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Quality of life in children and adolescents surviving cancer

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A B S T R A C T

Purpose: To explore subjective and proxy reported QoL (Quality of Life) in children and adolescents surviving cancer three years after diagnosis compared with healthy controls.
Method: Case-control study including 50 children and adolescents diagnosed with cancer between January 1, 1993 and January 1, 2003 and treated at the Paediatric Department of St. Olav's University Hospital in Trondheim, Norway. Data were collected using The Inventory of Life Quality in Children and Adolescents (ILC) and the KINDL QoL questionnaires (parent and self-reports), as well as by collecting data for any somatic late effects and psychological problems from the medical records of children surviving cancer.
Results: Adolescents surviving cancer as a group assessed their QoL as similar to that of their peers. However, adolescents surviving brain tumours or those with late effects reported lower QoL and an increased number of QoL domains perceived as problematic, even many years after diagnosis and treatment. Parents generally report a poorer QoL for their children surviving cancer and a greater number of QoL domains experienced as problematic compared with parent controls.
Conclusion: To improve the child's total functioning and well-being we conclude that when planning long-term follow-up care, rehabilitation of children and adolescents with cancer, especially for survivors with brain tumours, and with late effects should particularly take into account their subjectively perceived and proxy reported QoL, in addition to their psychological problems and psychosocial functioning.

Introduction

The diagnosis of cancer in childhood involves a crisis for both the child and its family, who face many challenges to achieve normality after diagnosis. As survival rates for childhood cancer have increased, research has focused on quality of life (QoL) issues (Koot and Wallander, 2001) as well as on late effects (Patenaude and Kupst, 2005) among survivors, and not only on measurement of treatment outcomes in terms of survival.

The QoL concept, consistent with the World Health Organisation's definition of health from 1948, has developed to cover the individual's well-being, happiness and satisfaction. However, evaluating the QoL of children represents a number of challenges both in terms of assessment, methods and in the use of proxy informants. A number of instruments aiming to assess QoL in children have been developed (Ravens-Sieberer and Bullinger, 2000; Varni et al., 2001; Mattejat and Remschimidt, 1998, 2006; Upton et al., 2008). Since there is no gold standard, QoL in children with specific disorders should in all probability be assessed using more than one instrument, as well as including different perspectives from both proxy informants as well as from children themselves.

At present, the results of studies on QoL in children surviving cancer are somewhat conflicting (Eiser et al., 2000; Baider et al., 1996; Zebrack and Zeltzer, 2003; Packer, 2008; Foster et al., 2009; McDougall and Tsonis, 2009; Sundberg et al., 2009; Zeltzer et al., 2009). While a number of studies have reported adverse outcomes (Grant et al., 2006; Speechley et al., 2006; Stam et al., 2006; Reinfjell et al., 2009; Gurney et al., 2009; Nathan et al., 2009; Hudson et al., 2003; Mulhern et al., 2004; Oeffinger et al., 2008), others have concluded that QoL (Langeveld et al., 2002, 2004; Zebrack and

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Chesler, 2002; Shankar et al., 2005; Zeltzer et al., 2008, 2009; Servitzoglou et al., 2009; Sundberg et al., 2009) and psychosocial adjustment (Gray et al., 1992; Elkin et al., 1997; Noll et al., 1997; Patenaude and Kupst, 2005; Meyerowitz et al., 2008) are satisfactory for the majority of long-term childhood cancer survivors. Finally, a few studies have found that the prevalence of depression in survivors of childhood cancer equal that of healthy controls (Gray et al., 1992; Zebrack and Zeltzer, 2003).

In addition to potential differences in the use of children or parents as informants, the conflicting results of QoL studies in children with cancer may be partly explained by differences in study populations (i.e. different diagnoses), study designs (i.e. time elapsed since diagnosis, use of healthy controls) and methods (different screening instruments). Moreover it is unclear how late effects may have affected QoL in children surviving cancer in these studies. Thus, in order to increase our understanding of how QoL is affected in children surviving cancer there is a need for further studies using other instruments, including perspectives from both the child and parent proxy, as well as a control group of healthy children and their parents. In addition, there is also a need to take into consideration the role of late effects for children and adolescents surviving cancer.

Two recently developed instruments; the Inventory of Life Quality in Children and Adolescents (ILC) (Mattejat and Remschimidt, 2006) and the Kinder Lebensqualität Fragebogen (KINDL) (Ravens-Sieberer and Bullinger, 2000) questionnaires have both a child self-report and parent proxy report and most importantly, the child self-report is relatively easy to complete. The psychometric properties of these instruments in children with chronic disorders have been well documented (Mattejat and Remschimidt, 2006; Ravens-Sieberer and Bullinger, 2000; Jozefiak et al., 2008; 2010) however, we have not found studies using these instruments in children surviving cancer.

