


# Health-related quality of life of children born to childhood cancer survivors in Germany

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## Abstract

**Objective:** Rising childhood cancer survival rates have increased the importance of health-related quality of life (HRQL) assessment. While survivors show comparable HRQL to peers, concerns that cancer treatment could impact the health of prospective children were reported. No previous publications address HRQL of childhood cancer survivor offspring.

**Methods:** We assessed survivor offspring HRQL using the parental KINDL questionnaire. Matched-pair analysis was conducted with data from the general population (KiGGS study) using age, gender and education (1:1,  $n = 1206$  cases). Multivariate analyses were conducted to detect the influence of parental diagnose and treatment on offspring HRQL.

**Results:** Overall, within KINDL dimensions, survivors reported comparable to higher HRQL for their children than the general population. Survivor parents reported significantly ( $p < 0.001$ ) higher psychological (86.7% vs. 83.0%, Cohen's  $d = 0.3$ ) and self-esteem (79.1% vs. 73.3%, Cohen's  $d = 0.5$ ) well-being scores for younger children (3–6-year-olds). As time since diagnosis increased, parents reported higher well-being scores. Accordingly, recently diagnosed survivors reported significantly lower psychological well-being scores ( $p = 0.28$ ; OR = 0.457; 95% CI = 0.228–0.918) for their children. With increasing age, average HRQL scores decreased in both cohorts; yet, this drop was less pronounced for survivor offspring. The biggest difference between age groups (7–10- vs. 14–17-year-olds) was found for school-specific well-being (6.2-point drop in survivor offspring vs. 18.2-point drop in KiGGS offspring).

**Conclusion:** Comparable to higher parentally assessed HRQL was reported for survivor offspring compared to peers. These findings are reassuring and consistent with self-reported HRQL in childhood cancer survivors. Type of parental cancer diagnosis and treatment showed no negative impact on offspring HRQL.

## KEYWORDS

childhood cancer, health-related quality of life, offspring, oncology, survivors, well-being

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## 1 | BACKGROUND

Assessing child and adolescent health-related quality of life (HRQL) has increasingly become an important topic.<sup>1</sup> Accordingly, restoring and/or maintaining physical and psychosocial well-being have become central aspects in childhood cancer treatment, especially in light of growing survival rates.<sup>2</sup> Childhood cancer survivors may experience treatment-related sequelae that potentially reduce HRQL.<sup>3</sup> Overall, survivors seem to adapt well in adulthood with reported peer-comparable HRQL.<sup>4</sup> Survivors reported current and future life satisfaction.<sup>5</sup> Adolescent survivors expressed positive changes in self-awareness, relationships and prospective plans following cancer treatment<sup>6</sup>—possibly revealing *posttraumatic growth* regarding positive interpretation and cognizance of cancer-related trauma.<sup>2,6</sup> Yet, female gender, low educational level, unemployment, unmarried status and increased time since diagnosis may impair survivor HRQL.<sup>4,5,7</sup> The subjective experience of illness and treatment seems to influence psychological well-being more than objective, illness-specific characteristics.<sup>8</sup> Neither relapse nor second malignancy was significantly associated with HRQL impairment.<sup>2</sup> The manifestation of multiple or severe sequelae, psychiatric symptoms and reduced posttraumatic growth, however, may impair HRQL.<sup>5,7</sup>

Childhood cancer survivors reported concerns regarding the health of prospective children.<sup>9</sup> Parental HRQL and parenting are known to influence a child's developmental environment and associated HRQL.<sup>10</sup> The lifestyle observed for survivor offspring<sup>11</sup> suggests a healthier upbringing. While survivor HRQL has been investigated, little is known about the HRQL of their offspring.

## 2 | OBJECTIVES

This novel study compares HRQL in children born to childhood cancer survivors with the general population.

## 3 | PATIENTS AND METHODS

### 3.1 | Study design and participants

From August 2015 to December 2016, we conducted a second Germany-wide survey wave addressing the health of childhood cancer survivor offspring. Participants received a questionnaire regarding health aspects of their offspring based on the *Robert Koch-Institute's* "Health examination survey for children and adolescents in Germany, KiGGS study" (2003–2006,  $n = 17,640$ <sup>12</sup>). This allowed comparability of data between children born to survivors with the general population. Our study concept and methods have been described previously.<sup>9,13</sup> Study conduction was approved by the *Charité-Universitätsmedizin Berlin* Ethical Board (EA2/237/05, EA2/103/11) and by the *German Society for Paediatric Oncology and Haematology*.

