

SMW

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Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • www.smw.ch

Supplementum 257

ad Swiss Med Wkly

2022;152

April 18, 2022

Abstracts of the

International Cancer Survivor Symposium

Online Symposium, February 3, 2022



INTERNATIONAL CANCER SURVIVOR SYMPOSIUM 2022

Online symposium, February 3, 2022

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3. Prize: 1000.– CHF (Sponsored by: Sanofi Switzerland)

Adriaan Penson, Radboud University Medical Center, Nijmegen, the Netherlands

The impact of cancer-related fatigue on HRQOL in long-term survivors of childhood cancer: a DCCSS LATER study

FOLLOW-UP CARE

ID: 106

Information needs among family members affected by childhood cancer: A systematic reviewAnica Ilic¹, Katharina Roser¹, Katrin Scheinemann^{2,3}, Gisela Michel¹

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Background: Families facing a childhood cancer diagnosis are confronted with uncertainty and fear. Psychological distress among family members could be relieved by providing them with adequate information, which may ultimately foster coping mechanisms. Despite providing pediatric patients and their families with medical information on the disease is a well-established practice in most countries, information needs are often reported as the most common unmet need in childhood cancer research.

Aim: The study aims at assessing and synthesizing the information needs related to childhood cancer among families of patients and survivors.

Methods: A systematic search of the literature concerning information needs of family members of childhood cancer patients and survivors was conducted in PubMed, PsycINFO, CINAHL, and Scopus. The search identified 3128 potentially relevant articles. Studies applying both quantitative and qualitative approaches were included in the systematic review and data were analyzed through narrative synthesis.

Results: The review includes 45 publications, most providing results specific to parents' information needs (n = 37) and applying quantitative methods (n = 36). The concept of information needs was not adequately explained and most studies did not distinguish between met and unmet information needs. Recurring areas of information needs were treatment-related information, diagnosis-specific information, and information on follow-up and rehabilitation.

Conclusion: The systematic review provides insights on the information needs and preferences of family members of childhood cancer patients and survivors, and identifies areas that need further consideration. Ultimately, the findings of the current review will allow to develop and provide adequate information to families of childhood cancer patients and survivors, contributing to relieve their psychological distress.

Funding: Swiss National Science Foundation (Grant no. 10001C_182129/1).

ID: 118

Adult survivors of childhood cancer: motivation and needs during follow-up careMaria Wertli³, Eva Maria Eugenia Tinner Oehler^{1,2}, Sara Mirjam Buchmüller³, Christine Buchmüller³, Gisela Michel⁴, Helene Affolter³, Dajanira Larissa De Giovanni³, Jochen Karl Rössler¹, Joerg Leuppi²

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Introduction: Nowadays, over 80% of children diagnosed with cancer survive their disease and require transition into adult follow-up care. Little is known about the specific motivation and needs of adult survivors of childhood cancer (ACCS). We aimed to assess expectations and priorities of ACCS entering an interdisciplinary follow-up program.

Methods: All ACCS attending the structured adult cancer survivor follow-up program of 2 Swiss hospitals were invited to participate in a long-term prospective study. Participants were asked to complete a questionnaire about their motivation and needs. Further, health behavior (monitoring/blunting) was assessed based on 4 different clinical situations.

Results: Of 60 ACCS who met the inclusion criteria, 40 (67%) completed the questionnaire. Median age was 26 years and 60% were female. Most frequently treated cancers were lymphoma (28%), leukemia (23%), sarcoma (18%), and brain tumors (13%). Treatment included surgery and chemotherapy in most patients; 43% underwent radiotherapy. Overall, 90% reported that their motivation to attend the visit was to get confirmation about a good health status. Further, 90% expected to receive information about long-term adverse effects of their disease and past treatment. The majority wanted "to know that the cancer has not returned" (85%), to receive the best medical care (85%), and to receive information about a healthy lifestyle (59%). Selected ACCS wished to talk about sexuality/fertility (49%), work/insurance (40%), and psychological/other support (5%). The benefit of support options was rated differently depending on the personal attitude towards health problems: ACCS with high monitoring attitude rated patient interest groups as helpful, while those with low scores did not.

Conclusion: Motivation to attend follow-up visits included the desire to obtain information about current health and adverse treatment and disease effects and receive the best medical care.

ID: 126

IONA – Interdisciplinary Oncological Follow-Up Clinic in ViennaAlexandra Böhm¹, Sarah Rinner², Teresa Missmann², Marlene Huemer², Felix Keil¹

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Introduction: Cancer in childhood and adolescence can be cured in many cases nowadays. In Vienna, patients are treated either in the St. Anna Children's Hospital or at the University Clinic for Pediatrics and Adolescent Medicine (Neuro-Oncology). Short-term follow-up is usually performed in the children's hospitals. Afterwards patients had to organize the necessary examinations themselves for many years. This so-called transition was not successful in many cases, as the detection and treatment of therapy and disease-associated secondary diseases requires appropriate expertise.

Methods: "IONA - Interdisciplinary Oncological Follow-Up Clinic" is now offering age-appropriate, medical and psychosocial long-term follow-up since the beginning of 2020. A team of one experienced hemato/oncologist, two clinical psychologists and a social worker are offering the so-called "survivors" a specialized care, including medical check-ups tailored to the treatment and advices on risk factors in order to identify and treat possible late effects early on. In addition, there is psychosocial care and, if necessary, neuropsychological diagnostics. The health center where IONA is located also offers an optimal multi-professional network for this group of patients.

Results: More than 300 survivors have been transitioned since IONA started in early 2020. The majority of them suffered from CNS tumor, acute leukemia or lymphoma and were assigned directly by the hospitals, which guarantees continuous care. There is also regular exchange between the attending physicians as well as the psychologists, social workers and administrative employees. During the COVID pandemic, video and audio telephony were also used to hold joint conversations.

