NASLCCC

North American Symposium on Late Complications after Childhood Cancer

JUNE 20–22 2019

Emory Conference Center Hotel
Atlanta, GA

St. Jude Children's® Research Hospital

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Contents

General Information

Program Overview

The North American Symposium on Late Complications after Childhood Cancer (formerly the International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer) provides a venue for the multidisciplinary exchange of innovative ideas among clinicians and researchers engaged in pediatric cancer survivorship clinical care and/or research. The symposium historically includes global participation of approximately 300 attendees from Europe, Asia, Oceania, South America, Canada and the United States.

The 2019 symposium will focus on two themes: interventions to remediate late effects and emerging late effects of novel therapies. Keynote speakers will provide overviews of the conference themes. Highly ranking abstracts featuring research results related to the conference themes as well as other relevant survivorship topics will be presented in the conference oral plenary and poster sessions.

Target Audience

Oncology, Psychology/Psychiatry, Radiation Oncology, Social Work, Survivorship

Mobile Phones and Pagers

As a courtesy to presenters and others, please ensure that mobile telephones and pagers are turned off or switched to silent mode during all presentations.

Name Badges

Admission to all sessions is by name badge only, and all attendees must be registered.

Registration Desk and Check In

The registration desk will be open in Emory Conference Center Hotel at the following times:
(Early registration available Wednesday.)

Thursday, June 20 • 2–7 p.m. | Friday, June 21 • 7 a.m.–5 p.m. | Saturday, June 22 • 7:30 a.m.–12 p.m.

Registration fee includes the Program/Proceedings, the welcome reception (Thursday, June 20), admission to all scientific sessions, poster session, conference materials, continental breakfast, and refreshment breaks.

Additional copies of the Program/Proceedings may be purchased at the registration desk. Cost: $10.00 (US) per copy.

Speaker Preparation Room

A Speaker Preparation Room will be available to review your presentation for your convenience. If needed, please inquire at the registration desk for the room location and details.

Ground Transportation

Information on Ground Transportation is available at the hotel concierge desk.

Poster Exhibition (Friday, June 21)

Poster viewing will be from 5:30–8:30 p.m. (presenters in attendance). Posters will be on display through Saturday, June 22, at noon.

Conference Survey

A link to the conference survey will be emailed to you after the conference ends. While not mandatory, your feedback is very valuable to us, so please complete the survey to help us plan future conferences.

Sponsor Acknowledgement

The North American Symposium on Late Complications after Childhood Cancer gratefully acknowledges support from St. Jude Children's Research Hospital.

Continuing Medical Education Information

Education Objectives

After attending this educational conference, you should be able to:

- Describe common long-term physical and emotional sequelae of childhood cancer
- Compare and implement appropriate interventions to prevent, remediate, or promote early detection of cancer- or treatment-related medical complications
- Compare and implement appropriate interventions to prevent, remediate, or promote early detection of cancer- or treatment-related psychosocial complications
- Identify emerging signals of late toxicity associated with novel cancer treatment strategies

Please note that session objectives will be presented during the symposium as appropriate.

Accreditation Information

St. Jude Children's Research Hospital is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Credit Designation

St. Jude Children's Research Hospital designates this live activity **for a maximum of 12.75** *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Credit Certificates

To claim *AMA PRA Category 1 Credit*™ or attendance credit for this activity and print a certificate, you must attend the sessions and then follow the instructions below:

- Go to *cme.stjude.org*.
- Enter the email address you used when registering for this conference and your password for the St. Jude CME system (if you do not remember your password or have not previously used this system, follow the instructions to set a password).
- Click the MyCME button in the red menu bar and choose Evaluations and Certificates.
- Choose "Complete Evaluation" by North American Symposium on Late Complications After Childhood Cancer to complete the short CME evaluation for this activity; you must complete this CME evaluation to claim credit.
- You will then be returned to the Evaluations and Certificates screen to print, download, or email your certificate.
- Print and/or save your certificate

If you have questions about claiming your CME or attendance certificate, please contact us at *cme@stjude.org*.
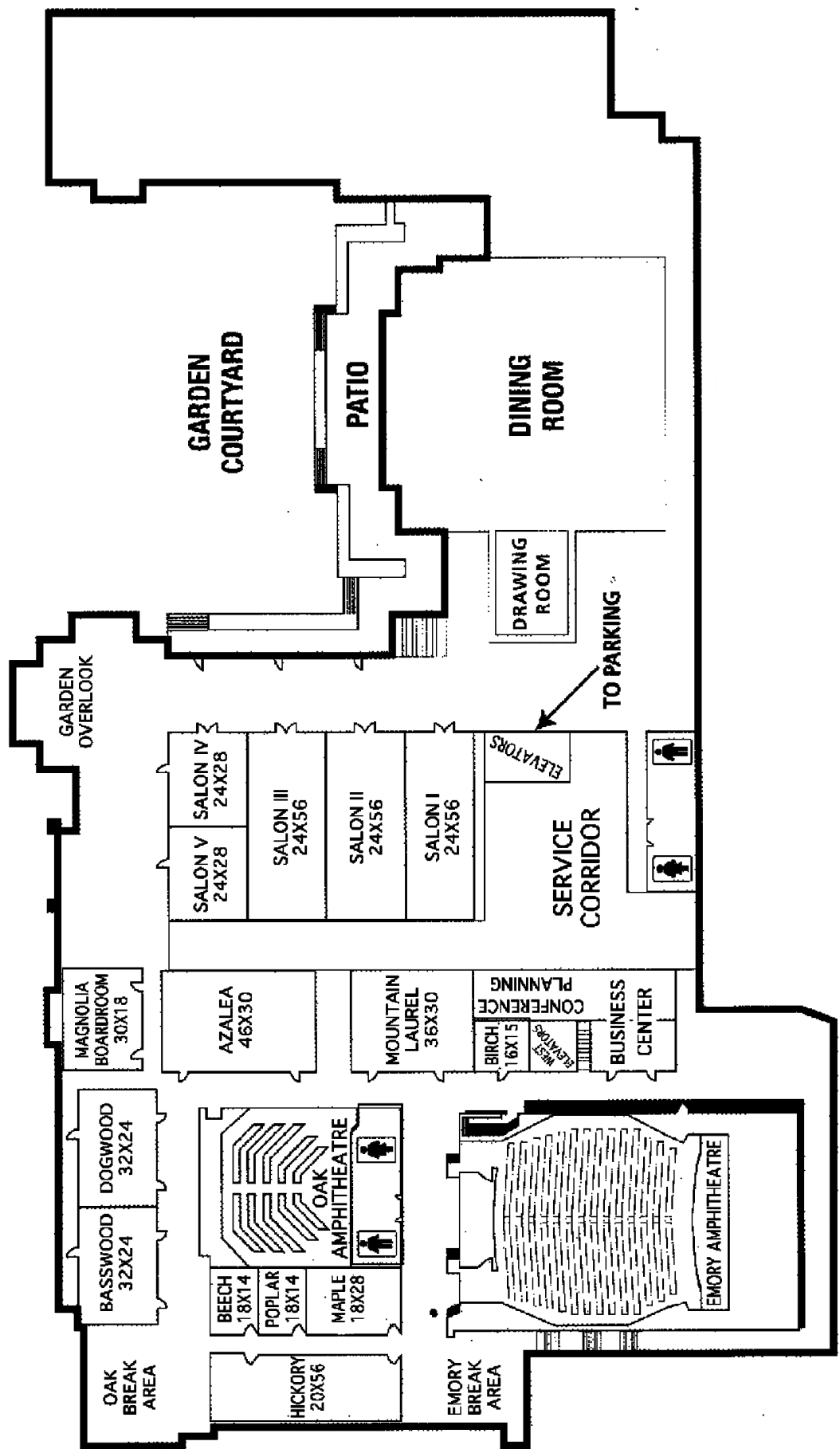
Disclosure of Financial Relationships

All individuals in a position to control the content of this CME activity (such as faculty, speakers, oral presenters, and planners) were asked to complete a statement regarding all relevant financial relationships between themselves or their spouse/partner and any commercial interest (defined by the ACCME as "any entity producing, marketing, re-selling, or distributing health care goods and services consumed by, or used on, patients"). St. Jude CME has reviewed and resolved any conflicts of interest that were identified.

Sharon Castellino, MD, has received grant/research support from Bristol-Myers Squibb. Tara Henderson, MD, MPH, has received grant/research support from Seattle Genetics.

No other speakers, planners, or other individuals with control over content have disclosed relevant financial relationships with commercial interests for themselves or their spouse/partner.

Emory Conference Center Hotel map

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DINING ROOM

DRAWING ROOM

GARDEN OVERLOOK

TO PARKING

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EMORY AMPHITHEATRE

OAK BREAK AREA

HICKORY
20X56

EMORY BREAK AREA

Keynote Speakers

Saro Armenian, DO, MPH
City of Hope, Departments of Pediatrics and
Population Sciences
Duarte, California, USA

Eric Chow, MD, MPH
Fred Hutchinson Cancer Research Center
University of Washington
Seattle Children's Hospital
Seattle, Washington, USA

Claire E. Wakefield, PhD, MPH
School of Women's & Children's Health,
University of New South Wales Medicine
Behavioural Sciences Unit, Kids Cancer Centre,
Sydney Children's Hospital
Sydney, Australia

Clinical Conundrum Speakers

Sogol Mostoufi-Moab, MD, MSCE
Department of Pediatrics
Divisions of Oncology and Endocrinology
The Children's Hospital of Philadelphia
University of Pennsylvania,
Perelman School of Medicine
Philadelphia, Pennsylvania, USA

Hanneke M. van Santen, MD, PhD
Department of Pediatric Endocrinology,
Wilhelmina Children's Hospital University
Medical Center Utrecht and Princess Maxima
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Discussants

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Professor, Pediatric Oncology
Vice Chair for Outcomes Research,
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BMT, Honorary Professor of Childhood Cancer
Great North Children's Hospital, and Northern
Institute of Cancer Research, Newcastle University
Newcastle upon Tyne, United Kingdom

Conference Program

THURSDAY, JUNE 20

2:00–7:00 p.m.	**Registration**
3:00 p.m.	**Welcome – Melissa M. Hudson, MD, Conference Chairperson**

Session I

3:15–4:15 p.m.	**Keynote Speaker: Saro Armenian, DO, MPH** *Interventions to Mitigate Health-Related Complications in Survivors*
4:15–5:30 p.m.	**Oral Abstract Presentation – Morbidity and Mortality** Moderator: Gregory T. Armstrong, MD, MSCE
4:15 p.m.	*Frailty Among Childhood Cancer Survivors: A Report from the Childhood Cancer Survivor Study (CCSS)* **Samah Hayek, DrPH**
4:30 p.m.	*Progression of Frailty in Young Adult Survivors of Childhood Cancer: A Report from the St. Jude Lifetime Cohort* **Robyn E. Partin, MS**
4:45 p.m.	*Chronic Health Conditions (CHC) and Late Mortality in Survivors of Acute Lymphoblastic Leukemia (ALL) in the Childhood Cancer Survivor Study* **Stephanie Dixon, MD**
5:00 p.m.	*Comparing Late Mortality Risks Among Childhood Cancer Survivors: A Report from the Childhood Cancer Survivor Study and British Childhood Cancer Survivor Study* **Miranda Fidler-Benaoudia, PhD**
5:15 p.m.	*Very Late Excess Mortality in Older Adults from the PanCareSurFup Study of 77,423 Five-Year Survivors of Childhood and Adolescent Cancer* **Julianne Byrne, PhD**
5:30–7:00 p.m.	**Welcome Reception**
7:00–9:00 p.m.	**Dinner** (Buffet for Emory Conference Center Hotel guests, Garden Level Dining Hall)

FRIDAY, JUNE 21

6:15–8:00 a.m.	**Dan Green Fun Run**
6:30–8:00 a.m.	**Breakfast Buffet** (Emory Conference Center Hotel guests, Garden Level Dining Hall)
	Continental Breakfast (All conference participants)
7:00 a.m.–5:00 p.m.	**Registration**

Session II

8:00 a.m.–9:00 a.m.	**Keynote Speaker: Claire Wakefield, PhD, MPH** *Intervening Early to Remediate the Psychosocial and Behavioral Late Effects of Childhood Cancer*
9:00–10:30 a.m.	**Oral Abstract Presentation – Cardiovascular** Moderator: Paul Nathan, MD, PhD, FRCP(C)
9:00 a.m.	*High Risk of Symptomatic Cardiac Ischemia in a Pan-European Cohort of Childhood Cancer Survivors: A PanCareSurFup Study* **Elizabeth (Lieke) Feijen, PhD**
9:15 a.m.	*Risk of Acute Coronary Syndromes and Heart Failure After Treatment for Testicular Germ Cell Cancer (TC) in the Platinum Era* **Michael Schaapveld, PhD**
9:30 a.m.	*Risk of Cerebrovascular Disease among 13,457 Five-Year Survivors of Childhood Cancer: A Population Based Cohort Study* **Raoul Reulen, PhD**
9:45 a.m.	*Reduction in Cardiac Events for Survivors of Childhood Cancer Treated in More Recent Eras: A Report from the Childhood Cancer Survivor Study* **Daniel Mulrooney, MD, MS**
10:00 a.m.	*Cost-Effectiveness of Screening Guidelines to Prevent Heart Failure in Childhood Cancer Survivors: A Report from the Childhood Cancer Survivor Study (CCSS)* **Matthew Ehrhardt, MD, MS**
10:15 a.m.	**Discussion – Roderick Skinner, PhD, FRCPCH**
10:30 a.m.	**Refreshment Break**

Session III

11:00 a.m.–12:00 p.m.	**Clinical Conundrums** Moderator: Lillian Meacham, MD
11:00 a.m.	*The Advantage of Thyroid Screening in Cancer Survivors: Cutting the Gordian Knot in this Clinical Conundrum* **Sogol Mostoufi-Moab, MD, MSCE**
11:20 a.m.	*Why We Should Not Screen for Thyroid Cancer in Childhood Cancer Survivors* **Hanneke M. van Santen, MD, PhD**
11:40 a.m.	**Group Discussion**
12:00 p.m.	**Lunch** (Buffet available for Emory Conference Center Hotel guests, Garden Level Dining Hall)

Session IV

1:30 – 3:15 p.m.	**Oral Abstract Presentation – Genetics** Moderator: Leslie L. Robison, PhD
1:30 p.m.	*Subsequent Neoplasm Risk Associated with Rare Variants in DNA Repair and Clinical Radiation Sensitivity Syndrome Genes: A Report from the Childhood Cancer Survivor Study* **Lindsay Morton, PhD**
1:45 p.m.	*A Novel Association Between GSTM1 Null Variant and Anthracycline-Induced Cardiac Dysfunction (ACD) in Childhood Cancer Survivors (CCS): A COG ALTE03N1 Report* **Purnima Singh, PhD, MSPH**
2:00 p.m.	*Risk Prediction of Anthracycline-Related Cardiomyopathy (AC) in Childhood Cancer Survivors (CCS): A COG-ALTE03N1 and CCSS Report* **Xuexia Wang, PhD**
2:15 p.m.	*Population-Based Genetic Risk Loci and the Risk for Diabetes Mellitus in the Childhood Cancer Survivor Study (CCSS)* **Nisha Rathore, MD**
2:30 p.m.	*The Generalizability of General-Population GWAS Hits in Childhood Cancer Survivors: An Analysis of 12 Anthropometric and Cardiometabolic Phenotypes in the St. Jude Lifetime Cohort Study (SJLIFE)* **Cindy Im, PhD**
2:45 p.m.	*Clonal Hematopoiesis in Survivors of Childhood Cancer* **Jonathan D. Fish, MD**
3:00 p.m.	**Discussion – Smita Bhatia, MD, MPH**
3:15 p.m.	**Refreshment Break**

Session V

3:45–5:15 p.m.	**Oral Abstract Presentation – Subsequent Neoplasms** Moderator: Flora Van Leeuwen, MD
3:45 p.m.	*Risk of Subsequent Primary Neoplasms in Survivors of Adolescent and Young Adult Cancer (Teenage and Young Adult Cancer Survivor Study): A Population-Based Cohort Study* **Michael Hawkins, DPhil**
4:00 p.m.	*286 Subsequent Primary Genitourinary (SPGU) Cancers in 69,460 5-Year Survivors of Childhood Cancer: A Pan-European Case-Control Study Nested Within the PanCareSurFup Cohort* **Michael Hawkins, DPhil**
4:15 p.m.	*230 Subsequent Primary Bone Tumours in 69,460 Survivors of Childhood Cancer: Pan-European Pooled Nested Case-Control Study Within PanCareSurFup* **Raoul Reulen, PhD**
4:30 p.m.	*Risk of Developing Leukemia After Chemotherapy and Radiotherapy for Childhood Cancer: An International Pooled Analysis* **Florent de Vathaire, PhD**
4:45 p.m.	*Survival Disparities for Second Primary Malignancies Diagnosed Among Childhood Cancer Survivors: A Population-Based Assessment* **Austin Brown, PhD**
5:00 p.m.	**Discussion – Michael Schaapveld, PhD**
5:15 p.m.	**Adjourn**
5:30–8:30 p.m.	**Poster Exhibition**
6:00–8:00 p.m.	**Cash Bar open**
7:00–9:00 p.m.	**Dinner** (Buffet available for Emory Conference Center Hotel guests, Garden Level Dining Hall)

SATURDAY, JUNE 22

7:30 a.m.	**Registration**
6:30–8:00 a.m.	**Breakfast Buffet** (Emory Conference Center Hotel guests, Garden Level Dining Hall)
	Continental Breakfast (All conference participants)

Session VI

8:00–9:00 a.m. **Keynote Speaker: Eric Chow, MD, MPH**
Emerging Late Effects of Novel Therapies

9:00–10:15 a.m. **Oral Abstract Presentation – Breast Cancer**
Moderator: Cecile M. Ronckers, PhD

9:00 a.m. *Subsequent Breast Cancer in Female Childhood Cancer Survivors in the St. Jude Lifetime Cohort Study (SJLIFE)*
Matthew Ehrhardt, MD, MS

9:15 a.m. *Increased Risk for Breast Cancer in Childhood Solid Cancer Survivors: Role of Nipple Radiation Dose and of Anthracyclines*
Florent de Vathaire, PhD

9:30 a.m. *Predicting Breast Cancer Risk in Childhood Cancer Survivors Treated with Chest Radiation: A Report from the Childhood Cancer Survivor Study (CCSS), and the Dutch Hodgkin Late Effects and DCOG-Later Cohorts*
Chaya Moskowitz, PhD

9:45 a.m. *Clinical Outcomes and Cost-Effectiveness of Breast Cancer Screening for Childhood Cancer Survivors Treated with Chest Radiation: A Comparative Modeling Study*
Jennifer M. Yeh, PhD

10:00 a.m. **Discussion – Tara Henderson, MD, MPH**

10:15 a.m. **Refreshment Break**

Session VII

10:30 a.m.–12:00 p.m. **Pediatric Cancer Cohort Updates**
Moderator: Sharon Castellino, MD, MSc

10:30 a.m. *Predicting Acute Ovarian Failure in Female Childhood Cancer Survivors: A Report from the Childhood Cancer Survivor Study (CCSS)*
Rebecca Clark, MSc

10:45 a.m. *Treatment Factors Associated with Fertility Impairment among Female Survivors of Childhood, Adolescent and Young Adult Cancer: A Case-Control Study (Pancarelife)*
Marleen van den Berg, PhD

11:00 a.m. *Temporal Changes in the Probability of a Live Birth in Female Childhood Cancer Survivors from the ALiCCS Cohort*
Sofie de Fine Licht, MSc, PhD

11:15 a.m. *Sexual Functioning Among Male Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)*
Jordan Gilleland Marchak, PhD

11:30 a.m. *Late-Onset Anorectal Disease and Psychosocial Impact in Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study*
Arin Madenci, MD, MPH

11:45 a.m. *The Cumulative Burden Risk-Prediction and Visualization Tool: A Report from the St. Jude Lifetime Cohort Study (SJLIFE)*
Nickhill Bhakta, MD, MPH

12:00 – 12:30 p.m. **Adjourn – Melissa M. Hudson, MD**

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Keynote Speaker Abstracts

INTERVENTIONS TO MITIGATE HEALTH-RELATED COMPLICATIONS IN SURVIVORS

Saro Armenian, DO, MPH
City of Hope, Duarte, California, USA

Over the past three decades, there have been a wealth of observational studies to inform the development of upfront clinical trials for children newly diagnosed with cancer, as well as clinical care guidelines for long-term survivors of childhood cancer. Several initiatives are under way to test and implement interventions to prevent or minimize the effect of treatment–related adverse outcomes. This presentation will provide a broad overview of completed and ongoing prevention trials across the survivorship spectrum, including primary prevention (before or during cancer treatment), secondary prevention (after completion of treatment), and integrated approaches to manage modifiable risk factors. We will highlight challenges to conducting prevention trials in this population, and identify gaps in knowledge to be addressed by current and future investigators.

