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Attention-deficit/hyperactivity disorder in pediatric cancer survivors: risk and medication use in a nationwide population-based study

Jae Sik Kim^{1†}, Jung Lee^{2,3†} and Joo Ho Lee^{4,5,6*} 

Abstract

Background Pediatric cancer survivors experience attention or behavioral deficits. This study assessed the risk and medication use of attention-deficit/hyperactivity disorder (ADHD) in pediatric cancer survivors compared with the general population.

Methods Using nationwide cohort data from Korea's National Health Insurance Service, we studied a pediatric cancer population (brain tumors [$n = 3,517$], acute lymphoblastic leukemia [ALL, $n = 2,093$], and other tumors [$n = 30,639$]) diagnosed between 2004 and 2011 and 125,663 healthy children. We analyzed the incidence of ADHD, medication patterns, and factors affecting ADHD using the Cox proportional hazards model and logistic regression analysis.

Results Patients with brain tumors had the highest 10-year ADHD incidence (4.0%, 95% confidence interval [CI] 3.3–4.6) compared with healthy children (2.0%, 95% CI 1.9–2.1), patients with ALL (2.9%, 95% CI 2.2–3.7), and patients with other tumors (2.6%, 95% CI 2.4–2.8). Brain tumor survivors had the highest ADHD risk (hazard ratio [HR] 1.85, 95% CI 1.57–2.17, $p < 0.001$). Chemotherapy was associated with increased ADHD in children diagnosed at ages 0–3 years (HR 2.89, 95% CI 1.14–7.38, $p = 0.03$), whereas radiotherapy increased ADHD in patients with ALL (HR 4.10, 95% CI 1.63–10.28, $p = 0.003$). The use of ADHD medications was significantly higher in younger age groups (0–3 years, HR 2.62, 95% CI 1.98–3.45, $p < 0.001$; and 4–12 years, HR 3.44, 95% CI 2.30–4.86, $p < 0.001$) and among brain tumor survivors (HR 1.79, 95% CI 1.32–2.31, $p < 0.001$). Brain tumor survivors required long-term (> 7 months) ADHD medication (odds ratio 2.06, 95% CI 1.20–3.59, $p = 0.01$).

Conclusions Pediatric cancer survivors, particularly those with brain tumors or diagnosed at a young age, face a higher risk of ADHD and increased use of ADHD medications. Chemotherapy significantly increases the risk of ADHD in infants and toddlers, whereas radiotherapy increases this risk in patients with ALL. Ongoing monitoring and tailored interventions for high-risk groups are needed.

[†]Jae Sik Kim and Jung Lee are joint first authors.

*Correspondence:
Joo Ho Lee
jooholee@snu.ac.kr

Full list of author information is available at the end of the article



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Keywords Attention-deficit/hyperactivity disorder, Brain tumor, Pediatric cancer, Population-based study, Survivorship

Background

Among children aged ≤ 14 years, central nervous system neoplasms have continued to be the most prevalent solid tumors [1–3]. Advancements in diagnostic and therapeutic interventions have significantly enhanced the survival rates for all childhood cancers [1, 4]. Consequently, there is a growing need to address the physical and psychological long-term adverse effects experienced by pediatric cancer survivors, as well as their overall quality of life. Because of the characteristics of the tumors, the effects of treatments (e.g., brain radiotherapy or intrathecal chemotherapy), and host-related factors such as age at tumor diagnosis and sex, survivors of pediatric brain tumors and acute lymphoblastic leukemia (ALL) commonly exhibit neurocognitive decline [5–7]. Anticancer drugs that do not penetrate the blood–brain barrier may manipulate the proinflammatory cytokine pathway, indirectly affecting the brain [8].

Cognitive impairments affecting attention and concentration are well documented among brain tumor survivors, often manifesting behavioral symptoms that closely resemble those observed in attention-deficit/hyperactivity disorder (ADHD) [9]. As one of the most common psychiatric conditions in childhood, ADHD is characterized by a persistent pattern of inattention, hyperactivity, and impulsivity [10]. A recent meta-analysis estimated that the global prevalence of ADHD is approximately 8% [11]. Similarly, a prevalence study conducted on a community sample of elementary school students in South Korea reported a rate of approximately 8.5% [12]. ADHD is linked to various aspects of an individual's life, including intelligence, academic achievement, adaptability, and even suicidal behavior [13–16].

According to a single institution retrospective study that examined 528 patients with pediatric brain tumors using hospital-based data, approximately 13.1% of these patients were diagnosed with ADHD [9]. However, few population-based studies have systematically compared the risk of ADHD in pediatric cancer survivors with the general population, limiting broader epidemiological insights. Moreover, most studies have focused solely on patients with pediatric brain tumors or ALL, leaving uncertainty regarding the risk of ADHD across various cancer types [17]. A previous study reported that the risk of major psychiatric disorders, including ADHD, is higher in pediatric cancer survivors than in the general population [18]. However, further research using a large population-based cohort is needed to investigate the interplay between ADHD risk and key clinical factors, including age at diagnosis, treatment history, and actual

use of ADHD medications. A detailed analysis of real-world medication usage and its clinical implications is essential to better understand the risk and management of ADHD in pediatric cancer survivors.

Recognizing this need, this study leverages data from the Korean National Health Insurance Service (NHIS), a comprehensive nationwide database covering nearly the entire Korean population [19, 20]. Korea offers readily available access to psychiatric specialists within primary care clinics, leading to psychiatrists' dominant role in ADHD diagnosis and management [21, 22]. The strict control over methylphenidate prescriptions, a frequently used ADHD medication with limited availability outside strict reimbursement guidelines, suggests that NHIS data provides a reliable reflection of ADHD diagnostic accuracy and real-world medication use. This unique combination makes the NHIS data a valuable resource for investigating the long-term impact of childhood cancer on ADHD risk in a population-based setting.

The present study aimed to analyze the risk and correlation of ADHD in pediatric patients with brain tumors, ALL, and other tumors using comprehensive big data. Moreover, the study examined the medication history of patients, assessing the medication needs and patterns for ADHD among survivors. The correlation between the type of treatment received for pediatric cancers and the subsequent development of ADHD was investigated. Through these analyses, we seek to underscore the critical importance of diligent monitoring and proactive treatment of ADHD among pediatric cancer survivors.

