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## Original Paper

# Health-related Quality of Life of Adults Surviving Malignancies in Childhood

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**While sophisticated data on specific problems are available, very little is known about the overall quality of life of long-term survivors of malignancies in childhood. We used a previously validated 15-dimensional questionnaire to examine the perceived health-related quality of life of 168 survivors, currently aged 16–35 years, who had been treated for a malignancy at a single institution between 1961 and 1993. All had been off therapy for at least 1 year (median, 12 years). In statistical terms, the quality of life score of the survivors was significantly better than that of 129 normal controls [0.966 versus 0.941 (theoretical maximum 1), respectively; $P < 0.001$]; however, a difference of this magnitude is most likely not clinically significant. There were no associations between original diagnosis and present quality of life, but the numbers in each diagnostic group were small. The survivors reported significantly better levels of vitality, distress, depression, discomfort, elimination and sleeping dimensions than the controls. Although we are presently not able to identify all the contributing factors, we speculate that the high perceived quality of life of long-term survivors of childhood malignancies is at least in part a consequence of denial mechanisms which compensate or even overcompensate the objectively measurable late effects of childhood cancer.** 

**Key words: quality of life, malignancies, prognosis, survivors, adult, childhood**
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## INTRODUCTION

ALTHOUGH THE treatment results of childhood cancer have improved dramatically over the last 20 years, emerging reports on late effects of both the disease and the therapy (for a concise review, see [1]) have raised serious concerns about the quality of life of the survivors. Unfortunately, while sophisticated data on specific problems are available, very little is known about the overall quality of life of the patients surviving into adulthood [2]. The few recently published studies on the quality of life of survivors have concentrated mostly on patients with severe malignancies [3–7], and have been presented mainly without adequate normal controls [3, 4, 7–9]. Further, the quality of life has been assessed by physicians (even by the physicians responsible for the treatment of the given patient—a situation prone to lead to biased estimates) or proxies instead of the patients themselves [3, 4, 8, 10, 11], although the patient is known to be the most appropriate source of this information [12–14].

Based on these previous reports and our own observations on poorer body image in adolescents and adults surviving leukaemia [15], we hypothesised that the health-related quality of life of adults surviving malignancies in childhood—especially those surviving leukaemia—would be inferior to that of the normal population. Further, we also attempted to establish whether the health-related valuations of the survivors would differ from the valuations of the controls.

## PATIENTS AND METHODS

Our study sample comprised all the 220 patients treated and followed up for a malignancy at the Children's Hospital, University of Helsinki between 1961 and 1993, who had been off therapy for at least 1 year and who were at least 16 years old at the time of the study. A 15-dimensional questionnaire (15D), developed and validated previously [16–20], was mailed to the patients with written instructions. We selected the 15D measure for the quality of life instrument of our study

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because it is multidimensional and subjective—both well-agreed criteria for a good quality of life instrument [12, 13, 21]—and because it contains questions from all the components of health-related quality of life we find important—namely physical, social and mental well-being.

The response rate after one reminder letter was 80% (176/220). Only the 168 complete answers (95%) were included for further analysis. The mean age of the respondents was 23 years (range, 16–35 years); 106 (63%) were male and 62 (37%) female. Their diagnoses had been acute lymphoblastic leukaemia ($n = 68$), various sarcomas ($n = 23$), Wilms' tumour ($n = 22$), Hodgkin's disease ($n = 15$), other lymphomas ($n = 13$), other leukaemias ($n = 10$), neuroblastoma ($n = 7$), and others ($n = 10$). None of the patients had survived a central nervous system (CNS) tumour. Due to the wide range of different malignancies and long entry period to the study, the therapy received by the patients varied considerably. Of all the respondents, three with acute lymphoblastic leukaemia (ALL) and two with acute non-lymphoblastic leukaemia (ANLL) had received a bone marrow transplant. The median duration of follow-up after discontinuation of therapy was 12 years. The age and sex distribution, diagnoses and duration of follow-up of the non-respondents did not differ significantly from those of the respondents.

As controls, we utilised 129 adults, aged 17–35 years and chosen randomly from the National Population Register to represent the general population, who had completed the 15D previously. Of the controls, 69 (53%) were women and 60 (47%) men. There were no significant differences in the level of education achieved or employment status of the patients and the controls.

A detailed description of the 15D measure has been previously published [16–20]. Briefly, it consists of 15 multiple choice questions, each representing one health-related dimension (mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality and sexual activity). The item selection was originally based on a thorough review of the literature on conceptualising health, after which experts from medical profession as well as nearly 3000 patients from health-care centres were invited to supplement the items. Based on these surveys, some items were added, others combined and some of the questions were rephrased.

