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IMPACT OF CHILDHOOD CANCER ON EDUCATION, PROFESSIONAL AND SOCIAL LIFE OF SURVIVORS IN CROATIA

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SUMMARY

Background: *The aim of this study was to investigate the impact of childhood cancer and its treatment on the education, occupation, and social life of young adults in Croatia. There have been no comparable studies on this particular growing population group in Croatia to date. The study is the starting point for comparing and improving the quality of life of survivors of childhood cancer in Croatia and other countries that follow this population.*

Subjects and methods: *The study was conducted using questionnaires distributed from October to November 2020. A total of 73 individuals were interviewed, including 40 survivors and 33 siblings as a control group. Data were collected on disease characteristics (for cancer survivors), school performance, occupational success, and quality of social life. The X2 test and Mann Whitney U test were used to compare differences between categorical and continuous variables, respectively.*

Results: *The type of childhood malignancy and the type of childhood malignancy treatment affected survivors' academic performance (p=0.140), but performance was not statistically significantly different from that of the control group (p=0.923). No difference was found in total monthly income (p=0.920). In social life, there were no differences in living with parents (p=0.002), married life (p=0.118), and offspring (p=0.196), although there was a tendency to lag behind their siblings.*

Conclusion: *Treatment of childhood malignancy affected academic achievement and occupational success, while in social life there tended to be differences between survivors and controls, so further study is needed.*

Key words: *Childhood cancer survivors, education, professional and social life*

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INTRODUCTION

Childhood cancer is a rare disease and at the same time one of the most frequent causes of death. In Croatia, on average per year (at age 0-19 years old), 167 children were diagnosed with cancer (aged 0-19), and 35 of them died. According to the study published in Lancet CONCORD- 3, the 5-year survival rate for childhood cancer in Croatia is above the European average and is 95% for lymphoma, 85% and 73% for ALL and CNS malignancies, respectively (Croatian Institute for Public Health 2018).

With the advances in treatment protocols, we can observe an increase in survival rates in the last decades. In the 1980s, the survival rate was about 54%, in the 1990s it increased to 75%, and at the beginning of the new century, it reached almost 80% overall for all childhood malignancies. Significant shifts in advances in the diagnosis and treatment of childhood cancer are resulting in a growing population with more or less known long-term consequences for health and overall quality of life (Erdmann et al. 2021). In recent decades, as the number of survivors has grown, a new question has arisen: how to maintain physical, emotional, and mental health during and after treatment for childhood cancer?

Childhood cancer affects the whole family, not just the child. The main focus of doctors is shifting from treating cancer to maintaining the quality of life. The way the family copes with cancer has a significant impact on the child's emotional, mental, and ultimately physical health. These issues have opened many new areas of research. Studies conducted on survivors mostly capture the physical consequences of the disease and treatment of childhood cancer. Newer areas of research are addressing the psychosocial impact of childhood cancer in adulthood, requiring long-term follow-up. Despite conflicting data, the outcome of the research conducted on survivors shows good overall physical and emotional functioning, comparable employability, longer retention in the parental home, lower rates in terms of marital life and parenthood compared to peers (Ernst et al. 2019, Brinkman et al. 2018, Tremolada et al. 2017, Inhestern et al. 2020, Zamora et al. 2017). Until the preparation of this study, no similar reports of survivors in Croatia were found.

This study examines the academic and career development and social life of childhood cancer survivors compared to their brothers and sisters as a control group.

The hypothesis of this study is: diagnosis and treatment of childhood cancer during and after treatment has a negative impact and slows down daily activities in education, professional and social life.

SUBJECTS AND METHODS

Data sources

Study participants were patients treated for childhood cancer ("survivors") who are members of the Firefly Youth (FY) group (N=40), and their siblings (N=33) as controls. More about FY is presented in the discussion. Participants were treated and currently live throughout Croatia. Survivors were treated at the Children's Hospital Zagreb and University Hospital Centre Zagreb. The ethics committee of the School of medicine, University of Zagreb approved this research.