In our study, we therefore chose to use both the ILC and KINDL questionnaires to gain a comprehensive description of various aspects of QoL in children who had survived their cancer diagnosis by more than three years, using healthy controls as a reference and including both the child's own perspective as well as the parent proxy perspective. Psychological problems and psychosocial functioning, related more indirectly to QoL will serve as background information. We expected to find reduced self-perceived and parent-reported QoL compared to the control group. Secondary aims were to explore the following questions:

- Do children surviving brain tumours have a lower QoL than children surviving leukaemia?
- Do childhood, cancer survivors with late effects have lower QoL than those without late effects?
- Do children surviving cancer and their parents report QoL issues differently from their respective controls?

Materials and methods

Study design

This is a population-based, case-control study which was carried out in the period between April 2007 and May 2008. It includes children and adolescents in Central Norway from the ages of six to 20 years who were diagnosed with cancer between January 1st, 1993 and January 1st, 2003. Eligible for participation were children who had completed their cancer treatment at the Paediatric Department, St. Olav's University Hospital, Trondheim, and survived at least three years after diagnosis. Data was collected by using questionnaires mailed to the child's families, as well as by reviewing the child's medical records. A control group was recruited by asking children and adolescents in the study group to invite one friend of the same gender and age (±one year) to participate, as well as one of the friend's parents. Questionnaires were sent to these invited families.

Study population

Children surviving cancer

Of 109 eligible children, a total of 50 (46%) participated; 29 (58%) males and 21 (42%) females, aged 6–20 years and born in the period of 1987–2001. The median age was 12.5 years (interquartile range: 10.0–16.0), with 29 (58%) being adolescents (12–20 years). The children took part in this study 4–16 years (median: 7.5; interquartile range: 6.0–10.2) after their cancer diagnosis and 1–13 years (median: 6.0; interquartile range: 4.0–7.2) after completion of treatment. The group included children with leukaemia ($n = 20$), malignant brain tumours ($n = 13$), lymphoma ($n = 5$) and solid or soft tissue tumours ($n = 12$) (Table 1). One of their parents responded to questionnaires, and 45 participants/parents consented to contact the child's teacher, whereof 36 teachers responded (Eilertsen et al., in press).

Control group

Of the 50 families in the study group, 40 gave written consent to contact one friend to participate as a control in the study, and 29 (73%) peers and one of their parents agreed to participate. Of these, 15 (52%) were males and 14 (48%) were females aged 5–20 years, born in the period of 1987–2001. The median age was 12.0 years (10–14.5), with 21 of the 29 (73%) being adolescents (Table 1). Of the 29 parents, 24 gave written consent to contact the child's teacher and 19 teachers responded (Eilertsen et al., in press).

Study variables

Quality of life (QoL)

In this study we define QoL as the subjective perceived well-being as reported by the child and her/his parent by proxy on

Table 1
Background information of children included in the study.

		Survivors		Controls		
		N	%	N	%	*P*-value
	Total	*50*	*100*	*29*	*100*	
Gender	Female	21	42	14	48	
	Male	29	58	15	52	0.59
Age	<12 yrs	21	42	8	27	
	>12 yrs	29	58	21	73	0.20
Family economical situation	Poor economy	7	14	2	7	
	Average economy	21	42	5	17	
	Good economy	18	36	11	38	0.19
Children live with[a]	Both parents or one parent with partner	36	72	24	82	
	Single parent	12	24	2	7	0.07

[a] 3 participants (2 young adults with cancer and 1 in the control group) lived on their own.

several life domains. To gain a comprehensive picture of various aspects of QoL in our study we used two different instruments; the Inventory of Life Quality in Children and Adolescents (ILC) (Mattejat and Remschimidt, 2006) and the Kinder Lebensqualität Fragebogen (KINDL) (Ravens-Sieberer and Bullinger, 2000) questionnaires. These instruments are developed for different research and clinical purposes and differ in items, content and length.

The inventory of life quality in children and adolescents (ILC)

The ILC questionnaire was developed as a short and practical instrument assessing QoL over the past week for use in working with child mental health issues (Mattejat and Remschimidt, 2006). The ILC was translated into Norwegian according to international standards and approved by the original authors. The Norwegian version of the ILC for adolescents (aged 12–18 years and may be used up to 20 years) and their parents have shown satisfactory reliability (Jozefiak et al., 2008, 2010). Both adolescent (self-report) and parent (proxy report for children and adolescents from 4 to 20 years) versions were used in the present study. The questionnaire includes six items addressing the child/adolescent's experience of *school performance, family functioning, friends and social integration, activities and hobbies, physical health,* and the child's *mental health*. In addition, it includes one *global QoL item (this question is as follows: "All these things considered: How are you currently feeling?").* Each of the seven items are rated on a 1–5 scale (1 = very good; 5 = very bad). The ILC QoL score was obtained by summing the seven items, transforming into a 0–28 scale (Mattejat and Remschimidt, 2006), 0 = very low QoL and 28 = very high QoL. In contrast to the subscale scores (seven domains), low values for the QoL scale score correspond to a poor QoL, whereas a high QoL scale score indicates a very good QoL. Further, the ILC Problem scale indicates the amount of life domains affected by problems. The problem score (range 0–7) is computed by dichotomising each of the seven items, thus ratings of 1 or 2 (= 0) signify no problem and ratings of 3, 4, 5 (=1) signify the present problem. The ILC has shown a moderate convergent validity with the KINDL (Child Self-report, general population, $r = 0.69$; $p < 0.01$; $n = 1961$) (Jozefiak, 2004).