EMERGING LATE EFFECTS OF NOVEL THERAPIES

Eric Chow, MD, MPH
Seattle Children's Hospital, Seattle, Washington, USA

In the past two decades, incremental improvements in the treatment of children and adolescents with cancer have led to 5-year survival rates reaching nearly 85%. In many instances, this has been achieved by delivering more intense multimodality therapy, combined with new agents and modalities. At the same time, with a greater understanding of the biology of many pediatric cancers, new agents are becoming available that offer the promise of more effective and less toxic treatment. These include agents that target various cell surface antigens and engage the adaptive immune system, as well as those that interfere with key signaling pathways involved in tumor development and growth. For local control, surgery and radiation techniques also have evolved, becoming less invasive, or featuring new techniques and particles that more precisely target the tumor and limit dose to normal tissue. Nevertheless, "targeted" agents, like conventional chemotherapy, radiotherapy, and surgery, may have off-target effects and deserve long-term follow-up of their safety and efficacy. These include injury to the endocrine, cardiovascular, and immunologic systems. New radiation and surgical techniques that theoretically reduce morbidity and improve long-term quality of life must also be validated with actual patient outcomes. In summary, while treatment options for children and adolescents diagnosed with cancer have never looked more promising, important research questions remain whether contemporary treatments will indeed be associated with improved long-term health and higher quality of life.

INTERVENING EARLY TO REMEDIATE THE PSYCHOSOCIAL AND BEHAVIORAL LATE EFFECTS OF CHILDHOOD CANCER

Claire E. Wakefield, PhD, MPH
School of Women's & Children's Health, UNSW Medicine, Sydney, Australia

This presentation will walk the audience through the available evidence on the impact of childhood cancer from the perspective of survivors and their families, focusing on psychosocial and neurocognitive late effects, as well as impacts on health behaviors (e.g. dietary intake and engagement with survivorship care). Once impacts have been established, Prof Wakefield will present the latest data on her team's suite of e-health interventions. She will present outcomes from two randomized controlled trials aiming to improve quality of life and resilience in adolescent and young adult survivors ('Recapture Life') and parents of young cancer survivors ('Cascade'). A description of the 'Re-engage' pilot and planned implementation trial will follow, highlighting a novel approach to encouraging long term survivors to access appropriate survivorship care. The presentation will conclude by presenting 'Ready Steady School', an online platform for students, parents and teachers to support survivors' return to school after cancer treatment.

Objectives:
1. Describe the long-term psychosocial and behavioral late effects of childhood cancer, including impacts on mental health, health behaviors and engagement with survivorship care.
2. Present new data on the safety, feasibility and efficacy of interventions designed to remediate the psychosocial and behavioral impacts of childhood cancer on survivors and their families.

Clinical Conundrum Abstracts

THE ADVANTAGES OF THYROID SCREENING IN CANCER SURVIVORS: CUTTING THE GORDIAN KNOT IN THIS CLINICAL CONUNDRUM

Sogol Mostoufi-Moab, MD, MSCE
Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA

Radiation exposure to the thyroid gland during childhood is a defined risk factor associated with secondary thyroid malignancy in childhood, adolescent, young adult cancer (CAYAC) survivors.[1] The risk of differentiated thyroid cancer (DTC) following radiation is strongly associated with radiation dose and young age at the time of irradiation treatment.[2,3] Secondary thyroid malignancy is most frequently diagnosed 10-20 years after primary cancer diagnosis, with reports as early as 4.2 years and as late as 38 years after primary cancer diagnosis.[1,4] In contrast to the indolent and rarely fatal course of most primary thyroid malignancies, secondary thyroid malignancies in CAYAC survivors are more likely to be multifocal at the time of diagnosis, and confer a 6.6-fold higher risk of mortality compared to pediatric patients with primary thyroid malignancy, independent of demographic, tumor, and treatment factors.[5] Earlier diagnosis of DTC is associated with lower recurrence and reduced surgical morbidity, including lower rates of hypoparathyroidism and recurrent laryngeal nerve injury. In addition to less extensive surgery, at risk survivors with early detection of DTC may require no or lower doses of radioactive iodine, further reducing potential risk of future malignancies due to radioactive iodine exposure.[6,7]

While physical exam remains the current standard of care for the detection of new thyroid nodules in CAYAC survivors, increasing evidence points to the inadequacy of this modality and the need for standardized screening programs using ultrasound (US) imaging. Thyroid US is considered the gold standard for detecting a thyroid nodule, with sensitivity and specificity of 95-100%.[8,9] In comparison, the sensitivity of neck palpation for detecting a thyroid nodule is less than 40% and specificity varies from 96-100%.[10] Given its high false negative rate, neck palpation has a poor diagnostic value for detecting the presence of a thyroid nodule that might represent DTC in CAYAC survivors. The current consensus among major thyroid societies is that thyroid US should be employed as part of routine monitoring workup of high risk populations and mainstay of management for patients with known or suspected familial predilections for thyroid cancer such as Cowden syndrome or familial adenomatous polyposis.[11]

Careful selection of the screening population using a risk prediction model will further help improve diagnostic and therapeutic yields.[12] With the advent of improved US technologies, including elastography and high-resolution US, greater characterization of specific anatomic features associated with benign and cancerous nodules is now possible with improved sensitivity and specificity.[13] The American Thyroid Association pediatric guidelines recommend fine needle aspiration biopsy (FNAB) of thyroid nodules that grow over time or display suspicious clinical or radiographic characteristics, irrespective of size. Molecular markers used in conjunction with FNAB can serve as additional diagnostic tools to obviate unnecessary surgery in the absence of genetic and molecular markers confirming thyroid malignancy in patients with indeterminate cytology.[14,15]

An allegory that captures today's thyroid cancer surveillance conundrum in CAYAC survivors is the legend of the Gordian knot. Alexander the Great faced the challenge of untying an intricate knot so entangled, making it impossible to see how it was fastened. An oracle declared that the individual capable of unraveling this Gordian knot was destined to become the ruler of Asia. While Alexander could not untie the knot, he reasoned that no rules specified how to loosen the knot. Hence, he sliced through the knot with a single stroke of his sword and ultimately went on to conquer Asia! Much like Alexander's approach, it would be technically easier to start fresh and fill the current knowledge gaps with carefully designed research studies aimed at improving surveillance and outcomes of DTC in CAYAC survivors. Research priorities and benefits of screening will provide a better understanding of the impact of genetic susceptibility on DTC risk in CAYAC survivors, changes in DTC risk by changes in clinical features of thyroid nodules over time, clarification of risk factors that may alter the latency time of radiation-induced DTC, and efficacy of DTC surveillance with neck palpation vs. thyroid US with respect to benefits and harms. US is a no risk procedure and the benefit of early diagnosis of a thyroid cancer in a high-risk population is clearly greater than the risk of the procedure. A gap in a provider's comfort level with interpreting US images, and in selecting which patients should undergo FNAB or continue with surveillance, should not be used to convey risk of the procedure in the CAYAC population at risk for secondary thyroid malignancy.

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THYROID CANCER IN CHILDHOOD CANCER SURVIVORS: WHY WE SHOULD NOT SCREEN FOR THYROID CANCER IN CHILDHOOD CANCER SURVIVORS

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During the North American Symposium on Late complications after Childhood Cancer we will have a pro and con debate about screening for differentiated thyroid cancer (DTC).

There are many arguments against screening for thyroid cancer in this population. Firstly, although indirect evidence may suggest that early detection of thyroid cancer by surveillance may be beneficial for CAYAC survivors, there is, to date, no data to support this hypothesis. Secondly, there is no data that secondary thyroid cancer behaves differently or more aggressively than sporadic thyroid cancer. The prognosis for children and adults with differentiated thyroid cancer is excellent. Thirdly, the screening tools for detection of thyroid cancer are misleading. Neck palpation is not very sensitive and may lead to under-diagnosis and false reassurance. On the other hand, neck ultrasound may be too sensitive (and lacks specificity), leading to over-diagnosis of thyroid incidentaloma and unnecessary concerns in the survivor.

For all these reasons, thyroid screening should not be advocated. The decision regarding whether to screen or not should be made by the health care provider in consultation with the survivor after careful consideration of the advantages and disadvantages of screening versus non-screening.

Oral Platform Presentations

1. SUBSEQUENT NEOPLASM RISK ASSOCIATED WITH RARE VARIANTS IN DNA REPAIR AND CLINICAL RADIATION SENSITIVITY SYNDROME GENES: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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Background: Radiotherapy for childhood cancer is associated with strikingly elevated risk for developing subsequent neoplasms (SNs). Whether mutations in DNA repair and radiation sensitivity genes modulate SN risks is largely unknown.

Methods: We conducted whole-exome sequencing in 5105 long-term childhood cancer survivors of European descent (mean follow-up=32.7 years). SnpEff and ClinVar identified potentially damaging rare variants in 476 DNA repair or radiation sensitivity genes. Conditional logistic regression assessed SN risk associated with these variants aggregated by gene or pathway (N=155 with =5 carriers). Controls were matched on sex, childhood cancer type and diagnosis age, radiation dose to the SN site, and survival. Exact p-values were calculated by permutation. Analyses used all survivors or subsets stratified on radiation dose.

Results: A total of 1108 (21.7%) survivors developed at least one SN type known to be related to ionizing radiation exposure (e.g., breast cancer, basal cell carcinoma, meningioma, thyroid cancer, sarcoma). Radiation-related SN risk was associated with homologous recombination (HR) gene variants for SN sites that received >0-<10 Gy (N=41/196 [20.9%] cases, 11.0% matched controls; odds ratio [OR]=2.20, 95% confidence interval [CI] 1.52-3.18; P=1.41x10-4), most notably for FANCM (3.1% cases, 0.5% matched controls; OR=9.91, 95%CI 3.73-26.4; P=2.85x10-4). For radiation-related SNs at sites with higher doses (=10 Gy), associations were not observed for the HR pathway (N=201/711 [14.4%] cases, 12.4% matched controls, P=0.17) but were observed for two individual genes implicated in double-strand DNA break repair, EXO1 (1.8% cases, 0.4% matched controls; OR=6.50, 95%CI 3.49-12.1; P=7.43x10-4) and NEIL3 (0% cases, 1.0% matched controls; P=3.23x10-4).

Conclusions: In this discovery study, we identified dose-specific novel associations between SN risk after radiotherapy for childhood cancer and potentially damaging rare variants in genes involved in double-strand DNA break repair, particularly HR. If replicated, these results could impact long-term screening of childhood cancer survivors and risk-benefit assessments of treatment approaches.

2. COMPARING LATE MORTALITY RISKS AMONG CHILDHOOD CANCER SURVIVORS: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY AND BRITISH CHILDHOOD CANCER SURVIVOR STUDY

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Background: It is unclear whether late-effect risks are comparable across international settings. We compared late mortality risks in the Childhood Cancer Survivor Study (CCSS) and British Childhood Cancer Survivor Study (BCCSS).

Methods: 46,474 5-year survivors of childhood cancer diagnosed from 1970-1999 and <15 years age were included: 28,248 from the CCSS and 18,226 from the BCCSS. Late mortality (death occurring at least 5 years from diagnosis) was assessed by linking to national vital statistics records. Adjusted ratios of the standardized mortality ratio (RSMR) and cumulative mortality probabilities were used to compare risks between cohorts. Treatment exposures were not available for the BCCSS, precluding comparison.

Results: The cumulative all-cause mortality at 10 years from diagnosis was significantly lower in the CCSS (4.8%; 95%CI:4.6%-5.0%) compared to the BCCSS (6.9%; 95%CI:6.5%-7.2%); this was due to a lower probability of death from recurrence/progression of the primary cancer (CCSS=3.3% vs. BCCSS=5.8%), with significant differences observed in survivors of leukemia (7.9% vs 4.0%), Hodgkin lymphoma (2.5% vs 1.3%), CNS tumors (6.4% vs 4.4%), and sarcoma (6.5% vs 4.0%). However, with increasing time from diagnosis, risks became more similar. The CCSS ultimately had a greater cumulative mortality at 40 years from diagnosis, attributable to a 2-fold higher mortality from subsequent neoplasms (SNs) (RSMR:2.0; 95%CI:1.8-2.3), cardiac (RSMR:1.7; 95%CI:1.4-2.3) and pulmonary (RSMR:1.9; 95%CI:1.4-2.5) causes, and other health-related deaths (RSMR: 2.4;95%CI:2.1-2.9). When assessed by follow-up interval, the differences between the CCSS and BCCSS increased significantly for deaths due to SNs, cardiac and pulmonary causes, and other health-related deaths as time increased. Among those diagnosed more recently, the gap in all-cause mortality widened, with CCSS survivors diagnosed 1990-1999 experiencing approximately half the excess (RSMR:0.5; 95%CI:0.5-0.6) observed in the BCCSS; this widening was driven by declines in the RSMR for most non-recurrence/progression causes of death.

Conclusions: Our findings suggest that North American survivors may have received more intensive regimens during this time period to achieve sustainable remission and cure. However, the cost of this approach was a higher risk of death from late-effects. Which approach confers a net survival advantage will depend critically on the magnitude of the excess risk of late-effect deaths as the cohorts age.

3. SUBSEQUENT BREAST CANCER IN FEMALE CHILDHOOD CANCER SURVIVORS IN THE ST. JUDE LIFETIME COHORT STUDY (SJLIFE)

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Background: Anthracycline-associated risk for subsequent breast cancer in childhood cancer survivors is hypothesized to be mediated by TP53 mutation-related gene-environment interactions. We characterized treatment/genetic risks and impact of screening for breast cancer in the St. Jude Lifetime Cohort.

Methods: Female participants underwent risk-based assessments, prior health event validation, chest radiation dosimetry, and whole genome sequencing. Breast biopsy reports were reviewed. A subgroup (n=139) underwent both breast magnetic resonance imaging (MRI) and mammography. Multivariable regression was used to calculate hazard ratios (HR) and 95% confidence intervals (95%CI).

Results: Among 1,467 women, 56 developed 68 breast cancers at a median age 38.6 (24.5-53.0) years. Cumulative incidences at ages 35 years were 1% (no chest radiation) and 8% (=10 Gy chest radiation). In adjusted models, breast cancer was associated with =20 Gy chest radiation vs. none (HR 7.6, 95%CI: 2.9-20.4), anthracycline exposure vs. none (1-249 mg/m2, HR 2.6, 95%CI: 1.1-6.2; =250 mg/m2, HR 13.4, 95%CI: 5.5-32.5), and having a breast cancer predisposition gene mutation (HR 23.0, 95%CI: 7.3-72.2). Anthracyclines =250 mg/m2 remained significantly associated with increased risk for breast cancer in models excluding survivors with cancer predisposition gene mutations, chest radiation =10 Gy, or both. Sensitivity/specificity were 53.8%/96.3% for mammography, 69.2%/91.4% for MRI, and 85.8%/99.7% for dual imaging. Breast cancers detected by imaging and/or prophylactic mastectomy compared to by physical findings were more likely to be in situ carcinomas, smaller, without lymph node involvement, and treated without chemotherapy.

Conclusions: Higher doses of anthracyclines are associated with increased risk for breast cancer independent of mutations in known cancer predisposition genes. Surveillance imaging identifies breast cancers less likely to require chemotherapy than those detected by physical findings.

4. CHRONIC HEALTH CONDITIONS (CHC) AND LATE MORTALITY IN SURVIVORS OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IN THE CHILDHOOD CANCER SURVIVOR STUDY

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Background: The impact of evolving risk-stratified therapy on long-term morbidity and mortality in survivors of childhood ALL remains largely unknown.

Methods: All-cause and health-related late mortality (HRM; captures death from late-effects occurring >5 yrs from diagnosis), subsequent (malignant) neoplasm [S(M)N], CTCAE graded CHC and neurocognitive outcomes were assessed in 5-yr survivors of ALL diagnosed <21 yrs of age from 1970-99. Therapy combinations defined 6 groups: 1970s- like (70s), standard and high risk 1980s- and 1990s-like (80sSR, 80sHR, 90sSR, 90sHR), relapse/transplant (R/BMT). Cumulative incidence and standardized mortality ratios (SMR) were calculated. Piecewise exponential and log-binomial models estimated rate ratios (RR) with 95% confidence intervals (CI).

Results: Among 6148 survivors (median age 31.5 yrs), 15-yr cumulative incidence of all-cause mortality was 5.8% (CI 5.3-6.2) and HRM was 1.5% (1.2-1.7). Compared to 70s, HRM was lower for 90sSR and 90sHR (RR 0.1, CI 0.0-0.3; 0.2, 0.1-0.7), similar to that in the US population (SMR; CI: 90sSR 1.1; 0.6-1.9, 90sHR 1.9; 0.8-3.7). 20-yr cumulative incidence of SN was 3.5% (CI 3.1-3.9). Compared to 70s, 90sSR had lower risk of benign meningioma (RR 0.1, CI 0.0-0.3) and SMN (0.3, 0.1-0.6) with no absolute excess risk compared to the US population. 90sSR was associated with a lower risk of CHCs (Table).