Methods

The participant datasets were obtained from the NHIS-National Health Information Database (NHIS-NHID), which comprises demographic data, mandatory public health insurance contributions, healthcare utilization, and other relevant information for the entire Korean population [20]. A pediatric cancer cohort ($n=50,976$, Fig. 1) was provided by the NHIS, which comprised patients aged ≤ 18 years who were diagnosed with cancers (Korean Standard Classification of Diseases C codes) between 2004 and 2011 and excluded those diagnosed with trisomy 21 and neurofibromatosis. A healthy control group ($n=135,772$) was selected from the entire pediatric population in the baseline year 2011. Three times the number of subjects from the pediatric cancer cohort were randomly matched based on sex and age. Individuals diagnosed with neurofibromatosis and trisomy 21 were also excluded from this group.

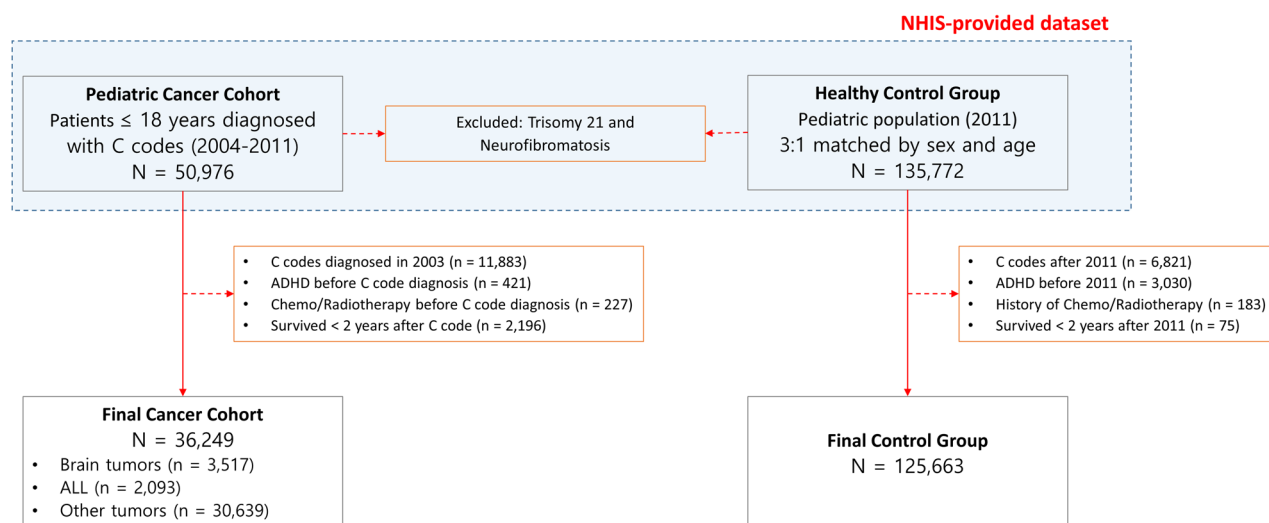


Fig. 1 Study population selection flowchart. *ADHD* attention-deficit/hyperactivity disorder, *ALL* acute lymphoblastic leukemia, *NHIS* National Health Insurance Service

Using the provided dataset, we applied additional inclusion and exclusion criteria. In the pediatric cancer cohort, individuals diagnosed with C codes in 2003 ($n = 11,883$) were excluded to allow for a wash-out period. Patients diagnosed with ADHD before receiving a C code diagnosis ($n = 421$) or those who received chemotherapy or radiotherapy before being diagnosed with a C code ($n = 227$) were excluded. Considering ADHD as a late sequela, the cohort was limited to patients who survived for more than 2 years after being diagnosed with a C code (excluding 2,196 patients). In the control group, children diagnosed with C codes after 2011 ($n = 6,821$), those diagnosed with ADHD before 2011 ($n = 3,030$), or those with a history of chemotherapy or radiotherapy ($n = 183$) were excluded. Survivors who had lived for less than 2 years ($n = 75$) were excluded in the study. Ultimately, the study included 36,249 patients with pediatric cancer (brain tumors, $n = 3,517$; ALL, $n = 2,093$; and other tumors, $n = 30,639$) and 125,663 control subjects. We categorized “other tumors” into the following subgroups for analysis: malignant neoplasms of the lip, oral cavity, and pharynx ($n = 3,541$); malignant neoplasms of the digestive organs ($n = 4,917$); malignant neoplasms of the respiratory and intrathoracic organs ($n = 1,827$); malignant neoplasms of the bone, articular cartilage, skin, breast, mesothelial, and soft tissues ($n = 4,845$); malignant neoplasms of the genital organs and urinary tract ($n = 4,056$); malignant neoplasms of the lymphoid, hematopoietic, and related tissues except for ALL ($n = 4,333$); and unclassified malignant neoplasms ($n = 7,120$) (Additional file 1). The NHIS-NHID data regarding these neoplasms were used from 2003 to 2021.

The follow-up for the healthy control group commenced from a fixed reference point set in the year

2011, whereas that for patients with pediatric cancer began from the date of their cancer diagnosis, and continued until death or the last follow-up date (December 31, 2021), whichever came first. Age was defined based on this index date—calendar year 2011 for controls and the date of cancer diagnosis for cancer patients. Cancer treatment was defined as surgery, chemotherapy, or radiotherapy procedure codes received within 3 months of a C code diagnosis. Because of database limitations for tracking prescriptions using drug codes, only procedural codes for injectable chemotherapeutic agents were used to determine chemotherapy treatment, thereby excluding oral chemotherapeutic agents. ADHD medication treatment was identified through prescriptions for methylphenidate, atomoxetine, or clonidine, which are the only medications approved for the treatment of ADHD in Korea.