Conclusions: IONA offers interdisciplinary, standardized long-term follow-up care for patients from the age of 18 who had a hemato/oncologic disease in their childhood, adolescence or young adulthood and who have completed their medical therapy and short-term follow-up care at the responsible clinic. IONA accompanies patients in their transition process through close cooperation with the referring hospitals.

ID: 123

Long-term follow-up for childhood cancer survivors: the Geneva experience

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Background: Although the 5-year survival for pediatric cancer is over 85% in Switzerland, two thirds of the survivors will develop chronic health conditions (CHCs) due to the disease or to the toxicity of treatments. In this context, a long-term personalized follow-up (LTFU) program was set up at the University Hospitals of Geneva (HUG) since 2015. We aimed to describe this program, more particularly the cumulative burden of the CHCs, and assess the satisfaction of patients and/or their parents with it.

Methods: A retrospective study was performed where data on follow-ups and CHCs were collected from medical charts. CHCs were classified and graded in severity with the CTCAE classification. This study was completed by a satisfaction survey among patients and/or their parents.

Results: Out of 83 eligible patients, 51 (61.4%) accepted to participate, with an average age of 17.4 years (range, 10 to 35) at the time of study. Forty-two patients (82.3%) presented one or more CHCs and almost half of them (20/42) described 3 or more CHCs. The total number of CHCs was 118 for the 51 participants, with a mean of 2.3 (range, 0 to 7) disorders per patient. The most frequently affected systems were neurological (14.4%), musculoskeletal (13.6%), endocrine (9.3%) and renal (9.3%) systems. Sarcoma, central nervous system tumors and neuroblastoma were the diagnoses associated with the highest average number of CHCs. Among the 118 questionnaires, we received 82 (69.5%) responses. The level of satisfaction was good to excellent for more than 90% of the participants, for all the items evaluated.

Conclusions: Childhood cancer survivors present a significant number of CHCs, confirming the need for appropriate long-term, multidisciplinary and patient-specific medical follow-up based on the primary diagnosis and therapies received. Moreover, the LTFU program at the HUG was highly appreciated by patients and/or their parents.

ID: 125

Long-term follow-up programs for childhood cancer survivors in French-speaking Switzerland

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Purpose: There are various long-term follow-up (LTFU) care models for child cancer survivors (CCS). Our aim is to describe the LTFU programs in French-speaking Switzerland.

Methods: Data regarding LTFU clinics at the University Hospitals of Lausanne and Geneva were collected retrospectively in November 2021.

Results: Two LTFU clinics have been developed in French-speaking Switzerland, in Geneva (HUG, 2015) and Lausanne (CHUV, 2018). The time of entry into LTFU is at 5 years after the end of treatment. All patients are followed in the same program at HUG, whereas CCS treated for CNS tumors are included in a specific multidisciplinary consultation at CHUV. All patients receiving hematopoietic stem cell transplants are followed in the transplant center (HUG). The transition begins at the age of 18 and 20 years in Lausanne and Geneva respectively. Two options are presented to CHUV patients: (1) a family doctor-led FU, preferred by patients living outside the canton; (2) FU in an adult general medicine outpatient clinic at CHUV with a shared-transition model involving the pediatric oncologist and the general practitioner. At HUG, all patients are transitioned to the adult oncology department and the pediatric oncologist participates in adult consultations. The number of annual pediatric visits is increasing over time: 34 (2018) - 94 (2021) at CHUV; 28 (2015) - 61 (2021) at HUG with 0 (2015) - 32 (2021) adult consultations. A multidisciplinary working group including the two LTFU clinics was created in 2019 and a harmonization of practices completed in 2020 based on COG (Children Oncology Group) and IGHG (International Guidelines Harmonization Group) recommendations.

Conclusion: Two LTFU clinics have been developed in French-speaking Switzerland since 2015. Programs differ in the two centers reflecting local preferences and regional needs, but a standardization of practices has been achieved thanks to a joint multidisciplinary working group.

ID: 113

Adult survivors of childhood cancer: health-related quality of life of patients from two follow-up care clinics

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Introduction: The interdisciplinary follow-up clinic at the Cantonal Hospital Baselland Liestal and the University Hospital, Inselspital Bern offer the first structured follow-up care for childhood cancer survivors (CCS) under the guidance of general internists in Switzerland. The program uses the „Passport for Care“-Application (COG-Long Term Follow Up Guidelines). We aimed at describing health-related quality of life (HRQOL) in CCS attending these clinics, comparing it to HRQOL in the Swiss general population, and assessing differences in HRQOL before and after the clinic visit.

Methods: Questionnaires filled in before and after the first clinic visit included the Short Form-36 version 2 (SF-36v2) assessing HRQOL compared to normative data in the Swiss general population (mean score: 50). The SF-36v2 provides two summary measures (physical and mental HRQOL). Means of the two summary measures were calculated for the whole sample and different sub-samples.

Results: In total, 103 CCS attended the clinics in Bern (53%) and Liestal (47%), 68% were female, their mean age was 31.5 years (range: 17.1–61.8 years).

Before the visit, physical (mean = 47.6, $p = 0.037$) and mental (47.5, $p = 0.040$) HRQOL were significantly lower in CCS compared to the Swiss general population. Physical and mental HRQOL did not differ between females and males ($p = 0.732$ and $p = 0.203$). Survivors >28 years ($n = 45$, 36 of which previously lost to follow up) reported significantly lower physical and mental HRQOL compared to younger survivors ($n = 47$, 7 of which previously lost to follow up): 44.8 vs. 50.2, $p = 0.017$ and 44.4 vs. 50.5, $p = 0.009$.

HRQOL before and after the clinic visit ($n = 54$) were similar: physical: mean = 47.1 vs. 45.7, $p = 0.168$ and mental: mean: 48.9 vs. 48.2, $p = 0.443$.

Conclusions: Especially the older – previously lost to follow up - CCS attending the clinics reported significantly lower HRQOL, both physical and mental. The clinics seem to be especially attractive to CCS with lower HRQOL.