The Kinder Lebensqualität Fragebogen (KINDL)

The KINDL (Ravens-Sieberer and Bullinger, 2000) was developed for epidemiological use in healthy and clinical groups of children and adolescents aged 4–16 years. This questionnaire includes generic forms for several age groups (4–7, 8–12, and 13–16 years) as well as a proxy report for parents. In the present study we used the KINDL for children from 8 years to young adults up to 20 years. The forms consist of 24 items equally distributed into the following six subscales: *physical well-being, emotional well-being, self-esteem, family, friends and school*. Each item addresses the child's experiences over the past week and is rated on a 5-point scale (1 = never; 5 = always). Mean scores are calculated for each of the six subscales as well as the *total quality of life scale*, which again are transformed to 0–100 scale (0 = very low and 100 = very high QoL). The KINDL questionnaire was completed by the participants themselves (self-report) while children from four to 20 years of age were also assessed by one of their parents (parent proxy report). The original KINDL showed satisfactory validity and reliability (www.Kindl.org). The Norwegian version, which had been translated according to international standards (Helseth and Jozefiak, 2004) showed also satisfactory reliability (Jozefiak, 2004).

Parents' socioeconomic status

Socioeconomic status (SES) was calculated according to Hollingshead's two factor index of social position scaled one (low) to five (high), based on a combination of parents' education and occupation (Hollingshead, 1958). Parents also evaluated their economical situation as "poor", "average" or "good".

Background data

Parents gave information about demographic data (where and whom they lived with, number of children and marital status). Parents of a child with cancer were also asked about their child's diagnosis, as well as their child's health status and late effects at the time of this study. Based upon these questions we defined a variable called late effects which included somatic health problems that could probably be related to the cancer diagnosis or its treatment. Somatic diagnoses and psychological problems were also collected from the child's medical records.

Ethics

Ethical approval was obtained from the Regional Committee for Medical and Health Research Ethics in Central Norway (Ref.nr. 4.2006.2610). Approval was given for a single written reminder, whereas permission was not given to get in touch with the child's family by telephone. A letter with written information was sent to families of all eligible children inviting them to participate. Written consent to participate in this study, as well as access to the child's medical records, was given by the participant or by one of the child's parents, if the child was under 16 years of age. Approval by the Norwegian Social Science Data Services (Ref.nr. 15372/JE) was obtained for a licence to maintain a register containing personal data.

Statistical analysis

SPSS for Windows version 17.0 (SPSS Inc, Chicago, IL) was used for data analysis. In accordance with the KINDL manual, and in order to compare our results with other studies, we have chosen to present location and distribution of the QoL scores as mean values and standard deviations, even if these were not normally distributed. However group differences were analysed using the Mann Whitney *U*-test. Group differences in proportions were analysed using Chi-square statistics. We did not correct for multiple comparison since our results were coherent and such methods used for adjusting for multiple comparisons (i.e. Bonferroni correction) are conservative as well as likely to detract the results (Bacchetti, 2002; Rothman, 1990; Altman, 1999; Rosner, 2000). Spearmans correlations coefficient was used to study the correlation between the ILC *Total quality of life* scores on the self-report and on the parent proxy report. To compare scores obtained in the control group with a representative sample obtained from the general population we used a one-sample *T*-Test. Two-sided *p*-values ≤ 0.05 were considered statistically significant.

Results

When comparing our control group with an extensive representative sample of the general population in the same geographical area there were no significant differences shown in the total sum scores of the parent report for either the ILC ($N = 1777$) or KINDL ($N = 1742$). Furthermore, no significant differences were shown in the adolescent report for the ILC questionnaire ($N = 1032$). However, a significant difference was found in the child report for the KINDL *Total quality of life* ($N = 1966$), when comparing our control group with the general population (Mean (SD): 75.3 (8.2) and 70.6 (12.4) respectively; $p = 0.011$).

There were no significant differences between children surviving cancer and the control group in view of the children's age and gender or in the parents' educational and economical status (Table 1). Mean socioeconomic status (SES) score was 3.8 (SD: 1.1)

for parents of children with cancer, compared to 3.7 (SD: 1.2) in the control group ($p = 0.8$). Twelve (24%) children with cancer lived with single parents compared to two (7%) children in the control group ($p = 0.07$) (Table 1).