The cohorts used in the analysis were extracted from the NHIS-NHID using SAS Enterprise Guide 7.1 (Cary, NC), and all statistical analyses were performed using R version 4.0.3. Descriptive statistics between healthy controls and patients with brain tumors, ALL, and other tumors were compared using Chi-squared tests or analysis of variance, where appropriate. The incidences of ADHD were calculated using the Kaplan–Meier method and compared using the log-rank test. The association between several variables and ADHD incidence was examined using the Cox proportional hazards model. Analyses were conducted using either the entire cohort or the cancer cohort, depending on the specific analysis. We included interaction terms between age and key variables, such as cancer type and treatment, to evaluate whether their associations with ADHD diagnosis varied across age groups. A logistic regression analysis

Table 1 Baseline characteristics of the study cohort

	Healthy control (N=125,663)	Brain tumors (N=3,517)	ALL (N=2,093)	Other tumors (N=30,639)	p-value
Follow-up duration (year) ^a	11.0 (11.0–11.0)	14.7 (12.3–16.4)	14.9 (12.0–16.3)	15.1 (13.0–16.6)	< 0.001
Survival duration					
< 5 years	53 (0.04)	121 (3.4)	103 (4.9)	479 (1.6)	< 0.001
< 10 years	177 (0.1)	212 (6.0)	148 (7.1)	721 (2.4)	< 0.001
Sex					< 0.001
Male	70,209 (55.9)	1,957 (55.6)	1,194 (57.0)	16,261 (53.1)	
Female	55,454 (44.1)	1,560 (44.4)	899 (43.0)	14,378 (46.9)	
Age (year)	12 (8–16)	11 (7–15)	7 (4–12)	12 (5–16)	< 0.001
0–3	6,514 (5.2)	363 (10.3)	428 (20.4)	5,710 (18.6)	< 0.001
4–12	58,199 (46.3)	1,698 (48.3)	1,146 (54.8)	10,876 (35.5)	
13–18	60,950 (48.5)	1,456 (41.4)	519 (24.8)	14,053 (45.9)	
Surgery	–	744 (21.2)	865 (41.3)	4,053 (13.2)	< 0.001
Chemotherapy ^b	–	159 (4.5)	1,100 (52.6)	1,722 (5.6)	< 0.001
Radiotherapy	–	73 (2.1)	41 (2.0)	67 (0.2)	< 0.001
ADHD	2,863 (2.3)	167 (4.7)	77 (3.7)	1,016 (3.3)	< 0.001
Age at ADHD	14 (9–18)	13 (9–17)	9 (7–15)	12 (8–17)	< 0.001

Data are presented as N (%) or median (interquartile range)

ADHD attention-deficit/hyperactivity disorder, ALL acute lymphoblastic leukemia

^aIn the case of the healthy control group, the year 2011 was used as a reference. Meanwhile, for patients with pediatric cancer, the date of cancer diagnosis was used

^bLimited to injectable chemotherapy agents

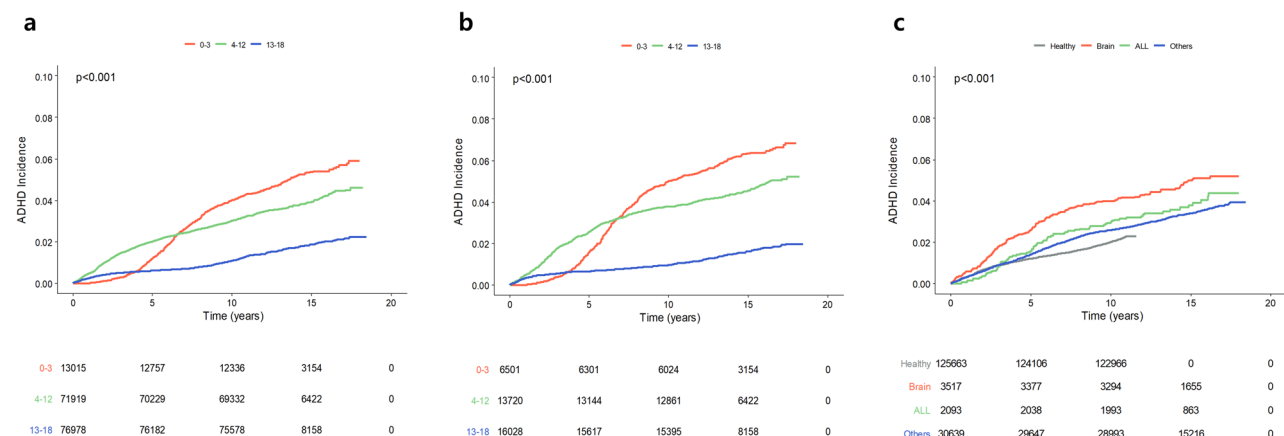


Fig. 2 Incidence of ADHD in the study population. Incidence of ADHD by age **a** the entire cohort and **b** cancer patient cohort. **c** Incidence of ADHD by cancer type in the entire cohort. ADHD attention-deficit/hyperactivity disorder, ALL acute lymphoblastic leukemia

was performed on a subsample of patients who received pharmacological treatment for ADHD ($n=1,633$; 1,186 boys) to evaluate the relationship between cancer type and long-term use of ADHD medications. The multivariate analysis included all variables used in the univariate analysis after confirming the absence of multicollinearity. Statistical significance was considered at a two-sided p -value of less than 0.05.

Results

Demographic and clinical characteristics

Table 1 shows the demographic and clinical characteristics of the study population. The follow-up duration significantly varied between the groups, with the healthy control group having the shortest duration (median,

11.0 years) and patients with other types of tumors having the longest duration (median, 15.1 years, $p<0.001$). This difference was attributable to the methodology used in the study. In terms of cancer treatment, surgery and injectable chemotherapy were frequently performed in pediatric patients with ALL, whereas radiotherapy was least often administered to patients with other types of tumors (all $p<0.001$). The healthy control group had the highest median age of ADHD diagnosis (14 years), indicating earlier presentation in cancer survivors ($p<0.001$).

Age and risk of ADHD

Figure 2a and b show the incidence of ADHD by age in the entire cohort and pediatric cancer survivor groups, respectively. The incidence of ADHD over a 5- to 10-year

period among children aged 0–3 years surpassed that of children aged 4–12 years, which is consistent with previous reports on incidence trends in the general population [23]. In the entire cohort, the 5-year incidence rates of ADHD were 1.2% (95% confidence interval [CI] 1.0–1.4) in the pediatric age group of 0–3 years, 2.0% (1.9–2.1) in the pediatric age group of 4–12 years, and 0.6% (0.5–0.7) in the pediatric age group of 13–18 years. Meanwhile, the 10-year incidence rates of ADHD were 4.0% (95% CI 3.7–4.3) in the pediatric age group of 0–3 years, 3.0% (2.9–3.1) in the pediatric age group of 4–12 years, and 1.1% (1.0–1.2) in the pediatric age group of 13–18 years. When considering only cancer survivors, this age-related pattern of the incidence rate remained consistent as the incidence of ADHD among children aged 0–3 years surpassed that of children aged 4–12 years within 5–10 years (5-year incidence rate, 1.6% [95% CI 1.3–1.9], 2.5% [2.3–2.8], and 0.6% [0.5–0.8] in the pediatric age groups of 0–3, 4–12, and 13–18 years, respectively; 10-year incidence rate, 5.0% [4.5–5.5], 3.8% [3.5–4.1], and 1.0%

[0.8–1.1] in the pediatric age groups of 0–3, 4–12, and 13–18 years, respectively).

