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RESEARCH ARTICLE

Cognitive, Motor, and Quality of Life Outcomes in Childhood ALL Survivors: A Comparative Study of Moscow-Berlin Protocols and Implications for Care

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Abstract

Introduction: To compare cognitive and motor abilities, and quality of life among children treated with the Moscow-Berlin protocols for acute lymphoblastic leukemia (ALL-MB-2008 and ALL-MB-2015). **Materials and Methods:** A total of 188 children aged 7–17 years (112 treated with ALL-MB-2008 and 76 with ALL-MB-2015) were assessed at the Medical Rehabilitation Scientific Center "Russkoye Pole," a branch of the National Medical Research Center of Pediatric Hematology, Oncology and Immunology named after Dmitry Rogachev, Ministry of Health of the Russian Federation. Cognitive and motor functions were evaluated using standardized neuropsychological tests. Quality of life was assessed using the Pediatric Quality of Life Inventory (PedsQL) and the SF-36 Health Survey.**Results:** Intermediate-risk group children treated with ALL-MB-2008 had worse performance in coding ($p<0.05$) and motor dexterity ($p<0.01$). High-dose methotrexate and cranial irradiation were associated with differences in PedsQL scores. Risk-group differences demonstrated small-to-moderate effect sizes, whereas treatment exposure effects were trivial. No significant protocol-based differences were found in cognitive or HRQoL outcomes. **Conclusion:** While protocol changes did not improve overall outcomes, risk- and gender-specific patterns highlight critical targets for survivorship care, particularly motor rehabilitation for intermediate-risk patients and psychosocial support for families of male survivors.

Keywords: Childhood cancer survivors, ALL-MB-2008, ALL-MB-2015, quality of life, cognitive outcomes, motor function

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Introduction

In survivorship care, nursing and supportive care professionals play a central role in the early identification of functional and psychosocial difficulties in childhood cancer survivors. Nurses are often the first members of the multidisciplinary team to observe subtle changes in a child's motor coordination, fatigue, attention, school functioning, and emotional adjustment during routine follow-up visits. In parallel, they frequently interact with caregivers and are therefore well positioned to detect signs of family burden, parental stress, and altered quality of life. From a supportive care perspective, neurocognitive performance, fine motor functioning, and health-related quality of life represent not only clinical outcomes, but also practical indicators of everyday challenges faced by survivors and their families. Understanding how these domains are affected by treatment intensity and risk stratification may support the development of nurse-led screening, timely referral to rehabilitation

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and psychological services, and more individualized, family-centered survivorship care.

While survival rates for childhood acute lymphoblastic leukemia (ALL) have significantly improved, the long-term toxicity of treatment continues to impair survivors' quality of life (QoL), cognitive function, and psychosocial well-being. In survivorship research, the concept of quality of life encompasses several related but distinct domains. Health-related quality of life (HRQoL) refers primarily to perceived physical, emotional, and social functioning associated with health status and is commonly assessed using standardized instruments such as the PedsQL and SF-36. In contrast, broader psychosocial well-being includes life satisfaction, emotional adjustment, family functioning, and social reintegration. Distinguishing these domains is important for interpreting survivorship outcomes and identifying targets for supportive care.

These late effects necessitate a stronger focus on supportive care strategies to mitigate lifelong burdens [1]. Meanwhile, patient survival rates have significantly increased due to substantial advances in childhood cancer treatment [2]. Acute lymphoblastic leukemia (ALL) is considered as one of the most common types of cancer in children [3]: estimate ALL to be diagnosed in approximately half of all cases of childhood malignancies. Fardell and colleagues [4] revealed ALL survivors to demonstrate a lower health-related quality of life as compared to that of peers or siblings; noteworthy, the overall life quality of ALL survivors appeared to be slightly higher than that of the brain tumor survivors. Hence, improving treatment protocols primarily aimed at reducing the toxicity the treatment might cause to improve not only the overall patient survival rate but also the quality of life. Retaining cognitive and motor abilities one of the most important constituents of quality of life [5].