The subject marks the level (1–5) of each dimension best describing his or her present health status (Table 1 illustrates the levels of the mobility dimension). In routine use, filling this questionnaire (taking 5–10 min) is the only thing required from the subject. The 15D score—representing health-related quality of life and ranging from 0 (worst possible) to 1 (best possible)—is calculated by combining the previously obtained dimension importance weights and within-dimension level desirability values (see below) with the subject's own assessments of his or her current health status.

*Table 1. The levels of the mobility dimension*

| | |
|---|---|
| 1. | I am able to walk normally (without difficulty) indoors, outdoors and on stairs. |
| 2. | I am able to walk without difficulty indoors, but outdoors and/or on stairs I have slight difficulties. |
| 3. | I am able to walk without help indoors (with or without an appliance), but outdoors and/or on stairs only with considerable difficulty or with help from others. |
| 4. | I am able to walk indoors only with help from others. |
| 5. | I am completely bed-ridden and unable to move about. |

The valuation questionnaire is considerably more difficult to fill out and also more time consuming (30–60 min) than the 15D questionnaire. For the purposes of this study, the 15D scores for both the patients and controls were calculated using importance weights and level desirability values obtained previously from 442 adults aged 17–65 years chosen randomly from the National Population Register. However, in analysing whether the valuations of the patients differ from those of the normal population, not all 442 but only the 129 controls aged 17–35 were evaluated. To obtain the dimension importance weights, the subjects are instructed to indicate the position of each of the 15 dimensions on an adjacent importance scale (0–100) placing the dimension considered most important at the top (at 100). The individual values given to a dimension by all subjects are first averaged, and then transformed so that the sum of the 15 individual important weights equals 1. The within-dimension five discrete functional states are valuated similarly using a 0–100 scale and placing the most desirable level at 100. In addition to these five levels, the states of being unconscious and being dead are valuated for each dimension. The individual values given to a level are averaged to obtain the desirability value of that value.

Analysis of variance, Mann–Whitney $U$ test, multiple regression (tobit) [22], and correlation coefficients were used to analyse the results. The study protocol was approved by the Institutional Review Board of the Children's Hospital, University of Helsinki.

## RESULTS

There were no significant differences in the health-related valuations (importance weights of the dimensions) between the patients and controls. Mental function and breathing were considered by both groups to be the most important dimensions, whereas vision was considered least important (Figure 1). In both groups, sexual activity was considered more important by men than by women ($P = 0.004$). For other dimensions, there were no associations between sex and valuations. Age and diagnosis had no effect on the valuations. Both the patients and the controls considered death the worst and unconsciousness the next worst state for all the dimensions.

The health-related quality of life (15D score) of the patients was statistically significantly better (0.966, S.D. = 0.047) than that of the controls (0.941, S.D. = 0.059; $P < 0.001$). There were no differences in the quality of life between patients with different malignancies (Table 2); the mean 15D score of patients surviving leukaemia was 0.971 as compared with 0.962 for patients surviving solid tumours ($P = 0.34$). The quality of life of the patients with bone marrow transplantation was slightly lower than that of others (mean 0.927, individual values 0.972, 0.789, 0.966, 0.907 and 1.0; $P = 0.06$). Sex was not associated with quality of life. There was an inverse correlation between the quality of life and age ($r = -0.16$, $P = 0.04$ and $r = -0.18$, $P = 0.05$, for patients and controls, respectively). After taking age into account, the duration of follow-up had no additional effect on the quality of life. In multivariate analysis, the quality of life of the patients was statistically significantly better than that of the controls even after taking age and sex into account ($P = 0.003$). The age