Adults aged 18 to 40 years who had completed treatment for a malignant disease diagnosed in childhood, and their adult siblings (aged 18 to 40 years) were included. Survivors who responded to the author's written invitation (via Facebook message) were invited to participate.

A total of 73 adult respondents, 40 of whom were survivors and 33 of whom were their siblings, affected the study sample. The siblings of the survivors were selected as a control group in order to approach the analysis of the impact of the disease and treatment more objectively, and whose respondents assumed common socioeconomic opportunities during adolescence.

The study was conducted using questionnaires distributed in October and November 2020. The collected data was analyzed through the Jamovi software using parametric and nonparametric tests.

Questionnaires

Two questionnaires were created for the research - one for survivors and the other for siblings. The questionnaires were in Google forms. Both questionnaires contained three sections of questions: 1. demographic (for survivors, they included questions about diagnosis, treatment, and disability), 2. educational attainment (for survivors, they included questions about education during treatment and help needed during follow-up), 3. career success (for survivors, they included a question about government benefits), and 4. social life. All questions were mandatory, and one question for survivors was qualitative - designed to describe personal satisfaction with health status.

In total, the questionnaire contained 25 questions for survivors and 11 questions for siblings. The questionnaire was distributed via private Facebook messages to survivors, who were asked to share the second questionnaire with their siblings.

Data analysis

A study conducted on survivors from Croatia comparable to this study was not found. This fact highlights the need for this and further research to answer the question of the long-term impact of the disease and treatment on the quality of life of this population and to provide guidelines for improving the quality of life not only of this population but also of other children and adolescents being treated for chronic and life-threatening diseases. All data collected were tested to validate the hypothesis that childhood cancer diagnosis and treatment complicate and slow down daily activities in education, work, and social life during and after treatment.

RESULTS

Demographic characteristics

The questionnaire was sent to 51 survivors. We received back 44 completed questionnaires, of which 4 were excluded from the analysis because the criteria for participation were not met (treatment in childhood, up to the age of 18 years).

The gender and age distribution of respondents by the group is shown in Table 1. Table 2 shows that of the total 40 survivors, 40.0% were treated for leukemia or lymphoma, 27.5% for other solid tumors, 22.5% for osteosarcoma or Ewing sarcoma, and 10.0% for CNS tumors. Median age and interquartile ranges for age at diagnosis, duration of treatment, and duration of disease remission by site, treatment modality, and disability and relapse were also reported.

The incidence of disability differed significantly between malignancy groups (p=0.098). No statistical significance was found for the recurrence rate (p=0.736). Overall, 20 (50.0%) survivors were classified as disabled and 4 (10.0%) relapsed.

Comparison of academic and professional life

For the academic comparison between survivors and controls, the criteria were the highest level of education (p=0.889), current study (p= 0.825), and employment status (p=0.352). No significant difference was found, although a lower trend in malignancy location and highest education level was observed in the survivor group (p=0.593). The data are presented in Table 3. Detailed representation of survivors' academic success was measured by independence in meeting school obligations and the highest level of education completed, age at diagnosis, and duration of treatment. No statistically significant difference was found, but there was a trend between independence and highest level of education (p=0.134).The data are presented in Table 4. Monthly income is considered as a variable of occupational success and is shown in Figure 1. The data shows that no significant statistical difference was found (p = 0.920). The impact of the disability as a long-term consequence of malignant disease on employment and/or study is presented in Table 5.

Comparison of social life

The social development of the survivors and the control group was assessed by questions on the housing situation, marital status, children, and sports habits. Significant statistical differences between survivors and controls were found for all living arrangements: with parents (p=0.002), alone (p =0.019), and renting (p=0.183). There are also trend toward lower family life between survivors and controls who are married (p=0.118) and have offspring (p=0.196). In leisure activities, survivors and control subjects have similar habits (p=0.862). Detailed data can be found in Table 6. A more detailed overview of housing situations and disabilities with statistically significant differences can be found in Table 7.