Neurotoxic effects of chemotherapy, such as high-dose methotrexate and cranial irradiation, are well-documented in ALL survivors, leading to deficits in executive function, memory, and motor skills. These impairments often persist into adulthood, affecting educational attainment, employment, and mental health. However, the comparative impact of modern treatment protocols (e.g., Moscow-Berlin 2008 vs. 2015) on QoL remains understudied, particularly in the context of risk stratification [6].

Beyond individual suffering, survivorship after acute lymphoblastic leukemia places substantial psychosocial strain on families. Parents often report elevated stress, financial hardship, and marital difficulties. Siblings may experience emotional neglect and reduced parental attention. These family-level challenges can further affect survivors' quality of life. Together, these findings highlight the need for holistic supportive interventions that address not only the child but the entire family system.

This study compares cognitive, motor, and HRQoL outcomes in ALL survivors treated with the Moscow-Berlin 2008 and 2015 protocols, with two key objectives:

1. To evaluate whether protocol modifications reduce long-term neurotoxicity;

2. To identify risk groups and gender-specific disparities requiring targeted supportive care.

Materials and Methods

Participants and Setting

The analysis included primary ALL patients, aged 7 to 17 years 11 months 29 days who were treated in Russian clinics participating in the Moscow-Berlin study between January 2008 and December 2022. Both protocols include the main chemotherapeutic agents used to treat ALL in children. The differences between ALL-MB-2008 and ALL-MB-2015 are due to a different approach to stratifying patients by risk groups, changes in the regimen and doses of drugs administered, and the criteria used to prevent radiotherapy from damaging the central nervous system. Patients were divided into standard (SRG), intermediate (ImRG) and high-risk groups (HRG) according to clinical criteria. The ALL-MB-2008 protocol includes specific criteria for clinical groups. In the SRG, initial leukocytosis has to be less than 30,000 μL-1, the age of the patient has to be above 1 year old, there has to be no CNS involvement, T-lineage immunophenotype, t (4;11) and/or t (9;22), morphological remission after induction therapy (at day 36 of protocol). In ImRG patients may be younger than 1 year old, achieving morphological remission by day 36 of therapy is contingent upon having at least one of the following: initial leukocytosis exceeding 50,000 μL−1, CNS involvement, T-lineage immunophenotype, mediastinal involvement, and/or splenomegaly exceeding 4 cm. In the HRG group of patients with precursor B lymphoblastic leukemia at diagnosis, it is necessary to have t (4;11), t (9;22), absence of remission on day 36, and leukocytosis of 100,000 μL-1 or higher [7]. The ALL-MB-2015 protocol includes the same cytotoxic agents, but uses the principle of more differentiated stratification of risk groups and therapy [8] .

The sample comprised 188 participants: 112 individuals (59 - boys, 53 - girls) treated in accordance with MB 2008 and 76 individuals (46 - boys, 30 - girls) treated in accordance with ALL-MB 2015. Descriptive statistics of participants' demographic and clinical characteristics, neurocognitive and motor measures, and quality of life questionnaires are presented in Table 1.

Treatment Protocols

Both ALL-MB-2008 and ALL-MB-2015 protocols incorporate standard chemotherapeutic agents, but differ in risk stratification and treatment intensity. The 2008 protocol stratifies patients into standard-risk (SRG), intermediate-risk (ImRG), and high-risk (HRG) groups based on clinical and laboratory parameters. The 2015 protocol refines risk stratification based on immunophenotyping and molecular genetic features.

The ALL-MB-2008 protocol stratified patients into three broad risk groups (standard, intermediate, high) based primarily on clinical and laboratory features at diagnosis (e.g., initial leukocyte count, age, CNS involvement, immunophenotype, and early response). High-dose methotrexate (HD-MTX, typically ≥1–5 g/m² courses) was used selectively in higher-risk subgroups,

and cranial radiotherapy (usually 12–18 Gy) was indicated for CNS involvement or high-risk features. The ALL-MB-2015 protocol introduced more refined, MRD-based risk stratification (expanding to multiple subgroups, including 12 categories in some implementations), with greater emphasis on immunophenotyping and molecular features. This enabled more precise therapy reduction: HD-MTX was largely avoided or minimized in standard- and intermediate-risk groups (none in our 2015 cohort received it), and criteria for omitting cranial radiotherapy were broadened based on better early response/MRD clearance, resulting in lower overall exposure to these neurotoxic modalities.