Cancer types and risk of ADHD

The 10-year incidence rates of ADHD in the healthy control, brain tumor, ALL, and other tumor groups were 2.0% (95% CI 1.9–2.1), 4.0% (3.3–4.6), 2.9% (2.2–3.7), and 2.6% (2.4–2.8), respectively ($p < 0.001$, Fig. 2c). ADHD was more frequently diagnosed in patients with brain tumors (4.7%), ALL (3.7%), and other tumors (3.3%) compared with the healthy control group (2.3%) ($p < 0.001$) (Table 1, Additional file 1). Compared with healthy children, the hazard ratio (HR) for ADHD in patients with pediatric cancer was 1.30 (95% CI 1.20–1.40, $p < 0.001$) after adjusting for sex, age, birth year, and survival duration. The multivariate analysis in Table 2 revealed that brain tumors presented the highest HR for ADHD compared with healthy controls (HR 1.85, 95% CI 1.57–2.17, $p < 0.001$). However, we did not find a significant association between ALL and ADHD ($p = 0.07$). Head and neck, gastrointestinal tract, genitourinary,

Table 2 Multivariate Cox regression for ADHD risk and use of ADHD medications in the cancer survivor cohort

	ADHD diagnosis		ADHD medication	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Sex				
Male vs. female	1.83 (1.63–2.07)	< 0.001	1.96 (1.60–2.38)	< 0.001
Age				
0–3 vs. 13–18	2.65 (2.25–3.12)	< 0.001	2.62 (1.98–3.45)	< 0.001
4–12 vs. 13–18	3.28 (2.61–4.12)	< 0.001	3.44 (2.30–4.86)	< 0.001
Birth year				
≥ 2000 vs. < 2000	1.16 (0.99–1.37)	0.07	1.42 (1.09–1.86)	0.01
Survival duration				
< 10 years vs. ≥ 10 years	0.28 (0.16–0.51)	< 0.001	0.58 (0.19–1.82)	0.35
Cancer type (vs. healthy, entire cohort)				
Malignant neoplasm of the brain and meninges	1.85 (1.57–2.17)	< 0.001	1.79 (1.32–2.31)	< 0.001
Acute lymphoblastic leukemia	1.24 (0.98–1.56)	0.07	1.17 (0.82–1.68)	0.38
Malignant neoplasms of the lip, oral cavity, and pharynx	1.44 (1.22–1.71)	< 0.001	1.31 (0.99–1.72)	0.06
Malignant neoplasms of digestive organs	1.19 (1.00–1.42)	0.049	1.08 (0.81–1.44)	0.60
Malignant neoplasms of respiratory and intrathoracic organs	0.97 (0.71–1.31)	0.82	0.92 (0.57–1.50)	0.75
Malignant neoplasms of bone, articular cartilage, skin, breast, mesothelial and soft tissue	1.07 (0.89–1.28)	0.48	0.85 (0.62–1.16)	0.29
Malignant neoplasms of genital organs and urinary tract	1.25 (1.05–1.50)	0.01	1.27 (0.96–1.66)	0.09
Malignant neoplasms of lymphoid, hematopoietic, and related tissue ^a	1.34 (1.14–1.57)	< 0.001	1.18 (0.91–1.55)	0.22
Unclassified malignant neoplasms	1.26 (1.10–1.44)	< 0.001	1.06 (0.85–1.33)	0.60
Cancer type (vs. Malignant neoplasm of the brain and meninges)				
Acute lymphoblastic leukemia	0.67 (0.50–0.92)	0.01	0.67 (0.42–1.06)	0.09
Malignant neoplasms of the lip, oral cavity, and pharynx	0.76 (0.61–0.95)	0.01	0.70 (0.49–0.998)	0.049
Malignant neoplasms of digestive organs	0.67 (0.53–0.84)	< 0.001	0.61 (0.42–0.88)	0.01
Malignant neoplasms of respiratory and intrathoracic organs	0.54 (0.38–0.75)	< 0.001	0.52 (0.30–0.89)	0.02
Malignant neoplasms of bone, articular cartilage, skin, breast, mesothelial and soft tissue	0.58 (0.46–0.73)	< 0.001	0.47 (0.32–0.70)	< 0.001
Malignant neoplasms of genital organs and urinary tract	0.67 (0.53–0.84)	< 0.001	0.70 (0.49–0.995)	0.047
Malignant neoplasms of lymphoid, hematopoietic, and related tissue ^a	0.73 (0.58–0.90)	0.004	0.67 (0.47–0.95)	0.03
Unclassified malignant neoplasms	0.66 (0.54–0.81)	< 0.001	0.58 (0.42–0.79)	< 0.001

ADHD attention-deficit/hyperactivity disorder, CI confidence interval, HR hazard ratio

^aExcept for acute lymphoblastic leukemia

lymphohematopoietic (excluding ALL), and other unclassified tumors were linked to a higher risk of developing ADHD. Compared with brain tumors, the risk of ADHD for other cancer types was lower with all HRs being less than 1.

Notably, the impact of the cancer type on ADHD risk varied by age group (Table 3). Compared with adolescents (13–18 years), children diagnosed with cancer

Table 3 Risk of ADHD by age, cancer type, and treatment (reference: 13–18-year-old age group)

	Age 0–3		Age 4–12	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Cancer type ^a				
Malignant neoplasm of the brain and meninges	1.15 (0.67–1.99)	0.62	1.38 (0.94–2.05)	0.11
Acute lymphoblastic leukemia	2.77 (1.06–7.26)	0.04	1.96 (0.77–4.97)	0.16
Malignant neoplasms of the lip, oral cavity, and pharynx	1.04 (0.62–1.73)	0.89	1.24 (0.79–1.95)	0.35
Malignant neoplasms of digestive organs	1.69 (1.08–2.64)	0.02	1.39 (0.92–2.08)	0.12
Malignant neoplasms of respiratory and intrathoracic organs	1.78 (0.79–4.03)	0.17	1.65 (0.81–3.35)	0.17
Malignant neoplasms of bone, articular cartilage, skin, breast, mesothelial and soft tissue	1.26 (0.76–2.10)	0.38	1.28 (0.84–1.97)	0.25
Malignant neoplasms of genital organs and urinary tract	1.90 (1.16–3.12)	0.01	1.49 (0.91–2.45)	0.11
Malignant neoplasms of lymphoid, hematopoietic, and related tissue ^b	2.32 (1.42–3.77)	< 0.001	1.42 (0.90–2.25)	0.14
Unclassified malignant neoplasms	1.50 (1.003–2.25)	0.048	1.52 (1.04–2.22)	0.03
Cancer treatment ^c				
Surgery	1.13 (0.70–1.80)	0.62	1.08 (0.69–1.68)	0.75
Chemotherapy ^d	2.89 (1.14–7.38)	0.03	2.42 (0.96–6.14)	0.06
Radiotherapy	7.93E+05 (0-inf)	0.98	4.45E+05 (0-inf)	0.98

