking, for HUI3 results (see Appendix).

The HUI3 results highlight the great variability in the type and severity of disability combinations reported for this population: only four unique health state vectors each described two or more subjects; most (24 of 30) unique health state vectors describe more than one disability; and only four unique states were in common across two or more radiotherapy–site groups. Perhaps most disconcerting is that more than half the children treated with craniospinal radiotherapy (6 of 11 children) were described as living in health states with utility scores less than 0.40. The health state of each of these children was unique, each of these children had disabilities in at least three attributes, and each of two of these children had at least two disabilities at the lowest functional levels. For example, the HUI3 health state of the child with the lowest utility score (utility score of − 0.27) is described as follows:

- Able to read ordinary newsprint with or without glasses but unable to recognise a friend on the other side of the

street, even with glasses or contact lenses;
- able to hear what is said in a group conversation with at least three other people, without a hearing aid;
- unable to be understood when speaking to other people, or unable to speak at all;
- cannot walk at all;
- limitations in the use of hands or fingers, requires the help of another person for all tasks;
- somewhat happy;
- unable to remember anything at all, and unable to think or solve day to day problems; and
- mild to moderate pain that prevents no activities.

Negative utility scores indicate that the associated health states are considered, on average by members of the general population, to be worse than being dead [14].

The global utility scores reflect the relative burdens of morbidity. Thus, children who had no radiotherapy or who were irradiated only to the posterior fossa had mean scores only slightly lower than those of survivors of standard risk acute lymphoblastic leukaemia who, in turn, are comparable to children in the general population [42]. By contrast, the mean utility scores presented in Table 4 suggest that, on average, those who received radiotherapy to the cerebral hemisphere(s) and those who had craniospinal irradiation may be expected to experience almost 20 and 30%, respectively, less quality-adjusted life years (QALYs—the duration of a health state weighted by its utility) than people in perfect health. Furthermore, the lowest HUI2 utility score for global HRQL was 0.12. If that child's health status were to remain stable at this level for 50 years, it would be 'worth' only 6 (undiscounted) QALYs. In a more complex example, if a child with cancer undergoes 2 years of therapy with a utility of 0.5, then survives 20 years with a utility of 0.8 only to develop cardiomyopathy with clinical manifestations lasting 3 years (with an average utility of 0.3), at the end of which he dies, the survival from diagnosis is 25 years, but the QALYs amount to only 17.9 $(2\times0.5)+(20\times0.8)+(3\times0.3)$ [43].

The relationships between age at diagnosis, radiotherapy and extent of radiotherapy on health status, especially in the cognitive and emotional domains, have been observed by many other investigators (as summarised by Seaver and colleagues [44]). Likewise, disease status (at the time of assessment of health status and HRQL), and the intervals from diagnosis and completion of therapy to the time of assessment are also important variables. Exceptions to these generalisations have been reported for specific circumstances [45, 46]. More general exceptions in children with brain tumours [29] probably reflect the insensitivity of the HRQL measures employed.

Despite different constructs, between HUI2 and HUI3 systems, for some attributes sharing the same name (e.g. emotion), there is very good agreement about the frequency of morbidity between HUI2 and HUI3 results (see cognition, emotion and mobility/ambulation). The most prevalent morbidity burden is associated with cognition, the attribute affected most commonly and severely. In this cohort of subjects, the prevalence of cognitive dysfunction is 66% which compares very unfavourably with the rate of 24% reported for 15–19-year-olds in the general population [4]. Pain is surprisingly frequent among survivors of brain tumours in childhood, mirroring our experience in a comparable population of adults [47], and attesting to the usefulness of the HUI generic health status classification systems in identifying under-recognised problems for clinical management.

Evidently the matter of perspective in health status assessment is critical. In particular, self–report by children surviving brain tumours should be most instructive. In the study by Lannering and associates [30], 44 of 46 children older than 12 years provided a global assessment of health status on a linear scale (0–100). Those with 'psychological emotional dysfunction' ($n=8$) gave a mean score of 51 which was significantly below the mean (79) for the remainder. Subsequent recorded experience of such self-reports has been decidedly limited [40, 44]. The recent development of health status measures designed for use by children as young as 4–5 years [48, 49] should help remedy this deficit. In the present study, even cognitively impaired children of at least 9.5 years of age could complete the 15-item HUI questionnaire, attesting to its acceptability. Inter-rater reliability (agreement) was heterogeneous among pairs of respondents (children, nurse and physicians) for both functional levels in individual attributes and global HRQL (utility) scores. This implies that viewpoint is an important factor. Unfortunately, in the study by Lannering and associates [30], although the mothers of the children provided independent assessments, the authors reported no information on inter-rater agreement.