In total, 902/906 survivors, previously identified as having biological children by the *VIVE study* on late effects in childhood cancer survivors,<sup>14</sup> were successfully contacted via the *German Childhood Cancer Registry*. Overall, 598/902 survivors (66.3%) completed questionnaires for 922 children. Written informed consent was obtained from all study participants. Responding survivors were more likely to be younger, female and moderately to highly educated than non-responders, while age at diagnosis and distribution of diagnoses did not significantly differ.<sup>13</sup> Questionnaires missing offspring age ( $n = 3$ ), gender ( $n = 6$ ), or from 0–2-year-old ( $n = 291$ ) or  $\geq 18$ -year-old offspring ( $n = 19$ ) were excluded, as KiGGS reference values are only available for 3–17-year-olds. This resulted in 603 (65.7%) assessable questionnaires. Survivor offspring were matched 1:1 with KiGGS offspring using gender, age and educational level in a case-control design for matched-pair analysis ( $n = 1206$ ).

### 3.2 | Measure instruments

Survivors assessed offspring HRQL using the *KINDL* questionnaire for parents (questions 21–26 ; *KINDL*-ID: 977). The *KINDL* questionnaire, a reliable, validated instrument, determines HRQL for both healthy and health-impaired children within the previous week.<sup>1,15</sup> Parents assessed 24 items within the dimensions *physical, psychological, self-esteem, family, friends* and *school*, using a five-point Likert scale (range: *never-always*). A total score was calculated; 100 indicated the highest HRQL.<sup>1</sup> Standard values for different age groups (range 3–17 years) are representative of the general population.<sup>1</sup> Survivors subjectively assessed their child's health status (question 6; range: *very good-very poor*), rated their anxiety regarding a perceived potential for cancer development in offspring (question 12; 100 mm visual analog scale: *low-high anxiety*) and reported any recent pain experienced by child (previous 3 months). Educational level of parents (rated: *low, medium, or high*) was calculated using *CASMIN* classification.<sup>16</sup> Survivor core data were provided by the *German Childhood Cancer Registry*.

### 3.3 | Statistical methods

Analyses were performed using IBM SPSS Statistics, Version 25. Survivor offspring group differences were tested nonparametrically (two-sided Chi-squared and Mann-Whitney U-tests for unpaired samples) with a 5% significance level. Bivariate analyses used McNemar and Wilcoxon signed-rank tests for paired nonparametric samples with a <5% significance level to detect group differences. Calculated effect sizes included unadjusted OR with 95% CI and Cohen's *d* effect size (thresholds: 0.2 = small, 0.5 = medium, 0.8 = large).<sup>17</sup> Binary logistic regression estimated adjusted ORs with 95% CI in multivariate analyses considering potential confounders (Table S1). To allow comparability with data from the general population, we categorized survivor offspring data according to categorization used within the KiGGS study data. Additional variables

included the following: parental-reported anxiety regarding a perceived possibility of cancer development in offspring (grouped: <20 mm = *none/low*, 20 mm–<60 mm = *medium*, >60 mm = *high/very high*); parental age at cancer diagnosis (grouped: 0–4, 5–9 and ≥10 years of age); time since diagnosis (grouped: 10–19, 20–29 and ≥30 years); and type of cancer (grouped: leukemia/lymphoma, brain tumors and extracranial tumors).

## 4 | RESULTS

### 4.1 | Survivor offspring characteristics

Gender distribution of assessed survivor offspring was well balanced (47.3% girls). The majority of children were under 11 years old (88.2%, range: 3–17 years). Survivor parents were more likely to subjectively assess their child's general health as *very good* or *good* than parents from the general population (96.8% vs. 91.3%,  $p < 0.001$ ). Survivor offspring lived with both parents significantly more often than offspring from the general population (83.6% vs. 66.0%,  $p < 0.001$ ) (Table 1).

### 4.2 | 3–6-year-olds

Survivor parents of 3–6-year-olds reported significantly ( $p < 0.001$ ) higher *physical* (86.3% vs. 81.8%, Cohen's  $d = 0.3$ ), *psychological* (86.7% vs. 83.0%, Cohen's  $d = 0.3$ ) and *self-esteem* (79.1% vs. 73.3%, Cohen's  $d = 0.5$ ) scores compared to parents from the general population (Table 2). When analyzing categories separately for boys and girls, significantly higher scores were also reported for *family* for survivor daughters compared to KiGGS daughters ( $p = 0.014$ , 82.6% vs. 80.9%, Cohen's  $d = 0.15$ ; Table 2). Survivor parents of 3–6-year-olds rated the well-being of their children highest in all categories compared to survivor children aged seven or older (Figure 1). However, in multivariate analyses, younger age (3–6 years) was only statistically significant for *psychological* well-being and *self-esteem* (Table S1).