	Grade 3-5 CHC				Neurocognitive Impairment	
	Any	Congestive heart failure	Stroke	Major joint replacement	Task Efficiency	Memory
70s	1.0	1.0	1.0	1.0	1.0	1.0
80sHR	0.8 (0.7-1.1)	0.9 (0.3-2.6)	0.8 (0.3-1.8)	1.7 (0.4-7.6)	1.0 (0.7-1.3)	0.8 (0.6-1.1)
80sSR	0.9 (0.7-1.1)	0.6 (0.2-1.7)	1.6 (0.7-3.3)	2.3 (0.7-7.7)	1.0 (0.8-1.4)	0.8 (0.6-1.0)
90sHR	0.8 (0.6-1.1)	0.4 (0.1-1.6)	1.0 (0.3-3.0)	**3.8 (1.5-9.3)**	0.8 (0.6-1.2)	**0.7 (0.5-0.96)**
90sSR	**0.4 (0.3-0.6)**	**0.0 (0.0-0.1)**	**0.4 (0.2-0.97)**	1.9 (0.7-5.6)	**0.5 (0.4-0.7)**	**0.6 (0.5-0.8)**
R/BMT	**2.3 (1.9-2.7)**	1.9 (0.8-4.5)	**4.0 (2.3-6.9)**	**5.6 (2.2-14.3)**	0.9 (0.7-1.2)	0.8 (0.6-1.0)

RR(CI) adjusted for age at diagnosis, attained age, sex, race.

Conclusions: More recent risk-stratified therapy has succeeded in reducing risk of late mortality and CHCs among long-term survivors of ALL.

5.   PROGRESSION OF FRAILTY IN YOUNG ADULT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE ST. JUDE LIFETIME COHORT

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Background: Childhood cancer survivors are at risk for premature aging; over 8% (ages18-60 years) meet Fried Frailty Criteria (=3 of low lean muscle mass, muscle weakness, slow walking speed, exhaustion, low energy expenditure). Longitudinal changes and new onset frailty has not been studied

Methods: Childhood cancer survivors (N=1501, 51.5% male, 14.9% black, median age at diagnosis 7 [0-22] years), were evaluated clinically to ascertain frailty at baseline (median age 30 [18-45] years) and five years later. Risk factors for incident frailty and impact of baseline frailty on mortality were evaluated in proportional hazard models.

Results: Frailty increased from 6.0% (95% CI 4.1-8.9) to 11.7% (95% CI 6.7-12.2) overall, and for all diagnoses (Table). Risk factors for new onset frailty among those not frail at baseline were amputation (HR 5.1, 95% CI 1.1-14.4), anthracyclines (HR 1.2, 95% CI 1.1-1.4 per 100 mg/m2), and carboplatin (HR 1.3, 95% CI 1.1-1.5 per 2000 mg/m2). Severe, disabling or life threatening chronic conditions (HR 1.2, 95% CI 1.1-1.4 per organ system) and inactivity (HR 2.0, 95% CI 1.2-3.2) also predicted new onset frailty. Sixty-nine participants died from baseline to follow-up. Accounting for age, sex and chronic conditions, baseline frailty was associated with a 2.9 (95% CI 1.6-5.2) increased hazard of death.

Diagnosis	N	% Frail Baseline	95% CI	% Frail Follow-up	95% CI
Acute lymphoblastic leukemia	501	6.2	5.7-6.7	9.6	8.8-10.3
Other leukemia	66	7.6	5.9-9.3	16.7	13.3-20.0
Central nervous system tumor	165	10.9	9.4-12.4	16.4	14.3-18.5
Hodgkin lymphoma	177	5.1	4.4-5.8	17.0	14.9-19.0
Non-Hodgkin lymphoma	117	6.0	5.0-7.0	7.7	6.4-9.0
Neuroblastoma	67	1.5	1.1-1.8	6.0	4.6-7.3
Ewing sarcoma	30	3.3	2.2-6.7	3.3	2.2-4.5
Osteosarcoma	48	8.3	6.2-14.6	16.7	12.7-20.6
Retinoblastoma	50	0.0	0.0-0.0	6.0	4.4-7.6
Soft tissue sarcoma	84	4.8	3.8-5.8	11.9	9.7-14.1
Wilms tumor	109	3.7	3.1-4.3	16.5	13.9-19.1
Other	62	8.1	6.2-9.9	9.7	7.5-11.9

Conclusions: Prevalent frailty nearly doubled in five years and was associated with increased risk for death. Given that previous treatment exposures cannot be altered, interventions to remediate chronic disease and promote activity may impact function and longevity for childhood cancer survivors.

6. COST-EFFECTIVENESS OF SCREENING GUIDELINES TO PREVENT HEART FAILURE IN CHILDHOOD CANCER SURVIVORS: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background: Childhood cancer survivors treated with anthracyclines or chest radiation therapy (RT) are at risk for left ventricular dysfunction (LVD) and subsequent heart failure (HF). The International Guideline Harmonization Group (IGHG) recommends risk-based screening echocardiograms for LVD, but evidence supporting its frequency and cost-effectiveness is limited.

Methods: Using data from the CCSS, we developed a microsimulation model of the clinical course of LVD and HF to estimate long-term health and economic outcomes associated with screening for IGHG-defined risk groups (low [anthracycline 1-99 mg/m2 and/or RT <15 Gy], moderate [100 to <250 mg/m2 or 15 to <35 Gy], high [=250 mg/m2 or =35 Gy or (=100 mg/m2 and =15 Gy)]). We compared 1, 2, and 5-year interval-based screening to no screening. Screening performance and pharmacological treatment effectiveness were based on published studies. Costs and quality of life weights were based on US averages and published studies. Outcomes included lifetime HF risk, quality-adjusted life years (QALYs), lifetime costs, and incremental cost-effectiveness ratios (ICERs). Strategies with ICERs <$100,000/QALY gained were considered cost-effective.

Results: Among the IGHG risk groups, the lifetime HF risk in the absence of screening was 37% (high), 25% (moderate) and 17% (low). Screening every 2 or 5 years was cost-effective for the high-risk group, and every 5 years for the moderate-risk group. In contrast, routine screening may not be cost-effective for the low risk group, representing ~40% of those for whom screening is currently recommended.

Risk group	Screening interval, years	Absolute lifetime HF risk reduction, % [a]	Lifetime costs, $ [b]	ICER, $/QALY
High	No screening	–	2,130	–
	5	2.1	4,520	26,780
	2	3.1	7,230	55,840
	1	3.7	11,220	138,040
Moderate	No screening	–	1,020	–
	5	1.4	3,450	55,450
	2	2.2	6,340	124,770
	1	2.6	10,680	309,510
Low	No screening	–	570	–
	5	1.0	2,990	101,330
	2	1.5	5,940	234,190
	1	1.8	10,390	570,310

[a] Relative to none; [b] Discounted at 3% annually

Conclusions: Our findings can inform screening guidelines and suggest that LVD/HF surveillance for low-risk survivors warrants careful consideration.

7. CLINICAL OUTCOMES AND COST-EFFECTIVENESS OF BREAST CANCER SCREENING FOR CHILDHOOD CANCER SURVIVORS TREATED WITH CHEST RADIATION: A COMPARATIVE MODELING STUDY

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Background: Survivors of childhood cancer previously treated with chest radiation face elevated breast cancer risk similar to BRCA1 carriers. Children's Oncology Group (COG) guidelines recommend annual mammography with breast MRI, yet the benefits and costs of various screening strategies are uncertain.

Methods: We used two breast cancer simulation models (Model 1 and 2) from the Cancer Intervention and Surveillance Modeling Network (CISNET) and data from the Childhood Cancer Survivor Study to reflect high breast cancer and competing mortality risks among survivors. We simulated 3 screening strategies: annual mammography with MRI starting at age 25 (COG25), annual MRI starting at 25 (MRI25), and biennial mammography starting at 50 (Mammo50). Performance of mammography+/-MRI was based on published studies in BRCA1/2 carriers who have similar cancer risk. Costs and quality of life weights were based on US averages and published studies.

Results: Among a simulated cohort of 25-year-old survivors treated with chest radiation, the lifetime breast cancer mortality risk in the absence of screening was 10-11% across models. Compared to no screening, Mammo50, MRI25, and COG25 screening avert approximately 23-25%, 56-62% and 56-71% of deaths, respectively; averted deaths for COG25 compared to MRI25 were higher in Model 1 than Model 2 (9% vs. <1%). In Model 1, both MRI25 and COG25 were cost-effective; in Model 2, MRI25 was preferable (more effective, less costly than COG25).

Strategy	Model 1				Model 2			
	False-positive tests*	Incremental Costs*†	QALYs gained*†	ICER	False-positive tests*	Incremental Costs*†	QALYs gained*†	ICER
Mammo50	259	–	–	–	257	–	–	–
No screening	0	1,033,840	-74.4	‡	0	839,750	-65.4	‡
MRI25	3283	5,629,340	285.3	$19,730	3764	6,651,870	175.4	$37,920
COG25	4188	8,439,630	350.5	$43,100	4879	9,463,560	171.6	‡

ICER, incremental cost-effectiveness ratio ($/QALY)
*Per 1000
†Discounted
‡Dominated

Conclusions: Compared to no screening, initiating annual screening at younger ages for at-risk survivors averts >50% of breast cancer deaths and is cost-effective. Additional data on test performance are needed to inform recommendations on screening modality.

8. RISK PREDICTION OF ANTHRACYCLINE-RELATED CARDIOMYOPATHY (AC) IN CHILDHOOD CANCER SURVIVORS (CCS): A COG-ALTE03N1 AND CCSS REPORT

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Background: CCS treated with anthracyclines are at risk for AC. While risk increases with dose, significant inter-patient variability in AC risk suggests a role for genetic predisposition in moderating the risk and provides an opportunity to identify patients at high or low risk.

Methods: We curated candidate single nucleotide polymorphisms (SNPs) associated with AC from previous publications and used these to develop a risk prediction model, drawing upon COG-ALTE03N1 (CCS with AC [155 cases] matched with CCS without AC [256 controls]). Final Model (clinical + genetic) was obtained using backward variable selection guided by effect on area under receiver operating characteristic curve (AUC). Bootstrapping corrected for optimism of AUC. Regression coefficient estimates from Final Model were used to calculate risk scores, which were used to create risk groups. We validated the model in an independent sample from CCSS (229 cases; 5,360 controls).

Results: Previously-published SNPs (rs1786814 [CELF4], rs11864374 [ABCC1], rs1800566 [NQO1], rs4673 [CYBA], rs2232228 [HAS3]) were verified in COG-ALTE03N1 and were included, along with GxE interaction of rs1786814, rs4673, rs2232228 in a Final Model containing age at cancer, sex, race, cumulative anthracyclines (mg/m2), chest radiation, diabetes, hypertension, dyslipidemia. This yielded an optimism-corrected AUC = 0.8138, which was superior (P=0.0002) to the Clinical Model (corrected AUC=0.7677). The sensitivity/specificity of the prediction model were 73.7%/ 81.3%. The prediction model was successfully replicated in CCSS (Final Model performed significantly better than the Clinical Model, P=0.02).

Table - Characteristics	COG-ALTE03N1 Cases (n=155)	COG-ALTE03N1 Controls (n=256)	CCSS Cases (n=229)	CCSS Controls (n=5360)
Median age at cancer dx	7.2 (0-21)	7.6 (0-2)	13 (0-20)	6 (0-20)
Cumulative anthracyclines (mg/m^2) Median (range)	340 (0-760)	175 (0-825)	230 (0-918)	0 (0-1120)
Radiation to heart (n, %)	35 (23)	33 (13)	115 (50)	1248 (23)

Conclusions: It is possible to identify CCS at high or low risk for AC on the basis of genetic and clinical information. This information can be used to inform interventions in CCS.

9. POPULATION-BASED GENETIC RISK LOCI AND THE RISK FOR DIABETES MELLITUS IN THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background: Genome-wide association studies (GWAS) have identified over 60 germline susceptibility loci for diabetes mellitus (DM) in the general population. However, these variants have not been systematically evaluated among childhood cancer survivors. Therefore, we assessed the role of known DM-associated genetic variants, individually and as a genetic risk score (GRS), on DM risk in childhood cancer survivors.

Methods: The study population consisted of 4,804 childhood cancer survivors of European ancestry enrolled in the CCSS, 360 of whom self-reported incident DM and consistent medication use. We identified 62 variants associated with DM ($P<5.0 \times 10^{-8}$) in two population-based GWAS: DIAGRAM and the UK Biobank (UKBB). We used multivariable logistic regression to evaluate for the association between each individual DM variant and DM risk in the CCSS. We further estimated the OR for DM using a GRS, calculated from the unweighted sum of risk alleles across the 62 variants. All models were adjusted for relevant DM demographic and treatment characteristics previously identified in the CCSS (see Table footnote).

Results: Among the 62 population-based DM-associated variants, 45 had the same direction of effect in the CCSS, of which six also achieved P<0.05 (Table). We identified a significant association of the GRS, derived from 62 population-based GWAS variants, with incidence of DM among childhood cancer survivors (OR=1.06, 95% CI=1.03-1.08, $P=1.2 \times 10^{-5}$). Furthermore, survivors with a GRS in the highest quartile were 1.89 times (95% CI=1.34-2.66, P=0.0003) more likely to develop DM compared to survivors in the lowest quartile of the GRS.

Table. Significant population-based DM-associated variants and DM risk in the CCSS

Variant	Locus	Study	Risk Allele	OR	95% CI	P-value	OR*	95% CI	P-value
		Population-based GWAS					**CCSS**		
rs6757251	*THADA* intron	DIAGRAM	C	1.139	1.093-1.187	1.9E-10	1.51	1.38-1.64	0.007
rs2972145	*MIR5702*	UKBB	C	1.003	1.002-1.004	6.3E-11	1.24	1.17-1.31	0.014
rs116647495	*ITPR3* intron	UKBB	C	1.009	1.006-1.012	1.2E-08	1.61	1.43-1.79	0.022
rs2258238	*HMGA2* intron	UKBB	T	1.005	1.003-1.006	1.9E-09	1.28	1.18-1.38	0.039
rs4239217	*HNF1B* intron	UKBB	G	1.003	1.002-1.004	1.5E-12	1.20	1.13-1.27	0.028
rs2023681	*HORMAD2-LIF*	DIAGRAM	G	1.127	1.082-1.175	3.9E-09	1.44	1.29-1.58	0.032
GRS** with 62 variants							1.06	1.03-1.08	1.2E-05
Quartile 1							Ref		
Quartile 2							1.22	0.88-1.71	0.2378
Quartile 3							1.60	1.13-2.26	0.0083
Quartile 4							1.89	1.34-2.66	0.0003

*Adjusted for body mass index, age at follow-up, sex, genotype-derived principal components of ancestry, cancer diagnosis, decade of diagnosis, alkylating chemotherapy (yes vs. no), and abdominal radiation (yes vs. no)
**Continuous GRS

Conclusions: We found that a GRS calculated from population-based DM susceptibility loci was associated with increased DM risk in survivors of childhood cancer. This information could be leveraged to identify childhood cancer survivors at highest risk for DM who could benefit from early interventions after therapy.

10. VERY LATE EXCESS MORTALITY IN OLDER ADULTS FROM THE PANCARESURFUP STUDY OF 77,423 FIVE-YEAR SURVIVORS OF CHILDHOOD AND ADOLESCENT CANCER

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Background: Overall, mortality beyond five years after diagnosis of childhood or adolescent cancer has dropped sharply over the last 60 years. Yet mortality in long-term survivors continues to be substantially higher than in the general population.

Methods: The PanCareSurFup (PCSF) consortium pooled data from 12 cancer registries and clinics in 11 European countries. We followed 77,423 five-year survivors of cancer diagnosed before age 20 from 1940 to 2008 to determine their risk of death, especially into their middle and older years. PCSF includes 392 deaths and 24,856 person-years observed between 50 and 78 years of age, making it the largest cohort of survivors with the longest follow-up available for research to date.

Results: At the end of follow-up, 9,166/77,423 survivors (11.8%) had died compared to 927 expected, an SMR (standardized mortality ratio) of 9.89 (95% confidence interval (CI) 9.69 to 10.09), and AER (absolute excess risk) of 6.47 per 1000 person years (PY) (95% CI 6.32- 6.62). The primary malignancy was the major cause of death (55.8%), followed by a subsequent malignancy (15%). For each era of treatment, the cumulative mortality function at any time after diagnosis was lower than in every previous era of treatment. However, this is largely attributable to reduced mortality from the primary malignancy while the cumulative mortality functions from other causes of death were relatively unchanged. For all types of first malignancies, except leukemia, both observed mortality rates and AERs first dropped, reaching a minimum between 20 and 30 years from diagnosis and increased from there to the end of follow-up. Overall, at 5-9 years from diagnosis the SMR was 33.92 (95% CI 32.91 – 34.94) and AER was 11.95/1000 (95% CI 11.59-12.32), while at 50-54 years from diagnosis the SMR was 3.75 (95% CI 2.85-4.83), but the AER was 20.47/1000 (CI 13.81 – 28.57). At the end of follow-up, i.e. between 45 and 60 years from diagnosis, the mortality rate exceeded that at entry (5 years after diagnosis) for survivors of most types of first malignancy.

Conclusions: The PanCareSurFup Late Mortality study confirms and extends our understanding of the growing absolute excess mortality rate of adult survivors of childhood and adolescent cancer compared to the general population even decades after initial diagnosis. These findings should raise awareness of the need for improved services for older adults who have survived cancer during childhood or adolescence.

11.   RISK OF SUBSEQUENT PRIMARY NEOPLASMS IN SURVIVORS OF ADOLESCENT AND YOUNG ADULT CANCER (TEENAGE AND YOUNG ADULT CANCER SURVIVOR STUDY): A POPULATION-BASED COHORT STUDY

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Background: Few studies have investigated the risks of subsequent primary neoplasms (SPNs) after adolescent and young adult (AYA) cancer. We investigated the risks of specific SPNs after each of 16 types of AYA cancer.

Methods: The Teenage and Young Adult Cancer Survivor Study is a population-based cohort of 200,945 5-year survivors of cancer diagnosed when aged 15–39 years in England and Wales from Jan 1, 1971, to Dec 31, 2006. The cohort was established using cancer registrations from the Office for National Statistics and the Welsh Cancer registry. Follow-up was from 5-year survival until the first occurrence of death, emigration, or study end date (Dec 31, 2012). In this analysis, we focus on the risk of specific subsequent primary neoplasms after 16 types of AYA cancer: breast; cervical; testicular; Hodgkin lymphoma (female); Hodgkin lymphoma (male); melanoma; CNS (intracranial); colorectal; non-Hodgkin lymphoma; thyroid; soft-tissue sarcoma; ovarian; bladder; other female genital; leukaemia; and head and neck cancer. We report absolute excess risks (AERs; per 10,000 person-years).