ID: 110**AYA Cancer Support CH**

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The association AYA Cancer Support CH emerged from the university project "Fresh Ideas for Cancer Care" of the Competence Center Medicine-Ethics-Law Helvetiae and the PhD program Biomedical Ethics and Law/Law Track of the University of Zurich.

The project showed that AYA are often too young or too old for existing cancer organisations in Switzerland and have very different problems and needs during or after cancer than other patient groups. Possible problems are, for example, impaired career entry, more difficult detachment from parents or less contact with peers, etc.

Within the framework of the project, an analysis of the existing support programs in Switzerland was carried out. It was found that Switzerland did not yet have its own youth cancer organization and that specific offers for AYA were fragmented within the different organisations and not always publicly announced. Additionally, the paper "Unterstützungsprogramme für junge Krebspatienten" (Staudinger, SZS 1/2020) proved that AYA fall through the social security net and thus suffer a more difficult career start. For these reasons, the platform ayacancersupport.ch was created, which aims to bundle all offers. With the founding of AYA Cancer Support CH (September 2021) a youth cancer organisation was established in order to fill existing gaps in services, such as in the area of career start. AYA Cancer Support CH is fulfilling these goals by expanding the social media presence in line with the target group, flyers and its first event, as well as awareness raising training sessions.

Furthermore, the association plans to hold more events, set up a contact point for questions about starting a career with cancer, promote collaborations with doctors to create own information content in language suitable for AYA and promote the development of an AYA community.

FATIGUE / PSYCHOSOCIAL PROBLEMS

ID: 122

The impact of cancer-related fatigue on HRQOL in long-term survivors of childhood cancer; a DCCSS LATER study

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Background: Late effects of treatment and their impact on health-related quality of life (HRQOL) has become a key goal of childhood cancer survivorship care. One of the most prevalent late effects is cancer-related fatigue (CRF). Since the impact of CRF on HRQOL is poorly understood, the current study aimed to investigate the association between CRF and HRQOL in a nationwide cohort childhood cancer survivors (CCS).

Methods: Participants were included from the Dutch Childhood Cancer Survivor Study (DCCSS) LATER cohort, a nationwide cohort of five-year CCS. Participants completed the Checklist Individual Strength (CIS) to indicate CRF (CIS-fatigue ≥ 35 and duration of symptoms ≥ 6 months) and the Short Form-36 (SF-36) and TNO and AZL QOL questionnaire (TAAQOL) as measures for HRQOL. Independent t-tests were calculated to identify differences in mean HRQOL domain scores between CRF and non-CRF participants. The association between CRF and impaired HRQOL (scoring 2 SD below population norm) was tested using multivariable logistic regression to adjust for potential confounders.

Results: A total of 1695 CCS participated in the study (23.1% with CRF). Mean total scores of all HRQOL domains were significantly lower for the CRF group compared to the non-CRF group, with mean differences ranging from 14.0 (95% CI 11.4–16.7) on sexuality to 41.6 (95% CI 38.2–45.0) on physical work limitations. CRF was associated with an impaired HRQOL on all studied domains with adjusted odds ratio's ranging from 2.5 (95% CI 1.7–3.8) for the sleep domain to 41.0 (95% CI 18.8–89.7) for the vitality domain.

Conclusion: Understanding the impact of late effects on HRQOL is crucial when aiming to improve the quality of CCS daily lives. The current study shows CRF to have a negative impact on multiple HRQOL domains, indicating the urge of structural screening and monitoring of fatigue symptoms, and developing possible prevention and intervention techniques.

ID: 109

Risk factors for cancer-related fatigue in adult childhood cancer survivors: A report from the CardioOnco Study

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Background: Cancer-related fatigue (CRF) is a distressing late effect in childhood cancer survivors (CCS) with prevalence between 10 and 85%, and little evidence on its risk factors. We aimed to describe the prevalence of CRF in adult CCS and assess its risk factors.

Methods: As part of the CardioOnco study, we invited adult 5-year CCS treated at Inselspital Bern between 1976–2015 to a cardiooncological outpatient clinic and sent them questionnaires. We assessed fatigue with the Checklist Individual Strength subjective fatigue subscore (CIS, during last 2 weeks) and the Visual Analog Scale (VAS, at the current day). Increased fatigue was defined as CIS score 27–35 and VAS score ≥ 70 . We collected information on previous cancer treatment and medical history and calculated mean CRF scores with ANCOVA adjusting for sex and age.

Results: We included 158 CCS (participation rate 29%) with median age at study of 33 years (IQR: 26–38). We found that 19% of CCS had increased fatigue with CIS and 11% with VAS. Mean CIS fatigue score was higher in women (21, CI 20–22) than men (18, CI 16–19, $p = 0.001$), in those treated with radiotherapy (22, CI 20–23 vs. 18, CI 17–19, $p < 0.001$), those with sleep disturbance (23, CI 21–24 vs. 18, CI 17–19, $p < 0.001$), and those with an endocrine abnormality (24, CI 22–25 vs. 18, CI 17–19, $p < 0.001$).

Conclusion: We found that one fifth of adult CCS experiences increased fatigue. Female CCS with history of radiotherapy and suffering from endocrine or sleep problems would profit from screening for CRF and further counselling with a specialist.

ID: 114

Can virtual reality immersion reduce anxiety, stress and pain in pediatric patients with cancer?