### 4.3 | 7–17-year-olds

Average HRQL scores for all categories did not differ significantly between 7- and 17-year-olds in either cohort (Table 2). Yet, differences were evident within gender-specific groups. Survivor parents of 14–17-year-old girls reported significantly higher scores for *physical* ( $p = 0.48$ ; 77.9% vs. 65.8%, Cohen's  $d = 0.7$ ) and total well-being ( $p = 0.35$ ; 76.7% vs. 70.5%; Cohen's  $d = 0.6$ ). Significantly higher *school-specific* well-being scores were reported for 11–13-year-old survivor daughters and 14–17-year-old survivor sons than for daughters ( $p = 0.028$ , 81.5% vs. 76.6%, Cohen's  $d = 0.3$ ) and sons ( $p = 0.027$ , 73.1% vs. 64.5%, Cohen's  $d = 0.6$ ) from the respective age groups within the general population (Table 2). The average total

HRQL scores decreased with age in both cohorts. This drop was less pronounced for survivor offspring (2.4 vs. 6.1-point drop, Table 2). The biggest difference between age groups (7–10- vs. 14–17-year-olds) was found for *school-specific* well-being (6.2-point drop in survivor offspring vs. 18.2-point drop in offspring from the general population, Table 2).

### 4.4 | Confounding factors in survivor offspring

Higher well-being scores were more likely reported by survivors who rated their child's health as *very good* (Table S1). Younger age (3–6 years) was associated with higher scores for *psychological* well-being ( $p = 0.011$ ; OR = 2.034, 95% CI = 1.176–3.518) and *self-esteem* ( $p < 0.001$ ; OR = 2.836, 95% CI = 1.710–4.703). Recent, child-reported pain led to lower scores for *physical* ( $p < 0.006$ ; OR = 0.476, 95% CI = 0.278–0.812), *psychological* ( $p = 0.021$ ; OR = 0.529, 95% CI = 0.308–0.909) and *family related well-being* ( $p = 0.018$ ; OR = 0.595, 95% CI = 0.387–0.913). Separate household upbringing was associated with lower scores for the category *friends* ( $p = 0.048$ ; OR = 0.535; 95% CI = 0.288–0.995). Parents who stated high anxiety that their offspring might develop cancer reported higher *family related well-being* ( $p = 0.030$ ; OR = 1.759; 95% CI = 1.055–2.93). Survivor mothers were more likely to report lower *physical* well-being for their children. Recently diagnosed survivors more often reported lower *psychological* well-being for their children ( $p = 0.28$ ; OR = 0.457; 95% CI = 0.228–0.918). Parental age at time of diagnosis showed no associations with well-being scores. Parents who had survived a brain tumor reported higher scores for *school* ( $p = 0.11$ , OR = 9.465; 95%-CI = 1.687–53.109), while extra-cranial tumors reported higher *physical* well-being ( $p = 0.12$ ; OR = 2.087; 95% CI = 1.177–3.703; Table S1).

## 5 | DISCUSSION

This novel analysis compares the HRQL of survivor offspring and the general population in Germany. Currently, there is limited data regarding health-related issues of survivor offspring. However, extensive research exists comparing the HRQL of childhood cancer survivors to their parents, siblings and peers. Parental HRQL is known to influence a child's HRQL.<sup>10</sup> Overall, offspring HRQL was rated comparable or higher by survivor parents than their peers. This is similar to HRQL studies of childhood cancer survivors which revealed comparable to higher HRQL scores for survivors.<sup>4</sup> Yet, there have also been reports of reduced HRQL, in particular for survivors who experienced increased anxiety, depression or posttraumatic stress syndrome.<sup>5</sup> In our study, the average total HRQL score decreased with increasing age in both cohorts. This trend has been described previously.<sup>1</sup> However, in survivor offspring, we observed a less pronounced drop in scores. Average family-related well-being scores were more consistent throughout survivor offspring age groups than for peers. Although decreasing HRQL with increasing

TABLE 1 Characteristics of childhood cancer survivor (CCS) and KiGGS offspring cohorts