Results: During the 2,631,326 person-years of follow-up 12,321 SPNs were diagnosed in 11,565 survivors, most frequently among survivors of breast cancer, cervical cancer, testicular cancer, and Hodgkin lymphoma. AERs of any SPNs were 19·5 per 10,000 person-years (95% CI 17·4–21·5) in survivors of breast cancer, 10·2 (8·0–12·4) in survivors of cervical cancer, 18·9 (16·6–21·1) in survivors of testicular cancer, 55·7 (50·4–61·1) in female survivors of Hodgkin lymphoma, and 29·9 (26·3–33·6) in male survivors of Hodgkin lymphoma. In patients who had survived at least 30 years from diagnosis of cervical cancer, testicular cancer, Hodgkin lymphoma in females, breast cancer, and Hodgkin lymphoma in males, we identified a small number of specific SPNs that account for 82%, 61%, 58%, 45%, and 41% of the total excess number of neoplasms, respectively. Lung cancer accounted for a substantial proportion of the excess number of neoplasms observed after each AYA cancer investigated in detail.

Conclusions: Our finding that a small number of specific SPNs account for a large percentage of the total excess number of neoplasms in long-term survivors of cervical, breast, and testicular cancer, and Hodgkin lymphoma provides an evidence base to inform priorities for clinical long-term follow-up. The prominence of lung cancer after each of these AYA cancers indicates the need for further work aimed at preventing and reducing the burden of this cancer in future survivors of AYA cancer.

12. TEMPORAL CHANGES IN THE PROBABILITY OF A LIVE BIRTH IN FEMALE CHILDHOOD CANCER SURVIVORS FROM THE ALiCCS COHORT

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Background: Over the past four decades, there has been a growing focus on fertility preservation in childhood cancer survivors. We used the unique Nordic registries to investigate if the fertility-sparing strategies increased the probability of live births in female childhood cancer survivors across decades compared with population comparisons.

Methods: In the Nordic cancer registries, we identified 8,887 females with childhood cancer in 1954-2008. A population comparison cohort of 62,908 women was randomly selected by age and country from the central population registries. All women were followed for a first live birth in the nationwide medical birth registries from 15 years of age or at 5-year survival, whichever occurred later. We calculated the cumulative probability of a first live birth and estimated the risk ratio (RR) of a live birth by maternal age across decades with population comparisons as reference adjusting for country and birth year.

Results: During 655,653 years of follow-up, we observed 3,068 and 29,892 live births among female survivors and population comparisons, respectively. At the age of 45 years, the probability of a live birth was 0.79 [95% CI 0.77-0.81] in survivors with population comparisons as reference. Risk ratios were lowest in survivors of germ-cell tumors (RR=0.48 [0.39-0.58]), CNS tumors (RR=0.64 [0.60-0.68]) and survivors with high radiation dose to the pituitary gland (RR=0.42 [0.34-0.52]). We observed a clear effect of treatment decade on the probability of live births. At 30 years of age, female survivors had a markedly lower probability of a live birth compared with population comparisons if diagnosed with cancer before 1990 (1954-1969, RR=0.65 [0.54-0.78]; 1970s, RR=0.67 [0.60-0.74]; 1980s, RR=0.69 [0.64-0.74]; 1990s, RR=0.91 [0.87-0.95]; 2000s, RR=0.94 [0.91-0.97]).

Conclusions: Overall, female childhood cancer survivors had a lower probability of a live birth than comparison women. However, in women treated most recently the probability of a live birth was approaching that of the women from the background population.

13. PREDICTING BREAST CANCER RISK IN CHILDHOOD CANCER SURVIVORS TREATED WITH CHEST RADIATION: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS), AND THE DUTCH HODGKIN LATE EFFECTS AND DCOG-LATER COHORTS

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Background: Chest radiotherapy (RT) increases breast cancer (BC) risk in childhood cancer survivors. Absolute risk BC prediction models applicable to this population are not available.

Methods: Among 1,150 female 5-year survivors diagnosed < 21 years old and treated with chest RT in CCSS (median age at last follow-up 43 years, median follow-up 32 years), 241 were diagnosed with invasive or in situ breast cancer. Using these data we combined BC relative risks with the competing risk of death to predict the absolute risk of BC based on treatment exposures and BC risk factors. Variables that maximized the competing risk time-dependent area under the curve (tAUC) were selected. Data from two Dutch cohorts on 470 female 5-year survivors of cancer diagnosed < 21 years old (median age at last follow-up 38 years, median follow-up 29 years, 84 with BC) were combined for validation.

Results: The final BC model included: chest RT field, receipt of chest RT within one year of menarche, exposure to anthracyclines, history of a first-degree relative with BC, and age at menopause. The estimated 10-year BC risk varied considerably based on these variables, from 2% to 41% (table), with highest risks among premenopausal women treated with mantle field RT within a year of menarche who had a first-degree relative with BC. In comparison, a typical 40-year old woman without a history of childhood cancer but with a first-degree relative with BC has a 10-year risk of about 3% (https://tools.bcsc-scc.org/bc5yearrisk/calculator.htm). The average tAUC on the validation cohort was 0.61.

Conclusions: BC risk varies widely among childhood cancer survivors treated with chest RT. Accurate risk prediction may aid in refining surveillance, counseling, and preventive strategies in this population.

14. RISK OF ACUTE CORONARY SYNDROMES AND HEART FAILURE AFTER TREATMENT FOR TESTICULAR GERM CELL CANCER (TC) IN THE PLATINUM ERA

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Background: Platinum-based combination chemotherapy (Pt-CT) for TC has been associated with increased coronary artery disease (CAD) risks, but estimates vary widely. Most studies only included patients treated up to the mid 1990's with follow-up after Pt-CT rarely extending beyond 20 years. Furthermore, no Pt-CT dose-response relationship with CAD risk has been established and risk of other heart diseases, such as heart failure (HF), has rarely been assessed.

Methods: Risks for CAD (with/without myocardial infarction (MI) separately) and HF were evaluated in a multicenter cohort using a case-cohort design, comprising 5,098 survivors, aged 12-50 years (median 31 years) and treated for TC between 1976-2006. Incidence of CAD/ HF was established from medical records, through questionnaires sent to general practitioners and through linkage with the cause of death registry. MI and HF rates were compared with corresponding general population rates. Dose response was assessed using a linear model: Hazard ratio $(HR)=1+\text{ß}Dose$. Departure from linearity was based on testing $F=0$ in a model with a quadratic dose-term: $HR=1+\text{ß}Dose+F\,Dose^2$.

Results: After a median follow-up of 14.1 years, 322 patients were diagnosed with CAD (155 MI) and 50 with HF (without prior CAD or MI). Cumulative incidence of MI was 5.4% (95%Confidence Interval (CI) 4.2%-6.7%) at 25 years for non-seminoma patients and 4.4% (95%CI 3.3-4.7%) for seminoma patients. The SIRs of MI or HF were not increased after seminoma, but non-seminoma patients had a 1.7-fold (95%CI 1.5-2.2) increased risk of MI compared to the general population. Although HF risk overall was not increased among non-seminoma patients (SIR 1.3, 95%CI 0.8-1.9), the SIR of HF was 1.7-fold (95%CI 1.1-2.6) increased after primary orchidectomy followed by CT. In multivariable analyses receipt of Pt-CT was associated with increased risk of MI (HR 2.3, 95%CI 1.7-3.90) and HF (HR 2.1, 95%CI 1.1-4.2), adjusting for age, supradiaphragmatic radiation dose and smoking. The HR of MI increased linearly with 33% (95%CI:20-45%) per additional 100mg/m2 Pt-CT (P-trend <0.001). The HR of heart failure as first cardiac event rose with 34% (95%CI:16-52%) per additional 100mg/m2 Pt-CT (P-trend <0.001).

Conclusions: Platinum-containing chemotherapy is associated with increased risks for CAD and HF. This is the first study showing a linear dose-response relationship for Pt-CT and MI, and the first study suggesting Pt-CT may increase HF risk in a dose-dependent manner.

15. RISK OF CEREBROVASCULAR DISEASE AMONG 13,457 FIVE-YEAR SURVIVORS OF CHILDHOOD CANCER: A POPULATION BASED COHORT STUDY

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Background: Survivors of childhood cancer are at increased risk of cerebrovascular disease (CVD), but no large-scale study has satisfactorily investigated the risks of CVD beyond age 50 years among survivors treated with cranial irradiation.

Methods: In total, 13,457 survivors included in the population-based British Childhood Cancer Survivor Study cohort were linked to Hospital Episode Statistics (HES) data for England. The risk of hospitalisation due to CVD was quantified by standardised hospitalisation ratios (SHR) and absolute excess risks (AER) per 10,000 person-years. Cumulative incidence by attained age was calculated accounting for the competing risk of death.

Results: Survivors of a central nervous system (CNS) tumour treated with cranial irradiation were at greatest risk of CVD (SHR=15.32, 95%CI:13.03-18.01), but CNS tumour survivors treated without cranial radiotherapy were still at 3-fold risk. Beyond age 60 years, on average, 3% of CNS tumour survivors treated with cranial irradiation were hospitalised annually for CVD (0.4% in the general population). For this group, the cumulative incidence was 11.6% at age 40, increased to 16.3% by age 50, and reached 26.0% by age 65, whilst this was expected to be only 4.2% from rates in the general HES population.

Conclusions: Among CNS tumour survivors treated with cranial irradiation the risk of developing CVD increases substantially between age 40 and 65 years. Clinically, such survivors should be: counselled with regards to the substantially increased risk; regularly monitored for hypertension, dyslipidaemia and diabetes; and advised on the potential benefits of exercise, healthy diet, smoking cessation and drinking within guidelines. Future research among such survivors should include: the recall for counselling and brain MRI (including MRA) to identify specific subgroups that could potentially benefit from pharmacological or surgical intervention; and establishment of a large-scale case-control study to determine the risk factors for the development of CVD for future prevention or intervention.

16. 286 SUBSEQUENT PRIMARY GENITOURINARY (SPGU) CANCERS IN 69,460 5-YEAR SURVIVORS OF CHILDHOOD CANCER: A PAN-EUROPEAN CASE-CONTROL STUDY NESTED WITHIN THE PANCARESURFUP COHORT

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Background: Very little is known about the risks and risk factors for genitourinary cancer after childhood cancer, but PanCareSurFup provides unprecedented numbers and statistical power to address these issues.

Methods: As part of PanCareSurFup, 12 countries across Europe contributed 286 cases and 286 matched controls to a case-control study nested within a cohort of 69,460 5-year survivors of childhood cancer for whom there was systematic ascertainment of subsequent primary neoplasms. Information on radiotherapy and chemotherapy exposures was abstracted from available medical records. Radiation dose reconstruction was undertaken to estimate the cumulative radiation dose to the site of the SPGU cancer in the case—and corresponding anatomical site in the matched control. Conditional logistic regression was used to calculate odds ratios (ORs) of developing a SPGU cancer for different levels of cumulative radiation dose from radiotherapy and different levels of cumulative dose of specific types of chemotherapy.

Results: There were 72, 46, 44, 35, 29, 23, 20 and 17 cancers of kidney, bladder, testis, ovary, cervix, corpus uteri, prostate and other sites, respectively. Considering all SPGU cancers together the risk of occurrence increased with increased dose of cumulative radiation (p-trend < 0.001) the risk reaching 7.2-fold (95%CI: 1.8, 29.4) within tissue exposed to at least 25 Gy compared with the risk in unexposed tissue. A similar dose-response (p-trend = 0.02) was found for kidney cancer and the corresponding risk estimate was 5.9-fold (95%CI: 0.6, 54.6). Increasing cumulative dose of alkylating agents increased the risk of all SPGU cancers (p-trend = 0.001) the risk reaching 14.0-fold (95%CI: 1.4, 141.4) among those exposed to cumulative doses of at least 20,000 mg/m2 compared with the risk among those not receiving alkylating agents. A similar dose-response (p-trend = 0.002) was found for bladder and kidney cancer combined and the corresponding risk estimate was 46.6-fold (95%CI: 1.5, 1464.8). There was also suggestive evidence of an increase in the risk of all SPGU cancers (p-trend = 0.032) and separately bladder and kidney cancers (p-trend = 0.069) with increased cumulative exposure to anthracyclines.

Conclusions: This largest every study of SPGU cancers after childhood cancer provides evidence that increased cumulative dose of radiation, alkylating agents and possibly anthracyclines are associated with an increased risk of all SPGU cancers combined and bladder and/or kidney cancers considered separately.

†Deceased 27th November 2018 to whom this research is dedicated.

17. HIGH RISK OF SYMPTOMATIC CARDIAC ISCHEMIA IN A PAN-EUROPEAN COHORT OF CHILDHOOD CANCER SURVIVORS: A PANCARESURFUP STUDY

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Background: Childhood cancer survivors are at significant risk of long-term adverse effects of their cancer and its treatment, including cardiac events. One of the objectives of the PanCareSurFup (PCSF) cardiac cohort study is to determine the cumulative incidence of symptomatic cardiac ischemia in European =5-year childhood cancer survivors.

Methods: Eight data providers (France, Hungary, Italy (2 cohorts), the Netherlands, Slovenia, Switzerland and the United Kingdom) participating in PCSF identified and validated symptomatic cardiac events among 36,205 eligible childhood cancer survivors in their cohorts. Data on severe, life-threatening or fatal cardiac ischemia were collected and graded according to the method previous described by our group (based on Criteria for Adverse Events v. 3.0 (grade 3-5)). We calculated cumulative incidences, both overall and for different subgroups based on treatment and malignancy, and used multivariate Cox regression to analyse risk factors.

Results: In all, 302 out of the 36,205 childhood cancer survivors developed severe, life-threatening or fatal cardiac ischemia during follow-up (median follow-up time after primary cancer diagnosis: 23.0 years). The cumulative incidence of ischemia by age 60 years was 5.4% (95% confidence interval (CI) 4.6%-6.2%). Men (7.1%;95% CI 5.8-8.4) had higher rates than women (3.4%; 95% CI 2.4-4.4) (p<0.0001). Treatment with radiotherapy and/or chemotherapy conferred 2-fold risk (95% CI 1.5-3.0) and ischemia appeared earlier than in childhood cancer survivors without treatment or surgery only (15% vs. 3% prior to age 30 years respectively; Figure 1 (P=0.04)).

Conclusions: This collaborative effort is the largest population of childhood cancer survivors. In our study we showed that at 60 years of age, 1 in 18 of all childhood cancer survivors developed a severe, life-threatening or fatal cardiac ischemia. Evidence-based lifestyle interventions are critical in this population to help prevent these life-threatening late adverse events.
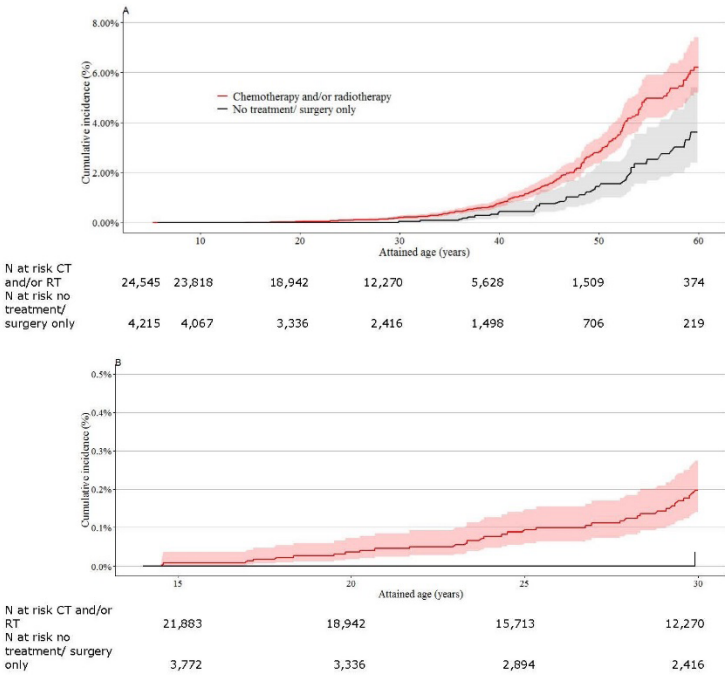
Figure 1. Cumulative incidence of symptomatic cardiac ischemia per treatment group with attained age as time-scale. **A** is for all attained ages, p-value for Gray's test is p<0.0002. **B** is zoomed in on attained ages 15-30 years, p-value for Gray's test is p=0.04. CT=any chemotherapy, RT= any radiotherapy.

18. REDUCTION IN CARDIAC EVENTS FOR SURVIVORS OF CHILDHOOD CANCER TREATED IN MORE RECENT ERAS: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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Background: Contemporary cancer protocols have incorporated modifications to minimize cardiotoxic exposures and preserve long-term health. We investigated the impact of these changes on late cardiac outcomes in a large cohort of adult survivors of childhood cancer.

Methods: Congestive heart failure (CHF), myocardial infarction (MI), valvular disease, pericardial disease, and arrhythmias were graded by the National Cancer Institute's Common Terminology Criteria for Adverse Events among 23,462 five-year cancer survivors [6,193 (26%) treated in the 1970s, 9,363 (40%) in the 1980s, and 7,906 (34%) in the 1990s] and 5,057 siblings. Cumulative incidence and 95% confidence intervals (95% CI) were estimated by treatment decade. Adjusted multivariable subdistribution hazard models were used to estimate hazard ratios (HR) and 95% CI for cardiac outcomes by decade. Mediation analysis examined risks with and without cardiotoxic exposures.

Results: For survivors [median age 6 years (range: 0-21) at diagnosis, 28 years (8.2-58) at follow-up], cardiac radiation (RT) exposure declined from 77% of those treated in the 1970s to 55% and 40% in the 1980s and 1990s. Anthracycline exposure increased from 28% to 50% to 64%. The 20-year cumulative incidence of CHF (0.69% for those treated in 1970s, 0.74% in the 1980s, 0.54% in the 1990s) and MI (0.38%, 0.24%, 0.19%) declined in more recent treatment eras (p<0.01). This change was not seen for valvular disease (0.06%, 0.06%, 0.05%), pericardial disease (0.04%, 0.02%, 0.03%) or arrhythmias (0.08%, 0.09%, 0.13%). Compared to survivors diagnosed in the 1970s, the risk of CHF, MI, and valvular disease decreased in the 1980s and 1990s, but only significantly for MI (HR 0.64 95% CI 0.47-0.89 and 0.52 95% CI 0.32-0.83). The overall MI risk was attenuated by adjustment for cardiac RT exposure (HR 0.94 95% CI 0.80-1.11), mostly among Hodgkin lymphoma (HL) survivors (HR 0.82 95% CI 0.69-0.98 [unadjusted for RT]; 1.03 95% CI 0.83-1.28 [adjusted for RT]).

Conclusions: Reductions in exposure to cardiotoxic cancer therapies have resulted in declines in adverse cardiac outcomes, particularly for the RT-associated risk of myocardial infarction among HL survivors.