CI confidence interval, HR hazard ratio, inf infinity

^aThe hazard ratios were adjusted for sex, birth year (≥ 2000 vs. < 2000), and survival duration (< 10 years vs. ≥ 10 years)

^bExcept for acute lymphoblastic leukemia

^cThe hazard ratios were adjusted for sex, birth year (≥ 2000 vs. < 2000), survival duration (< 10 years vs. ≥ 10 years), cancer types, and treatment modalities

^dLimited to injectable chemotherapy agents

at the age of 0–3 years had a significantly higher risk of ADHD: ALL (HR 2.77, 95% CI 1.06–7.26, $p = 0.04$), digestive organ malignancies (HR 1.69, 95% CI 1.08–2.64, $p = 0.02$), genital and urinary tract malignancies (HR 1.90, 95% CI 1.16–3.12, $p = 0.01$), and lymphoid and hematopoietic malignancies excluding ALL (HR 2.32, 95% CI 1.42–3.77, $p < 0.001$). By contrast, children diagnosed with these cancer types at the age of 4–12 years did not show a significantly higher risk of ADHD. Meanwhile, children diagnosed with unclassified tumors at the age of 0–3 and 4–12 years had a significantly elevated ADHD risk (HR 1.50, 95% CI 1.003–2.25, $p = 0.048$; HR 1.52, 95% CI 1.04–2.22, $p = 0.03$, respectively).

Treatment types and risk of ADHD

In the entire cancer cohort, radiotherapy marginally increased the risk of ADHD ($p = 0.10$) (Additional file 2). However, in patients with ALL, radiotherapy was significantly associated with an increased risk of ADHD ($p = 0.003$). No significant associations between the treatment type and ADHD risk were observed for other cancer types.

The impact of treatment types on ADHD risk also varied by age group (Table 3). Among cancer treatments, chemotherapy was associated with an increased ADHD risk in children diagnosed at the age of 0–3 years (HR 2.89, 95% CI 1.14–7.38, $p = 0.03$). By contrast, no significant associations were observed between the treatment type and ADHD risk in older children or in the entire cancer cohort.

Use of ADHD medications across cancer types

The proportions of patients diagnosed with ADHD who received medications were 40.3% (1,154 of 2,863 cases), 39.5% (66 of 167 cases), 41.6% (32 of 77 cases), and 37.5% (381 of 1,016 cases) in the healthy control, brain tumor, ALL, and other tumor groups, respectively, indicating no significant variance ($p = 0.46$). However, across the cancer types, the use of ADHD medications was significantly associated with brain tumors among the different tumor types (HR 1.79, 95% CI 1.32–2.31, $p < 0.001$) (Table 2, Additional file 1). Furthermore, the use of ADHD medications was significantly associated with younger age groups (0–3 or 4–12 years).

The median duration of ADHD medication use was significantly longer in the brain tumor (369 days, interquartile range [IQR] 97–758) and ALL (418 days, IQR 112–1,082) groups than in the healthy control group (209 days, IQR 50–665) ($p = 0.002$). Table 4 shows that brain tumor survivors were significantly more likely to require long-term ADHD medications (defined as > 7 months) compared with healthy controls (odds ratio 2.06, 95% CI 1.20–3.59, $p = 0.01$).

Table 4 Multivariate logistic regression for the duration of ADHD medication use (> 7 months)^a

Cancer type (vs. healthy)	OR (95% CI)	p-value
Malignant neoplasm of the brain and meninges	2.06 (1.20–3.59)	0.01
Acute lymphoblastic leukemia	1.56 (0.75–3.39)	0.24
Malignant neoplasms of the lip, oral cavity, and pharynx	1.27 (0.73–2.25)	0.40
Malignant neoplasms of digestive organs	0.88 (0.48–1.59)	0.68
Malignant neoplasms of respiratory and intra-thoracic organs	1.20 (0.45–3.31)	0.71
Malignant neoplasms of bone, articular cartilage, skin, breast, mesothelial and soft tissue	1.18 (0.62–2.25)	0.62
Malignant neoplasms of genital organs and urinary tract	0.67 (0.38–1.18)	0.17
Malignant neoplasms of lymphoid, hematopoietic, and related tissue ^b	1.13 (0.65–1.96)	0.67
Unclassified malignant neoplasms	1.24 (0.78–1.96)	0.37

CI confidence interval, OR odds ratio

^aThe odds ratios were adjusted for sex, age (0–3 years vs. 4–12 years vs. 13–18 years), birth year (≥ 2000 vs. < 2000), and survival duration (< 10 years vs. ≥ 10 years)^bExcept for acute lymphoblastic leukemia

Discussion

We provided nationwide evidence that pediatric cancer survivors face a higher risk of ADHD compared with the general population. Malignant neoplasms of the brain and meninges; lip, oral cavity, and pharynx; digestive organs; genital and urinary tract; lymphoid and hematopoietic tissues (excluding ALL); and unclassified neoplasms were associated with ADHD risk. Although some of our results align with findings from a previous Taiwanese population-based study [18], the larger cohort size in our study enabled us to identify ADHD risk in previously unexamined cancer types. Notably, our study uniquely identified that ALL was not associated with ADHD risk. Moreover, survivors of lip, oral cavity, and pharynx neoplasms had a higher risk of ADHD, whereas no significant association was observed for cancers of the respiratory and intrathoracic organs.