Quality of life – ILC results

Parents of children (6–20 years) surviving cancer reported a lower mean total score for their children on the *Quality of life scale,* compared to the control group (Table 2). Moreover, they also reported an increased number of domains as being problematic on the *Problem score*, compared to the control group (Table 2). On the parent report this finding was particularly evident among survivors as a group but also among survivors of brain tumours ($p < 0.001$ for both scales) and leukaemia (*Quality of life scale:* $p = 0.04$ and *Problem scale*: $p = 0.03$). On the adolescent self-report (12–20 years) this was evident for survivors with brain tumours (*Quality of life scale*: $p = 0.01$ and *Problem scale*: $p = 0.02$), while no differences on the adolescent self-report were found for survivors as a group or with leukaemia, compared to their controls (Table 2).

With regards to *school performance,* parents of children surviving cancer reported a lower QoL (i.e. showed higher mean scores) compared to the control group, which was mainly evident among survivors with brain tumours ($p = 0.008$). There were no differences reported on the adolescent self-report.

With regard to *family functioning* children surviving cancer did not differ significantly from control children on any reports. Although, for children with brain tumours their parents reported a statistical tendency (Mean 1.69; SD: 0.8) compared with Mean 1.30 (SD: 0.5) in the control group ($p = 0.08$), suggesting a lower family functioning for the brain tumour group.

Parents reported a significantly lower QoL (i.e. higher mean score) on the *friends and social* integration domain for children surviving cancer as a whole ($p = 0.003$), with brain tumours ($p < 0.001$) and leukaemia ($p = 0.008$), when compared to the control group. In addition, on the self-report adolescents surviving brain tumours reported significantly ($p = 0.01$) higher mean scores on the *friends and social* integration domain compared to the control group.

Results from the parents' score on the *activity and hobbies* domain were lower ($p = 0.04$) (higher mean scores) for children with brain tumours, while the difference between the control group and children surviving cancer as a whole ($p = 0.06$) as well as leukaemia ($p = 0.07$) were borderline, non-significant. No significant differences were shown on the adolescent self-report.

On the *physical health domain,* children surviving cancer did not differ from control children on any reports except on the parent report for children surviving brain tumours ($p = 0.02$), when compared to the control group. Yet, on the *mental health domain* parents reported significantly lower mental health (higher mean scores) for children surviving cancer as a whole ($p = 0.004$), with brain tumours ($p < 0.001$) and leukaemia ($p = 0.03$) when compared to controls. On the self-report adolescents surviving brain tumours ($p = 0.01$) also reported lower mental health (higher mean scores) compared with controls.

Parents reported significantly lower global QoL (higher mean scores) for children surviving cancer as a whole ($p = 0.005$), with brain tumours ($p < 0.001$) as well as leukaemia ($p = 0.05$). However, no differences were found on the adolescent self-report.

The ILC showed a moderate to strong correlation between the *Quality of life scale scores on the* self-report and the parent proxy report both within the group of children surviving cancer ($r_s = 0.65$; $p < 0.001$) as well as within the control group ($r_s = 0.61$; $p = 0.004$).

Quality of life – KINDL results

Parents of children (8–20 years) surviving cancer with brain tumours reported a significantly lower QoL (lower mean scores) on the *KINDL total quality of life scale* compared to the control group ($p = 0.004$). No differences were reported by children on the self-report (Table 3).

Parents of children surviving cancer reported lower mean scores (i.e. lower QoL) or a tendency to lower mean scores for their children on the *physical and emotional well-being,* as well as the *friends' subscales.* Parents reported no significant findings on the *self-esteem*, *family or school subscales.* However, on the self-report, only

Table 2
Quality of Life as assessed by The Inventory of Life Quality (ILC) Questionnaire, completed by parents and adolescents.