19. 230 SUBSEQUENT PRIMARY BONE TUMOURS IN 69,460 SURVIVORS OF CHILDHOOD CANCER: PAN-EUROPEAN POOLED NESTED CASE-CONTROL STUDY WITHIN PANCARESURFUP

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Background: Survivors of childhood cancer are at high risk of developing subsequent primary neoplasms (SPNs) of the bone, but, to our knowledge, only a few small studies quantified the risk by cumulative radiation and chemotherapy doses.

Methods: As part of PanCareSurFup, 12 countries across Europe contributed 230 cases of a bone SPN and 230 matched controls to a case-control study nested within a cohort of 69,460 5-year survivors of childhood cancer. Information on radiotherapy and chemotherapy exposures was abstracted from available medical records. Radiation dose reconstruction was undertaken to estimate the cumulative radiation dose to the site of the bone SPN for the case—and corresponding site in the matched control. Conditional logistic regression was used to calculate odds ratios (ORs) of developing a bone SPN for different levels of cumulative radiation exposure and cumulative doses of specific type of chemotherapy. The attributable risk percentage among the exposed was also estimated.

Results: The OR of a survivor developing a bone SPN following bone tissue exposure to 5-9 Gy was 14.7-fold (95%CI: 4.1, 52.5) when compared to unirradiated survivors. The OR increased significantly with increasing doses of radiation (Ptrend<0.001) up to 52-fold (95%CI:9.3, 239.3) for doses exceeding 40 Gy. After adjustment for cumulative alkylating agent dose the linear trend remained significant with the OR for survivors exposed to 5-9 Gy being 10-fold (95%CI:1.0-100.7). At least 90% of all bone SPNs that developed after exposure to cumulative radiation doses exceeding 5 Gy were attributable to radiation exposure. Increasing exposure to alkylating agents was associated with a linear increase in the OR of developing bone SPNs (Ptrend=0.006).

Conclusions: Previous reports suggested that childhood cancer survivors are at risk of a bone SPN when bone tissue is exposed to cumulative radiation doses exceeding 10 Gy, but not below. However, here we demonstrate that the risk of developing a bone SPN is also substantially increased for survivors with bone tissue exposed to cumulative radiation doses of 5 to 10 Gy.

†Deceased 27th November 2018 to whom this research is dedicated.

20. PREDICTING ACUTE OVARIAN FAILURE IN FEMALE CHILDHOOD CANCER SURVIVORS: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background: Acute ovarian failure (AOF), which is the permanent loss of menstruation within 5 years of cancer diagnosis or failure to achieve menarche before age 18, is an established late effect of cancer treatment. Precise individual risk prediction of AOF may direct appropriate counseling and fertility preservation. We sought to develop and validate a risk prediction model as the initial step to creating an AOF risk scoring system for clinical use.

Methods: Treatment exposure and self-reported menstrual history information were obtained from 5,886 female participants in the CCSS (median age at evaluation = 13 years (range: 5-26 years)). Alkylating agent exposure was quantified using the cyclophosphamide equivalent dose (CED). Three classes of candidate risk prediction models, i.e. logistic regression models, random forests, and support vector machines, were developed and evaluated using 100 random training-test data splits. Model performance including discrimination, predictive power, and calibration were assessed with the AUC, the average positive predictive value (AP), and calibration plots respectively. The final model was externally validated using the St. Jude Lifetime Cohort Study (SJLIFE).

Results: AOF occurred in 354 survivors (6.0%) following cancer treatment. Final models from each class performed very well, with internally validated AUCs above 0.80 and APs above 0.50. Calibration plots indicated good calibration, with the observed and predicted number of cases aligning well for low and high risk patients. Since the prediction performance of the three models was similar, the logistic regression model was selected as the final model for external validation due to its simple interpretation compared to the random forest and support vector machine. Predictors in the final model included ovarian radiation dose, exposure to preparatory regimens for a bone marrow transplant, age at cancer diagnosis, and CED. When externally validated, the model was calibrated, with an AUC of 0.96 and an AP of 0.91.

Conclusions: The logistic regression model performed very well during both internal and external validation, indicating the excellent ability of the model to predict the risk of AOF. A risk scoring system will be developed using the final logistic regression model to provide individual risk prediction for AOF to childhood cancer patients.

21. A NOVEL ASSOCIATION BETWEEN GSTM1 NULL VARIANT AND ANTHRACYCLINE-INDUCED CARDIAC DYSFUNCTION (ACD) IN CHILDHOOD CANCER SURVIVORS (CCS): A COG ALTE03N1 REPORT

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Background: ACD is a leading cause of mortality in CCS. Previous studies have identified genomic variants that moderate the ACD risk. An agnostic evaluation of differential gene expression between those with and without ACD has not been explored, and could provide insights into the mechanism of cardiotoxicity.

Methods: Gene expression profiles in leukocyte RNA from anthracycline-exposed non-Hispanic white (NHW) CCS (20 with ACD [cases]; 20 without ACD [controls]) used Illumina HumanHT-12 v4.0 Expression Beadchips. Gene expression profiles in human iPSC-derived cardiomyocytes (hiPSC-CMs – Day 30) from 6 childhood cancer patients (3 each with and without CD) treated with 1µM doxorubicin or vehicle for 24 h, used RNA-seq. Genotyping in leukocyte DNA from anthracycline-exposed NHW CCS (65 cases; 76 controls) to determine if the differentially-expressed genes mapped to genetic variants that modified ACD risk, used conditional logistic regression analysis adjusted for sex, age at cancer diagnosis, chest radiation and anthracycline dose. Patient characteristics are in Table.

Results: Gene-expression in survivors: Glutathione S transferase mu 1 (GSTM1) was differentially-expressed; RT q-PCR showed significant downregulation of GSTM1 in cases (0.67 ± 0.57 vs. 1.33 ± 1.33, p=0.049). hiPSC-CMs gene expression: GSTM1 was downregulated in patients with ACD (logFC = -1.4). Genotyping: Using PCR for GSTM1 null, we observed a significant association between CD risk and GSTM1 null genotype (OR=3.0; 95%CI, 1.4-6.2, p=0.003).

Table. Patient Characteristics

Variables	Gene Expression			Genotyping		
	Cases (N=20)	Controls (N=20)	p-value	Cases (N=65)	Controls (N=76)	p-value
Median age at cancer dx (y)	6 (2-9)	6 (1-13)	0.8	8 (4-13)	9 (3-14)	0.8
Median anthracycline dose (mg/m²)	295 (241-350)	218 (121-266)	**0.002**	320 (241-375)	255 (150-368)	**0.02**

Conclusions: We report an association between GSTM1 null genotype and ACD, previously unreported likely because GWAS studies did not examined gene deletions. GSTM1 is involved in detoxification of anthracyclines. This finding could facilitate identification of childhood cancer survivors at increased risk of ACD.

22. TREATMENT FACTORS ASSOCIATED WITH FERTILITY IMPAIRMENT AMONG FEMALE SURVIVORS OF CHILDHOOD, ADOLESCENT AND YOUNG ADULT CANCER: A CASE-CONTROL STUDY (PANCARELIFE)

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Background: We aimed to identify specific treatment-related factors associated with risk of fertility impairment among female survivors of childhood, adolescent and young adult (CAYA) cancer. In addition, possible relationships between cumulative doses of chemotherapeutic agents and radiotherapy body sites and the risk of fertility impairment were investigated.

Methods: This case-control study was performed within PanCareLIFE, a pan-European research consortium (http://www.pancarelife.eu). For the current study we matched cases (survivors who were fertility impaired) to controls (survivors who were not fertility impaired) on a 1:2 basis. Matching criteria were: age at time of study, age at cancer diagnosis, country, and treatment era. Fertility impairment was defined using both questionnaire data (primary or secondary amenorrhea, use of artificial reproductive techniques, and an unfulfilled wish to conceive) and hormonal data (AMH and FSH). Multivariable logistic regression models were used to investigate the role of chemotherapeutic agents and radiotherapy body sites as risk factors for fertility impairment using two approaches: (1) a calculated score for alkylating agent exposure (Cyclophosphamide Equivalent Dose (CED) score); (2) dose categories of individual chemotherapeutic agents and radiotherapy body sites. All models were corrected for body mass index.

Results: In total, 450 cases and 882 matched controls were selected from 11 survivor cohorts in 8 countries. Preliminary results showed a positive dose-effect relationship between fertility impairment and CED-score (adjusted for treatment with radiotherapy), with survivors with a CED-score > 7121 mg/m2 being at a significantly increased risk of fertility impairment (OR (95% CI)=2.6 (1.9-3.6) p<0.001). Moreover, multivariable analysis showed that cumulative dose variables of the following treatments were significantly associated with fertility impairment: busulfan, carmustine, cyclophosphamide, melphalan, procarbazine, lower abdominal radiotherapy, and total body irradiation (TBI). Busulfan, lower abdominal radiotherapy, and TBI seem to be associated with fertility impairment at any dose, whereas gonadotoxicity of melphalan and procarbazine is suggested at medium/high (>140 mg/m2) or high dose (>5600 mg/m2) therapy, respectively.

Conclusions: We identified survivors at high risk for fertility impairment and, consequently, for a reduced reproductive life span. Clinicians should counsel both girls and young women who are about to start anti-cancer treatment, as well as adult female survivors, about future parenthood. Timely referral for fertility preservation technologies may be appropriate, following guidelines. This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement No. 602030.

## 23.   CLONAL HEMATOPOIESIS IN SURVIVORS OF CHILDHOOD CANCER

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Background: Aging is associated with the accumulation of somatic mutations and the development of clonal hematopoiesis (CH). Age-related CH is associated with increased overall mortality, and specifically cardiovascular mortality. Survivors of childhood cancer (SCC) experience phenotypic 'premature aging', including increased overall cardiovascular mortality. As SCC have been exposed to genotoxic therapies that can hasten the acquisition of somatic mutations, we hypothesize that SCC experience genotypic 'premature aging' manifesting as a higher prevalence of CH than their peers.

Methods: Study subjects were consecutive SCC seen in a long-term follow-up program who were >18 years, >5 years from completion of cancer treatment, did not undergo stem cell transplant and were enrolled in our registry. Participants underwent whole exome sequencing (WES), and were compared to de-identified age and sex-matched controls without a cancer history previously sequenced on the same platform. Somatic analysis focused on 309 previously reported CH variants in 160 genes, with control exome coverage of 120x-200x, and SCC exome coverage of 60x–160x (average 110x). A variant allele fraction cutoff of 5% was used. Fisher's two-tailed test was used to compare overall CH prevalence, and the Wilcoxon test to compare the number of CH variants, in SCC versus controls.

Results: To date, 62 SCC underwent WES, and were compared to 186 control samples. At the time of sample collection, SCC had a mean age of 26.6 years (range 18.4-50), and were 13.6 years from the completion of therapy (range 6.6-32.2). 54.8% were female. All were treated with combination chemotherapy (83.9% with anthracyclines, and 75.8% with alkylators), and 53.2% received radiation. 19% of SCC had CH, compared with 6% of controls (p=0.0039). SCC with CH had a greater number of CH variants than controls with CH (p=0.0013) (Figure 1). We also examined 260 non-CH-associated variants from previously reported 40 non-CH-associated genes, and there was no difference in variant numbers per patient between the SCC and controls.
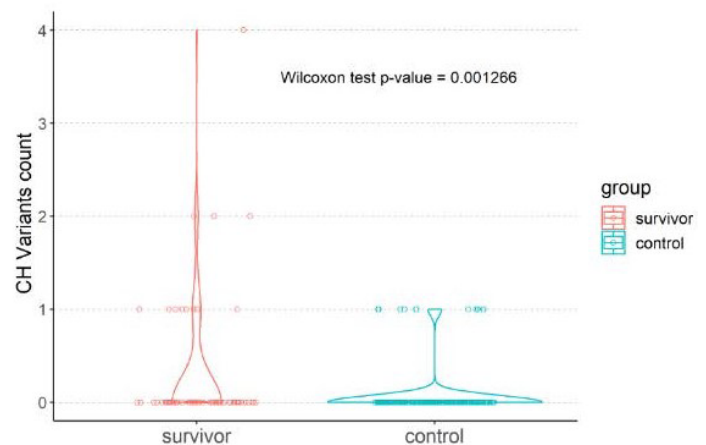
Figure 1. CH Variants (AF>0.05) count in each sample

Conclusions: SCC experience a higher prevalence of CH, and a greater number of CH variants, than age and sex-matched controls. Given the association between the development of CH and risk for cardiovascular mortality, this suggests a possible mechanism for the premature development of cardiovascular disease in SCC. Future studies will focus on the association of CH with the increased prevalence of chronic disease and mortality in SCC.

24. RISK OF DEVELOPING LEUKEMIA AFTER CHEMOTHERAPY AND RADIOTHERAPY FOR CHILDHOOD CANCER: AN INTERNATIONAL POOLED ANALYSIS

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Background: Previous studies of childhood cancer survivors have demonstrated increased risk for therapy-related leukemias. However, studies had limited numbers of subjects, limiting understanding of risks associated with specific treatments.

Methods: We initiated collaborative analyses of studies with detailed treatment data to more thoroughly investigate the respective roles of radiotherapy and chemotherapy in the occurrence of therapy-related leukemia after childhood cancer, pooling 147 therapy-related leukemia cases and 522 individually-matched controls (childhood cancer survivors with no secondary leukemia) from France, Great Britain, and an American-led consortium. Radiation dose to the active bone marrow and cumulative doses of chemotherapy were calculated based on data abstracted from medical records; pooled multivariable odds ratios were calculated using conditional logistic regression.

Results: For the combined data, the unadjusted odds ratios associated was significantly elevated for both chemotherapy (odds ratio = 6.2, 95% CI: 2.9–13.3) and radiotherapy (odds ratio = 1.6, 95% CI: 1.0–2.4). However, when chemotherapy and radiotherapy were included simultaneously in a multivariable analysis, the odds ratio for chemotherapy remained similar (odds ratio = 6.1, 95% CI: 2.8–13.2), but the radiotherapy-related risk estimate was slightly attenuated (odds ratio = 1.5, 95% CI: 0.98–2.3). In the multivariable model including radiation dose to the active bone marrow and cumulative exposure to topoisomerase II inhibitors (anthracyclines and epipodophyllotoxins), alkylating agents, platinum compounds, and vinca-alkaloids, only topoisomerase II inhibitors were independently associated with an increased therapy-related leukemia risk (odds ratio = 4.1, 95% CI: 2.2–7.7) and the risk increased with increasing cumulative dose of topoisomerase II inhibitors (P-trend = 0.0002). Risk was even higher (odds ratio = 14.5, 95%CI: 5.2–40.3) when patients received both topoisomerase II inhibitors and alkylating agents, compared to childhood cancer survivors who did not receive chemotherapy.

Conclusions: These results are particularly important given increases in topoisomerase II inhibitors use in current treatment approaches and have implications for the follow-up of childhood cancer survivors for therapy-related leukemia.

25.   SEXUAL FUNCTIONING AMONG MALE SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background: Cancer and/or subsequent treatment can have a profound impact on future sexual functioning. Multiple factors, including aging and chronic medical conditions, affect sexual performance. The purpose of this study was to characterize sexual functioning among a large sample of adult male survivors of childhood cancers.

Methods: The Sexual Function Questionnaire (SFQ) is a self-administered questionnaire designed to assess overall sexual function, using nine physical and psychosocial sub-domains. The SFQ was completed by 1595 adult male survivors from the Childhood Cancer Survivor Study (CCSS), diagnosed between 1970-86, and 269 siblings as a comparison group. Survivors whose SFQ Total scores were >2 standard deviations below the siblings' mean were categorized as reporting sexual dysfunction. Demographic variables were reported on questionnaires and treatment variables were abstracted from medical records. Multivariable logistic regression was used to identify predictors of poor sexual function.

Results: Survivors median [range] age at survey = 37.8 years [22.0 - 59.4], median years from diagnosis = 28.4 [21.4-39.2]. Sibling age at survey = 38.9 years [21.5 - 60.8]. Compared to the frequency of 4.9% in siblings, 8.3% of survivors reported sexual dysfunction. Male survivors were more likely to report sexual dysfunction if they were older at the time of survey (compared to 20-29 year reference; 40-49 years Odds Ratio [OR] 2.24, 95% Confidence Interval [CI] 1.07-4.69; =50 years OR 3.44, 95% CI 1.28-9.26), had lower educational attainment (Post-graduate reference; college graduate OR 2.28, 95% CI 1.06-4.91; some college OR 2.43, 95% CI 1.07-5.51; did not attend college OR 3.46, 95% CI 1.52-7.87), or reported problems with learning or memory (OR 1.80, 95% CI 1.02-3.18). Men who were employed were less likely to report sexual dysfunction (OR 0.32, 95% CI 0.20-0.52) than those who were unemployed. Men who received high dose cranial (OR 4.70, 95% CI 2.23-9.92) or high dose testicular (OR 4.44, 95% CI 1.84-10.72) radiation were more likely to report poor sexual functioning compared to those treated with no radiation.

Conclusions: A significant subset of adult male survivors report sexual dysfunction. The literature indicates that men typically do not voluntarily report sexual problems to their healthcare providers, nor do providers frequently ask about sexual concerns. Understanding the prevalence and predictors of sexual dysfunction among adult male childhood cancer survivors will allow clinicians to better identify and treat men to mitigate these problems.

26. LATE-ONSET ANORECTAL DISEASE AND PSYCHOSOCIAL IMPACT IN SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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Background: The prevalence of late-onset anorectal disease after childhood cancer treatment and associated psychosocial morbidity is not known.

Methods: 25,530 survivors diagnosed between 1970-1999 (median age at cancer diagnosis 6.1 years, interquartile range 3.0-12.4; age at survey 30.2, 23.8-37.7) and 5036 siblings self-reported the presence or absence of late-onset anorectal disease, defined as fistula-in-ano, anorectal stricture, or anorectal subsequent malignant neoplasm (SMN) >5 years from primary cancer diagnosis. Psychosocial outcomes were evaluated using the Brief Symptom Inventory-18 (BSI-18) and the 36-Item Short Form Health Survey (SF-36), and dichotomized into impaired vs. not impaired using thresholds set at the population norm highest 10th percentile (T-score =63) values for the BSI and the lowest 16th percentile (T-score <40) for the SF-36. Piecewise exponential models compared the rate of late-onset anorectal disease between survivors and siblings, and evaluated the associations between cancer treatments and late-onset anorectal disease among survivors. Multivariable logistic regression with generalized estimating equations examined associations between late-onset anorectal disease and emotional distress, as defined by the Brief Symptom Inventory-18 (BSI-18), and Health Related Quality of Life, using the 36-Item Short Form Health Survey (SF-36).