It is worth noting that the 10-year cumulative incidence of ADHD observed in this study (2.0%–4.0%) is lower than the previously reported global and Korean prevalence estimates derived from community-based studies [11, 12]. This discrepancy is largely due to our reliance on NHIS claims data, which reflects only those seeking formal hospital treatment rather than the broader symptomatic population captured in community-based surveys. As shown in previous Korean registry-based research, ADHD incidence in claims data is often recorded at significantly lower rates than in other datasets [22]. However, this implies that our cohort consists of clinically

significant cases where symptoms were severe enough to warrant specialized medical intervention and formal pharmacological management. By focusing on relative risk comparisons between cancer survivors and healthy controls within this consistent dataset, we have identified critical risk factors while accounting for the conservative nature of claims-based incidence.

Among pediatric cancer survivors, brain tumor survivors had the highest incidence of ADHD, highlighting the significant neurocognitive burden associated with this cancer type. Brain tumors often affect regions involved in cognitive and executive function which could explain the higher prevalence of ADHD in this group [24]. Surgical resection, cranial radiation, neuro-penetrating chemotherapy, and associated brain injuries may lead to long-term deficits in attention regulation, impulse control, and working memory, further increasing the susceptibility for ADHD [25]. Although ALL survivors did not show a significant association with ADHD risk, radiotherapy in patients with ALL significantly increased the incidence of ADHD. The significant association could be explained by the fact that, in most cases of ALL, radiotherapy is administered as cranial radiotherapy for central nervous system involvement or irradiation to the total body, including the brain [26]. Brain damage from radiation exposure, rather than ALL itself, may play a key role in ADHD development. By contrast, patients with ALL who did not receive radiotherapy may have had a lower risk because of the absence of direct neurotoxic effects on the brain.

Although oral chemotherapy is a major component of pediatric ALL therapy, we excluded it from our treatment exposure analyses due to limitations of the NHIS–NHID database. Reliable identification of oral chemotherapeutic agents across the study period (2004–2011) proved challenging given changes in drug-specific coding over time, and prescription claims do not necessarily reflect actual intake, adherence, or dose intensity, raising concerns about exposure misclassification. We therefore focused on procedural codes for injectable chemotherapeutic agents, which are more consistently captured in administrative claims. Notably, induction chemotherapy for ALL at major pediatric centers in Korea uniformly includes intravenous agents [27], and most reimbursed first-line regimens mandate concomitant intravenous chemotherapy; thus, substantial misclassification of treated ALL patients as untreated is unlikely. However, our inability to capture long-term oral chemotherapy exposure may have limited assessment of cumulative treatment effects, and treatment-related findings should be interpreted accordingly.

Pediatric cancer survivors, particularly those with brain tumors, were treated with medications significantly longer than healthy controls, indicating a greater ADHD

severity and disease burden. Brain tumor survivors have a significant risk of chronic neurocognitive late effects, leading to global cognitive decline and long-term academic and social challenges [28, 29]. Moreover, brain tumor survivors diagnosed with ADHD have been shown to exhibit poorer cognitive function compared to children with neurodevelopmental ADHD [30]. These difficulties are further exacerbated by the plateauing of core neurocognitive abilities, affecting the quality of life [31, 32]. Methylphenidate has demonstrated effectiveness in managing “secondary ADHD” due to acquired brain injury [33, 34], with studies supporting its long-term benefits in attention regulation, academic performance, and overall well-being [35–37]. Using national registry-based epidemiological data, the present study reinforces the persistent neurocognitive impact in brain tumor survivors and emphasizes the necessity of long-term pharmacological management.

The present study observed an age-related pattern in ADHD incidence, with higher initial rates in the 4–12 year group, followed by a later increase in the 0–3 year group after 5 years in both the entire cohort and the cancer survivor cohort. This finding is unsurprising given that the established median age of ADHD diagnosis is around 6–7 years, with even more severe cases generally identified after age 4 [23]. Nonetheless, this finding underscores the importance of long-term follow-up in childhood cancer survivorship. In the pediatric cancer cohort, the results showing a significantly higher ADHD diagnosis rate in the 0–3 year-old age group at 10 years compared with that at 5 years suggest that the survivors diagnosed and treated for cancer in this age group require close monitoring for ADHD over an extended period, particularly throughout their school years.

As we consider the practical implications of our findings, it's essential to revisit the application of ADHD diagnoses in pediatric cancer survivors, a complex and actively debated issue. Although ADHD is traditionally considered a neurodevelopmental condition, current Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria do not strictly preclude its diagnosis when attentional symptoms arise from a known medical condition [38]. However, the age-of-onset requirement in the DSM criteria leads some providers to hesitate in diagnosing ADHD in adolescent cancer survivors. As a result, our study may underestimate ADHD incidence in older age groups within this population. While the term secondary ADHD has been applied to pediatric cancer survivors, drawing similarities to the functional impairments of survivors of pediatric cancer and neurodevelopmental ADHD, ongoing research suggests that nuanced differences may exist in neuropsychological profiles, treatment response, and side effect sensitivity to stimulant medications [30, 39, 40]. Specifically, secondary ADHD often

represents one facet of the broader spectrum of later cognitive deficits observed in pediatric cancer survivors, encompassing areas beyond attention, such as memory or processing speed [30, 41, 42]. Consequently, addressing the diverse neurocognitive challenges faced by pediatric tumor survivors calls for multiple, targeted intervention approaches tailored to their individual profiles. Future research should prioritize identifying subgroups of patients based on unique neurocognitive and psychosocial characteristics, ultimately linking these profiles to appropriate and personalized interventions.

This study had several limitations. Because of its retrospective nature, this study was inherently subject to potential biases, such as selection and information bias, and limitations in data collection. The exclusive use of claims-based diagnostic and procedure codes restricted the clinical granularity of our analysis, as it lacked detailed information on cancer stage, radiation fields or doses, oral chemotherapy exposure, and standardized neuropsychological assessments. The challenges associated with searching for specific surgical codes led us to verify only the performance of the surgery, rather than detailing the specific names of the surgery. Similarly, the limitations in the available data concerning specific treatment sites restricted our ability to confirm only the administration of radiotherapy. Moreover, the statistical power of our study might have been affected by the relatively low proportion of patients undergoing treatment. In the study by Shabason et al., approximately 81.3% of patients with pediatric brain tumors underwent surgery, 40.0% received radiotherapy, and 36.6% were treated with chemotherapy [9]. By contrast, our study had a markedly lower number of treated patients, which might be attributed to several factors. Only treatments and diagnoses that were covered by insurance claims were included in our analysis. Patients diagnosed or treated outside the insurance system, possibly through nonreimbursed services—particularly advanced radiation modalities used in patients with brain tumors, including intensity-modulated radiotherapy and proton therapy, during the study period—were not captured in the dataset. While the vast majority of ADHD diagnoses and medication prescriptions in Korea are known to be made by psychiatrists [21, 22], we lack detailed information regarding the specific assessment processes used, such as whether objective neuropsychological evaluations were conducted. Moreover, the fact that most non-pharmacological ADHD treatments are non-reimbursed and therefore uncaptured by our data represents a further limitation of this study. Lastly, we could not account for unmeasured confounders such as socioeconomic status, school-based interventions, and cognitive rehabilitation, as these variables are not available in the NHIS database. Future cohort studies incorporating these factors are warranted to identify

key determinants of later cognitive outcomes in pediatric cancer survivors.