Neurocognitive and Motor Assessments

Neurocognitive performance was evaluated using the Coding subtest (processing speed), Digit Span (working memory), Controlled Oral Word Association Test (verbal fluency), and the Rey-Osterrieth Complex Figure Test (visuospatial construction). Fine motor performance was measured using the Grooved Pegboard test, assessing motor coordination and speed [9-12].

Quality of Life Assessment

Children's health-related quality of life was assessed using the Pediatric Quality of Life Inventory (PedsQL), including both self-reports and parent proxy-reports. Parents additionally completed the SF-36 Health Survey. In this study, SF-36 scores were interpreted as reflecting parental perceptions of the child's health status and functional limitations, as well as the perceived impact of the child's condition on daily family life, rather than a direct measure of family well-being [13-15].

Timing of Assessments

Cognitive and motor assessments were conducted between 2018 and 2019. Quality of life questionnaires were completed between 2016 and 2023. The mean duration of remission at the time of assessment was 57.9 months for cognitive/motor evaluations and 61.3 months for quality of life surveys.

Statistical Analysis

The Shapiro–Wilk test was applied to assess normality. Depending on data distribution and variance, statistical comparisons were conducted using Fisher's or Welch's one-way ANOVA, Student's t-test, or the Mann–Whitney U test. Analyses examined between-group differences in cognitive, motor, and HRQoL outcomes, stratified by treatment protocol, gender, risk group, and exposure to high-dose MTX or cranial irradiation. Effect sizes (Cohen's d) were calculated for primary between-group comparisons to assess the magnitude of observed differences. No correction for multiple comparisons was applied across cognitive, motor, and QoL domains; therefore, results should be interpreted cautiously due to an increased risk of Type I error.

Missing data in questionnaires and cognitive or motor tests were handled using pairwise deletion, meaning that all available data were used for each analysis.

Results

The analysis showed no significant differences between the groups treated with the 2008 and 2015 protocols in the cognitive and motor tests, as well as quality of life questionnaires. In the ALL-MB-2008

Table 1. Description of the Sample of Participants

Demographic and clinical characteristics	Descriptive Statistics	ALL-MB 2008	ALL-MB 2015
N		112	76
Age	Mean (SD)	10.01 (2.50)	9.64 (2.80)
	Range	6-16	6-17
Sex	Males	59	46
	Females	53	30
Remission (period from the start of therapy) in months		71.9 (19.3)	37.1 (9.7)
High dose methotrexate		22	0
Cranial irradiation		18	6
Intermediate risk group (ImRG)		50	34
Standard risk group (SRG)		58	42
High risk group (HRG)		4	0

Table 2. Differences between Boys and Girls in Cognitive and Fine Motor Tests, and Quality of Life Questionnaires in the ALL MB 2008 Protocol

Test/ Scale	Statistical test	N (boys/ girls)	Mean (SD)/ Median boys	Mean (SD)/ Median girls	U	Z	p-value
PedsQL.child Physical functioning	Mann–Whitney U	58/ 53	79.80 (16.60) / 81.30	70.10 (19.00) 71.90	2284	2.95	0.003**
PedsQL.child Total Scale Score	Mann–Whitney U	58/ 53	76.00 (14.1) / 79.9	70.2 (16.70) 72.80	2146	2.21	0.038*

* p < .05, ** p < .01, *** p < .001

protocol group, significant differences were found in the PedsQLTM Physical Functioning ($p<0.01$) and children version Total Scale Score ($p<0.05$) (boys showed higher scores in both tests)? The Table 2.

In ALL-MB 2015, group differences were found in the scores of boys' and girls' parents on the SF-36 quality of life scales. According to parents, girls are much more physically active than boys, while girls are more likely to experience physical ailments (pain of varying severity). The SF-36 questionnaire, completed by parents, reflects their perception of the child's health status and functional limitations, and the extent to which these challenges affect everyday family routines. In the ALL-MB 2015 protocol group, the parents of girls showed higher scores than the parents of boys. The results are presented in Table 3.