Results: By 45 years after diagnosis, 394 survivors (fistula, n=291; stricture, n=116; anorectal SMN, n=26) and 84 siblings (fistula, n=73; stricture, n=23; anorectal SMN, n=1) had developed late-onset anorectal disease (adjusted RR=1.2 for survivors vs. siblings, 95% CI=1.0-1.5). Among survivors, pelvic radiotherapy =30 Gy within 5 years of cancer diagnosis was associated with late-onset anorectal disease (30-49.9 Gy vs. none, adjusted rate ratio=1.6, 95% CI=1.1-2.3; =50 Gy vs. none, adjusted rate ratio=5.4, 95% CI=3.1-9.2). The 40-year post-diagnosis cumulative incidence (95% CI) of late-onset anorectal disease was 3.9% for 30-49.9 Gy and 9.7% for =50 Gy, compared with 2.7% for no radiation). Late-onset anorectal disease was associated with psychosocial impairment in all BSI-18 and SF-36 domains (Table).

Conclusions: Late-onset anorectal disease is uncommon among childhood cancer survivors but associated with previous history of higher dose directed pelvic radiotherapy. For survivors who experience late-onset anorectal disease, there is substantial psychosocial morbidity.

Table. Association between late-onset anorectal disease and impaired health-related quality of life and psychological outcomes

Measure	Odds ratio[a]	95% CI
SF-36 physical component		
Physical health	2.0	1.5 - 2.6
Physical role	2.2	1.7 - 2.9
Bodily pain	2.0	1.5 - 2.5
General health	2.1	1.6 - 2.7
Summary	2.3	1.7 – 3.0
SF-36 mental component		
Vitality	1.7	1.4 - 2.3
Emotional role	2.4	1.9 - 3.2
Social function	2.1	1.6 - 2.7
Mental health	1.9	1.4 - 2.5
Summary	1.9	1.5 - 2.6
BSI		
Depression	2.1	1.6 - 2.8
Anxiety	2.5	1.8 - 3.4
Somatization	2.5	1.9 - 3.2
Global Status Index	2.4	1.8 - 3.3

[a]Adjusted for gender, race, highest attained education, household income, body mass index, age at cancer diagnosis, age at outcome evaluation as cubic splines, pelvic radiotherapy, cranial radiotherapy. *BSI-18*, Brief Symptom Inventory-18; *CI*, confidence interval; *SF-36*, Medical Outcomes Study 36-Item Short-Form Health Survey.

27. SURVIVAL DISPARITIES FOR SECOND PRIMARY MALIGNANCIES DIAGNOSED AMONG CHILDHOOD CANCER SURVIVORS: A POPULATION-BASED ASSESSMENT

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Background: Curative therapy places childhood cancer survivors at increased risk of second primary malignancies (SPMs). However, there have been few population-based attempts to characterize differences in outcomes between SPMs in childhood cancer survivors compared with outcomes from first primary malignancies (FPMs).

Methods: We extracted clinical and demographic information from childhood cancer survivors who developed SPMs and from individuals with comparable FPMs using data from the Surveillance, Epidemiology, and End Results (SEER) program. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated with Cox proportional hazards models comparing overall survival (OS) between individuals with and without a history of childhood cancer. OS was evaluated both overall and within specific cancers diagnosed in =50 childhood cancer survivors. Models accounted for potential confounders, including sex, race, age, treatment decade, histology, and disease stage.

Results: Compared with individuals with FPMs (n=1,332,203), childhood cancer survivors (n=1,409) with a similar SPM as the FPMs experienced poorer OS (HR=1.86, 95% CI: 1.72-2.02) after accounting for age, sex, race, and decade of diagnosis (Figure). A history of childhood cancer remained a poor prognostic factor for all specific cancers evaluated, including: breast (HR=2.07, 95% CI: 1.63-2.62), thyroid (HR=3.59, 95% CI: 2.08-6.19), acute myeloid leukemia (HR=2.38, 95% CI:1.87-3.05), brain (HR=2.09, 95% CI:1.72-2.55), melanoma (HR=2.57, 95% CI: 1.55-4.27), bone (HR=1.88, 95% CI:1.37-2.57), and soft tissue sarcoma (HR=2.44, 95% CI: 1.78-3.33).

Conclusions: Compared to individuals without a prior cancer diagnosis, survivors of childhood cancer with an SPM experience inferior outcomes. These survival disparities persist across cancer types, therapeutic exposures, and clinical factors.
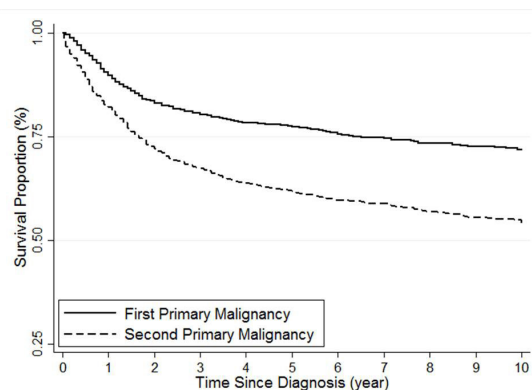
28. FRAILTY AMONG CHILDHOOD CANCER SURVIVORS: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

Samah Hayek, DrPH[1], Todd Gibson, PhD[1], Wendy Leisenring, PhD[2], Jennifer Guida, PhD[3], Monica Gramatges, MD, PhD[4], Philip Lupo, PhD[4], Rebecca Howell, PhD[5], Kevin Oeffinger, MD[6], Smita Bhatia, MD, MPH[7], Kim Edelstein, PhD[8], Melissa Hudson, MD[11], Leslie Robison, PhD[1], Paul Nathan, MD, MSC[9], Yutaka Yasui, PhD[1], Kevin Krull, PhD[1], Gregory T. Armstrong, MD, MSCE[1], Kirsten K. Ness, PT, PhD, FAPTA[1]

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Background: Childhood cancer survivors are at increased risk for frailty, which is a loss of physiological capacity that is typically observed among older adults. Purpose: Estimate the prevalence of frailty among survivors, and examine direct and indirect effects of treatment, lifestyle, and chronic disease factors on frailty.

Methods: CCSS participants who were > 5-year survivors of childhood cancer, diagnosed between 1970-1999 at <21 years of age (n=10,899, 48% male), and siblings (n=2,097, 42% male) were included. Frailty was defined from self-reported data at mean ages of 37.6±9.4 and 42.9±9.8 years for survivors and siblings, respectively, as =3 of the following: low lean mass, exhaustion, low energy expenditure, slow walking, and weakness.

Results: The prevalence of frailty among survivors was higher compared to siblings (5.8%, 95% CI: 5.4-6.3% vs. 1.9%, 95% CI 1.4-2.5%). Prevalence was highest in survivors of CNS tumors (9.5%, 5.2-13.8%), bone sarcomas (8.1%, 5.1-11.1%) and Hodgkin lymphoma (7.5%, 4.9-10.1%). In models adjusted for sex, age at assessment, and race/ethnicity, treatment exposures were associated with frailty (Table). After adjusting for the presence of chronic diseases and lifestyle factors, these associations were attenuated.

Table 1: Direct and indirect effects of treatment on frailty (n=681)

	Adjusted for Demographics		Adjusted for Demographics, Chronic Disease and Lifestyle	
	PRR[1]	(95%CI)	PRR[2]	(95%CI)
Cranial radiation	1.44	(1.32-1.58)	1.21	(1.10-1.33)
Abdominal radiation dose >40 Gy	1.38	(0.98-1.96)	1.15	(0.80-1.64)
Pelvic radiation dose ≥34 Gy	1.46	(1.20-1.80)	1.39	(1.13-1.71)
Cisplatin dose ≥600 mg/m²	1.51	(1.07-2.12)	1.24	(0.88-1.75)
Amputation	1.36	(1.13-1.63)	1.17	(0.92-1.47)
Thoracotomy	1.47	(1.26-1.73)	1.35	(1.14-1.58)

[1]Adjusted for sex, race and age at assessment. [2]Adjusted for sex, race, age at assessment, CTCAE graded 3-4 chronic diseases, smoking, physical activity and obesity.

Conclusions: The prevalence of frailty among survivors (6.0% at 38 years of age) was similar to the general population aged =65 years (9.0%). Radiation, platinum, amputation and thoracotomy increased risk for frailty. Findings suggest interventions to prevent, delay onset, or remediate chronic disease and/or promote healthy lifestyle are needed to preserve function in this population.

29. INCREASED RISK FOR BREAST CANCER IN CHILDHOOD SOLID CANCER SURVIVORS: ROLE OF NIPPLE RADIATION DOSE AND OF ANTHRACYCLINES

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Background: Although breast cancer risk is the most frequent secondary cancer risk in women after cancer during childhood, the International Late Effects of Childhood Cancer Guideline Harmonization Group recommends screening only if more than 20, Gy of radiation was delivered to the chest, starting at age 25 and after at least 8 years after radiotherapy. The evidence for an increased breast cancer risk after 10 to 19 Gy was considered moderate or low and even very low after radiation doses between 1 to 9 Gy.

Methods: We studied 3,470 women after childhood and adolescent cancer treated before 2001 in 5 cancer treatment centers in France. Individual chemotherapy drug doses were collected and radiation dose received to the nipple of the breasts and to other organs was estimated for each patient.

Results: One hundred fifteen women developed at least one breast cancer. All but 17 breast cancers occurred after the age of 30. The risk of breast cancer increased linearly with increasing radiation doses to the breast nipple (p < 0.001). Of the 94 women who had received 20 Gy or more as an average radiation dose to the 2 nipples, 24 developed breast cancer (cumulative incidence at age 50y: 34% (95%CI: 25%-44%). Lower radiation doses also increased breast cancer risk: when adjusting for other risk factors, including chemotherapy, the women who received 1 to 9 Gy, and 10 to 19 Gy as maximal dose to the breast nipples? had a relative risk of 2.7 (95%CI: 1.5-4.9) and 4.8 (95%CI: 2.4-9.4) compared to those we did receive no radiotherapy, respectively. Ovaries and pituitary irradiation significantly reduced breast cancer risk. Anthracyclines administration did not increased the risk of breast cancer: as compared to risk for those who did not received anthracyclines, the relative risk of breast cancer was 1.9 (95%CI: 1.2-3.0) in the 772 women who received less than 300 mg/m2 and 1.2 (95%IC: 0.6-2.4) in those who received more, despite an average follow-up of 27 years after anthracycline administration.

Conclusions: The risk of breast cancer was significantly increased after radiation dose (even < 20 Gy). Guidelines for follow-up of survivors may consider exposures below 20 Gy, if a positive risk-benefit ratio is demonstrated. This novel finding supports the need to update monitoring guidelines for breast cancer to optimize the long-term follow-up in survivors of childhood cancer.

30. THE CUMULATIVE BURDEN RISK-PREDICTION AND VISUALIZATION TOOL: A REPORT FROM THE ST. JUDE LIFETIME COHORT STUDY (SJLIFE)

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Background: A comprehensive account of the multimorbidity among survivors of childhood cancer was previously reported using the cumulative burden metric. Separately, risk-prediction models based on patient-specific demographic factors, and chemotherapy and radiation exposures have been reported for single chronic health conditions (CHCs). Integrated risk factor-specific prediction models for multimorbidity accounting for competing risks are lacking.

Methods: 5522 childhood cancers survivors (mean age=35.3, range 18.9-67.9) met SJLIFE eligibility (treated at St. Jude Children's Research Hospital, survived =10+ years and =18+ years old as of June 2015) and underwent longitudinal and/or retrospective clinical assessments for 168 different CHCs. 78 CHCs were further classified into 32 categories of CHCs for disease burden risk estimation. A risk factor-specific cumulative burden prediction tool, burden of cumulative chronic disease events with termination by a competing-risk event (BCCT), was developed. The BCCT method consists of two Cox proportional hazards sub-models: a model for recurrent chronic disease events and a model for death as a terminal event. Predicted data by the final model were integrated into interactive, dynamic online visualizations tools built using customized JavaScript.

Results: Cumulative burden risk-prediction models that include user-entered demographic (gender, race, age at diagnosis), chemotherapy (continuous dose: bleomycin, etoposide, cisplatin, carboplatin, vincristine, intravenous and intrathecal methotrexate, cyclophosphamide, anthracycline; yes/no exposed: steroids) and radiation (continuous dose: chest/neck, heart, brain, abdominal and pelvis) terms were developed for 32 CHC categories. Four web-based visualization tools (age series line charts, absolute and proportional stacked bar charts, ranked heatmaps and treemaps) were constructed. Using the web-based interface, users can vary and compare combinations of terms in order to assess the impact of multimodal therapy on overall and each CHC category, simultaneously, in real time.

Conclusions: We have developed a web-based risk-prediction and visualization tool as a means for users to interact with late effects burden estimates derived from SJLIFE. After validation procedures are completed, we will make these tools available on the St. Jude Cloud to provide clinicians, clinical investigators and patients a platform to identify clinical interventions, conduct pre-clinical analyses for clinical trials and develop future patient-oriented educational material.

31. THE GENERALIZABILITY OF GENERAL-POPULATION GWAS HITS IN CHILDHOOD CANCER SURVIVORS: AN ANALYSIS OF 12 ANTHROPOMETRIC AND CARDIOMETABOLIC PHENOTYPES IN THE ST. JUDE LIFETIME COHORT STUDY (SJLIFE)

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Background: Large-scale (N>10,000) meta-analyses of genome-wide association studies (meta-GWAS) have identified robust associations (P<5x10-8) between single nucleotide polymorphisms (SNPs) and many complex traits/ diseases. Methods that leverage knowledge of established meta-GWAS hits, i.e., candidate SNP/gene or genetic risk score approaches, to explore genetic predictors for late effects in survivors of pediatric cancer have broad appeal. The suitability of these methods depend on the generalizability of meta-GWAS hits in survivors, who are at greater risk for various health conditions due to cancer treatment exposures.

Methods: We compiled 46 large-scale meta-GWAS for 12 anthropometric/cardiometabolic phenotypes (published before 11/20/2017). The generalizability of 1,376 robust SNP associations was evaluated in SJLIFE, a retrospective cohort study of =5-year survivors (European ancestry, N=2,229). We used measured SNPs from whole genome sequencing and linear/logistic regression models informed by reference meta-GWAS. We estimated the expected replication power in SJLIFE and tested whether observed replication frequencies were greater/less than expected with Poisson generalized estimating equations.

Results: Given meta-GWAS effect sizes and available power in SJLIFE, we anticipated to replicate ~279 meta-GWAS hits overall. We observed significantly fewer replications than expected (observed-to-expected ratio=0.68, P=2.4x10-9). A median replication rate of 13.2% (IQR=11.4-20.2%) was observed across phenotypes. While three phenotypes showed similar replication frequencies to expected (waist-to-hip ratio, triglycerides, type 2 diabetes), the remaining nine phenotypes exhibited significant (P<0.05) or suggestive (P<0.2) replication depletion. When treatments had greater contributions to phenotype variation, treatment-exposed subgroups had greater replication depletion compared to unexposed counterparts. Analyses of functional annotations revealed that SNPs with non-replicated signals were depleted for phenotype-specific annotations compared to replicated SNPs.

Conclusions: Because of strong associations between treatments and cardiometabolic phenotypes, not all general-population meta-GWAS hits apply in childhood cancer survivors. Treatment-induced epigenetic alterations are a potential explanation for observed replication depletion in survivors, even when meta-GWAS hits are robust; we plan to explore this hypothesis with forthcoming DNA methylation data.

Poster Abstracts

P1.   NEW INSIGHTS IN CISPLATIN AND RADIATION-INDUCED LONG TERM OTOTOXICITY: A FRENCH CHILDHOOD CANCER SURVIVORS STUDY (FCCSS) REPORT

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Background: Very few is known on long term ototoxicty and on the role of radiation dose to the cochlea.

Methods: Of 7670 5-year childhood cancer survivors from the FCCSS treated before 20 years of age in 1942-2000 for solid cancer or lymphoma, 5243 with ototoxicity long-term follow-up data were included. Severe ototoxicity, defined as the need of hearing aids or Brock grade 3-4 hearing loss, was identified from self-administrated questionnaires, clinical visits and cohort linkage with the French Hospital Database and health insurance information system (SNIIRAM). The mean RT dose at inner ear was estimated using home-made software. Multivariable Cox models adjusted for gender, age at diagnosis, time period and social deprivation index was used to identify risk factors for severe ototoxicity.

Results: After a mean follow-up of 30 years, 199 cases of severe ototoxicity were identified. cisplatin (RR = 2.8, 95%CI = 1.9-4.0), melphalan (RR = 3.3, 95%CI = 1.9-5.7) and busulfan exposure (RR = 2.6, 95%CI = 1.6-4.4) were significantly associated with severe ototoxicity. Radiation dose to the inner ear was an independent risk factor for long term ototoxicity. Among the 4020 patients who did not received ototoxic chemotherapy, 113 severe ototoxicity occurred, the RR being 1.5 (IC95%:0.78-3.0), 2.2 (IC95%: 0.89-4.9), 6.6 (3.4-12.9), and 19.3 (IC95%:11.5-35.2), for inner ear dose of, respectively less than 1.0 Gy, 1 to 10 Gy, 10 to 30 Gy and more to 30 Gy, as compared to patients who did not received radiotherapy. In these patients, the Excess of Relative Risk of severe ototoxicity per gray to the inner ear was, in overall, 0.35 (IC95%CI: 0.22-0.57), reaching from 0.28 (IC95%CI: 0.17-0.49) to 0.49 (IC95%CI: 0.27-0.88), and 0.91 (IC95%: 0.18-2.82) for survivors from attained age, respectively less than 30, 30 to 50 and more than 50 years. Severe ototoxicties occuring after radiotherapy and ototoxic chemotherapy occured earlier than the ones occurring after radiotherapy alone.

Conclusions: Ototoxicity is not only a short term problem of cisplatin compounds and of high radiation dose to inner ear, but also an important long term effect of inner ear irradiation at moderate radiation dose.

P2.   A GENOME-WIDE ASSOCIATION STUDY (GWAS) OF BODY MASS INDEX (BMI) IN ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL): A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS) AND ST. JUDE LIFETIME COHORT (SJLIFE)

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Background: Obesity is an important late effect in survivors of childhood ALL. Many genetic variants are associated with BMI in the general population, yet genetic predisposition for obesity in ALL survivors is poorly understood. We conducted a GWAS of BMI among ALL survivors from the CCSS and SJLIFE.

Methods: The GWAS discovery analysis included 1,458 ALL survivors in the CCSS. Replication included 398 independent subjects from SJLIFE. BMI (kg/m2) was regressed on additive variants adjusted for age at diagnosis, age at follow-up, treatment (yes/no) with cranial radiotherapy (CRT), sex, and genotype-derived principal components.

Additional analyses were conducted stratifying on CRT, a risk factor for obesity among survivors. In addition, we used inverse-variance weighted meta-analyses to combine the CCSS and SJLIFE effect estimates for SNPs potentially associated with BMI (P<10-7) in the CCSS.