Characteristics	CCS offspring		KiGGS offspring		p-Value ( $\alpha = 0,05$ )
	MD (n)	n (%)	MD (n)	n (%)	
Total		603 (100.0)		603 (100.0)	
Gender <sup>a</sup>	-		-		1.0
Female		285 (47.3)		285 (47.3)	
Male		318 (52.7)		318 (52.7)	
Age at time of survey <sup>a</sup>	-		-		1.0
3–6-year-olds		362 (60.0)		362 (60.0)	
7–10-year-olds		134 (22.2)		134 (22.2)	
11–13-year-olds		54 (9.0)		54 (9.0)	
14–17-year-olds		53 (8.8)		53 (8.8)	
Educational attainment <sup>a</sup>	-		-		1.0
High		243 (40.3)		243 (40.3)	
Medium		269 (44.6)		269 (44.6)	
Low		91 (15.1)		91 (15.1)	
Migrant background	1	131 (21.8)	5	157 (26.3)	0.061
The child lives with...	4		3		<0.001
... mother and father		501 (83.6)		396 (66.0)	
...the mother <sup>b</sup>		90 (15.0)		193 (32.2)	
...the father <sup>b</sup>		4 (0.7)		1 (0.2)	
Other <sup>c</sup>		4 (0.7)		10 (1.7)	
Health insurance	-		3		0.221
Statutory		515 (85.4)		531 (88.5)	
Private		65 (10.8)		47 (7.8)	
Other		23 (3.8)		22 (3.7)	
Pain during previous three months	7	364 (61.1)	109	276 (55.9)	0.223
Subjective health status	5		3		<0.001
Very good/good		579 (96.8)		548 (91.3)	
Moderate		18 (3.0)		49 (8.2)	
Poor/very poor		1 (0.2)		3 (0.5)	

Note: The bold numbers are relevant, statistically significant results.

Abbreviation: MD, missing data.

<sup>a</sup>Matching variables.

<sup>b</sup>Including single parents/a new partner.

<sup>c</sup>Includes living with the grandparents, foster/adoptive parents or in a home.

age is reported to be more evident in girls,<sup>18</sup> our multivariate analysis did not detect an effect of gender for the different categories among survivor offspring.

## 5.1 | Physical well-being

Childhood cancer patients showed a higher prevalence of physical activity compared to siblings, healthy peers or their parents.<sup>19,20</sup> A

previous study reported that survivor offspring participated in indoor sports at about the same frequency, but less often in outdoor activities than peers.<sup>11</sup> Our cohort of survivor offspring scored comparable to slightly higher *physical well-being* values than peers, in particular, 3–6-year-olds and 14–17-year-old survivor daughters. Survivors of brain tumor, bone tumor, soft tissue sarcoma or neuroblastoma experienced higher levels of physical limitations<sup>21,22</sup>—potentially reducing HRQL.<sup>2,5</sup> We detected no negative effect owing to parental cancer diagnosis/treatment for *physical*

TABLE 2 KINDL-R average scores stratified for age groups and gender (parent-reports)