Since in the ALL-MB-2015 protocol group no participants has received high-dose MTX therapy, the analysis was performed in the only cohort of patients from the 2008 protocol between the patients having got high-dose MTX and those who did not. Differences were found in the PedsQLTM life scale ($p<0.05$) between the patients treated with high-dose MTX (n=18, mean=75.83, SD=17.26) and those not treated (n=146, mean=64.86, SD=20.54).

Differences were also revealed between the patients having received cranial irradiation and those who did not in the overall cohort of patients from the both protocols on scales of PedsQLTM Physical functioning ($p<0.05$): patients with without cranial irradiation (n=165, mean=72.54, SD=18.43) and patients with cranial irradiation (n=24, mean=84.38, SD=13.86); PedsQLTM Social functioning ($p<0.05$): patients with without cranial irradiation (n=163, mean=77.58, SD=21.61) and patients with cranial irradiation (n=24, mean=84.38, SD=13.86). In total score of the PedsQLTM ($p<0.05$): patients with without cranial irradiation (n=163, mean=71.34, SD=15.26) and patients with cranial irradiation (n=24, mean=79.24 78.81, SD=13.50).

Comparative statistical analysis of the differences shown in children's groups in neurocognitive outcomes, as well as quality of life was performed only between the Intermediate risk (ImRG) and the Standard risk (SRG) groups due to insufficient numbers of patients in the high-risk group in the overall cohort of the 2008 and 2015 protocols. Significant differences were found in the Coding test ($p<0.05$), where the ImRG group performed worse than the SRG group, and in the Grooved Pegboard test ($p<0.01$), where the ImRG group also showed lower scores. Effect size analysis indicated moderate differences between ImRG and SRG in motor performance (GP: $d = 0.50$) and small-to-moderate differences in processing speed (Coding: $d = 0.37$). In contrast, high-dose MTX and cranial irradiation were associated with trivial effect sizes ($|d| < 0.10$). More detailed results are presented in Table 4. These differences highlight the intermediate-risk group as particularly vulnerable to persistent neurocognitive and motor impairments, even under modern protocols.

Discussion

The aim of this article was to explore the differences in the effects of the ALL-MB-2008 and 2015 protocols on cognitive and motor function, and the quality of life. No significant differences between patients treated according to the ALL-MB-2008 and ALL-MB-2015 protocols were found for cognitive and motor functions. Similarly, no significant differences in quality of life were found between the patients treated according to the ALL-MB-2008 and ALL-MB-2015 protocols, either on quality of Life.

The number of studies confirm that the toxicity of the treatment protocol and drugs used to treat ALL often lead to a reduction in quality of life [16]. This is associated with a decrease in physical activity, bodily pain and somatic complaints [17]. Studies show that administering high doses of methotrexate and cranial irradiation are associated with the most significant cognitive and motor impairments following treatment of ALL [18].

The observed differences in processing speed and fine motor performance are consistent with known neurobiological effects of ALL treatment. High-dose methotrexate and CNS-directed therapies have been associated with alterations in white matter integrity, particularly within frontoparietal networks supporting

Table 3. Differences between Boys and Girls in Quality of Life Questionnaires in the ALL-MB Protocol 2015

Test/ Scale	Statistical test	N (boys/ girls)	Mean (SD)/ Median boys	Mean (SD)/ Median girls	U	Z	p-value
SF-36 Physical Functioning	Mann–Whitney U	44/ 29	77.40 (14.60)/ 80.00	86.72 (14.53)/ 95.00	387	-2.99	0.003**
SF-36 Role-Physical	Mann–Whitney U	44/ 29	74.09 (18.31)/ 80.00	82.41 (15.68)/ 90.00	457.5	-2.2	0.027*
SF-36 Bodily Pain	Mann–Whitney U	44/ 29	70.18 (15.73)/ 75.00	80.76 (15.82)/ 85.00	379	-3.02	0.003**

* p < .05, ** p < .01, *** p < .001.