Results: We identified 23 SNPs in 17 loci associated with BMI at P<10-7 in CCSS. However, only one SNP replicated (P=0.01) in SJLIFE (Table). This variant, rs113934659, was strongly associated with BMI among subjects not treated with CRT (6.1 kg/m2 per T allele, PMeta = 2.4x10-9) and mapped to an intron in LEFTY1, which encodes a TGF-beta ligand and is primarily expressed in the colon and pancreas. Based on bioinformatics data from ENCODE, rs113934659 is located in an enhancer chromatin state in gastric tissue and the endoderm.

SNP	Locus	Risk Allele	CCSS AF	CCSS beta	CCSS P	SJLIFE beta	SJLIFE P	Meta beta	Meta P
Overall GWAS									
rs189224538	*CYP7B1-LINC00251*	G	0.007	7.3	6.0E-9	1.0	0.72	6.3	3.9E-8
CRT-yes									
rs149426421	*U6-KCNMB2*	T	0.011	6.7	9.4E-8	12.4	0.07	6.9	1.9E-8
rs575792008	*LINC00856*	A	0.006	7.5	9.4E-8	10.8	0.12	7.7	2.3E-8
CRT-no									
rs113934659	*LEFTY1*	T	0.024	6.7	9.1E-8	4.8	0.01	6.1	2.4E-9

Conclusions: We identified a potentially novel genetic locus of low frequency with large effect sizes for BMI in survivors of childhood ALL. Notably, LEFTY1 rs113934659 may regulate gene transcription in the gastrointestinal tract.

P3.   NEUROCOGNITIVE OUTCOMES IN ADULT SURVIVORS OF NEUROBLASTOMA: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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Background: Long-term survivors of neuroblastoma may be at risk for neurocognitive impairment due to young age at diagnosis and intensive multimodal therapies.

Methods: 837 survivors of neuroblastoma (57% female; median [range] age 25 [17-58] years, age at diagnosis 1 [0-21] years) and 728 siblings (56% female; age 32[16-43] years) self-reported neurocognitive problems using a neurocognitive questionnaire. Impairment was defined as scores =90th percentile of siblings in emotional regulation (ER), organization, task efficiency (TE), and memory. Multivariable log-binomial models evaluated associations with treatment exposures, era and chronic conditions (Grade 2-4 CTCAE v5) adjusting for sex, age, and race. Analyses were stratified by age at diagnosis (=1 and > 1 year) as proxy for risk group.

Results: Rates of impairment were 19.7% (ER), 25.3% organization, 21.9% TE and 19.4% for memory. Survivors had 50% higher risk of impaired TE (=1 year relative risk [RR] 1.48, 95% confidence interval [CI] 1.08-2.03; > 1 year: RR 1.58, CI 1.22-2.06) and ER (=1 year RR 1.51, CI 1.07-2.12; > 1 year RR 1.44, CI 1.06-1.95) versus siblings. Among survivors =1 year at diagnosis, treatment with platinum (RR 1.74, CI 1.01-2.97), hearing loss (RR 1.95, CI 1.26-3.00), cardiovascular (RR 1.83, CI 1.15-2.89) and neurologic (RR 2.00, CI 1.32-3.03) conditions were associated with higher risk of impaired TE. Female sex (RR = 1.54, CI, 1.02-2.33), cardiovascular (RR 1.71, CI 1.08-2.70) and respiratory (RR 1.99, CI 1.14-3.49) conditions were associated with higher risk of impaired ER. Among survivors > 1 year at diagnosis those treated in 1970-79 vs. 1990-99 had 80% higher risk of impaired ER (RR 1.77, CI 1.02-3.06). Hearing loss (RR 1.56 (1.09-2.24), respiratory (RR 2.35, CI 1.60-3.45) and cardiovascular (RR 1.74, CI 1.12-2.69) conditions were associated with higher risk of impaired TE.

Conclusions: Adult survivors of neuroblastoma are at-risk for neurocognitive impairment. Differences associated with age at diagnosis, chronic disease and treatment exposures may inform risk-stratified inventions to improve neurocognitive outcomes. Reduced risk in later eras may reflect improved supportive care and knowledge of late effects.

P4. SHORTER NAIVE T CELL TELOMERE LENGTH IS ASSOCIATED WITH THYROID SUBSEQUENT MALIGNANT NEOPLASM: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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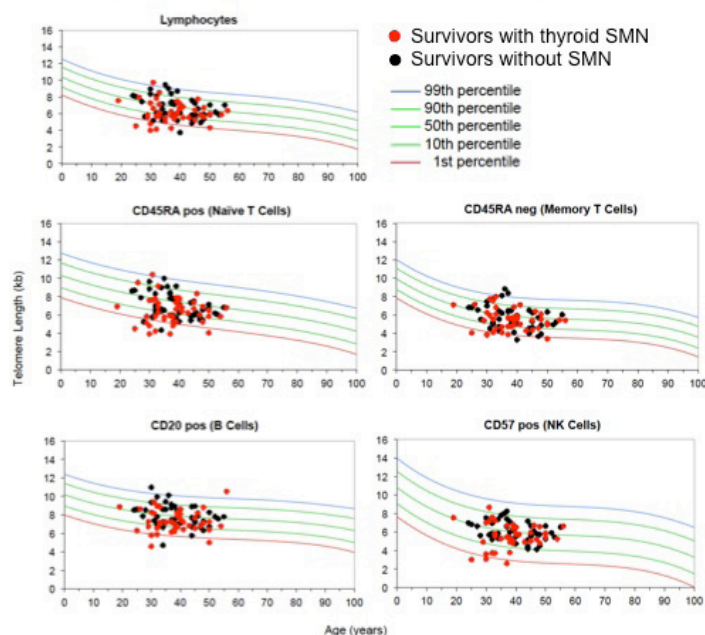
Background: Reduced blood telomere content has been associated with an increased risk for subsequent malignant neoplasms of the thyroid (thyroid SMN) in survivors of childhood cancer. Here, we further investigate this association by examining telomere length (TL) in leukocyte subsets.

Methods: Survivors were enrolled to the CCSS, a multicenter, retrospective cohort of 5-year + survivors of childhood cancer. Cases were survivors with thyroid SMN, and matched (1:1) to survivor controls without SMN by primary diagnosis, year of primary diagnosis (decade), chemotherapy (yes/no), radiation field, and follow-up time (exceeding time to SMN for the case). Stem cell transplant recipients were excluded. Absolute TL was determined from viably frozen leukocytes (lymphocytes, naïve T, memory T, B, and NK cells) by telomere flow cytometry fluorescence in situ hybridization (telomere flow FISH, Repeat Diagnostics), and transformed to age-adjusted percentiles based on age at sample collection. For each leukocyte subset, we used McNemar's test to compare frequency of very low (VL, =1st age-adjusted percentile) or low (L, >1st to =10th percentile), and a paired t-test to compare age-adjusted TL between cases and controls. Odds ratios were determined by conditional logistic regression.

Results: Of the 52 matched pairs identified, 46 pairs (92 survivors) had sufficient cell recovery for flow FISH: primary diagnoses included Hodgkin lymphoma (20 pairs), acute lymphoblastic leukemia (13 pairs), CNS tumors (7 pairs), neuroblastoma (2 pairs), non-Hodgkin lymphoma (3 pairs), and kidney tumor (1 pair). All survivors had age-adjusted TL below the population median. Cases had shorter age-adjusted TL than controls in 4/5 leukocyte subsets: lymphocytes (p=0.04), naïve T cells (p=0.02), B cells (p=0.01), and NK cells (p=0.01). Naïve T cell TL was VL in 9 cases/46 pairs vs. 2 controls/46 pairs, p=0.04). The odds of L or VL naïve T cell TL was greater in cases compared with controls (OR=2.8, 1.11-7.19, p=0.03), even after adjusting for age at diagnosis.

Telomere length in leukocyte subsets in survivors with thyroid SMN and survivors without SMN (n=46 pairs)

Conclusions: Survivors of childhood cancer had shorter age-adjusted leukocyte TL than the general population. This negative deviation was more pronounced among survivors with thyroid SMN than among those without SMN, which may reflect a differential risk among survivors for excess premature aging in the hematopoietic compartment. SMN treatment effect on TL is unlikely, as treatment for thyroid SMN is primarily surgical. In cancer-naïve populations, VL lymphocyte TL is a sensitive and specific indicator of underlying defects in telomere maintenance. In survivors of childhood cancer, VL TL in naïve T cells may identify defects in T cell-mediated cancer surveillance and augmented risk for thyroid SMN.

P5. HIGH HOSPITALIZATION RATES IN 5,650 LONG-TERM CHILDHOOD CANCER SURVIVORS: A DCOG-LATER LINKAGE STUDY

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Background: Insight in hospitalizations in long-term childhood cancer survivors is useful to understand the impact of long-term morbidity. We aimed to investigate hospitalization rates and underlying types of diagnoses in a Dutch nationwide long-term childhood cancer survivor cohort compared to matched controls, and to investigate the determinants.

Methods: We linked 5,650 five-year childhood cancer survivors from the DCOG-LATER cohort and 109,605 age- and sex-matched controls to the Dutch Hospital Discharge register, which contained detailed information on day- and inpatient hospitalizations from 1995-2016. Relative hospitalization rates (RHRs) were calculated using a Poisson regression model. Adjusting for multiple hospitalizations per person via generalized estimated equations, using a Poisson model, we investigated determinants for hospitalizations for all types of underlying diagnoses among survivors.

Results: Survivors were twice as likely to be hospitalized than reference persons (RHR 2.0, 95% confidence interval (CI) 1.9-2.2). Although survivors had more hospitalizations for 17/18 types of underlying diagnoses, they were especially more likely to be hospitalized for endocrine conditions, (RHR: 6.0, 95% CI 4.6-7.7), subsequent neoplasms (RHR: 5.6, 95% CI 4.6-6.7) and symptoms without underlying diagnoses (RHR: 5.2, 95% CI 4.6-5.8) For those types of conditions, female sex and radiotherapy were determinants.

Conclusions: Childhood cancer survivors have high hospitalization rates for many types of underlying diagnoses and radiotherapy is an important treatment-related determinant. Our results emphasize the importance of increasing awareness of these hospitalizations among physicians involved in survivorship care, and investigating ways of preventing possible unnecessary hospitalizations.
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P6. LONG-TERM RISK OF CHRONIC KIDNEY DISEASE AFTER TREATMENT OF CHILDHOOD CANCER: A COHORT STUDY

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Background: Childhood cancer survivors (CCS) are at risk for renal late effects which may require medical management and could impair their quality of life. However, very little is known about the long term risks and risk factors for kidney disease after childhood cancer. The aims of this study were to assess the incidence and to evaluate the risks of chronic kidney disease (CKD) among 5-year survivors of childhood cancer.

Methods: The FCCSS (French Childhood Cancer Survivor Study) cohort includes 7670 5-year CCS diagnosed between 1946 and 2000 before age 21 in France. CKD was defined as decreased glomerular filtration rate (GFR) <60 ml/min/1.73m² and/or the presence of histological, morphological, biological (proteinuria, albuminuria or hematuria) abnormalities for more than 3 months. Urinary infections, urinary incontinence and acute kidney failure were not included. CKD cases were identified from self-questionnaires, medical records, long-term follow-up consultation reports, the causes of death, and the French national health insurance reimbursement database (SNIIRAM). Thirty-six patients with bilateral nephroblastoma were excluded. The cumulative incidence for CKD were estimated using the non-parametric Aalen–Johansen estimator. Time since childhood cancer diagnosis was used as time scale and death from causes other than CKD was considered a competing event.

Results: In this study 150 patients with CKD were identified and validated. These patients were followed for a median of 45.2 years (range 6.1-64.4) and were diagnosed of their CKD at a median age of 52.2 years (range 9.3-70). Among the CKD patients, there were 51 (34%) with end stage kidney disease (ESKD), 27 (18%) received a kidney transplantation and 48 (32%) had a unilateral nephrectomy. The cumulative incidence 50 years after childhood cancer diagnosis (50y-CumInc) of developing all stages CKD and ESKD among all CCS was 5% (3.7%-6.6%) and 2.2% (1.3%-3.3%) respectively. The 50y-CumInc of CKD was higher among patients treated with radiation (Gray test, P=0.002), with a cumulative incidence of 7.2% (4.4%-10.9%) with radiotherapy compared to 4.5% (3.1%-6.3%) with no radiotherapy. The 50y-CumInc of CKD was also higher among nephrectomized patients (Gray test, P=0.04) compared to patients who didn't receive a nephrectomy.

Conclusions: Few studies have examined the long-term risk of CKD among CCS. In this study, patients treated with radiotherapy or nephrectomy were at highest risk of developing CKD. Studies are ongoing to determine the role of radiation dose, location and association with chemotherapy. These new findings will be useful for both survivors and those involved in their clinical management and follow-up.

P7. TITLE: SLEEP DISTURBANCES AND PHYSICAL AND MENTAL HEALTH AMONG ADULT SURVIVORS OF CHILDHOOD CANCER: THE ST. JUDE LIFETIME COHORT

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Background: In the general population, sleep disturbances are causal risk factors for physical and mental health morbidity and mortality. Sleep disturbances are prevalent among adult survivors of childhood cancer, though little is known about associations between sleep and physical and mental health in this vulnerable population.

Methods: Survivors (n=642; 53% female; mean [range] age=34.5 [19-61] years; 26 [11-50] years post-diagnosis) completed the Pittsburgh Sleep Quality Index (PSQI) and underwent comprehensive physical examinations. Poor sleep quality was dichotomized using the PSQI clinical cut-off (>5). Short sleep duration was defined as sleeping <7 hours per night. Clinically-assessed outcomes were defined using modified CTCAE criteria for cardiac, pulmonary, and endocrine conditions (grade =2) and clinically significant anxiety and depression (T-scores =63 on the Brief Symptom Inventory-18). Covariates included treatment exposures (cranial radiation, thoracic radiation, anthracyclines, antimetabolites) and demographics (age, age at diagnosis, sex, race/ethnicity). Modified Poisson regression models were used to estimate relative risks (RR) and 95% confidence intervals (CI).

Results: Poor sleep quality and short sleep duration was reported by 64% (95% CI 60.2-68.1%) and 43% (95% CI 39.2-47.0%) of survivors, respectively. In adjusted multivariable models, poor sleep quality was associated with increased risk of pulmonary (RR=1.72, 95% CI=1.20-2.46) and endocrine (RR=1.25, 95% CI=1.03-1.53) conditions. Short sleep duration was associated with an increased risk of cardiac (RR=1.23, 95% CI=1.02-1.49) and pulmonary (RR=1.36, 95% CI 1.01-1.83) conditions. Symptoms of anxiety and depression were more common in survivors with poor sleep quality (depression: RR=4.45, 95% CI=2.20-9.02; anxiety: RR=7.38, 95% CI=2.72-20.0) and short sleep duration (depression: RR=2.02, 95% CI=1.33-3.06; anxiety: RR=1.87, 95% CI=1.16-3.02).

Conclusions: Sleep disturbances were associated with adverse physical and mental health after adjustment for treatment exposures. Although the directionality of these associations cannot be ascertained, sleep is a modifiable health behavior and interventions to improve sleep may improve overall health in survivors.

P8. MELATONIN INTERVENTION FOR NEUROCOGNITIVE DEFICITS IN ADULT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE ST. JUDE LIFETIME COHORT

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Background: Neurocognitive deficits and sleep disturbances are highly prevalent among adult survivors of childhood cancer. Exogenous melatonin treatment has been associated with improved neurocognition in non-cancer adults with mild cognitive impairment. The effect of melatonin on neurocognitive function in survivors of childhood cancer has not previously been examined.

Methods: Survivors (n=580; mean age=33.5 (SD 8.8) years; 25.6 (SD 9.0) years post-diagnosis) were randomized to a 6-month trial of 3mg sustained release melatonin vs. placebo across 3 strata (1: neurocognitive impairment (NI) only; 2: NI and sleep impairment (SI); 3: SI only). Neurocognitive performance was objectively assessed at baseline and post-intervention using standardized measures of intelligence, attention, memory, processing speed, and executive function. Independent sample T-tests compared mean change scores from baseline to 6 months, separately for each stratum. A clinically significant treatment response was defined as >0.3SD improvement from baseline to post-intervention.

Results: For each stratum, intent-to-treat analyses revealed no significant differences in mean change scores for neurocognitive performance or sleep parameters from baseline to post-intervention for melatonin vs. placebo. However, among survivors with NI only, a larger proportion randomized to melatonin vs. placebo demonstrated a treatment response for attention span (48% vs 31%, P=0.06), long-term memory (49% vs 33%, P=0.07), visuomotor speed (63% vs 41%, P=0.02), and nonverbal reasoning (46% vs 28%, P=0.04). Among survivors with SI only, a larger proportion treated with melatonin demonstrated a treatment response for shifting attention (44% vs 28%, P=0.05) and short-term memory (39% vs 19%, P=0.01). Survivors who reported improved sleep from baseline to 6 months, regardless of intervention arm, demonstrated improved performance on multiple measures of attention (focused: P<0.001; inattention: P=0.001; selective: P<0.001; shifting: P=0.002).

Conclusions: Melatonin was not associated with improved neurocognitive performance in adult survivors of childhood cancer; however, a subset of survivors demonstrated a clinically significant treatment response. Improved sleep may confer benefit to neurocognitive performance. Interventions targeting sleep should be considered for this population.

P9. SERUM BIOMARKERS FOR DETECTION OF CARDIOMYOPATHY IN SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE ST. JUDE LIFETIME COHORT

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Background: Childhood cancer survivors are at increased risk for cardiovascular morbidity and mortality. Little is known about the utility of cardiac biomarkers (NT-proBNP, cardiac troponin-T [TnT]) for long-term surveillance.

Methods: Cross-sectional analyses of 1213 survivors =18 years of age and =10 years from cancer diagnosis (786 exposed to cardiotoxic therapy [174 radiation therapy (RT) alone, 366 anthracycline alone, 246 both] and 427 unexposed). TnT >0.01 ng/ml and NT-proBNP levels > 97.5th percentile age- and sex-specific cutoffs were considered abnormal. Three-dimensional left ventricular ejection fraction (LVEF), global longitudinal strain (GLS), diastolic function and cardiomyopathy (CM) according to the CTCAE v4.03 were evaluated. Generalized linear models estimated risk ratios (RR) and 95% confidence intervals (CI).

Results: Among survivors (median 8.7 [range 0.0-23.6] years at diagnosis; 35.5 [range 19.1-62.2] years at evaluation), NT-proBNP and TnT were abnormal in 22.5% and 0.4%, respectively. A dose-dependent increased risk for abnormal NT-proBNP was seen with exposure to chest RT (referent no RT, 1-<20 Gy RR 1.62 [CI 1.07-2.46], 20-<30 Gy RR 1.68 [1.23-2.30], =30 Gy RR 3.66 [2.89-4.64]; p for trend <0.0001) and anthracycline (referent no anthracycline, 1-200mg/m2 RR 1.39 [1.01-1.91], 201-350mg/m2 RR 2.28 [1.74-2.99], >350mg/m2 RR 2.99 [2.27-3.95]; p for trend <0.0001). Survivors with CM at the time of evaluation had abnormal NT-proBNP (grade 2 CM RR 1.46, CI 1.08-1.99; grade 3-4 CM 2.66, 2.02-2.39). However, among exposed survivors previously undiagnosed with clinical CM, NT-proBNP had poor sensitivity and moderate specificity in identifying those with new onset of abnormal LVEF (<53%), GLS or diastolic dysfunction: sensitivity (29%, 30%, 33%), specificity (75%, 77%, 76%). Also, 132 (20.2%) had abnormal NT-proBNP with normal LVEF (=53%).