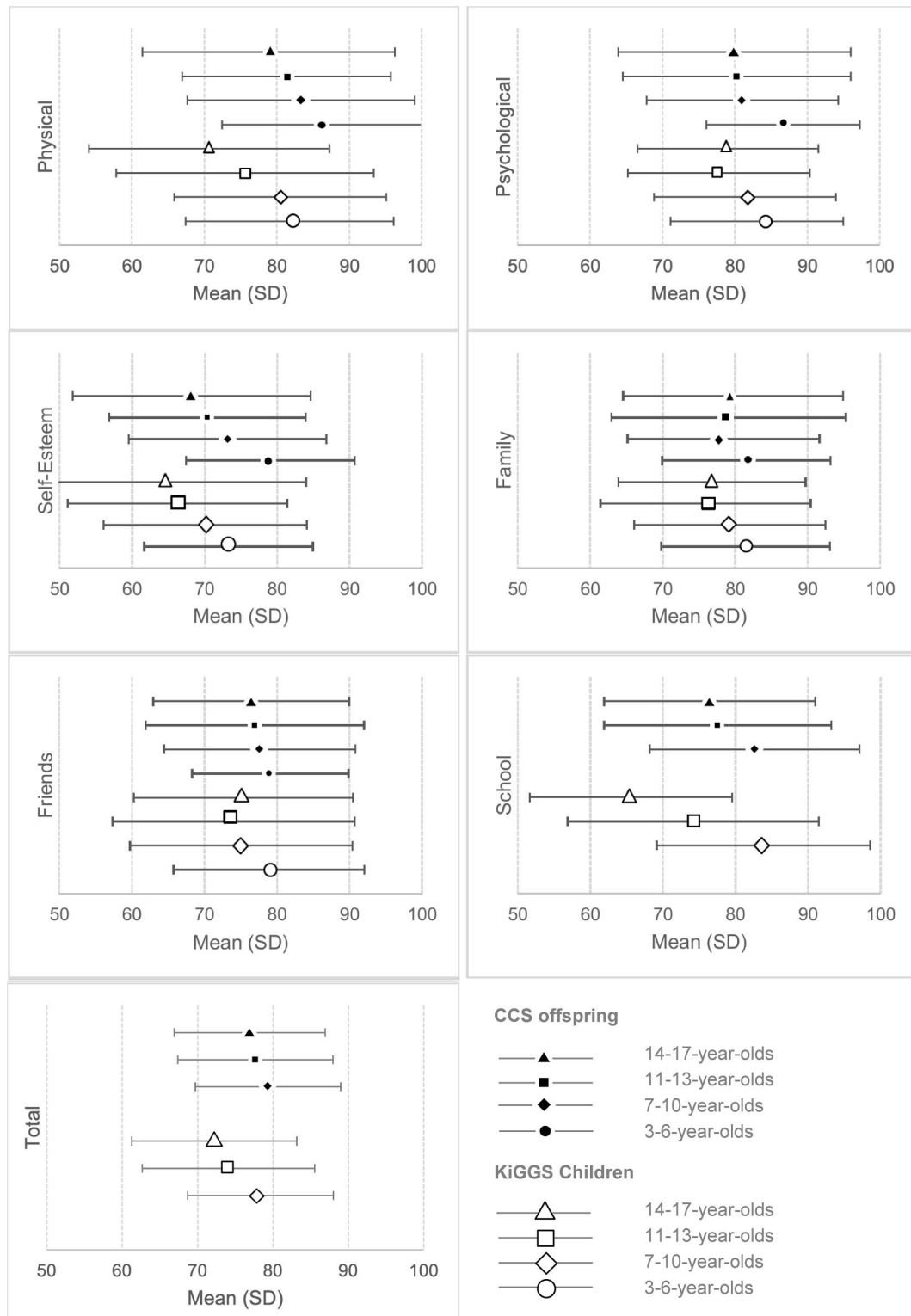
	Physical		Psychological		Self-esteem		Family		Friends		School		Total	
	Mean (SD)	p (Cohen's d)	Mean (SD)	p (Cohen's d)	Mean (SD)	p (Cohen's d)	Mean (SD)	p (Cohen's d)	Mean (SD)	p (Cohen's d)	Mean (SD)	p (Cohen's d)	Mean (SD)	p (Cohen's d)
3-6-year-olds	N = 709 (MD = 15)		N = 708 (MD = 16)		N = 702 (MD = 22)		N = 712 (MD = 12)		N = 701 (MD = 23)		-	-	-	-
Total														
Survivor offspring	86.3 (13.9)	<0.001	86.7 (10.6)	<0.001	79.1 (11.6)	<0.001	81.5 (11.6)	0.148	79.0 (10.8)	0.103	-	-	-	-
KIGGS	81.8 (14.4)	(0.318)	83.0 (11.9)	(0.328)	73.3 (13.2)	(0.467)	81.4 (12.4)	-	78.9 (13.1)	-	-	-	-	-
Girls														
Survivor offspring	85.1 (14.0)	0.010	86.6 (10.4)	<0.001	79.5 (11.2)	<0.001	82.6 (11.1)	0.014	79.6 (11.2)	0.165	-	-	-	-
KIGGS	81.2 (14.4)	(0.275)	82.3 (12.0)	(0.383)	73.1 (14.7)	(0.490)	80.9 (12.3)	(0.145)	79.0 (11.9)	-	-	-	-	-
Boys														
Survivor offspring	87.5 (13.7)	<0.001	86.7 (10.8)	<0.001	78.7 (12.1)	<0.001	80.5 (12.0)	0.811	78.6 (10.4)	0.372	-	-	-	-
KIGGS	82.3 (14.3)	(0.371)	83.7 (11.8)	(0.265)	73.4 (11.6)	(0.447)	81.9 (12.6)	-	78.7 (14.3)	-	-	-	-	-
7-10-year-olds	N = 267 (MD = 1)		N = 267 (MD = 1)		N = 266 (MD = 2)		N = 267 (MD = 1)		N = 264 (MD = 4)		N = 256 (MD = 12)		N = 267 (MD = 1)	
Total														
Survivor offspring	83.3 (16.7)	0.096	81.0 (13.2)	0.864	73.2 (13.6)	0.508	78.4 (13.2)	0.524	77.6 (13.2)	0.813	82.6 (14.4)	0.811	79.3 (9.7)	0.599