	Survivors		Leukaemia		Brain tumor		Controls
	Mean (SD)	*P*-value	Mean (SD)	*P*-value	Mean (SD)	*P*-value	Mean (SD)
ILC - parent report 4–20 yrs	$n = 50$		$n = 20$		$n = 13$		$n = 26$
Quality of life scale[c]	21.54 (5.0)	0.004	22.05 (4.4)	0.035	18.46 (5.6)	0.000	24.92 (3.2)
Problem scale[b]	1.56 (1.9)	0.002	1.35 (1.8)	0.026	2.62 (2.1)	0.000	0.44 (1.3)
School[a]	2.16 (1.2)	0.077	2.15 ((1.2)	0.195	2.69 (1.3)	0.008	1.62 (0.7)
Family[a]	1.46 (0.6)	0.315	1.35 (0.5)	0.628	1.69 (0.8)	0.084	1.30 (0.5)
Friends[a]	2.34 (1.3)	0.003	2.30 (1.2)	0.008	3.07 (1.6)	0.001	1.46 (0.6)
Activity - hobbies[a]	1.84 (1.0)	0.061	1.85 (0.9)	0.071	2.30 (1.4)	0.036	1.42 (0.6)
Physical health[a]	1.84 (0.9)	0.106	1.65 (0.8)	0.522	2.23 (1.0)	0.015	1.50 (0.7)
Mental health[a]	1.94 (0.8)	0.004	1.85 (0.7)	0.027	2.15 (0.8)	0.004	1.42 (0.6)
Global evaluation[a]	1.88 (0.8)	0.005	1.80 (0.8)	0.051	2.38 (0.9)	0.000	1.34 (0.6)
ILC - Adolescent report- 12–20 yrs	$n = 28$		$n = 12$		$n = 7$		$n = 21$
Quality of life scale[c]	22.11 (5.1)	0.200	24.75 (2.2)	0.663	18.86 (5.1)	0.012	23.81 (3.8)
Problem scale[b]	1.15 (1.7)	0.581	0.25 (0.5)	0.250	2.60 (1.9)	0.017	0.89 (1.7)
School[a]	2.02 (0.9)	0.391	1.75 (0.6)	0.951	2.28 (0.8)	0.117	1.79 (0.7)
Family[a]	1.35 (0.6)	0.451	1.25 (0.5)	0.752	1.42 (0.8)	0.553	1.23 (0.5)
Friends[a]	1.85 (1.2)	0.393	1.25 (0.5)	0.285	2.42 (1.5)	0.094	1.47 (0.6)
Activity - hobbies[a]	1.75 (0.9)	0.800	1.41 (0.5)	0.464	2.14 (1.1)	0.265	1.67 (0.8)
Physical health[a]	2.03 (1.1)	0.151	1.83 (0.9)	0.497	2.28 (1.1)	0.121	1.61 (0.8)
Mental health[a]	2.00 (1.3)	0.751	1.33 (0.5)	0.207	3.28 (1.5)	0.010	1.71 (0.8)
Global evaluation[a]	1.85 (0.9)	0.473	1.41 (0.5)	0.443	2.28 (1.0)	0.101	1.67 (0.8)

All *P*-values refer to comparisons with controls.
NB: c = high QoL scores whereas a and b = high subscale scores (domains) indicate a poor QoL.
[a] Range 0–28.
[b] Amount of domains effected range 0–7.
[c] Sub-domains range 1–5.

Table 3
Quality of Life as assessed by the KINDL Questionnaire, completed by parents and adolescents.

	Survivors		Leukaemia		Brain tumor		Controls
	Mean (SD)	*P*-value	Mean (SD)	*P*-value	Mean (SD)	*P*-value	Mean (SD)
KINDL - parent report 8–20 yrs	$n = 47$		$n = 19$		$n = 13$		$n = 24$
Total quality of life	68.82 (14.0)	0.065	69.61 (11.9)	0.129	63.62 (10.9)	0.004	74.99 (11.0)
Physical well-being	68.35 (24.7)	0.036	71.05 (24.9)	0.257	62.01 (17.5)	0.002	81.77 (13.2)
Emotional well-being	69.41 (19.6)	0.086	68.75 (16.8)	0.053	66.82 (19.2)	0.058	77.34 (14.4)
Self-esteem	62.50 (18.2)	0.545	61.11 (12.4)	0.284	56.73 (17.6)	0.266	64.06 (14.4)
Family	75.00 (11.2)	0.843	75.98 (11.5)	0.601	69.71 (8.4)	0.199	74.39 (13.7)
Friends	69.14 (19.7)	0.066	70.72 (19.1)	0.140	61.05 (21.4)	0.013	78.64 (11.9)
School	68.35 (18.8)	0.456	69.07 (16.0)	0.582	65.38 (17.4)	0.302	73.36 (13.6)
KINDL - Child & adoles report 8–20 yrs	$n = 44$		$n = 19$		$n = 8$		$n = 23$
Total quality of life	73.11 (11.60)	0.625	74.72 (10.67)	0.869	69.02 (15.16)	0.305	75.30 (8.19)
Physical well-being	72.30 (22.36)	0.305	74.67 (23.88)	0.848	65.62 (20.89)	0.039	80.52 (11.31)
Emotional well-being	76.46 (17.05)	0.979	80.59 (12.65)	0.440	68.75 (20.98)	0.217	78.26 (11.59)
Self-esteem	62.64 (20.10)	0.612	59.53 (23.04)	0.759	63.02 (23.04)	0.376	62.50 (13.05)
Family	77.98 (16.25)	0.709	82.23 (14.77)	0.582	69.79 (18.43)	0.054	79.89 (13.18)
Friends	77.46 (17.23)	0.692	81.90 (12.82)	0.336	70.31 (23.85)	0.633	79.61 (10.69)
School	71.80 (17.95)	0.459	69.40 (16.91)	0.864	76.70 (18.13)	0.101	70.45 (12.82)

All *P*-values refer to comparisons with controls.

children surviving a brain tumour reported lower mean scores on the *physical well-being* and *family subscales* (Table 3).