Table 4. Differences between Intermediate Group Risk (ImRG) and Standard Group Risk (SRG) Patients on Cognitive and Fine Motor Tests and Quality of Life Questionnaires in the ALL-MB 2008 and 2015 Protocols.

Test	Statistical test	N (ImRG/ SRG)	ImRG Mean (SD)	SRG Mean (SD)	F	p
Coding	Fisher	83/ 99	43.65 (13.51)	47.56 (12.85)	3.977	0.048*
GP	Fisher	68/ 66	81.66 (25.00)	74.32 (13.63)	4.417	0.037*

* p < .05, ** p < .01, *** p < .001, GP – Grooved Pegboard Tbi

processing speed and executive functioning [8, 19]. Disruption of myelination and connectivity may contribute to slower coding performance in intermediate-risk survivors. Fine motor deficits may additionally reflect cerebellar and corticospinal pathway vulnerability, as cerebellar circuits are critically involved in motor coordination and cognitive efficiency [23]. Thus, the functional findings observed in this study align with established evidence of treatment-related neurotoxicity affecting distributed neural networks.

In our patient cohort, only a small number of children received high-dose methotrexate and cranial irradiation compared to the general patient sample. Patients receiving high-dose methotrexate in the School Life domain of the PedsQLTM had higher scores compared to those not receiving high-dose methotrexate. The finding that survivors exposed to high-dose methotrexate or cranial irradiation reported comparatively higher quality of life scores should be interpreted cautiously within a psychological framework. Rather than reflecting reduced treatment burden, this pattern may indicate adaptive processes such as response shift, in which individuals recalibrate internal standards and expectations following serious illness. In addition, resilience and post-traumatic growth may contribute to more positive subjective evaluations of well-being despite ongoing functional limitations. Survivors who underwent intensive treatment may also experience greater meaning-making and gratitude associated with survival. Thus, higher HRQoL scores in this subgroup likely reflect psychological adaptation rather than the absence of late effects, underscoring the need for longitudinal research incorporating measures of coping and resilience.

Similarly, patients who underwent cranial irradiation showed higher scores in physical functioning and total scale score in the PedsQLTM compared to those who did not receive cranial irradiation. Importantly, HRQoL scores do not fully capture broader psychosocial adaptation. Survivors may report relatively favorable HRQoL despite ongoing functional limitations, reflecting processes of adaptation, recalibration of expectations, and changes in internal standards. Therefore, HRQoL outcomes should be interpreted alongside indicators of psychosocial well-being and family burden rather than as a comprehensive measure of overall life satisfaction.

At the same time, small number of patients and the overall relatively lower toxicity of the ALL-MB-2008 and 2015 protocols may have influenced these results [19]. After undergoing a prolonged and intensive treatment involving remedies and irradiation with toxic effects on the body and nervous system, patients may experience an improvement in their quality of life at the end of therapy [20]. This subjective factor of life valuation might produce impact on test results and quality of life questionnaires. Research on cancer survivors indicates that patients may experience not only distress but also signs of psychological adjustment and well-being, and even post-traumatic growth [21]. Childhood cancer survivors are reported to experience post-traumatic growth after diagnosis and treatment, as reported by Zhang and colleagues, childhood cancer survivors while cancer diagnoses not infrequently may be psychologically traumatic for children, as the experience may induce the increase in psychological maturity and provoke cognitive changes in survivors [22].

Meanwhile, we found significant differences between the high-dose methotrexate groups in life at school, and in the Physical Functioning and Total Score for the cranial irradiation and no the PedsQL TM. The significantly poorer performance of intermediate-risk patients (ImRG) compared to standard-risk patients (SRG) in processing speed (Coding test, $p<0.05$) and fine motor dexterity (Grooved Pegboard test, $p<0.01$) represents a key and highly actionable finding. This subgroup emerges as a primary target for intensified survivorship monitoring and early intervention, including routine nurse-led screening of motor function, timely referral to occupational therapy and neurocognitive rehabilitation, and tailored supportive care pathways.