KIGGS	80.5 (14.6)	-	81.3 (12.5)	-	70.1 (14.0)	-	79.3 (13.2)	-	75.1 (15.3)	-	83.3 (14.7)	-	78.3 (9.6)	-
Girls														
Survivor offspring	82.6 (15.2)	0.613	80.3 (13.3)	0.564	75.0 (14.6)	0.898	79.1 (11.8)	0.491	79.6 (13.3)	0.423	84.4 (13.6)	0.340	80.1 (9.3)	0.694
KIGGS	79.1 (15.5)	-	81.4 (12.1)	-	70.4 (11.5)	-	78.9 (12.5)	-	74.1 (16.2)	-	80.5 (16.8)	-	77.4 (9.2)	-
Boys														
Survivor offspring	83.8 (16.1)	0.087	81.5 (13.2)	0.799	72.0 (12.9)	0.470	77.9 (13.19)	0.784	76.3 (13.0)	0.770	81.6 (14.9)	0.491	78.8 (9.9)	0.734
KIGGS	81.3 (14.1)	-	81.3 (12.9)	-	69.9 (14.3)	-	79.5 (13.7)	-	75.8 (14.8)	-	85.9 (12.9)	-	79.0 (9.9)	-
11-13-year-olds	N = 106 (MD = 2)		N = 105 (MD = 3)		N = 106 (MD = 2)		N = 105 (MD = 3)		N = 104 (MD = 4)		N = 98 (MD = 10)		N = 103 (MD = 5)	
Total														
Survivor offspring	81.3 (14.4)	0.884	80.2 (15.7)	0.807	70.4 (13.5)	0.554	79.1 (16.2)	0.391	77.0 (15.0)	0.936	77.6 (15.7)	0.666	77.7 (11.4)	0.873
KIGGS	75.6 (17.8)	-	77.8 (12.5)	-	66.3 (15.1)	-	75.9 (14.5)	-	74.0 (16.7)	-	74.2 (17.3)	-	74.1 (10.3)	-
Girls														
Survivor offspring	84.2 (11.8)	0.691	84.3 (12.6)	0.346	72.8 (10.2)	0.377	84.4 (14.6)	0.301	80.7 (12.4)	0.369	81.5 (14.2)	0.028	81.2 (9.3)	0.070
KIGGS	76.3 (15.0)	-	77.2 (13.6)	-	68.9 (15.5)	-	73.6 (14.7)	-	72.0 (14.5)	-	76.6 (18.7)	(0.295)	74.8 (9.3)	-