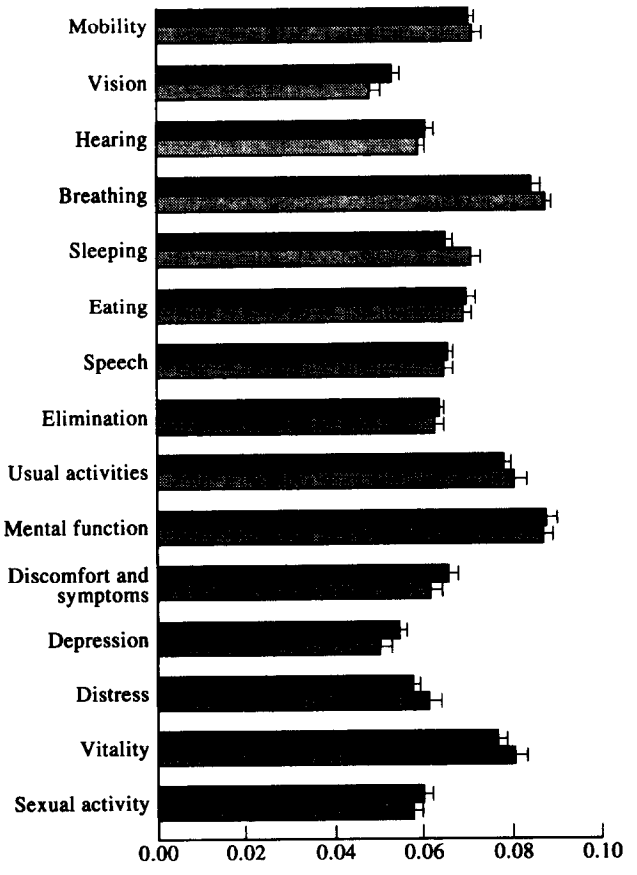


**Figure 1. Health-related valuations of the survivors and controls. The importance weights (mean ± S.E.) of the 15 dimensions included in 15D as judged by the adult survivors of malignancies in childhood (solid bars) and controls (shaded bars).**

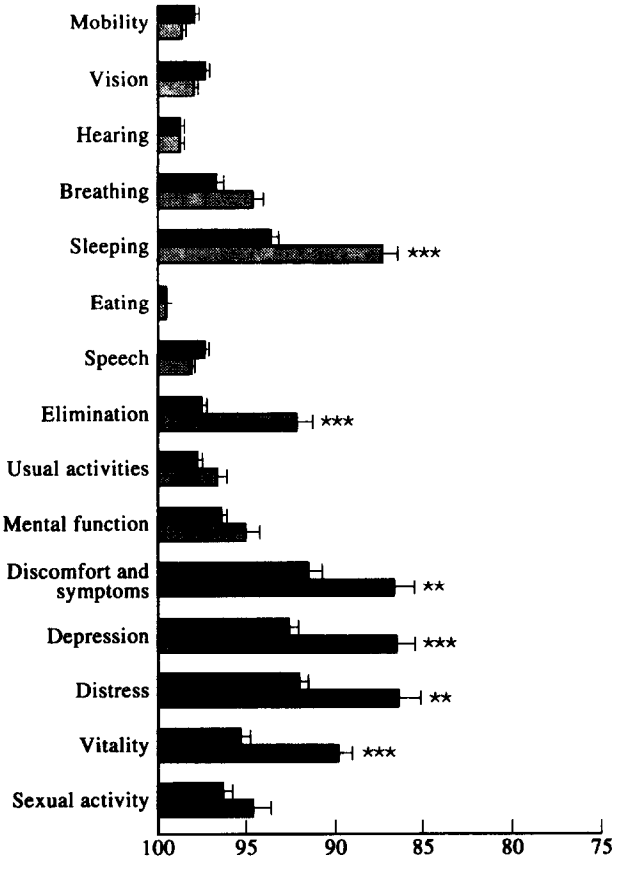


**Figure 2. The health-related quality of life profiles of the survivors and controls. The mean (± S.E.) scores for each dimension obtained by the adult survivors of malignancies in childhood (solid bars) and controls (shaded bars). For each dimension, best level equals 100 and worst level equals 0. Significant differences (Mann–Whitney *U* test) are marked with *($P < 0.01$) or * *($P < 0.001$).**

*Table 2. The health-related quality of life (15D scores) of the survivors by diagnosis*

| Diagnosis | *n* | Mean | Median | Min. | Max. |
|---|---|---|---|---|---|
| ALL | 68 | 0.970 | 0.983 | 0.789 | 1.000 |
| Other leukaemias | 10 | 0.975 | 0.983 | 0.907 | 1.000 |
| Hodgkin's disease | 15 | 0.972 | 0.981 | 0.893 | 1.000 |
| Other lymphomas | 13 | 0.982 | 0.983 | 0.947 | 1.000 |
| Wilms' tumour | 22 | 0.947 | 0.982 | 0.759 | 1.000 |
| Neuroblastoma | 7 | 0.933 | 0.987 | 0.784 | 1.000 |
| Sarcoma | 23 | 0.959 | 0.973 | 0.832 | 1.000 |
| Others | 10 | 0.978 | 0.994 | 0.933 | 1.000 |
| Total | 168 | 0.966 | 0.982 | 0.759 | 1.000 |

and sex standardised mean 15D scores of the survivors and controls were 0.964 [95% confidence interval (CI) 0.963–0.965] and 0.939 (95% CI 0.937–0.941), respectively. There were no differences in other sociodemographic variables between patients and controls.