In addition, significant differences were revealed between the Intermediate risk group (ImRG) and the Standard risk group (SRG) in functional domains. Compared to the ImRG group, patients in the SRG group performed worse on the Coding test and spent more time on the Grooved Pegboard test. Risk factors for the development of neuromuscular dysfunction, which contributes to deterioration of motor skills, are chemotherapy, spinal and cranial irradiation during cancer treatment [23]. Motor nervous system problems persist for a long time in those treated for childhood ALL [24]. Differences in the quality of life between boys and girls were also found in both the ALL-MB-2008 protocol (the PedsQLTM Total Score). In the ALL-MB-2015 protocol, boys performed worse on the COWAT. Observed gender differences in our cohort align with prior evidence in pediatric ALL survivorship, where female survivors often report greater pain prevalence and interference, alongside potential neurocognitive vulnerabilities. These patterns may stem from differential reporting biases and socialization effects (girls/caregivers endorsing somatic complaints more readily due to gender norms), biological factors (e.g., sex-specific methotrexate susceptibility or pain processing), and psychosocial variations (e.g., coping styles). Inconsistent directions across informants and domains underscore the multifactorial nature, warranting further research [25]. However, these findings remain controversial and warrant further comparative investigation across risk groups and treatment protocols.

Modern methods of cancer treatment are reaching their limits, so specialists face the task of integrating children into society. One of the important indicators of integration is the quality of life - to what extent the life of a child and then an adult is filled with opportunities. Therefore, it is important to determine what determines the quality of life of survivors and in what ways it can be improved - which will be the subject of further research.

These findings highlight the need for risk-adapted supportive care, including nursing-led monitoring of motor and cognitive functioning and family-centered psychosocial support during survivorship. Our analyses primarily focused on between-group comparisons. Given

the observational design, future studies could benefit from multivariable regression models to adjust for potential confounding factors such as age at diagnosis or remission duration when assessing the impact of treatment protocol, risk group, or specific treatment exposures.

Limitations

This study has several limitations. The small sample size, particularly for subgroups receiving high-dose methotrexate (n=18) or cranial irradiation (n=24), limits the reliability of subgroup analyses. Several potential confounders, including socioeconomic status, educational support, and family environment, were not controlled, and self-reported QoL measures may be subject to response bias. Cognitive assessments, though standardized, did not cover all domains, and changes in supportive care over time were not analyzed.

Importantly, the large difference in remission duration between treatment protocols (71.9 vs. 37.1 months) is a major potential confounder for cognitive and QoL outcomes. Counterintuitive higher PedsQL scores in some subgroups may reflect chance variation, selection bias, or unmeasured confounders. These limitations highlight the need for future longitudinal studies with larger samples, comprehensive assessments, and analyses adjusting for confounders such as remission duration and treatment exposure.

Clinical implications

• Routine nursing screening of fine motor function in intermediate-risk ALL survivors

• Early referral to motor rehabilitation and occupational therapy

• Attention to gender-specific patterns when discussing QoL with families

• Integration of parent-reported QoL as a marker of family burden

• Psychoeducation for families regarding adaptive coping after intensive treatment

In conclusion, this comparative study of ALL-MB-2008 and 2015 protocols revealed several key findings with important clinical implications. While we found no significant differences in cognitive, motor, or quality of life outcomes between the two protocols overall, our results highlight important risk- and gender-specific patterns that warrant attention.

The study demonstrated that intermediate-risk patients showed poorer performance in coding and motor tasks compared to standard-risk patients, suggesting the need for targeted neuropsychological monitoring and motor rehabilitation in this subgroup. Interestingly, contrary to some previous research, patients receiving high-dose methotrexate and cranial irradiation in our cohort reported better quality of life scores in certain domains, possibly reflecting adaptive psychological mechanisms or the relatively lower toxicity of modern protocols.

Our findings underscore the complex interplay between treatment factors and psychosocial adaptation, with evidence of both challenges and resilience among survivors. The observed gender differences in quality of life and cognitive outcomes point to the need for tailored support strategies in survivorship care programs.

These results emphasize that while protocol modifications between 2008 and 2015 did not produce dramatic differences in outcomes, individualized approaches considering treatment risk groups, specific neurocognitive vulnerabilities, and gender-related factors remain crucial for optimizing long-term outcomes. Future research should further explore the mechanisms of post-treatment adaptation and develop targeted interventions to support survivors' quality of life and functional outcomes.