Conclusions

This study provides comprehensive nationwide evidence that pediatric cancer survivors face an increased risk of ADHD, with variations based on cancer type, age at diagnosis, and treatment exposure. Among survivors, patients with brain tumors exhibited the highest incidence of ADHD and required the use of ADHD medications for a longer duration, indicating a greater disease burden and severity. Considering the complex interplay between cancer type, treatment modality, and developmental stage, individualized follow-up strategies are needed. Furthermore, these findings highlight the critical need for healthcare providers, especially clinicians, to incorporate vigilant ADHD monitoring and proactive management strategies into the long-term care plans of these patients. Moreover, a comprehensive, multidisciplinary approach is essential to address the multifaceted physical and neurodevelopmental challenges encountered by this vulnerable population.

Abbreviations

ADHD	Attention-deficit/hyperactivity disorder
ALL	Acute lymphoblastic leukemia
CI	Confidence interval
DSM	Diagnostic and Statistical Manual of Mental Disorders
HR	Hazard ratio
inf	Infinity
IQR	Interquartile range
NHID	National Health Information Database
NHIS	National Health Insurance Service
OR	Odds ratio

Supplementary Information

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Additional file 1.

Additional file 2.

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Author contributions

JSK—Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing—original draft; Writing—review and editing. JHL—Formal analysis; Supervision; Writing—review and editing. JHL—Conceptualization; Formal analysis; Resources; Supervision; Writing—review and editing. All authors read and approved the final manuscript.

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Data availability

The authors do not have proprietary rights to the NHIS-NHID data used in this study. Upon the conclusion of the research, the original data were deleted, making data sharing not feasible.

Declarations

Ethics approval and consent to participate

This study was exempted from the approval of the Institutional Review Board of Seoul National University Hospital (No. E-2203-002-1302) because it used the publicly available NHIS-NHID that is not individually identifiable. This study was also approved by the Data Provision Review Committee of the NHIS (NHIS-2022-1-559).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Department of Radiation Oncology, Soonchunhyang University Seoul Hospital, Soonchunhyang University College of Medicine, Seoul, Republic of Korea

²Integrative Care Hub, Children's Hospital, Seoul National University Hospital, Seoul, Republic of Korea

³Department of Child and Adolescent Psychiatry, Children's Hospital, Seoul National University Hospital, Seoul, Republic of Korea

⁴Department of Radiation Oncology, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-Ro, Jongno-Gu, Seoul 03080, Republic of Korea

⁵Cancer Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea

⁶Institute of Radiation Medicine, Medical Research Center, Seoul National University College of Medicine, Seoul, Republic of Korea

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References

1. Park HJ, Moon E-K, Yoon JY, Oh C-M, Jung K-W, Park BK, et al. Incidence and survival of childhood cancer in Korea. *Cancer Res Treat*. 2016;48:869–82.
2. Kang MJ, Jung K-W, Bang SH, Choi SH, Park EH, Yun EH, et al. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2020. *Cancer Res Treat*. 2023;55:385–99.
3. Central Brain Tumor Registry of the United States. Fact sheet for pediatric brain tumors. 2022. Accessed 23 May 2024. <https://cbtrus.org/cbtrus-published-factsheets/>
4. Wells EM, Packer RJ. Pediatric brain tumors. *Continuum (Minneapolis)*. 2015;21:373–96.
5. Robinson KE, Kuttlesch JF, Champion JE, Andreotti CF, Hipp DW, Bettis A, et al. A quantitative meta-analysis of neurocognitive sequelae in survivors of pediatric brain tumors. *Pediatr Blood Cancer*. 2010;55:525–31.
6. Moleski M. Neuropsychological, neuroanatomical, and neurophysiological consequences of CNS chemotherapy for acute lymphoblastic leukemia. *Arch Clin Neuropsychol*. 2000;15:603–30.
7. Beamish J, Drijver J, Partanen M. Cognitive and adaptive functioning outcomes after cancer diagnosis in early childhood: a systematic review. *EJC Paediatr Oncol*. 2025;5:100237.
8. Rönnbäck L, Hansson E. On the potential role of glutamate transport in mental fatigue. *J Neuroinflammation*. 2004;1:22.
9. Shabason EK, Brodsky C, Baran J, Isaac L, Minturn JE, Ginsberg JP, et al. Clinical diagnosis of attention-deficit/hyperactivity disorder in survivors of pediatric brain tumors. *J Neurooncol*. 2019;143:305–12.