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Children and adolescents with pediatric cancer undergo potentially painful medical procedures as part of their treatment. Anxiety and stress can exacerbate the perceived pain. Virtual reality (VR) immersion offers a powerful distraction from such adverse affects. Regarding the use of VR for pediatric cancer patients, empirical evidence and guidelines for its implementation are still lacking. Thus, we will conduct a within-subjects pilot study (N = 16) to investigate if a VR-session can reduce anxiety, distress and pain in pediatric oncology patients aged 8 to 18 years. Patients will participate in both conditions (VR; control) in random order, each time for 20 minutes during a potentially painful medical procedure. In the VR condition,

calm music and a friendly voice will guide the patients through a three-dimensional VR-experience, which was designed for medical purposes and to promote relaxation and calm, rhythmic breathing. Participants will choose among five nature-themed VR-environments. In the control condition, participants will choose among five books and magazines to read. Before and after either session (VR; control), self- and parent-rated anxiety, stress and pain will be assessed by means of concise scales and questionnaires. After either session, a questionnaire will assess the enjoyment, the feasibility and the immersive element of the experience. The parents and the medical personnel will be asked to evaluate the feasibility as well. We hypothesize less anxiety, stress and pain in the VR condition compared to the control condition post session when controlled for pre session levels. Additionally, we expect the VR-experience to be perceived as immersive and enjoyable by the patients. The results and experiences from this planned study will further guide the implementation of VR-interventions into our clinical practice. Depending on the findings of this exploratory study, we will consider conducting a larger, randomized controlled trial.

ID: 117

Small but mighty: cross-sectional associations between dietary daily nicotinamide intake and fatigue and other patient-reported outcomes in colorectal cancer survivors, 2 to 10 years post-diagnosis

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Supplementation with nicotinamide adenine dinucleotide (NAD⁺) precursors including dietary nicotinamide has been found to boost tissue NAD⁺ levels and ameliorate oxidative stress-induced damage that contributes to aging and aging-related diseases. The association between dietary NAD⁺ precursors and patient-reported health-related outcomes in cancer survivors has not been investigated. This study aimed to determine associations of dietary nicotinamide intake with different patient-reported outcomes in colorectal cancer survivors, 2 to 10 years post-diagnosis. A total of 145 eligible participants were recruited into this cross-sectional study. Dietary nicotinamide intake level was calculated based on data from 7-day food diaries. Fatigue was assessed with the Checklist Individual Strength (CIS), which is a subscale of the cancer-specific European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC), and anxiety and depression were assessed with Hospital Anxiety and Depression Scale (HADS). Oxidative stress marker serum protein carbonyl contents and serum NAD⁺ levels were measured. A hierarchical linear regression model with confounder adjustment was performed to analyze the association of nicotinamide intake, serum protein carbonyl contents, and NAD⁺ levels with patient-reported outcomes. The median values of daily nicotinamide intake for male and female participants were 19.1 and 14.4 mg, respectively. Daily dietary nicotinamide intake was associated with a lower level of fatigue (β : -14.85 (-28.14, -1.56)) and a lower level of anxiety and depression (β : -4.69 (-8.55, -0.83)). Subgroup analyses by sex showed that a beneficial association between nicotinamide intake and patient-reported outcomes was mainly found in men. To conclude, our findings suggested that higher dietary NAD⁺ precursor nicotinamide intake was cross-sectionally associated with less fatigue and less other patient-reported outcomes in CRC survivors.

ID: 102

Recommendations for the surveillance of education and employment outcomes in survivors of childhood, adolescent and young adult cancer: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group

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Purpose: Educational achievement and employment outcomes are critical indicators of quality of life in survivors of childhood, adolescent, and young adult (CAYA) cancer. We aimed to provide an evidence-based clinical practice guideline (CPG) with internationally harmonized recommendations for surveillance of education and employment outcomes in survivors of CAYA cancer diagnosed before 30 years of age.

Methods: This CPG was developed by a multidisciplinary panel under the umbrella of the International Late Effects of Childhood Cancer Guideline Harmonization Group. After evaluating concordances and discordances of four existing CPGs, we performed a systematic literature search through February 2021. We screened articles for eligibility, assessed quality, and extracted and summarized the data from included articles. We formulated recommendations based on the evidence and clinical judgement.

Results: Of 3930 articles identified, 83 articles originating from 17 countries were included. On a group level, survivors were more likely to have lower educational achievement and more likely to be unemployed than comparisons. Key risk factors for poor outcomes included primary diagnosis of a central nervous system tumor and experiencing late effects. We recommend that healthcare providers be aware of the risk of educational and employment problems, implement regular surveillance, and refer survivors to specialists if problems are identified.

Conclusions: We present a harmonized CPG that aims to facilitate evidence-based care, positively influence education and employment outcomes, and ultimately minimize the burden of disease and treatment-related late adverse effects for survivors of CAYA cancers.

ID: 105

Education, employment, and finances in adolescent and young adult cancer survivors – a systematic review

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Introduction: Adolescents and young adults (AYA) with cancer face unique challenges, also after treatment. With this systematic review, we aimed to describe i) what is currently known about education, employment, and finances, and ii) risk factors for adverse education, employment, and financial hardship in AYA cancer survivors.

Method: We performed a systematic literature search in PubMed, Scopus, and PsycINFO. We included original research articles on AYA (15–39 years of age) cancer survivors (> = 2 years after diagnosis) and our outcomes of interest. We narratively synthesized the results of included articles.

Results: We included 25 articles (16 quantitative, 9 qualitative). The majority of AYAs with cancer had to interrupt their education. Most AYA cancer survivors were employed, but they started their paid work at an older age than the general population. No disadvantages in income or disability pension were observed. AYA cancer survivors reported more absent work days than comparisons.

Risk factors for lower education were a stay in the intensive care unit during treatment and suffering from late effects related to vision or hearing. Female gender, longer time since and younger age at diagnosis were risk factors for unemployment. AYAs with extensive chemotherapy treatment and younger age at diagnosis were at higher risk for financial hardship.

Discussion: To facilitate successful re-entry in education or employment, and to minimize financial burden, future research should focus on the development of age-tailored interventions for AYA cancer survivors. Such intervention may be particularly beneficial in the last years of school or first years of employment.