Somatic late effects in children and adolescents surviving cancer

At the time of this study, 20 (40%) parents indicated that their child had somatic late effects, something which was also confirmed through the children's medical records. The late effects were pituitary ($n = 6$) and gonad ($n = 3$) deficiency, growth problems ($n = 1$), diffuse muscle pain ($n = 5$), lung problems ($n = 2$), dry eyes ($n = 1$), blindness ($n = 2$), impaired eyesight ($n = 1$), trembling/shaky hands ($n = 1$), as well as weight problems ($n = 2$) and problems with teeth enamel ($n = 2$).

Of these 20 children, eight (40%) were diagnosed with leukaemia, nine (45%) with brain tumours, three (15%) with solid or soft tissue tumours. There were no late effects registered for children diagnosed with lymphoma.

Psychological problems in children and adolescents surviving cancer

Sixteen of the 20 children registered with somatic late effects also had psychological problems; eight (50%) children surviving brain tumours and six (38%) with leukaemia. According to medical records, 12 of these 16 children (75%) had been referred to Child and Adolescent Psychiatric Services due to symptoms of anxiety ($n = 4$), depression ($n = 4$), behavioural problems ($n = 4$), eating problems ($n = 1$) or suspected ADHD ($n = 2$). The remaining four (25%) children had concentration problems, fatigue, cognitive and learning disabilities, or were socially isolated. Through the children's medical records there were no other children registered in this study with psychological problems.

The association between somatic late effects and quality of life

Parents to children surviving cancer with late effects, reported a significant difference and a lower QoL (ie. showed lower mean scores) on the ILC as well as an increased number of domains perceived as problematic (ie. higher mean scores) on the ILC problem scale, compared to the control group (Table 4). Similar results were also reported on the adolescent self-report (Table 4). Moreover, children surviving cancer *with* late effects showed corresponding results on both the parent report as well as the adolescent self-report when compared to children *without* late effects.

Furthermore, parents reported a significant difference and a lower QoL (ie. showed lower mean scores) on the *KINDL total quality of life scale* for children surviving cancer *with* late effects compared to control children, as well as children *without* late effects (Table 4). However, on the self-report children with late effects showed no significant difference on the *KINDL total quality of life scale* than control children, and only a statistical tendency was shown between children *without* and *with* late effects (Table 4).

Discussion

In this study, adolescents surviving cancer as a group reported equal QoL compared with healthy controls. Equal QoL was also

Table 4
Quality of Life as assessed by ILC and KINDL in children with and without somatic late effects.

	Survivors No late effects		Survivors Late effects		Control
	Mean (SD)	*P*-value	Mean (SD)	*P*-value	Mean (SD)
ILC - Parent report 4–20 yrs	$n = 30$		$n = 20$		$n = 26$
Quality of Life scale (range 0–28)	23.93 (3.6)	0.234	17.95 (4.7)c	0.000	24.92 (3.2)
Problem scale (range 0–7)	0.69 (1.2)	0.356	2.89 (1.9)c	0.000	0.44 (1.2)
ILC - Adolescent report 12–20 yrs	$n = 19$		$n = 9$		$n = 21$
Quality of Life scale (range 0–28)	23.32 (4.7)	0.733	19.56 (5.3)a	0.021	23.81 (3.8)
Problem scale (range 0–7)	0.56 (0.9)	0.623	2.33 (2.3)a	0.055	0.89 (1.7)
KINDL - Parent report 8–20 yrs	$n = 28$		$n = 19$		$n = 24$
Total quality of life	74.60 (12.8)	1.000	60.30 (11.35)c	0.000	74.99 (11.0)
KINDL - Child & adolescent report 8–20 yrs	$n = 27$		$n = 17$		$n = 23$
Total quality of life	75.90 (9.8)	0.755	68.69 (13.1)	0.147	75.30 (8.2)

All unmarked *P*-values refer to comparisons with controls; *P*-values marked a, b or c refer to late effects versus no late effects a = $P < 0.05$; b = $P < 0.01$; c = $P < 0.001$.

reported by the subgroup of adolescents surviving leukaemia, while adolescents surviving brain tumours and survivors with late effects reported lower QoL and increased number of QoL domains perceived as problematic, when assessed with the ILC. In consistence with the self-report, parents of survivors with brain tumours and with late effects rated their child's QoL as lower than parents of controls. However, in contrast to adolescents themselves, parents also reported an overall lower QoL and a greater number of QoL domains perceived as problematic for their children surviving cancer as a group, as well as for the subgroup of children surviving leukaemia. When using the KINDL questionnaire differences in QoL between cases and controls were consistent with the ILC results for children surviving brain tumours and with late effects.