Table 1. Gender and age distribution of respondents by group

		Survivors (N=40)	Controls(N=33)	p
Sex	Male	20(50.0%)	14(42.4%)	0.518
	Female	20(50.0%)	19(57.6%)	
Age	18-21 years	10(25.0%)	7(21.2%)	0.853
	22-25 years	14(35.0%)	12(36.4%)	
	26-30 years	7(17.5%)	6(18.2%)	
	30-35 years	9(22.5%)	7(21.2%)	
	36 and more years	0(0.0%)	1(3.0%)	

Table 2. Median and interquartile ranges of age at diagnosis, duration of treatment, and duration of disease remission by location, childhood malignancy treatment modalities, and disability and relapse

	CNS(N=4)	Leukemia and lymphoma (N=16)	Osteosarkoma and Ewing's sarcoma (N=9)	Other solid tumors (N=11)
Age at diagnose (years)	9.5 (IQR6.0-12.8)	13.0 (IQR11.0-14.3)	15.0 (IQR13.0-15.0)	7.0 (IQR3.5-15.5)
Duration of the treatment (months)	48 (IQR30.0-75.0)	12.5 (IQR12.0-18.0)	18 (IQR15.0-24.0)	12 (IQR6.0-21.0)
Durationof the remission (months)	114 (IQR99.0-135.0)	102 (IQR84.0-132.0)	156 (IQR108.0-180.0)	156 (IQR144.0-258.0)
Operation	3(75.0%)	7(43.8%)	9(100.0%)	10(90.9%)
Chemotherapy	3(75.0%)	16(100.0%)	9(100.0%)	8(72.7%)
Radiotherapy	4(100.0%)	10(62.5%)	2(22.2%)	4(36.4%)
Transplantation	0(0.0%)	5(31.3%)	2(22.2%)	0(0.0%)
Disability	3(75.0%)	7(43.8%)	7(77.8%)	3(27.3%)
Relapse	1(25.0%)	1(6.3%)	1(11.1%)	1(9.1%)

CNS= central nervous system

Table 3. Comparison of survivors (overall and by location) with controls in terms of education and occupational attainment

		Survivors (N=40)					Controls (N=33)
		CNS(N=)	Leukemia and lymphoma (N=16)	Osteosarkoma and Ewing's sarcoma (N=9)	Other solid tumors (N=11)	Total in all sites	
Highest level of education p=0.889	Graduate study / master's degree	0 (0.0%)	2 (12.5%)	2 (22.2%)	3 (27.3%)	7 (17.5%)	8 (24.2%)
	Undergraduate study	1 (25.0%)	3 (18.8%)	4 (44.4%)	2 (18.2%)	10 (25.0%)	8 (24.2%)
	Highschool	2 (50.0%)	10 (62.5%)	3 (33.3%)	6 (54.5%)	21 (52.5%)	16(48.5%)
	Primary school	1 (25.0%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	2 (5.0%)	1 (3.0%)
Still in education system p=0.825	Students			22 (55.0%)			19(57.6%)
	Not studying			18 (45.0%)			14(42.4%)
Employed/ studying p=0.352	Yes			35 (87.5%)			21(93.9%)
	No			5 (12.5%)			2 (6.1%)

CNS= central nervous system

Table 4. Academic performance, median, and interquartile range of independence in fulfilling school responsibilities of survivors as a function of age at diagnosis and duration of treatment for malignant disease

Academic success of survivors		Independent performance of school obligations	Help with instructions	Class attendance according to a customized program
Highest level of education	Graduate study/ master's degree	6 (25.0%)	1 (7.7%)	0 (0.0%)
	Undergraduate study	7 (29.2%)	3 (23.1%)	0 (0.0%)
	Highschool	10(41.7%)	9 (69.2%)	2 (66.7%)
	Primary school	1 (4.2%)	0 (0.0%)	1 (33.3%)
Age at diagnose (in years)		13 (IQR6.5-15.0)	13 (IQR11.0-16.0)	7 (IQR5.5-7.0)
Duration of the treatment (in months)		12 (IQR10-18)	16 (IQR12-24)	48 (IQR33-84)