ID: 103

Social, emotional, and behavioural functioning in young childhood cancer survivors with chronic health conditions

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Objective: The cancer diagnosis and its intensive treatment may affect long-term psycho-social adjustment of childhood cancer survivors. We aimed to describe social, emotional, and behavioural functioning, and their determinants in young childhood cancer survivors.

Methods: The nationwide Swiss Childhood Cancer Survivor Study sends questionnaires to parents of survivors aged 5–15 years, who have survived at least 5 years after diagnosis. We assessed social, emotional, and behavioural functioning using the Strengths and Difficulties Questionnaire (SDQ). The SDQ includes 4 difficulties scales (emotional, conduct, hyperactivity, peer problems), a total difficulties indicator, and 1 strength scale (prosocial). We compared the proportion of survivors with borderline and abnormal scale scores to reference values and used multivariable logistic regression to identify determinants.

Results: Our study included 756 families (response rate 72%). Thirteen percent of survivors had abnormal scores for the total difficulties indicator compared to 10% in the general population. The proportion of survivors with abnormal scores was highest for the emotional scale (15% vs. 8% in general population), followed by the peer problems scale (14% vs. 7%), hyperactivity (8% vs. 10%), and conduct scale (6% vs. 7%). Few survivors (4% vs. 7%) had abnormal scores on the prosocial scale. Children with chronic health conditions had a higher risk of borderline and abnormal scores in all difficulties scales (all $p < 0.05$). More than one third of survivors with two or more chronic health conditions had borderline and abnormal scores in emotional (38%) or peer problem domains (34%).

Conclusions: Most childhood cancer survivors do well in social, emotional, and behavioural life domains, but children with chronic health conditions experience difficulties. Therefore, healthcare professionals should offer specific psycho-social support to these survivors.

LATE EFFECTS AND CHRONIC DISEASE AFTER TREATMENT FOR CHILDHOOD AND AYA CANCER

ID: 119

The effect of a 1-year physical activity intervention on cardiovascular health in long-term childhood cancer survivors – a randomised controlled trial (The SURfit Study)

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Purpose: No randomized controlled trial (RCT) has so far investigated the effect of a physical activity (PA) intervention on cardiovascular health in long-term childhood cancer survivors (CCS). We aimed to assess the effect of a 1-year PA intervention on a cardiovascular disease (CVD) risk score, single CVD risk factors, physical fitness, PA and safety in adult CCS.

Methods: We randomized 151 CCS ≥ 16 y at enrollment, < 16 y at diagnosis, and ≥ 5 y in remission, identified from the Swiss Childhood Cancer Registry. Participants of the intervention group were asked to perform an additional ≥ 2.5 h of intense physical activity/week, controls continued exercise as usual; assessments were performed at baseline, 6 months (T6) and 12 months (T12). Our primary endpoint was change in a CVD risk score (average z-score of waist circumference, blood pressure, fasting glucose, inverted high-density lipoprotein cholesterol, triglycerides and inverted cardiorespiratory fitness) at T12. We performed intention-to-treat (primary) and 3 per protocol analyses.

Results: We found a robust and significant a reduction of the CVD risk score in the intervention group compared to the control group at T6 and T12. Our primary estimate showed a difference in the reduction of the CVD risk z-score of -0.18 (95% CI -0.29 to -0.06, $p = 0.003$). We further found a positive effect on some of the single CVD risk factors and physical fitness at T6 and T12 but no effect on the PA parameters. The intervention was safe.

Conclusion: This high-quality RCT could show a robust and significant effect of a one-year PA intervention to reduce CVD risk in long-term survivors of childhood cancer. PA should be routinely recommended during follow-up care of CCS to reduce their CVD burden.

ID: 111

Risk of second primary neoplasms among childhood cancer survivors in Europe: a population-based study

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Introduction: Childhood cancer survivors (CCS) are at high risk of developing second primary neoplasms (SPN). Within the Cancer Risk in Childhood Cancer Survivors (CRICCS) study, funded by Children with Cancer UK, we aimed to assess the incidence of SPN among CCS in Europe, on behalf of the CRICCS Consortium.

Methods: We pooled data from 73 population-based cancer registries (PBCR) operating in 31 European countries that collected data over variable periods in the range 1949–2011. Malignant tumours diagnosed in patients before the age 20 years and malignant SPN they developed at any age were included. All cancers were classified according to the International Classification of Childhood Cancer. Only CCS with no SPN in the 5 years since the first cancer diagnosis were included. We computed cumulative incidence (CI) of SPN in CCS.

Results: The 149,205 5-year CCS were followed-up for a median of 13.6 years and accumulated 2.4 million person-years, during which 1,937 SPN developed. Incidence rate of SPN was 81.1 per 100,000

person-years. The median age at SPN diagnosis was 27 years. The three most common SPN groups were carcinomas, soft tissue sarcomas, and CNS tumours. The CI of SPN increased with time since diagnosis from 0.4% at 10-years to 5.5% at 40-years. CNS and bone tumours developed in younger CCS (median age 14 years) than carcinomas, soft tissue sarcomas, and leukaemias (median age 32, 23, and 19 years, respectively). Carcinomas were the most common SPN after any first primary except for retinoblastoma, which was most often followed by a bone tumour.

Discussion: Our study shows that CCS have high SPN incidence, which increases with time and aging. Variations in sequence of the different cancer types will be explored further. These results highlight the importance of follow-up of CCS, both in medical setting and in PBCRs, to prevent SPN.

ID: 115

Prospective multicentre cohort study for diagnosing cardiac dysfunction in Swiss childhood cancer survivors – the CardioOnco Study

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Background: Cardiovascular disease is the leading nonmalignant cause of death among childhood cancer survivors. Anthracyclines and chest radiation are known treatment-related risk factors. Cardiovascular disease can remain asymptomatic for years and progress to high morbidity and mortality. Conventional echocardiography is the standard technique to diagnose cardiac dysfunction, but speckle-tracking echocardiography may be more sensitive. Also, cardiopulmonary exercise testing (CPET) predicts cardiovascular morbidity and mortality in non-childhood cancer patients. In our previous project (2016-19), we established a cardiovascular follow-up clinic in Bern. We invited all 530 eligible ≥ 5 -year survivors formerly treated in Bern to a cardiac assessment including conventional and speckle-tracking echocardiography; 289 completed the assessment (55% response rate).