TABLE 2 (Continued)

	Physical		Psychological		Self-esteem		Family		Friends		School		Total	
	Mean (SD)	<i>p</i> (Cohen's <i>d</i> )	Mean (SD)	<i>p</i> (Cohen's <i>d</i> )	Mean (SD)	<i>p</i> (Cohen's <i>d</i> )	Mean (SD)	<i>p</i> (Cohen's <i>d</i> )	Mean (SD)	<i>p</i> (Cohen's <i>d</i> )	Mean (SD)	<i>p</i> (Cohen's <i>d</i> )	Mean (SD)	<i>p</i> (Cohen's <i>d</i> )
Boys														
Survivor offspring	78.8 (16.2)	0.541	76.6 (17.5)	0.341	68.3 (15.9)	0.988	74.6 (16.3)	0.070	73.6 (16.6)	0.330	74.0 (16.4)	0.155	74.5 (12.4)	0.233
KIGGS	74.9 (20.4)	-	78.4 (11.6)	-	68.9 (15.5)	-	79.3 (13.1)	-	75.9 (18.6)	-	71.5 (15.5)	-	73.4 (11.4)	-
14–17-year-olds	<i>N</i> = 102 (MD = 4)		<i>N</i> = 103 (MD = 3)		<i>N</i> = 103 (MD = 3)		<i>N</i> = 102 (MD = 4)		<i>N</i> = 102 (MD = 4)		<i>N</i> = 97 (MD = 9)		<i>N</i> = 101 (MD = 5)	
Total														
Survivor offspring	78.8 (17.4)	0.073	79.9 (16.1)	0.105	68.2 (16.4)	0.112	79.7 (15.2)	0.783	76.4 (13.5)	0.237	76.4 (14.6)	0.080	76.9 (10.9)	0.066
KIGGS	70.7 (16.6)	-	79.0 (12.5)	-	64.8 (19.2)	-	76.8 (12.9)	-	75.4 (15.1)	-	65.6 (14.0)	-	72.2 (10.1)	-
Girls														
Survivor offspring	77.9 (15.5)	<b>0.048</b>	80.6 (16.0)	0.263	67.4 (15.1)	0.050	78.4 (13.7)	0.830	76.8 (11.4)	0.055	79.0 (13.1)	0.840	76.7 (9.8)	<b>0.035</b>
KIGGS	65.8 (17.0)	(0.744)	77.5 (14.3)	-	61.2 (17.7)	-	77.6 (13.0)	-	74.3 (13.0)	-	66.5 (15.2)	-	70.5 (10.7)	0.604
Boys														
Survivor offspring	79.9 (19.7)	0.509	79.2 (16.5)	0.300	69.2 (18.0)	0.720	81.3 (16.9)	0.767	76.0 (15.8)	0.952	73.1 (16.0)	<b>0.027</b>	77.2 (12.4)	0.587
KIGGS	76.0 (14.8)	-	80.7 (10.1)	-	68.9 (20.5)	-	75.8 (12.9)	-	76.6 (17.4)	-	64.5 (12.6)	(0.597)	74.1 (8.9)	-

Notes: Due to non-significant results, no effect sizes are calculated. The bold numbers are relevant, statistically significant results.

Abbreviations: MD, missing data; SD, standard deviation.



**FIGURE 1** Average scores of parentally assessed health-related quality of life (HRQL) in childhood cancer survivor (CCS) offspring compared to children from the German general population (KiGGS children), measured by the *KINDL-R* instrument (100 indicating the highest HRQL). Presented by *KINDL* dimensions and for age groups. SD, standard deviation

HRQL in survivor offspring. In fact, we observed an association with higher *physical* well-being scores for offspring born to survivors of extracranial tumors. In accordance with previous studies,<sup>1</sup>

our cohort reported lower *physical* well-being scores if the child had experienced pain (past 3 months), or when mothers had assessed their HRQL.



## 5.2 | Psychological well-being and self-esteem

Childhood cancer patients may experience psychosocial well-being impairment during and following cancer treatment.<sup>8,23</sup> As adolescence is an especially vulnerable developmental phase, it is not surprising that survivors of cancer during adolescence reported reduced HRQL, a reduction of self-esteem and increased anxiety.<sup>2</sup> Mental health issues and increased risk for psychiatric symptoms occur in a relevant proportion of survivors.<sup>24,25</sup> Adult survivors were more likely to be symptomatic and to experience impaired HRQL.<sup>26</sup> While previous studies showed that children whose parents (have) suffer (ed) from adult cancer showed significantly increased rates of anxiety than peers,<sup>27</sup> in our cohort of survivor offspring *psychological* and *self-esteem* scores were comparable to slightly higher than those of their peers, especially in younger children (3–6-year-olds). In our study, recently diagnosed parents were more likely to report lower *psychological* well-being for their child. This is in line with previous reports of survivors experiencing decreased psychiatric symptoms with increasing age as a possible sign of *posttraumatic growth*.<sup>24</sup> In contrast, there are also reports that increased time since diagnose is associated with diminished overall HRQL, possibly explained by occurrence of sequelae.<sup>7</sup>

## 5.3 | Family

Childhood cancer challenges families and can disrupt family structures.<sup>28</sup> Studies showed lower levels of posttraumatic stress symptoms in patients whose families functioned well.<sup>29</sup> Generally, the wish to have biological children is widespread among childhood cancer survivors and its fulfillment is linked to a higher quality of life.<sup>30</sup> Establishing a family potentially stabilizes and further integrates survivors into society. Survivors entered marriage and parenthood less often and tended to be older than the general population.<sup>30–32</sup> In our cohort, the majority of survivor offspring were reported to live with both parents and at a significantly higher rate than offspring from the general population. While overall average scores for *family* did not differ and were found to be consistent throughout age groups in both cohorts, significantly higher levels were reported for survivor daughters than daughters from the general population. Similar to reports from the *KiGGS study*,<sup>1</sup> survivors whose child had recently experienced pain assessed their offspring with lower *family* scores. Survivor parents who reported high anxiety regarding a perceived possibility of cancer development in offspring were more likely to report high well-being for *family*.