Declarations

Ethical Approval

The study was approved by the institutional Ethics Committee (Protocol No. 10/2017, dated 12.12.2017). Written informed consent was obtained from legal guardians of all minors under the age of 15, and assent was obtained from children older than 15 years, in accordance with the Declaration of Helsinki.

Data availability

A deidentifed dataset supporting the fndings of this study is available from the corresponding author upon reasonable request.

Competing interests

The authors declare no competing interests.

Author Contributions

Conceptualization: Alena Deviaterikova; Methodology: Elena Glebova, Tatiana Nikitina; Investigation: Alena Deviaterikova, Elena Zhukovskaya; Formal Analysis: Alexander Karelin, Shcheglova Anastasiia, Shapovalova Valeriia; Writing original draft: Alena Deviaterikova; Writing review & editing: Vera Tochennikova, Tatiana Ionova. All authors read and approved the final manuscript.

References

1. Hubbard AK, Spector LG, Fortuna G, Marcotte EL, Poynter JN. Trends in International Incidence of Pediatric Cancers in Children Under 5 Years of Age: 1988–2012. JNCI Cancer Spectrum. 2019 03 01;3(1):pkz007. https://doi.org/10.1093/jncics/pkz007
2. Butler E, Ludwig K, Pacenta HL, Klesse LJ, Watt TC, Laetsch TW. Recent progress in the treatment of cancer in children. CA: A Cancer Journal for Clinicians. 2021 07;71(4):315-332. https://doi.org/10.3322/caac.21665
3. Montes-Rodríguez IM, Soto-Salgado M, Torres-Cintrón CR, Tomassini-Fernandini JC, Suárez E, Clavell LA, Cadilla CL. Incidence and Mortality Rates for Childhood Acute Lymphoblastic Leukemia in Puerto Rican Hispanics, 2012–2016. Cancer Epidemiology, Biomarkers & Prevention. 2023 08 01;32(8):1030-1037. https://doi.org/10.1158/1055-9965.EPI-22-1227
4. Fardell JE, Vetsch J, Trahair T, Mateos MK, Grootenhuis MA, Touyz LM, Marshall GM, Wakefield CE. Health-related quality of life of children on treatment for acute lymphoblastic leukemia: A systematic review. Pediatric