Objectives: We are setting up a multicentre, longitudinal follow-up study to assess the prevalence of early cardiac dysfunction, compare conventional with speckle-tracking echocardiography, and investigate fitness in survivors of childhood cancer using CPET.

Methods: We will additionally invite survivors treated in Basel, Geneva, Lucerne, and St. Gallen. All ≥ 5 -year survivors diagnosed since 1976 at an age of < 20 years treated in one of the five children's hospitals (new centres: $N = 1200$) are eligible for inclusion. We will stratify participants into high-risk (treated with anthracyclines and/or chest radiation) and standard-risk survivors (treated with nonanthracycline-containing chemotherapeutic regimens). High-risk survivors will have longitudinal assessments, standard-risk survivors

only baseline assessments. Anticipating a response rate of 55%, we will assess N = 660 new survivors.

Study procedures: We will select our study population from the Childhood Cancer Registry and extract treatment data from patient records. The cardiac assessment includes conventional and speckle-tracking echocardiography, and CPET.

Impact: This multicentre study will investigate the predictive value of speckle-tracking echocardiography and the additional value of CPET in identifying survivors at risk for cardiac dysfunction. Ultimately, this will help improve follow-up care and long-term outcome in this vulnerable population.

ID: 116

Cerebral blood flow and its association with cognitive and motor performance in pediatric cancer survivors

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Pediatric cancer survivors (PCS) frequently experience long-term cognitive and motor difficulties as well as functional and structural brain alterations. However, little is known about cerebral blood flow (CBF) and its possible relationship with cognition and motor abilities in PCS. We therefore examined (1) CBF, cognitive functions, and motor abilities in PCS and (2) investigated the possible associations between these three domains.

Forty children after non-central nervous system cancer (aged 7–16 years; ≥one year following termination of cancer treatment) and 40 healthy children and adolescents were included in this cross-sectional analysis. All participants underwent MRI including arterial spin labeling. We investigated global CBF and the cerebral flow territories of the anterior, middle, and posterior cerebral artery (ACA, MCA, and PCA). Cognitive functions (i.e. fluid intelligence, executive functions, and processing speed) were assessed with neuropsychological tests and motor abilities (i.e. coordination and strength) using the German Motor Test.

CBF (global, ACA, MCA, and PCA) did not differ between PCS and controls. Working memory ($p = .034$) and motor performance ($p = .002$) were significantly worse in PCS than controls. CBF was negatively correlated with age ($r = -.659$) and body mass index ($r = -.602$) in controls, but not in PCS. In PCS, but not in controls, CBF was negatively correlated with working memory ($r = -.526$) and motor performance ($r = -.555$).

Our results might point towards an altered relationship between maturation and CBF in PCS. Furthermore, the association between CBF and functional outcome in PCS might indicate different brain-behavior mechanisms after cancer and its treatment.

ID: 107

Risk factors for overweight and obesity after childhood acute lymphoblastic leukemia in North America and Switzerland: a comparison of two cohort studies

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Background and aims: Survivors of childhood acute lymphoblastic leukemia (ALL) are at increased risk for obesity. We aimed to identify differences between the cohorts in the prevalence of overweight and obesity in childhood ALL survivors compared to siblings; identify risk factors for overweight and obesity, and compare the direction and strength of associations between cohorts.

Methods: The North American Childhood Cancer Survivor Study (CCSS) and the Swiss Childhood Cancer Survivor Study (SCCSS) include ≥5 years survivors of childhood cancer. Adult survivors of childhood ALL diagnosed prior to age 21 years between 1976–1999 were included. CCSS participants were individually matched (3:1) to SCCSS participants on sex and age at assessment. Self-reported heights and weights were used to calculate BMI for 429 Swiss and 1287 North American survivors and compared with 678 Swiss and 2034 North American siblings. We assessed risk factors for being overweight (25–29.9 kg/m²) and obese (≥30 kg/m²) by using multinomial logistic regression.

Results: Overweight and obesity were more common in North American than in Swiss survivors (overweight: 30 vs. 24%; obesity: 29 vs. 7%) and siblings (overweight: 30 vs. 25%; obesity: 24 vs. 6%). North American survivors were more likely to be obese than their siblings (OR = 1.26; 95%CI: 1.03–1.55). In Switzerland, we found the same trend (1.25; 0.72–2.16). Among all survivors, risk factors for obesity were: residency in North America (5.8; 3.7–8.9), being male (1.6; 1.2–2.1), having an older attained age (≥45 years: 5.5; 2.6–11.5), black race (3.2; 1.6–6.4), a low household income (2.2; 1.4–3.6), and age <5 years at diagnosis (1.6; 1.1–2.3). Interaction tests found no difference in risk factors effect between cohorts.

Conclusions: Obesity after childhood ALL is more prevalent in North America compared to Switzerland and seems to be explained mostly by socio-economical than treatment differences.