10. Furman L. What is attention-deficit hyperactivity disorder (ADHD)? *J Child Neurol*. 2005;20:994–1002.
11. Ayano G, Demelash S, Gizachew Y, Tsegay L, Alati R. The global prevalence of attention deficit hyperactivity disorder in children and adolescents: an umbrella review of meta-analyses. *J Affect Disord*. 2023;339:860–6.
12. Kim MJ, Park I, Lim MH, Paik KC, Cho S, Kwon HJ, et al. Prevalence of Attention-Deficit/Hyperactivity Disorder and its comorbidity among Korean children in a community population. *J Korean Med Sci*. 2017;32:401–6.
13. Frazier TW, Demaree HA, Youngstrom EA. Meta-analysis of intellectual and neuropsychological test performance in attention-deficit/hyperactivity disorder. *Neuropsychology*. 2004;18:543–55.
14. Arnold LE, Hodgkins P, Kahle J, Madhoo M, Kewley G. Long-term outcomes of ADHD: academic achievement and performance. *J Atten Disord*. 2020;24:73–85.
15. Burns E, Martin AJ. ADHD and adaptability: the roles of cognitive, behavioural, and emotional regulation. *Aust J Guid Couns*. 2014;24:227–42.
16. Septier M, Stordeur C, Zhang J, Delorme R, Cortese S. Association between suicidal spectrum behaviors and Attention-Deficit/Hyperactivity Disorder: a systematic review and meta-analysis. *Neurosci Biobehav Rev*. 2019;103:109–18.
17. Butler RW, Mulhern RK. Neurocognitive interventions for children and adolescents surviving cancer. *J Pediatr Psychol*. 2005;30:65–78.
18. Hsu T-W, Liang C-S, Tsai S-J, Bai Y-M, Su T-P, Chen T-J, et al. Risk of major psychiatric disorders among children and adolescents surviving malignancies: a nationwide longitudinal study. *J Clin Oncol*. 2023;41:2054–66.
19. Jeong H-S. Korea's National Health Insurance—lessons from the past three decades. *Health Aff*. 2011;30:136–44.
20. Seong SC, Kim Y-Y, Khang Y-H, Park JH, Kang H-J, Lee H, et al. Data resource profile: the National Health Information Database of the National Health Insurance Service in South Korea. *Int J Epidemiol*. 2016;46:799–800.
21. Song I, Lee MS, Lee E-K, Shin J-Y. Patient and provider characteristics related with prescribing of ADHD medication: nationwide health insurance claims database study in Korea. *Asia-Pac Psychiatry*. 2018;10:e12289.
22. Hong M, Kwack YS, Joung Y-S, Lee SI, Kim B, Sohn SH, et al. Nationwide rate of attention-deficit hyperactivity disorder diagnosis and pharmacotherapy in Korea in 2008–2011. *Asia Pac Psychiatry*. 2014;6:379–85.
23. Visser SN, Danielson ML, Bitsko RH, Holbrook JR, Kogan MD, Ghandour RM, et al. Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United States, 2003–2011. *J Am Acad Child Adolesc Psychiatry*. 2014;53:34–46.e2.
24. Sahrizan NSA, Manan HA, Abdul Hamid H, Abdullah JM, Yahya N. Functional alteration in the brain due to tumour invasion in paediatric patients: a systematic review. *Cancers (Basel)*. 2023;15:2168.
25. Castellino SM, Ullrich NJ, Whelen MJ, Lange BJ. Developing interventions for cancer-related cognitive dysfunction in childhood cancer survivors. *J Natl Cancer Inst*. 2014;106:dju186.
26. Hiniker SM, Agarwal R, Modlin LA, Gray CC, Harris JP, Million L, et al. Survival and neurocognitive outcomes after cranial or craniospinal irradiation plus total-body irradiation before stem cell transplantation in pediatric leukemia patients with central nervous system involvement. *Int J Radiat Oncol Biol Phys*. 2014;89:67–74.
27. Lee NH, Ju HY, Yi ES, Choi YB, Yoo KH, Koo HH. Survival of children with acute lymphoblastic leukemia with risk group–based protocol changes: a single-center experience with 460 patients over a 20-year period. *Cancer Res Treat*. 2025;57:558–69.
28. Stavinocha PL, Askins MA, Powell SK, Pillay Smiley N, Robert RS. Neurocognitive and psychosocial outcomes in pediatric brain tumor survivors. *Bioengineering (Basel)*. 2018;5:73.
29. Willard VW, Berlin KS, Conklin HM, Merchant TE. Trajectories of psychosocial and cognitive functioning in pediatric patients with brain tumors treated with radiation therapy. *Neuro Oncol*. 2019;21:678–85.
30. Hardy KK, Willard VW, Gioia A, Sharkey C, Walsh KS. Attention-mediated neurocognitive profiles in survivors of pediatric brain tumors: comparison to children with neurodevelopmental ADHD. *Neuro Oncol*. 2018;20:705–15.
31. King TZ, Ailion AS, Fox ME, Hufstetler SM. Neurodevelopmental model of long-term outcomes of adult survivors of childhood brain tumors. *Child Neuropsychol*. 2019;25:1–21.
32. Semmel ES, Quadri TR, King TZ. Oral processing speed as a key mechanism in the relationship between neurological risk and adaptive functioning in survivors of pediatric brain tumors. *Pediatr Blood Cancer*. 2020;67:e28575.
33. Hagan AJ, Verity SJ. Translating methylphenidate's efficacy on selective and sustained attentional deficits to those reported in childhood cancer survivors: A qualitative review. *Appl Neuropsychol Child*. 2023;12:74–87.
34. Nicholls E, Hildenbrand AK, Aggarwal R, McCarthy L, Daly B. The use of stimulant medication to treat neurocognitive deficits in patients with pediatric cancer, traumatic brain injury, and sickle cell disease: a review. *Postgrad Med*. 2012;124:78–90.
35. Conklin HM, Reddick WE, Ashford J, Ogg S, Howard SC, Morris EB, et al. Long-term efficacy of methylphenidate in enhancing attention regulation, social skills, and academic abilities of childhood cancer survivors. *J Clin Oncol*. 2010;28:4465–72.
36. Netson KL, Conklin HM, Ashford JM, Kahalley LS, Wu S, Xiong X. Parent and teacher ratings of attention during a year-long methylphenidate trial in children treated for cancer. *J Pediatr Psychol*. 2011;36:438–50.
37. Verity SJ, Halliday G, Hill RM, Ryles J, Bailey S. Methylphenidate improves cognitive function and health-related quality of life in survivors of childhood brain tumours. *Neuropsychol Rehabil*. 2024;34:133–53.
38. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington: American Psychiatric Publishing; 2013.
39. Daly BP, Brown RT. Scholarly literature review: management of neurocognitive late effects with stimulant medication. *J Pediatr Psychol*. 2007;32:1111–26.
40. Conklin HM, Lawford J, Jasper BW, Morris EB, Howard SC, Ogg SW, et al. Side effects of methylphenidate in childhood cancer survivors: a randomized placebo-controlled trial. *Pediatrics*. 2009;124:226–33.
41. Kahalley LS, Conklin HM, Tyc VL, Wilson SJ, Hinds PS, Wu S, et al. ADHD and secondary ADHD criteria fail to identify many at-risk survivors of pediatric ALL and brain tumor. *Pediatr Blood Cancer*. 2011;57:110–8.
42. Krull KR, Khan RB, Ness KK, Ledet D, Zhu L, Pui C-H, et al. Symptoms of attention-deficit/hyperactivity disorder in long-term survivors of childhood leukemia. *Pediatr Blood Cancer*. 2011;57:1191–6.

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