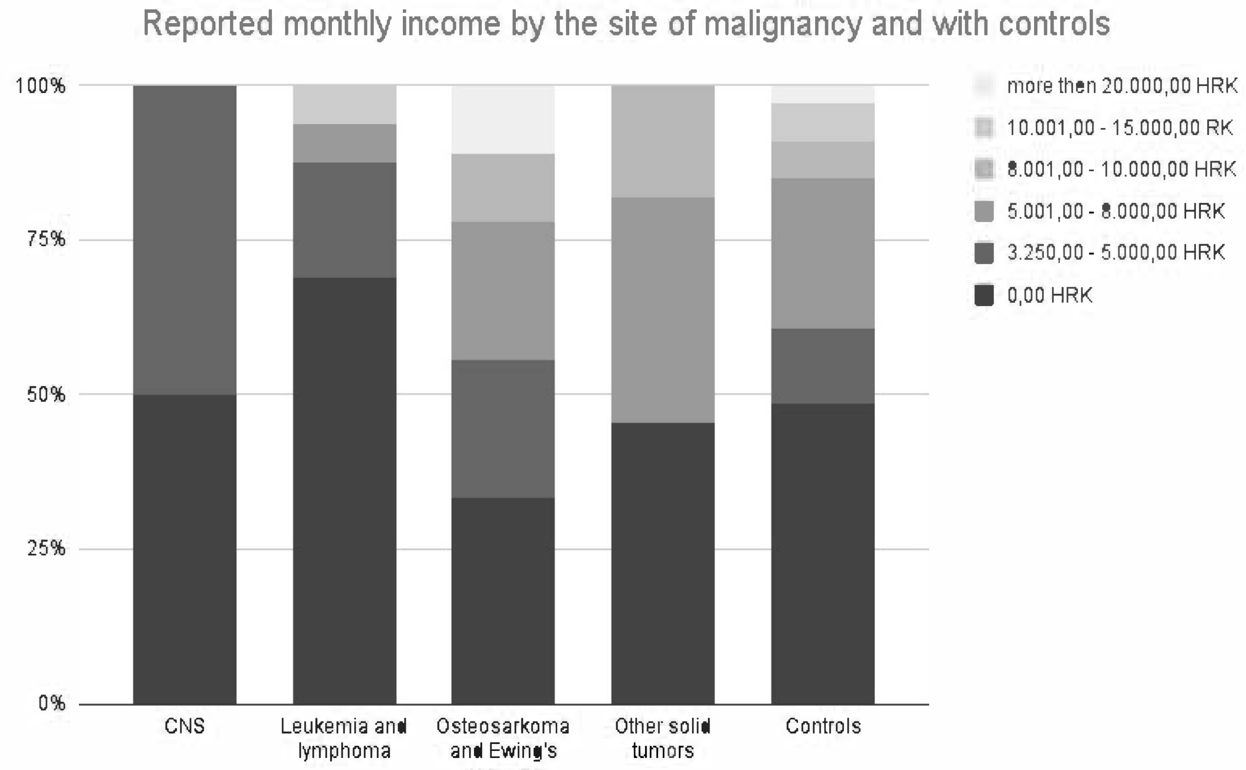

Figure 1.

Reported monthly income by location of malignancy and among controls (p=0920)

Table 5. Survival rate and disability

		Person with disability	Person without disability	p
Site of malignant disease	CNS (N=4)	1 (25.0%)	3 (75.0%)	0.098
	Leukemia and lymphoma (N=16)	7 (43.8%)	9 (56.3%)	
	Osteosarkoma and Ewing's sarcoma (N=9)	7 (77.8%)	2 (22.2%)	
	Other solid tumors (N=11)	3 (27.3%)	8 (72.7%)	
Employed/studying		18 (85.0%)	17 (87.5%)	0.633
Unemployed/not studying		2 (15.0%)	3 (12.5%)	
Highest level of education	Graduate study / master's degree	1 (5.0%)	6 (30.0%)	0.112
	Undergraduate study	5 (25.0%)	5 (25.0%)	
	Highschool	12 (60.0%)	9 (45.0%)	
	Primary school	2 (10.0%)	0 (0.0%)	