Blood & Cancer. 2017 09;64(9):e26489. https://doi.org/10.1002/pbc.26489
5. World Health Organization .CureAll framework: WHO global initiative for childhood cancer: increasing access, advancing quality, saving lives.2021.
6. Romanova E, Deviaterikova A, Tolchennikova V, Karelin A, Kasatkin V. Short-term sensorimotor training incorporating cognitive tasks for pediatric survivors of posterior fossa tumors: a pilot study. Journal of Neuro-Oncology. 2025 01;171(2):393-402. https://doi.org/10.1007/s11060-024-04858-1
7. Meleshko AN, Savva NN, Fedasenka UU, Romancova AS, Krasko OV, Eckert C, Aleinikova OV. Prognostic value of MRD-dynamics in childhood acute lymphoblastic leukemia treated according to the MB-2002/2008 protocols. Leukemia Research. 2011;35(10):1312-20
8. Van Der Plas E, Modi AJ, Li CK, Krull KR, Cheung YT. Cognitive Impairment in Survivors of Pediatric Acute Lymphoblastic Leukemia Treated With Chemotherapy Only. Journal of Clinical Oncology. 2021 06 01;39(16):1705-1717. https://doi.org/10.1200/JCO.20.02322
9. Baranova LA, Dvoryashina MD. (1976) Intellekt i ego prilozheniya. Psikhologicheskie metody v kompleksnom issledovanii studentov. (In Russian)..
10. Mironets S, Deviaterikova A, Glebova E, Kasatkin V. Phonological Verbal Fluency Test for Russian-Speaking Children. Folia Phoniatrica et Logopaedica. 2023;75(4):235-242. https://doi.org/10.1159/000529686
11. Meyers JE, Meyers KR. Rey complex figure test under four different administration procedures. The Clinical Neuropsychologist. 1995 02;9(1):63-67. https://doi.org/10.1080/13854049508402059
12. Ruff RM, Parker SB. Gender- and Age-Specific Changes in Motor Speed and Eye-Hand Coordination in Adults: Normative Values for the Finger Tapping and Grooved Pegboard Tests. Perceptual and Motor Skills. 1993 06;76(3_suppl):1219-1230. https://doi.org/10.2466/pms.1993.76.3c.1219
13. Nikitina TP. (2005) Razrabotka i otsenka svoistv PedsQL dlya issledovaniya kachestva zhizni detei 8–18 let. Nauchno-issledovatel'skii institut detskoi gematologii. (In Russian).
14. Varni JW, Seid M, Kurtin PS. PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. Medical Care. 2001 08;39(8):800-812. https://doi.org/10.1097/00005650-200108000-00006
15. Sherbourne CD, Hays RD, Mazel R. User's manual for the Medical Outcomes Study (MOS) core measures of health-related quality of life.1995.
16. Müller C. Social and Psychosocial Late Effects. Childhood Cancer Survivors with Chronic Diseases. 2023;37-74. https://doi.org/10.1007/978-3-031-31797-2_4
17. Cho S, Wurz A, Henry B, Tran A, Duong J, Noel M, Neville A, et al. Exploring pain among young people who have completed treatment for acute lymphoblastic leukemia: experiences of youth and caregivers. Supportive Care in Cancer. 2023 07;31(7):415. https://doi.org/10.1007/s00520-023-07888-z
18. Müller C. Reducing Methotrexate-Induced Toxicity. Childhood Cancer Survivors with Chronic Diseases. 2023;:89-97. https://doi.org/10.1007/978-3-031-31797-2_7
19. Alessi I, Caroleo AM, De Palma L, Mastronuzzi A, Pro S, Colafati GS, Boni A, et al. Short and Long-Term Toxicity in Pediatric Cancer Treatment: Central Nervous System Damage. Cancers. 2022 03 17;14(6):1540. https://doi.org/10.3390/cancers14061540
20. Schilstra CE, McCleary K, Fardell JE, Donoghoe MW, McCormack E, Kotecha RS, Trahair TN. Prospective longitudinal evaluation of treatment-related toxicity and health-related quality of life during the first year of treatment for pediatric acute lymphoblastic leukemia. BMC cancer. 2022;22(1):985. https://doi.org/10.1186/s12885-022-09939-1
21. Andrykowski MA, Lykins E, Floyd A. Psychological Health in Cancer Survivors. Seminars in Oncology Nursing. 2008 08;24(3):193-201. https://doi.org/10.1016/j.soncn.2008.05.007
22. Zhang S, Liu C, Wang F, Ni Z. Post-traumatic growth among childhood cancer survivors: A qualitative meta-synthesis. European Journal of Oncology Nursing. 2023 04;63:102289. https://doi.org/10.1016/j.ejon.2023.102289
23. Rodwin RL, Chen Y, Yasui Y, Leisenring WM, Gibson TM, Nathan PC, Howell RM, et al. Longitudinal Evaluation of Neuromuscular Dysfunction in Long-term Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study. Cancer Epidemiology, Biomarkers & Prevention. 2021 08 01;30(8):1536-1545. https://doi.org/10.1158/1055-9965.EPI-21-0154
24. Lehtinen SS, Huuskonen UE, Harila-Saari AH, Tolonen U, Vainionpää LK, Lanning BM. Motor nervous system impairment persists in long-term survivors of childhood acute lymphoblastic leukemia. Cancer. 2002 05;94(9):2466-2473. https://doi.org/10.1002/cncr.10503
25. Usenova A, Akhunbaev S, Tumanbaev A, Lim E. The Relationship between Gene Polymorphisms od the XRCC1 and TP53 with the Gender of Children with Acute Leukemia. Asian Pacific Journal of Cancer Prevention. 2023 02 01;24(2):613-621. https://doi.org/10.31557/APJCP.2023.24.2.613

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