ID: 108

Outcome of adolescent and young adult sarcoma patients after pencil beam scanning (PBS) proton therapy. (PT)Filippo Grillo Ruggieri¹, Christina Schröder¹, Dominic Leiser¹, Alessia Pica¹, Damien Charles Weber^{1,2,3}¹Center for Proton Therapy, Paul Scherrer Institute, ETH Domain, Villigen, Switzerland; ²University Hospital Zürich, Zürich, Switzerland; ³University Hospital Bern, Bern, Switzerland; filippo.grillo@psi.ch**Purpose:** To evaluate clinical outcome of AYA sarcoma patients after pencil beam scanning proton therapy.**Methods and material:** From 12/2000 to 01/2019 67 patients aged 15 to 39 years (median, 24) with sarcoma and benign soft tissue tumors were treated with PBS PT. Soft tissue sarcoma were 34/67 (50.8%), malignant bone tumors 24/67 (35.8%), benign tumors 9/67(13.5%). Four (6.0 %) presented at diagnosis with N+ disease and 7 (10.4 %) were metastatic. Forty-two (62.7%) were treated after partial or total resection, 25 (37.3%) with definitive proton therapy, and 42 (62.7%) received concurrent or sequential chemotherapy. Median proton dose was 61.6 Gy RBE (range, 9–78). Fifty-seven patients received ≥ 50 Gy RBE, 15 ≥ 70 Gy RBE. PT-dosimetric and clinical outcome were analyzed including toxicity, local and distant failure, progression-free (PFS) and overall survival (OS).**Results:** After a median follow-up of 31 months (range, 1–209), 23 local failures (n = 14 in field) were observed. The estimated 3-year LCR rate was 59%. Nine (13.4%) patients had distant failure only. The estimated 3-year DMFS was 65%. Twenty-four (35.8%) patients died, all of tumor related etiology. Median OS after PT was not reached. The 3-year survival rates was 69%. Late toxicity was observed in 20 (29.9 %) patients, 6 (9.0 %) had G3 late toxicity (3 unilateral cataract, 1 severe mastoiditis, 1 osteonecrosis and 1 paraplegia). No G4 or G5 late toxicity. Nine patients had fertility preservation before treatment, median age 18 years (range, 15–25), 8 females vs. 1 male. The 3-year high-grade ($\geq G3$) toxicity free survival was 96 %. Sixty-three per cent of patients regained employment during follow-up, 34.8% were unable to work due to early recurrence.**Conclusion:** For AYA patients with sarcoma, PBS proton therapy leads to expected control rates with low rates of high-grade radiation induced late toxicity.

ID: 112

Severity of hearing loss after platinum chemotherapy in childhood cancer survivorsSven Strebel^{1,2,3}, Luzius Mader¹, Tomáš Sláma^{1,4}, Nicolas Waespe^{1,2,10}, Annette Weiss^{1,5}, Ross Parfitt⁶, Antoinette am Zehnhoff-Dinnesen⁶, Martin Komp⁷, Nicolas X. von der Weid⁸, Marc Ansari^{2,9}, Claudia E. Kuehni^{1,10}¹Institute of Social and Preventive Medicine, University of Bern, Switzerland; ²CANSEARCH research platform in pediatric oncology and hematology, Department of Pediatrics, Gynecology and Obstetrics, University of Geneva, Geneva, Switzerland; ³Graduate School for Health Sciences, University of Bern, Switzerland; ⁴Graduate School for Cellular and Biomedical Sciences, University of Bern, Switzerland; ⁵Bavarian Care and Nursing Authority, Amberg, Germany; ⁶Department for Phoniatrics and Pedaudiology, University Hospital Münster, Münster, Germany; ⁷Department of ENT, Head and Neck Surgery, University Hospital Bern, University of Bern, Bern, Switzerland; ⁸Department of Pediatric Oncology and Hematology, University Children's Hospital Basel (UKBB), University of Basel, Basel, Switzerland; ⁹Department of Women, Child and Adolescent, Division of Pediatric Oncology and Hematology, Geneva University Hospital, Switzerland; ¹⁰Division of Pediatric Hematology/Oncology, Department of Pediatrics, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; sven.strebel@ispm.unibe.ch**Background:** Hearing loss is a potential side effect after childhood cancer treatment. We aimed to describe the severity of hearing loss in a representative national cohort of childhood cancer survivors (CCS) using audiogram data, and to identify clinical risk factors.**Method:** We included all CCS who were diagnosed at age ≤ 18 years in Switzerland and had been treated with platinum-based chemotherapy between 1990 and 2014. Audiograms, treatment-related information, and demographic data were extracted from medical records and the Swiss Childhood Cancer Registry. Two trained reviewers independently assessed the severity of hearing loss at latest follow-up using the Münster Ototoxicity Scale. We used ordered logistic regression to identify clinical risk factors for a higher severity grade.**Results:** We included 274 CCS in our analysis. Median time from cancer diagnosis to last audiogram was 5.0 years (interquartile range [IQR] 2.3–8.1). We found 53 (19%) CCS with mild, 78 (28%) with moderate, and 76 (28%) with severe hearing loss. Higher severity grades were associated with younger age at diagnosis (odds ratio [OR] 2.4, CI: 1.3–4.3 for <5 years), treatment in earlier years (OR 6.8, CI: 3.1–15.0 for 1990–1995), higher cumulative doses of cisplatin (OR 15.3, CI: 5.4–43.5 for >450 mg/m²), concomitant cranial radiation (OR 4.5, CI: 2.6–7.8), and hematopoietic stem cell transplantation (OR 2.5, CI: 1.1–5.9).**Conclusion:** Three out of four CCS treated with platinum-based chemotherapy experienced some degree of hearing loss. Patients diagnosed at a young age, treated with high cumulative doses of cisplatin, concomitant cranial radiation, and hematopoietic stem cell transplantation could profit from close monitoring of their hearing function.**Funding:** We would like to express our gratitude to the CANSEARCH Foundation and to the Swiss Cancer League (HSR-4951-11-2019) for their financial support.

FERTILITY

ID: 120

Pregnancy and pregnancy outcomes after hematopoietic stem cell transplantation during childhood: A cross-sectional survey of the EBMT Pediatric WP

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Introduction: Infertility is one of the major late effects after hematopoietic stem cell transplantation (HSCT) with a substantial impact on quality of life. Aim of the study was to analyze pregnancies and their outcome in survivors of childhood HSCT. Adoptions were not considered. **Material and Methods:** In a first step, pregnancies were identified in the EBMT database. Additional data were collected by a survey, which was conducted between July 2017– June 2018.