## 5.4 | Friends/relationships

The average scores for *friends* did not differ between our cohorts. This is in contrast to reports among childhood cancer survivors who were described as having reduced social relationships<sup>33</sup> and peer relationship difficulties.<sup>34</sup> Survivors are reported to achieve fewer

milestones of autonomy, or later social and psychosexual development, than peers.<sup>35,36</sup> This was especially true for brain tumor survivors and those who received radiotherapy.<sup>37</sup> We found that parental cancer diagnosis and treatment had no influence on *friends* well-being scores. When survivor offspring were raised in separate households, lower scores were reported. This corresponds to reports for the general population.<sup>38</sup>

## 5.5 | School

Offspring born to survivors and from the general population were reported to have comparable *school*-specific well-being. Yet, among the general population, scores for *school* dropped to a much larger extent with increasing age. Significantly higher *school*-specific scores were reported for 11–13-year-old survivor daughters and 14–17-year-old sons than for peers. Survivors are reported to have had more difficulties in school, having had to repeat a grade or to have attended special education programs more often than siblings or peers.<sup>31,32</sup> Nevertheless, survivors achieved comparable to higher educational levels with better employment rates, although they are usually older than peers when first employed.<sup>31,39</sup> Brain tumor survivors, though, were less likely to obtain higher educational degrees than other cancer survivors.<sup>32,39</sup> We could not detect a negative effect of parental cancer diagnosis or treatment on *school*-specific well-being for survivor offspring. Nonetheless, survivors of a brain tumor reported higher *school*-specific well-being in their offspring.

## 5.6 | Limitations

This study posed certain limitations. In Germany, a register containing information on survivor offspring does not exist. To reduce the study burden for survivors, recruitment was based on a previous survey identifying survivors with biological children. Selection bias cannot be ruled out. Although non-responder analyses showed no differences between parental cancer diagnoses or age at diagnosis, it confirmed that persons of female gender, younger age and those with a higher level of education were more likely to participate. However, we did not have information on the current parental health status and/or information regarding secondary cancer or relapse history; both potentially played a salient role regarding the child's current health and well-being. Offspring HRQL was parentally assessed using the *KINDL* instrument. Comparisons of self-assessment and parental assessment using the *KINDL* instrument showed that parents tend to overestimate *physical*, *self-esteem* and *school* well-being—resulting in higher overall well-being scores for their children—and tend to underestimate a child's *psychological* and *family* HRQL.<sup>15</sup> However, while parental reports were slightly more reliable, neither the parent nor child questionnaire was shown to be superior regarding measurement validity.<sup>40</sup> Due to a large proportion of younger children in our offspring cohort, no valid self-assessment was possible for all age groups. Parental assessment,



therefore, allowed inter-age group comparability. Corresponding data were available from the general population for matched-pair analysis, allowing comparability between cohorts. Possible cohort effects due to the time interval between the Offspring study and the KiGGS study cannot be ruled out. Nevertheless, the KiGGS study provided the best overall basis for comparisons with our study collective. In order to simplify study participation, one questionnaire version was used to survey different aspects of survivor offspring health, including HRQL. Accordingly, the school category was omitted for the 3–6-year-olds. Overall, the exploratory nature of this study, which does not allow for confirmatory conclusions, must be considered when interpreting the data.

## 5.7 | Clinical implications

Late effects occur in a relevant proportion of childhood cancer survivors. Besides medical reasons, concerns regarding potential health impairment in their offspring was previously reported as a reason for survivors for not fulfilling an existing desire for biological children.<sup>30,36</sup> Our study findings are reassuring, as we can report that survivor offspring have peer comparable to higher HRQL. We could not detect a negative influence of the previous cancer diagnose or treatment on HRQL in survivor offspring. These study results can make a valuable contribution to supporting patient/survivor counseling and reassure prospective parents who have a history of cancer.

## 6 | CONCLUSIONS

Survivors assessed their offspring's HRQL comparably or higher than peers. Type of parental cancer diagnosis and treatment appeared to have no negative effect on offspring HRQL. In light of the anxiety that survivors express regarding potential health issues in their children, these findings are reassuring and correspond with self-reported survivor HRQL.

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### CONFLICT OF INTEREST

The authors declare no conflict of interest.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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