Both the patients and the controls reported good levels of physical dimensions, such as eating, mobility and breathing, and of sensory dimensions, usual activities and mental function (Figure 2). In contrast, emotional dimensions, such as depression, distress and vitality, and also sleeping and discomfort were less satisfactory in both groups. The difference in the quality of life between the patients and the controls consisted mainly of the differences in dimensions sleeping, depression, vitality, distress, elimination, and discomfort (Figure 2), for which the patients reported a significantly better status (less problems) than the controls. The survivors of leukaemia reported slightly better levels of the breathing and discomfort dimensions than survivors of solid tumours ($P = 0.03$ and $P = 0.04$, respectively).

## DISCUSSION

We have demonstrated that the perceived health-related quality of life of adolescents and adults surviving malignancies in childhood is at least as good as that of normal population. Further, there were no associations between original diagnosis and present quality of life, although the numbers in each diagnostic group were too small to allow definitive conclusions to be drawn. Despite the statistically significant difference in the quality of life scores between the patients and the controls, the difference—0.025—is most likely not clinically significant; in earlier studies, an improvement of 0.034 in the 15D score has been experienced by the patients as higher level of quality of life [23]. Interestingly, there was no dimension on which the status of the patients would have been significantly inferior to that of the controls.

In contrast to our results, Feeny and associates [4] previously reported that the health status of survivors of high-risk

acute lymphoblastic leukaemia was inferior to that of normal controls. However, there were possible sources of bias in the study design. First, there are only seven attributes in the system. While each attribute includes several parameters—for example seeing, hearing and speaking are all encompassed within the domain of sensation—it may be difficult for an individual to rate the relative importance of the parameters and thus give a correct answer. Second, the data were not quantitative—the patients and controls were compared by counting the attributes affected, and the deficits of the patients were argued to be less readily ameliorated than those found in the general population. Further, the health status assessment of the patients was based on clinical records, analysed retrospectively by the physician, whereas the controls had been interviewed on telephone using a different set of attributes. In another study with the same system [8], there was no statistically significant difference between quality of life of survivors of either standard- or high-risk leukaemia and normal population. However, the patients and the controls were again assessed with a different set of attributes.

The quality of life of 342 survivors of CNS tumours [5], asssed by asking questions on employment, income, ability to drive a car and health status perception as a single estimate, was found to be lower than that of their siblings. Unfortunately, our series did not include patients surviving CNS malignancies, due to low survival of these patients.

The overall quality of life of survivors of bone marrow transplantation was recently indicated to be high by multiple measures [6]. They reported less depression, tension, confusion and fatigue than their controls, adding credibility to the present results. Further, both previous experiences [16–20, 24] and our observations on patients with different hereditary diseases (Apajasalo and colleagues, unpublished observations) indicate that 15D is a reliable and sensitive instrument for analysis of quality of life. Also, our study—and 15D in general—complies well with the criteria developed by Gill and Feinstein [25] to evaluate face validity of quality of life measurements.

There was an inverse correlation between age and 15D score in our study. One might initially think this was due to physical effects of certain types of therapy (e.g. craniospinal irradiation or some chemotherapeutic agents) worsening with time. This does not seem to be the case, since the effect was found in both patient and control groups. Contrary to expectation [26], the duration of follow-up had no additional effect on quality of life after taking present age into account.

Our study is exceptional in that the entire cohort of patients treated and followed up for a malignancy at a single institution was evaluated. However, this approach has some limitations. The study population was heterogeneous with regard to diagnosis, treatment and follow-up time. Further, the quality of life of the 24% of the probands who did not wish to participate in the study or provided incomplete answers might be lower than that of the probands assessed. In addition, issues such as perceived isolation, abnormal peer and family relationships, self-esteem and body-image, which are recognised issues to some survivors, may not be sufficiently identified through a generic measure such as the 15D. Finally, in spite of the considerable sensitivity and comprehensiveness of the 15D as a single number measure of HRQOL, there is still a possibility of a small ceiling effect in relatively healthy groups as those under study.

The observed excellent perceived health-related quality of life can be explained in many ways. One explanation may lie in the changes in personality and view of life brought about by the disease and its treatment: the patients may, after experiencing a life-threatening disease, find their present life more satisfying and possible defects in their present health status less significant. This alternative is supported by the finding that the most significant differences between survivors and controls were found in the most subjective dimensions, such as vitality and distress. However, in spite of the experiences of the patients, their valuations of health-related dimensions did not differ from those of the general population of the same age, indicating that the difference in perceived quality of life may not be totally explained by previous experiences.

Although we are presently unable to identify all the mechanisms leading to high perceived health-related quality of life of long-term survivors of childhood malignancies, denial is likely to be involved. Fear of recurrency, employment and insurance problems as well as potential discrimination by peers and partners may lead to a situation where a person ignores even objective symptoms and findings. These denial mechanisms may compensate or even overcompensate the objectively measurable late effects.


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