Results: In totally, 62'988 pediatric patients were transplanted in EBMT centers between 1995 to 2016. In 484 patients, a conception after HSCT was reported in a median 10.7 years (IQR 6.5–15.9 years) after HSCT. 341/484 patients (70%) had an allograft, 204 (60%) were females. The median age for males and females at transplant was 15.0 (range 0.6 - 17.9 years), regardless of autologous or allogeneic HSCT. 283 patients (58%) had conditioning regimen containing alkylating agents, irradiation or both. Detailed information was sent by centers for 99/484 (20.5%) patients and partners on 114 pregnancies. In 70/99 (71%) patients' pregnancies were of post-HSCT female. Underlying disease conditions for HSCT was malignant in 52/99 (52%) and 73/99 (73%) received a myeloablative conditioning regimen. Regarding fertilization, 13/25 (52%) patients with TBI (2/13 had 2 Gy only) conceived naturally, 10/25 (40%) required assisted fertilization and 2 used cryopreserved sperms. In patients conditioned without TBI, 69/74 (93%) had a natural conception, 4/74 (5%) required assisted fertilization and 1 used cryopreserved sperms. In 90/98 (92%) patients pregnancy resulted in live birth.

Conclusion: Risk of fertility impairment after HSCT is high in patients. Nevertheless, pregnancies are possible in patients transplanted during childhood. Pregnancy assisted fertilization techniques may increase pregnancy rate. Young patients undergoing HSCT should be counselled before and after regarding infertility risk and possible fertility preservation options

ID: 124

Testicular tissue cryopreservation for fertility preservation in prepubertal and adolescent boys facing highly gonadotoxic treatment: a six year experience from a Swiss multi-center network

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Background: One of the major adverse effects of oncologic treatments and hematologic stem cell transplantation (HSCT) is the risk of infertility. According to the Childhood Cancer Survivor Study, prevalence of infertility in male is 46%. Testicular tissue cryopreservation (TTC) is an experimental procedure of fertility preservation for prepubertal boys aiming at preserving spermatogonic stem cells, which could be used for assisted reproduction in the future. We report our experience with a research protocol of TTC.

Methods: Data were prospectively collected on patients who underwent TTC at the Lausanne University Hospital, Geneva University Hospitals and Basel University Children's Hospital between 2015 and 2020. Inclusion criteria were pre-pubertal boys aged more than 3 months or peri and post-pubertal boys with unsuccessful sperm cryopreservation, who were scheduled to undergo high-risk gonadotoxic treatment (risk of infertility estimated to 80% or more). The Andrology and Reproductive Biology Laboratory at Lausanne University Hospital centralized all samples.

Results: Testicular tissues from 35 patients were collected. Four families declined TTC. The mean age of patients was 8.5 years (range 0.5–18.5 years). Underlying diseases were a malignant disorder in 31 patients including 15 (42.9%) hematological malignancies and 16 (45.7%) solid tumors. Four (11.4%) patients had a benign hematological condition. The main indication for TTC was conditioning for HSCT (25 patients, 71.4%). A minor hematoma and a minor wound dehiscence were the only two reported adverse events. Tumoral cells were found in one testicular biopsy of a leukemic patient. Five patients died during the follow-up. Testicular tissue was destroyed in 2 cases and banked in 3 cases according to the preferences indicated at the time of consent.

Conclusions: Our data demonstrate the feasibility of a program of TTC coordinated by a multidisciplinary team of fertility preservation. Advances in assisted reproduction open great hopes to reduce adverse effects of gonadotoxic treatments.

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The BISKIDS biobanking study: DNA self-sampling in childhood cancer survivors in Switzerland

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Background: Germline genetic research is only feasible with sufficient patient numbers which is difficult to obtain for rare diseases such as childhood cancer. With self-collection kits, participants can contribute genetic samples conveniently from their home. In this nationwide cross-sectional study, we analyzed predictive factors of participation in DNA self-collection.

Methods: We identified childhood cancer survivors from the Swiss Childhood Cancer Registry for invitation to germline DNA self-sampling in September 2019. Participants received saliva sampling kits by postal mail at their home, were asked to fill them, sign an informed consent, and send them back by mail. Two reminders were sent to non-participants by mail. We compared demographic, clinical, and treatment information of participants with non-participants using univariable and multivariable logistic regression models.

Results: We invited 928 childhood cancer survivors in Switzerland with a median age of 26.5 years (interquartile range 19–37), of which 463 (50%) participated. After the initial send out of the sampling kit, 291 (63%) had participated, while reminder letters led to 172 additional participants (37%). Foreign nationality (odds ratio [OR] 0.5; 95%-confidence interval [CI] 0.4–0.7), survivors aged 30–39 years at invitation (OR 0.5; CI 0.4–0.8), and survivors with a known cancer predisposition syndrome (OR 0.5; CI 0.3–1.0) were less likely to participate in germline DNA collection. Survivors with a second primary neoplasm (OR 1.9; CI 1.0–3.8) or those living in a French or Italian speaking region (OR 1.3; CI 1.0–1.8) tended to participate more.

Conclusions: Half of invited childhood cancer survivors participated in germline DNA self-sampling relying completely on mailing of sampling kits in Switzerland. Written reminders increased the response by about one third. More targeted recruitment strategies may be advocated for specific subgroups.

Funding: We would like to thank the CANSEARCH Foundation, the Swiss National Science Foundation (31BL30_185396), and Swiss Cancer Research (KFS-4722-02-2019, KLS/KFS-4825-01-2019).

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SWISS MEDICAL WEEKLY

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Listed in: Index Medicus / MEDLINE; Web of science; Current Contents; Science Citation Index; EMBASE

Editing company:
EMH Swiss Medical Publishers Ltd.
Swiss Medical Weekly
Farnsbürgerstrasse 8
CH-4132 Muttenz, Switzerland

ISSN online supplement: 2504-1622

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2022.

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