CNS= central nervous system

Table 6. Comparison of housing, family life, and physical activity between groups

		Survivors (N=40)	Controls (N=33)	p
Housing	With parents	29(72.5%)	12(36.4%)	0.002
	Independent in own property	7(17.5%)	14(42.4%)	0.019
	Independent on lease	4(10.0%)	7(21.2%)	0.183
Family life	In marriage	7(17.5%)	11(33.3%)	0.118
	Children	6(15.0%)	9 (27.3%)	0.196
Sports	Not active	19(47.5%)	15(45.5%)	0.720
	Recreational. 1-2 times a week	12(30.0%)	8(24.2%)	
	Recreational. minimal 3 times a week	9(22.5%)	10(30.3%)	

Table 7. A review of housing after malignant disease and disability

Housing	Person with disability	CNS (N=4)	Leukemia and lymphoma (N=16)	Osteosarkoma and Ewing's sarcoma (N=9)	Other solid tumors (N=11)
With parents (p=0.063)	Yes	3 (75.0%)	7 (43.7%)	3 (33.3%)	2 (18.2%)
	No	1 (25.0%)	8 (50.0%)	2 (22.2%)	3 (27.3%)
Independent in own property (p=0.312)	Yes	0 (0.0%)	0 (0.0%)	2 (22.2%)	1 (9.1%)
	No	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (36.4%)
Independent on lease(p=0.248)	Yes	0 (0.0%)	0 (0.0%)	2 (22.2%)	0 (0.0%)
	No	0 (0.0%)	1 (6.3%)	0 (0.0%)	1 (9.1%)

CNS= central nervous system

DISCUSSION

Survivors are a growing population that requires long-term monitoring of disease outcomes and treatment. Diagnosis of malignant disease in early childhood carries the risk of cognitive impairment and poorer academic performance due to neurotoxicity of brain tissue, whose development is most active at age 10. Neurotoxicity is most pronounced in individuals treated for CNS tumors diagnosed in early childhood but is also evident in individuals treated for acute lymphoblastic leukemia (ALL) in the form of attention deficits and poor math skills. Survivors of childhood cancer who participated in this study showed no significant differences in academic performance compared to controls, but within the group of survivors, differences were evident according to the location of the malignancy. Other studies show such a result (Molcho et al. 2018, Saatci et al. 2019). In terms of the highest academic achievement, there is a trend toward lower achievement among survivors of CNS tumors, leukemia, and lymphoma.

Numerous studies point to lower overall intelligence compared to individuals treated in later childhood, while others point to impaired development of executive and emotional functions in individuals treated in the teen and adolescent years. The complexity of neurotoxicity resulting from the treatment of childhood malignancies leads to neurocognitive dysfunction and a negative impact on academic development (Gummersall et al. 2020, Barrera et al. 2005, Ghaderi et al. 2016, Koch et al. 2004). Long-term follow-up is particularly emphasized as it is a factor that significantly influences return to society (Miller et al. 2015, Robison et al. 2005).

The group FY is part of Firefly - Association for helping children and families facing malignant diseases. The vision of the Association is a society in which the family of a child with a malignant disease has equal access to all relevant systems during and after treatment that meet the individual needs of the child and family. The Association has been active since 2000. FY (ages 16-29) came together in May 2013 when it responded to a call to help children now in treatment. Soon the group began projects and became active on an international level. Their goal is to make the time of treatment and the time after easier for children and young people facing a malignant disease. This is done through continuous education of the surrounding community about malignant diseases. It is also done through activities carried out by young people who have been treated for malignant diseases in their childhood. They are linked at national, regional, and international levels. (Firefly 2021).