Quality of life

The highly significant differences in mean scores as particularly reported by parents, involving the case and control group may support a causal relation between aspects of the cancer diagnosis, its treatment and diminished QoL. Our findings of lower QoL reported by parents are consistent with a number of previous studies and reviews of QoL studies in childhood cancer survivors using either the proxy or self-report (Grant et al., 2006; Speechley et al., 2006) as well as three other studies in older age groups, using other outcome measures as well as other control groups (i.e. siblings) (Stam et al., 2006; Reinfjell et al., 2009; Zeltzer et al., 2009). However, most studies found that on the whole, survivors of childhood cancer fare the same or have a good QoL (Langeveld et al., 2002, 2004; Zebrack and Chesler, 2002; Shankar et al., 2005; Zeltzer et al., 2008, 2009; Servitzoglou et al., 2009; Sundberg et al., 2009) and function well psychologically (Gray et al., 1992; Elkin et al., 1997; Noll et al., 1997; Patenaude and Kupst, 2005; Meyerowitz et al., 2008). Yet, only a few studies had reported results by both parent proxy and adolescent self-report, compared with controls.

In addition, our findings of a lower QoL score and an increased number of domains perceived as problematic were found among almost all survivors *with* physical late effects. Parents in our study, reported 20 (40%) children as having late effects, including sixteen having psychological problems and twelve being referred to the Department of Child and Adolescent Psychiatry. In contrast, no psychological problems were recorded among children without physical late effects. However, we cannot rule out the consequences of long-term psychological strain because of the effects of the cancer disease and its treatment. In various studies suggesting that childhood cancer survivors function well psychologically (Zeltzer et al., 2009; Gray et al., 1992; Langeveld et al., 2002) despite a seemingly traumatic childhood experience, it was unclear if survivors were suffering from late effects or not. Taken into consideration, these findings may support the suggestion of a biological and psychological source for a poorer QoL experience among children who have survived cancer.

Differences in QoL in children surviving cancer may be related, as stated above, to both somatic and psychiatric side effects as well as psychological strain of the cancer illness. Side effects can be caused by the child's cancer diagnosis (i.e. brain tumours; leukaemia), type and length of the cancer treatment (i.e. radiation, surgery, neurotoxic side effects of drugs, bone marrow transplant) and its complications (i.e. severe systematic infections, bleeding, scars). The psychological strain of the cancer illness can be caused by the suffering from a life-threatening disease or its long-term, intensive and severe treatment. Long absences from normal social and school activities, which are consistent with cancer treatment, may also lead to a poorer QoL for the child. Furthermore, inappropriate attitudes or approaches among other children and adults both at school and at home can influence their expectations of the child with cancer and how they treat them, which may contribute to a poorer QoL for the child surviving cancer.

Child and parent proxy reports

In keeping with other studies (Eiser et al., 1995; Sawyer et al., 1999; De Clercq et al., 2004; Russell et al., 2006; Upton et al., 2008), we found a strong correlation between the total QoL ILC scores reported by parents and by their adolescent child, suggesting that in the case of cancer, parents and adolescents share much of the same perspective. Moreover, our finding of lower QoL among children with brain tumours and late effects compared with controls were consistent for parent proxy report and adolescent self-report. For these subgroup analyses the differences in mean values were considerable and may be consistent with a causal relation between adolescents surviving brain tumours or having late effects, and a poorer QoL. These results emphasise the need for addressing the issue of diagnosis and presence of late effects in QoL studies in childhood cancer survivors. Our results are consistent with other studies of reduced QoL among children surviving brain tumours (Upton et al., 2005; Cardarelli et al., 2006; Varni et al., 2007; Penn et al., 2009; Yoo et al., 2010), as well as among studies and reviews of late effects and QoL of childhood cancer (Pemberger et al., 2005; Calaminus et al., 2007; Eiser et al., 2007; Ishida et al., 2010a, b).

Nonetheless, there were some notable differences between the results obtained from parents and adolescents themselves when compared with healthy controls. In general, adolescents surviving cancer reported a QoL similar to controls, while parents reported an overall poorer QoL for their children surviving cancer compared to controls. This is consistent with other QoL studies of childhood cancer comparing parent and child ratings with controls (Sawyer et al., 1999; Russell et al., 2006; Varni et al., 2007).