The usefulness of measures of health status and HRQL in children surviving brain tumours has been emphasised by this study. The accompanying paper by our colleagues Glaser and associates [7] provides evidence about the generalisability of the HUI to applications outside Canada and the generalisability of the outcomes reported here. In these contexts, measures of health status and HRQL fulfil a discriminative function, distinguishing differences in health status within and among populations. The evaluation of changes in the health status of an individual over time will be addressed in future studies, and the prospect that such measures may be predictive of ultimate clinical outcome offers an exciting opportunity for study [10].

Finally, we readily acknowledge that the heterogeneous small sample of children severely limits the precision of health status and HRQL estimates reported here. The Appendix provides HUI health state vectors that may be pooled with data from other centres to improve the precision of results. We encourage other researchers to use these data, or collaborate with us, to increase the sample sizes of homogeneous groups.

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APPENDIX
FREQUENCY DISTRIBUTIONS OF HEALTH STATES AND GLOBAL UTILITY SCORES BY RADIOTHERAPY VOLUME GROUPS

HUI2 attribute levels

Sen	Mob	Emt	Cog	S-c	Pn
1	1	1	1	1	1
2	1	1	1	1	1
1	1	1	2	1	1
1	1	2	1	1	1
1	1	1	2	1	2
1	2	1	2	1	1
2	1	1	2	1	1
1	1	2	1	1	2
1	1	2	2	1	1
2	1	1	2	1	2
3	1	1	1	1	1
1	1	2	2	1	2
2	1	2	2	1	2
1	1	1	1	4	1
3	2	1	2	2	2
2	1	3	2	1	1
3	1	2	3	1	1
3	2	1	2	1	3
3	2	2	3	2	1
3	4	1	1	1	1
3	3	1	3	4	2
4	4	1	2	2	1
4	5	2	4	4	2

Radiotherapy group

Utility score	None	PF	ST	CS	All
1.00	4	2	1		7
0.95	1				1
0.95	3	3	1		7
0.93	1			1	2
0.92	1			2	3
0.92		1			1
0.90		1	2		3
0.90	1				1
0.88	1			1	2
0.87				1	1
0.85	1				1
0.85		1			1
0.80		1			1
0.79	1				1
0.73				1	1
0.71	1				1
0.69				1	1
0.65				1	1
0.64				1	1
0.61	1				1
0.46				1	1
0.37			1		1
0.12				1	1
Totals	16	9	5	11	41

HUI3 attribute levels

Vsn	Hrg	Sph	Amb	Dxy	Emt	Cog	Pn
1	1	1	1	1	1	1	1
2	1	1	1	1	1	1	1
1	1	1	1	1	2	1	1
1	1	1	1	1	1	2	1
1	1	1	1	1	1	3	2
2	1	1	1	2	1	3	1
1	1	1	1	1	2	2	1
1	1	1	1	1	2	3	2
2	1	1	1	2	1	2	1
1	1	1	1	1	2	1	3
1	1	1	1	1	1	4	1
1	1	1	1	1	1	4	2
1	1	1	1	1	2	4	1
1	1	1	1	2	1	4	1
2	1	1	1	1	1	4	2
2	1	1	1	2	1	4	1
1	1	1	1	2	1	4	2
1	1	1	1	1	2	4	2
5	1	1	1	1	1	1	1
2	1	1	1	2	2	4	2
2	1	1	1	1	3	4	1
1	1	1	2	3	1	4	1
1	1	2	5	3	1	1	1
1	4	1	2	2	1	4	3
1	1	2	1	2	2	5	1
4	1	2	2	4	1	4	2
5	1	2	2	2	1	5	1
6	1	1	6	1	1	2	1
5	1	2	4	3	1	5	2
3	1	5	6	6	2	6	2

Radiotherapy group

Utility score	None	PF	ST	CS	All
1.00	6	2	1		9
0.97	1				1
0.93				1	1
0.89		1			1
0.88	1			1	2
0.84			1		1
0.83			1		1
0.82		1			1
0.80			1		1
0.80	1				1
0.77	1	1			2
0.72				1	1
0.71	1	1			2
0.71	1				1
0.70		1			1
0.69		1			1
0.67	1				1
0.67				1	1
0.66	1				1
0.60				1	1
0.58	1				1
0.48		1			1
0.37	1				1
0.35				1	1
0.33				1	1
0.24				1	1
0.14				1	1
0.08			1		1
−0.01				1	1
−0.27				1	1
Totals	16	9	5	11	41

Sen, sensation; Mob, mobility; Emt, emotion; Cog, cognition; S-c, self–care; Pn, pain; Vsn, vision; Hrg, hearing; Sph, speech; Amb, ambulation; Dxy, dexterity; PF, posterior fossa; ST, supratentorium; CS, craniospinal.