Most of the respondents in this study were attending primary school at the time of treatment. Respondents whose treatment lasted during the elementary school years had the opportunity to attend school during their hospitalization. Unfortunately, this opportunity does not yet exist for high school students due to organizational reasons. Education for high school students depends mainly on the individual approach and efforts of the educational institution itself (student-parent-teacher). Overcoming such challenges is quite possible, as we were shown by the Covid-19 pandemic, as a result of which educational institutions turned to the new technological conditions and offered education to all students. The results of this study show the interdependence of malignancy and academic success through independence in fulfilling school obligations, age, and duration of treatment. For example, a survivor who was treated at age 7 and whose treatment lasted an average of 48 months recorded a high school diploma as the highest level of education completed after a tailored program. It is considered likely that these are CNS tumor survivors.

Assistance with school responsibilities was measured by instructions and a tailored educational program (p=0.275). Twenty-four (60.0%) survivors reported receiving no assistance with school responsibilities, 13 (32.5%) received assistance in the form of instructions, and 3 (7.5%) survivors followed the tailored program. The academic performance of the survivors compared to the control group showed no significant statistical difference (p=0.923). However, lower trend were found within the survivor group according to malignancy (p=0.593). In terms of academic achievement, it is important to note that 22 (55.0%) of the survivors are still in the education system and no significant statistical difference was found compared to 19 (57.6%) of the siblings (p=0.825). Comparing employment and/or school attendance between the groups, no significant statistical difference was found (p=0.352). In a more detailed analysis of academic performance within the group of survivors, assistance in fulfilling school responsibilities was rated with the highest educational level of education, showing a trend towards better performance among survivors who fulfilled their school responsibilities independently. It was observed that survivors who attended an individualized curriculum had a lower age at malignancy diagnosis, 7 (IQR 5.5-7.0) years. Survivors' academic success was also influenced by the duration of treatment, such that a shorter duration of treatment was observed among survivors who met their school obligations independently and vice versa. Studies have shown that they are absent from regular schooling for an average of 40 to 60 days after returning from treatment, and irregular school attendance may persist for up to three years after diagnosis. Compared to younger children, teenagers are at particularly high risk for prolonged absence from school due to hospitalization and home sick, which can be as long as two years (Inhestern et al. 2020, Koch et al. 2004, Pini et al. 2012, Ou et al. 2017). Poorer educational outcomes than the general population are associated with low family socioeconomic status and parental educational attainment. However, post-secondary education of parents and high self-esteem of survivors act as protective factors that can help with coping and increase psychological caring (Barrera et al 2005). Risk factors for academic and career success include female survivors, diagnosis of the disease in early childhood, and cranial radiation therapy associated with severe physical, psychological, and social problems (Maule et al 2017). The answer lies in support, i.e., the relationship between the educational institution, parents, and survivors, which can be crucial for professional and social development, i.e., mental health (Saatci et al. 2019). The measure of career development used in this study is total monthly income. The results showed no significant difference between survivors (with or without disability) and controls. In Croatia, there are measures to promote employment of people with disabilities that have an impact on the employment of survivors with disabilities and showed no difference compared to survivors without disabilities. Overall, in the group of survivors, 15 (38.5%) reported receiving social benefits. There was also no statistically significant difference in total monthly income between survivors with and without disabilities (p=0.751). Nevertheless, a difference in the realization of monthly income according to the location of the malignant disease is observed in the group of survivors (p=0.238), and we can speak of a trend towards a higher monthly income in the group of survivors treated for other solid tumors.Within the survivor group, no difference was found between study and highest educational attainment. Within the group of survivors is observed lower trend (p=0.134) in the ratio of employed/student depending on the age at which the malignant disease was diagnosed, such that lower employment is observed in survivors diagnosed with the malignant disease in adolescence and vice versa. A significant factor associated with education and employment in the labor market was disability, with a statistically significant difference according to malignancy diagnosis of 0.098. Most survivors with disability status were treated for osteosarcomas and Ewing sarcomas (77.8%), and the fewest for CNS tumors (25.0%). The impact of disability on employability/study showed no significant statistical difference (p=0.633). However, the lower trend (p=0.122) is observed at the highest educational level. Other studies show the lower total income between survivors and the general population (Brinkman et al. 2018, Frederiksen et al. 2018).