The discrepancy on QoL between the child and parent report for children surviving cancer compared with controls is most likely a consequence of the different perspectives about the child's health and well-being and not a question of which perspective is right or wrong (Varni et al., 2005; Upton et al., 2008; Jozefiak et al., 2008). Parents may vary in their awareness, sensitivity and tolerance of children's health concerns (Upton et al., 2008). In addition, the impact of the child's disease and actual problems may have an influence on the parents' experience of stress (Angold et al., 1998; Jozefiak, 2004; Davies et al., 2008) and thus, their perception of the child's QoL. On the other hand, children living with a chronic illness may assess their own QoL and possible problems differently, dependent upon their subjective experience of how they feel mentally and physically. Furthermore, younger children have a limited cognitive capacity (Eiser and Morse, 2001). They also tend to live more in the present on a "here and now" level, not having the same sense of time as adults. Many children may respond to stressors by repressing their own issues as an important defence mechanism for coping, whereas other children and adolescents may show resilience and positive coping strategies (Woodgate, 1999a, b; Borge, 2010), which can result in increased growth and the potential for enhanced QoL (Haase, 1997; Woodgate, 1999a, b). Sequentially can improved QoL lead to improved resilience to stressors (Woodgate, 1999a, b). Therefore, as stated by both Parsons et al., (1999) and Upton et al., (2008) the main question is not essentially, "who is right?" but rather, "what does the parent proxy and self-report contribute to our further understanding of paediatric QoL?"

Obtaining information about QoL provided by both children and their parents is therefore important in contributing to a richer and more comprehensive understanding from different informant

perspectives. In this study our results are in accordance with other studies reporting a discrepancy between the self-report and proxy report in different clinical and general population studies (Theunissen et al., 1998; Chang and Yeh, 2005; Yeh and Chang, 2005; Jozefiak et al., 2008, 2009, 2010). However, our study also showed that comparing QoL child vs. proxy report *directly* in studies of children surviving cancer could be misleading without including a control group. With the use of both the child self-report and parent proxy report, as well as the use of two different QoL instruments (ILC and KINDL questionnaires) our results suggest that especially adolescents surviving brain tumours and survivors of late effects have an overall poorer QoL compared with a healthy control group.

Strengths and limitations of the study

Strengths of this study are the comprehensive assessment of QoL by both the child self-report and parent proxy report for children surviving cancer with different diagnoses and the inclusion of a control group comprising both children and parents. Moreover, the two instruments used, KINDL and ILC, are well-established questionnaires that have shown satisfactory reliability and validity in former studies including in Norway. Both the IL C and KINDL *Total quality of life* scores in our control group were representative for the general population when they were compared with data of a reference population; except for KINDL where our control group obtained higher scores on the adolescent self-report. The latter finding would only have been a problem had adolescents surviving cancer scored significantly lower than control adolescents. Finally, the main findings were essentially the same regardless of the instruments used, which may also be considered as a strength.

The observed differences found between children surviving cancer and controls were statistically highly significant, thus making chance an unlikely cause of the main findings. However, the limited number of participants, resulted in low power to demonstrate small differences between the groups, and lack of statistically significant findings should therefore be interpreted with caution. Moreover, using friends as controls (Elkin et al., 1997; Buizer et al., 2006) may introduce a methodological bias since peers are likely to share common interests (Eiser et al., 2000) and attitudes with the case group, and therefore may be more similar in terms of their subjective experience of QoL. This bias would be expected to decrease the differences between groups. However, the control children's scores on the ILC and KINDL questionnaires did not differ essentially from that of a representative sample from the general population in the same geographical area. We therefore consider it less likely that this bias significantly affected our results. Another potential limitation is the low response rate (44%), although not uncommon in long-term follow-up studies using mailed surveys (Fewtrell et al., 2008; Langeveld et al., 2004). We consider it however less likely that the non-responders differed systematically from responders as there were no differences regarding background data such as age, gender or diagnoses.

Key variables such as age, gender and parents' socioeconomic status did not differ between the group of children surviving cancer and controls, making confounding by these variables less likely.

Implications

To improve the child's total functioning and well-being our results indicate the need to develop adequate supportive interventions and programs when planning long-term follow-up care and rehabilitation of children and adolescents with cancer, especially for survivors with brain tumours, and with late effects. Our results also indicate the need to particularly take into account subjectively perceived and proxy reported QoL, in addition to children and adolescents' psychological problems and psychosocial functioning. Further, it is essential to compare clinical QoL reports, either self-report and/or parent proxy report, always to a normative frame of reference.

Further research is needed to obtain an even more comprehensive understanding of QoL in survivors of childhood cancer. Based on our results we suggest that focus be given to potential factors such as resilience that can contribute to the experience of a good QoL, as well as more in-depth studies using both self and proxy reports in addition to quantitative and qualitative methods. Results can therefore be used to guide interventions and improve strategies to enhance the child's total functioning and well-being.

Conclusion

In conclusion, our study shows that adolescents surviving cancer as a group assess their QoL as similar to that of their peers. However, adolescents surviving brain tumours or those with late effects reported lower QoL and an increased number of QoL domains perceived as problematic, even many years after diagnosis and treatment. Our study also shows that parents generally report a poorer QoL for their children surviving cancer, as well as a greater number of QoL domains experienced as problematic compared with parent controls.

Conflicts of interest

None.

Ethical approval

Ethical approval was obtained from the Regional Committee for Medical and Health Research Ethics in Central Norway (Ref.nr. 4.2006.2610).

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