In terms of social life, this study examined housing situation, marital life, offspring, and sports activities. Housing situation was observed at three levels: Living with parents, living independently in their own home, and living independently in a rented apartment. Compared to control subjects, survivors lagged significantly at all levels. To examine this fact in more detail, the variable disability was used, which showed a significant influence on the housing situation.

A significant statistical difference within the survivor group was analyzed using the impact of diagnosis and disability on housing. As many as 3 (75.0%) survivors who were treated for a CNS tumor and diagnosed with a disability live with their parents. They are followed by 7 (43.7%) survivors treated for leukemia and lymphoma. Not a single CNS, leukemia, and lymphoma survivor lives alone. Only 4 survivors live in a rental apartment/house. Most of them are being treated for osteosarcoma and Ewing's sarcoma and have a confirmed level of disability. Survivors also lag behind their siblings in the areas of married life and offspring, but not in the areas of leisure and sports. Large cohort studies found lower rates of marriage or cohabitation compared to siblings and the general population (Brinkman et al. 2018). Fertility and parenthood are issues that continue to be neglected in the treatment process. Some treatments (radiation therapy) have been shown to impact fertility, but during the time a child or adolescent is being treated, this issue is less important than life itself. Organizational (sperm and egg banks) and cultural factors also influence how this issue is dealt with. In the long term, survivors may suffer from anxiety, insecurities, and hurt romantic relationships (Ernst et al. 2019, Robison et al. 2005). Behind every success (educational and professional) is mental health, which is a consequence of psychosocial development. Malignancy is a burden that brings anxiety, depression, inattention, and antisocial behavior, which can lead to a risk for social isolation and low peer acceptance. Studies show that self-esteem plays an important role in (re)building social relationships, body experience/image, academic performance and work life (Tremolada et al. 2017). Close collaboration between parents, health care providers, and the educational institution can help reintegrate survivors into society, thus alleviating this burden (Inhestern et al. 2020). In terms of social risks, epidemiological studies portray survivors as a group that utilizes more mental health services, which translates into limited or even positive effects on their adjustment (Brinkman et al. 2018). In this context, some researchers have noted post- traumatic stress disorder and even post-traumatic growth. Post-traumatic growth can be defined as spiritual growth and appreciation of life. The experiences of childhood cancer survivors often describe personal strength, appreciation of life, closer relationships with parents, siblings, and partners, and spiritual growth (Zamora et al. 2017). In this study, questions were asked about current health status and treatment outcomes. Half of the survivors described their health status as satisfactory despite the effects and disabilities, which could be a sign of post-traumatic growth.

In this study, the current health status and consequences of the disease and its treatment were reported by the survivors in an open-ended type of responses. As many as 19 (47.5%) survivors reported having no consequences. 9 (45.0%) survivors with a confirmed level of disability reported that their health status was good and that they had no serious health consequences that affected their daily functioning. 5 (12.5%) survivors reported no health consequences related to posttraumatic growth. The most commonly reported consequences by other respondents were problems with the kidneys, cardiovascular and endocrine systems, skeletal system, and damage to the nerves and vestibular center. Only one respondent reported psychological trauma.

CONCLUSION

Childhood cancer survivors are a growing population in Croatia whose needs have not yet been adequately explored. In this study, members of FY were interviewed, whose characteristics include active participation in the work of the association. Therefore, the main limitations of the study are the small sample and the participants being active at the group level. The hypothesis made for this study is partially confirmed in terms of social life. In terms of education and professional life, the hypothesis is refuted, but the limitations of the study should be considered and further research should be conducted. Further research is needed to determine the conditions of survivors in Croatia and accordingly define guidelines to improve the quality of life.

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Conflicts of Interest:

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Contribution of individual authors:

Ms. Ana Radunić study design, data collection, first draft, statistical analysis

Prof. Rudolf Gregurek study design, approval of the final version

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