Conclusions: Abnormal NT-proBNP levels were prevalent and associated with prior cardiotoxic therapy and established CM but were not sensitive for detection of new onset CM. Longitudinal follow-up is needed to determine whether abnormal NT-proBNP in the large number of survivors without CM is predictive of future CM.

P10. TOTAL NEUROCOGNITIVE BURDEN IN LONG-TERM SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE ST. JUDE LIFETIME COHORT STUDY

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Background: The total neurocognitive burden in long-term survivors of childhood cancer has not been characterized. Previous studies have examined neurocognitive dysfunction by individual tests or cognitive domains, without reference to comorbidity.

Methods: 2,726 adult survivors (median [range] age 33 [18-66] years; 48% female) and 355 community controls (age 34 [18-70] years; 55% female) completed neuropsychological tests resulting in 20 indices of neurocognitive function (4 indices in each of 5 domains). Moderate to severe neurocognitive impairment was defined as age-adjusted z-scores = -2.0 compared to normative data. Burden was defined as the total number of impaired measures per participant. Multivariable logistic regression analyses were used to compare burden between survivors and controls, and to examine the effects of treatment, sex, age at diagnosis, and time since diagnosis within survivors.

Results: 31% of survivors and 11% of controls were impaired on = 2 measures, and 11% of survivors and 2% controls were impaired on = 5 measures. Within domains, survivors were 4-9 times more likely to have = 2 impaired measures compared to controls (IQ/academics RR 9.21, 95% CI 2.93-29.01; attention RR 3.92, 95% CI 2.06-7.45; processing speed RR 7.07, 95% CI 2.60-19.17; memory RR 3.74, 95% CI 2.02-6.92; executive function RR 6.94, 95% CI 2.56-18.83). Survivors of CNS tumors, acute lymphoblastic leukemia, rhabdomyosarcoma, Wilms tumor, acute myeloid leukemia, osteosarcoma, and Hodgkin lymphoma (burden = 3.67, 1.81, 1.51, 1.50, 1.39, 1.29, 1.27, respectively) had significantly greater total burden compared to controls (burden = 0.55, all p's<0.02). Among survivors, cranial radiation therapy (CRT) moderated the association between burden and age at diagnosis (interaction p<0.001) with greater burden for those who received CRT at younger ages. Compared to male survivors, female survivors demonstrated greater burden with younger age at diagnosis but lower burden with older age (interaction p<0.001). Females also showed lower burden with less time since diagnosis, but greater burden with more time (interaction p=0.01). Female survivors demonstrated lower risk of impairment in processing speed (RR 0.72, 95% CI 0.52-0.99) but higher risk in memory (RR 1.89, 95% CI 1.44-2.48).

Conclusions: Long-term survivors of childhood cancer are at elevated risk for greater neurocognitive burden compared to community controls, indicating the need for multifaceted interventions.

P11. LONG TERM MORBIDITY AND MORTALITY AMONG SURVIVORS OF INFANT NEUROBLASTOMA: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background: Infants with neuroblastoma typically have low-risk disease with excellent survival. Therapy has been de-intensified over time to minimize late effects, however the impact on survivors' risk of late mortality, subsequent malignant neoplasms (SMN), and chronic health conditions (CHC) is unclear.

Methods: We evaluated late mortality, SMNs and CHCs (graded according to CTCAE v4.03), overall and by diagnosis era, among 990 5-year neuroblastoma survivors diagnosed at <1 year of age between 1970-1999. Cumulative mortality, standardized mortality ratios (SMR), and standardized incidence ratios (SIR) of SMNs were estimated using the National Death Index and SEER rates, respectively. Cox proportional hazards estimated hazard ratios (HR) and 95% confidence intervals (CI) for CHC, compared to 5,051 CCSS siblings.

Results: Among survivors (48% female; median attained age: 24 years, range 6-46), there was increased treatment with surgery alone across the 1970s, 1980s and 1990s (21.5%, 35.3%, 41.1%, respectively), decreased treatment with combination surgery + radiation (22.5%, 5.3%, 0.3%, respectively) and surgery + radiation + chemotherapy (28.7%, 14.7%, 9.3%, respectively). The 20-year cumulative mortality was 2.3% (95% CI, 1.4-3.8), primarily due to SMNs (SMR$_{SMN}$=10.0, 95% CI, 4.5-22.3). The 20-year cumulative incidence of SMN was 1.2% (95% CI, 0.3-3.2), 2.5% (95% CI, 1.3-4.4), and zero for those diagnosed in the 1970s, 1980s, and 1990s, respectively. SIR was highest for renal SMNs (SIR 12.5, 95% CI, 1.7-89.4). Compared to siblings, survivors were at increased risk for grade 1-5 CHC (HR 2.1, 95% CI, 1.9-2.3) with similar HR across eras (HR$_{1970s}$=1.9, 95% CI, 1.6-2.2; HR$_{1980s}$=2.2, 95% CI, 1.9-2.6; HR$_{1990s}$=2.0, 95% CI, 1.7-2.4). The HR of severe, disabling, life-threatening and fatal CHC (grades 3-5) decreased in more recent eras (HR$_{1970s}$=4.7, 95% CI, 3.4-6.6; HR$_{1980s}$=4.4, 95% CI, 3.2-6.2; HR$_{1990s}$=2.9, 95% CI, 2.0-4.3).

Conclusions: Survivors of infant neuroblastoma remain at increased risk for late mortality, SMN, and CHCs many years after diagnosis. However, the risk of grade 3-5 CHCs has declined in more recent eras, likely reflecting de-intensification of therapy for low and intermediate risk disease.

P12. ADVERSE EVENTS (AEs) IN CHILDHOOD CANCER PATIENTS TREATED WITH TARGETED THERAPY

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Background: Targeted therapies inhibit pathways integral to proliferation and survival of cancer cells. Due to rarity of childhood cancer, toxicity profiles of targeted therapies have not been systematically examined. We describe the risk of AEs in childhood cancer patients treated with targeted therapy.

Methods: We used a matched case-control design. Cases (n=44) included patients treated with conventional + targeted therapy matched to controls (n=76) treated with conventional therapy only, on primary cancer, age at diagnosis, sex, race/ethnicity, year of diagnosis, and time from diagnosis. AEs were determined using CTCAE v5.0. The 1,721 individual observed AEs were consolidated into 10 organ-system-based health conditions. Cox regression analysis was used, with targeted therapy exposure as a time-varying variable. Analyses were adjusted for exposure to radiation and surgery.

Results: Median age at diagnosis was 11.1y (0.4-21.3y) for cases and 8.4y (0.5-19.7y) for controls. Cases and controls were followed for a mean of 4.8y (cases: 3.3y; controls: 5.7y) from diagnosis to last follow-up or death. Cancer diagnoses included: ALL (n=46), sarcoma (n=32), brain tumors (n=26), other (n=16). Targeted therapies included Dasatinib (31.8%), Bevacizumab (25%), Imatinib (20.5%), other (20.7%). The following AEs were more prevalent in cases: hematuria (61.4% vs 27.6%, p=0.0003), liver injury (97.7% vs 76.3%, p=0.002), neuropathy (54.6% vs 29.0%, p=0.005), pericardial effusion (15.9% vs 2.6%, p=0.008), pleural effusion (43.2% vs 5.3%, p<0.001). Targeted therapy exposure was associated with a higher risk of gastrointestinal (OR=2.1, 95%CI, 1.1-3.9, p=0.02), musculoskeletal (OR=4.8, 95%CI, 1.8-12.7, p=0.002), cardiac (OR=2.5, 95%CI, 1.3-4.7, p=0.007), endocrine (OR=2.7, 95%CI, 1.4-5.0, p=0.003), pulmonary (OR=4.8, 95%CI, 2.2-10.4, p <0.001) and dermatologic (OR=2.3, 95%CI, 1.0-5.1, p=0.04) complications.

Conclusions: Exposure to targeted therapies was associated with increased risk of key AEs. Further analyses need to examine the association of AEs with specific targeted therapies.

P13.   RISK OF SUBSEQUENT COLORECTAL CANCERS AFTER A SOLID TUMOR IN CHILDHOOD: EFFECTS OF RADIATION THERAPY AND CHEMOTHERAPY

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Background: Very few previous studies have addressed the question of colorectal cancer (CRC) after childhood cancer treatment. We aimed to quantify the roles of radiation therapy and chemotherapy agents in the occurrence of subsequent CRC.

Methods: A nested case–control study was conducted using 36 CRC cases and 140 controls selected from 7032 five-year survivors of the French Childhood Cancer Survivor Study (FCCSS) cohort, treated from 1945 to 2000 in France. The radiation dose-distribution metrics at the site of CRC and doses of individual chemotherapeutic agents were calculated. Conditional logistic regressions were performed to calculate odds ratios (ORs).

Results: Overall, patients who received radiotherapy with estimated dose to colon had a 4.3-fold (95% CI, 1.3–17.6) increased risk for CRC compared with patients who did not receive radiotherapy, after adjustment for chemotherapy. This risk increased to 8.9-fold and 19.3-fold among patients who received radiation doses ranging from 20 to 29.99 Gy and =30 Gy, respectively. Our data reported a significantly elevated OR for anthracyclines, after controlling for radiotherapy and MOPP regimen. But, restricted analyses excluding patients who had received =30 Gy showed that only radiation doses ranging from 20 to 29.99 Gy produced a significant increase in subsequent CRC risk (OR = 7.8; 95% CI, 1.3–56.0), after controlling for anthracyclines and MOPP regimen.

Conclusions: The risk of subsequent CRC was significantly increased after radiation dose (even < 30 Gy). This novel finding supports the need to update monitoring guidelines for CRC to optimize the long-term follow-up for subsequent CRC in survivors of childhood cancer.

P14.   POST-HEMATOPOEITIC STEM CELL TRANSPLANT VACCINE ADHERENCE IN PEDIATRIC PATIENTS

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Background: Hematopoietic stem cell transplant (HCT) has become a treatment of choice for multiple medical conditions. Infections are a leading cause of mortality after HCT and vaccination is one of the most important preventive strategies available for post-HCT patients. The Infectious Disease Society of America (IDSA) has guidelines regarding re-vaccination. Our goal was to retrospectively determine adherence to all recommended vaccines based on the 2013 IDSA guidelines up to 2 years post-HCT in a large pediatric HCT program.

Methods: We retrospectively reviewed electronic medical records of all patients who underwent HCT or received post-HCT care at Children's Healthcare of Atlanta (CHOA) from January 2010 to December 2016. We reviewed vaccine administration data using the Georgia Registry of Immunization Transactions and Services, and determined adherence to IDSA guidelines. Post-HCT vaccination schedules were provided to families prior to their transition back to their health care provider. Pneumococcal, influenza, and meningococcal vaccines were administered to patients with sickle cell disease (SCD) during follow up in the multidisciplinary "Ex-Sickle" late-effects clinic. We compared vaccination coverage in SCD post-HCT to coverage in other diseases. We used multivariate logistic regression to identify risk factors for low compliance. Our final model included age group, gender, and health insurance coverage and clinic type. P-values <0.05 were considered statistically significant. Statistical analyses were performed using R (version 3.4.2).

Results: Of 237 patients surviving two years post-HCT, none were fully adherent to IDSA guidelines (Table 1). Given that no patients were fully adherent, the remainder of our results focused on whether patients received any of doses of the recommended vaccinations, regardless of time since HCT. Leukemia/Lymphoma (LL) patients had lower odds of receiving pneumococcal polyscaaharide vaccine (PPV23) (OR: 0.12; 95% CI: 0.05, 0.29) and meningococcal vaccine (MCV)(OR: 0.40; 95% CI: 0.16, 0.96) compared to patients with SCD patients. Solid Tumor/Brain Tumor (ST/BT) patients had lower odds of receiving pneumococcal conjugate vaccines (PCV 13) (OR: 0.17; 95% CI: 0.05, 0.45), PPV 23 (OR: 0.10; 95% CI: 0.04, 0.26), and MCV (OR: 0.11; 95% CI: 0.04, 0.28) when compared to SCD patients. Immune Deficiency (ID) patients had lower odds of receiving PPV 23 (OR: 0.06; 95% CI: 0.01, 0.24) and MCV (OR: 0.08; 95% CI: 0.02, 0.29) vaccines relative to SCD patients.

Table 1: Number (percent) of patients that were not vaccinated, were vaccinated but did not adhere to, and adhered to IDSA 2013 guidelines by vaccine.

Vaccine	Disease					
	LL[1]	ST/BT[2]	Hem[3]	ID[4]	SCD[5]	other
Dtap/Tdap						
Adhered	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)
Did Not Adhere	56 (63.6%)	44 (62.9%)	17 (70.8%)	10 (50.0%)	23 (69.7%)	2 (100.0%)
Not Vaccinated	32 (36.4%)	26 (37.1%)	7 (29.2%)	10 (50.0%)	9 (27.3%)	0 (0.0%)
HiB						
Adhered	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Did Not Adhere	50 (56.8%)	31 (44.3%)	13 (54.2%)	9 (45.0%)	20 (60.6%)	2 (100.0%)
Not Vaccinated	38 (43.2%)	39 (55.7%)	11 (45.8%)	11 (55.0%)	13 (39.4%)	0 (0.0%)
Hep B						
Adhered	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)
Did Not Adhere	47 (53.4%)	29 (41.4%)	13 (54.2%)	10 (50.0%)	20 (60.6%)	2 (100.0%)
Not Vaccinated	41 (46.6%)	41 (58.6%)	11 (45.8%)	10 (50.0%)	12 (36.4%)	0 (0.0%)
Hep A						
Adhered	2 (2.3%)	2 (2.9%)	0 (0.0%)	1 (5.0%)	1 (3.0%)	0 (0.0%)
Did Not Adhere	49 (55.7%)	30 (42.9%)	15 (62.5%)	9 (45.0%)	18 (54.5%)	1 (50.0%)
Not Vaccinated	37 (42.0%)	38 (54.3%)	9 (37.5%)	10 (50.0%)	14 (42.4%)	1 (50.0%)
PCV 13						
Adhered	2 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.1%)	0 (0.0%)
Did Not Adhere	59 (67.0%)	34 (48.6%)	14 (58.3%)	14 (70.0%)	26 (78.8%)	2 (100.0%)
Not Vaccinated	27 (30.7%)	36 (51.4%)	10 (41.7%)	6 (30.0%)	5 (15.2%)	0 (0.0%)
PCV 23						
Adhered	2 (2.3%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	10 (30.3%)	0 (0.0%)
Did Not Adhere	15 (17.0%)	12 (17.1%)	4 (16.7%)	1 (5.0%)	12 (36.4%)	2 (100.0%)
Not Vaccinated	71 (80.7%)	58 (82.9%)	20 (83.3%)	18 (90.0%)	11 (33.3%)	0 (0.0%)
IPV						
Adhered	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)
Did Not Adhere	49 (55.7%)	43 (61.4%)	14 (58.3%)	10 (50.0%)	21 (63.6%)	2 (100.0%)
Not Vaccinated	39 (44.3%)	27 (38.6%)	10 (41.7%)	10 (50.0%)	11 (33.3%)	0 (0.0%)
MMR						
Adhered	2 (2.3%)	2 (2.9%)	0 (0.0%)	1 (5.0%)	1 (3.0%)	0 (0.0%)
Did Not Adhere	33 (37.5%)	34 (48.6%)	9 (37.5%)	8 (40.0%)	12 (36.4%)	1 (50.0%)
Not Vaccinated	53 (60.2%)	34 (48.6%)	15 (62.5%)	12 (60.0%)	20 (60.6%)	1 (50.0%)
MCV						
Adhered	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (9.1%)	0 (0.0%)
Did Not Adhere	49 (55.7%)	18 (25.7%)	16 (66.7%)	4 (20.0%)	22 (66.7%)	1 (50.0%)
Not Vaccinated	39 (44.3%)	52 (74.3%)	8 (33.3%)	16 (80.0%)	8 (24.2%)	1 (50.0%)
VZV						
Adhered	3 (3.4%)	2 (2.9%)	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)
Did Not Adhere	30 (34.1%)	34 (48.6%)	10 (41.7%)	6 (30.0%)	12 (36.4%)	1 (50.0%)
Not Vaccinated	55 (62.5%)	34 (48.6%)	14 (58.3%)	14 (70.0%)	20 (60.6%)	1 (50.0%)
HPV						
Adhered	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Did Not Adhere	26 (29.5%)	3 (4.3%)	7 (29.2%)	1 (5.0%)	8 (24.2%)	0 (0.0%)
Not Vaccinated	62 (70.5%)	67 (95.7%)	17 (70.8%)	19 (95.0%)	25 (75.8%)	2 (100.0%)
Influenza						
Adhered	4 (4.5%)	2 (2.9%)	0 (0.0%)	0 (0.0%)	2 (6.1%)	0 (0.0%)
Did Not Adhere	78 (88.6%)	57 (81.4%)	23 (95.8%)	17 (85.0%)	27 (81.8%)	2 (100.0%)
Not Vaccinated	6 (6.8%)	11 (15.7%)	1 (4.2%)	3 (15.0%)	4 (12.1%)	0 (0.0%)

1. LL = leukemia/lymphoma
2. ST/BT = solid tumor/brain tumor
3. Hem = hematologic diseases
4. ID = immune deficiency
5. SCD= sickle cell disease

Conclusions: These data uncover a major gap in vaccine delivery in a large pediatric HCT program. SCD patients exhibited higher post-HCT vaccine adherence suggesting the benefit of follow up in a multidisciplinary late-effects clinic.

P15. IMPACT OF PROTEIN SUPPLEMENTATION ON LEAN MUSCLE MASS IN ADULT SURVIVORS OF CHILDHOOD CANCER ENGAGED IN RESISTANCE TRAINING

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Background: Muscle weakness, low lean muscle mass and poor physical performance are prevalent among adult survivors of childhood cancer. We evaluated the effects of resistance training with and without protein supplementation on lean muscle mass, and muscle strength among childhood cancer survivors.

Methods: This double-blind placebo-controlled trial enrolled survivors aged =18 to <45 years. Participants were randomized to resistance training with daily protein supplement (21g protein/day, 90kcal) (RT+S) or resistance training with placebo (sucrose, 90kcal) (RT+P). Both groups received educational materials, access to a local fitness center and a tailored resistance training program with tapered supervision. Lean muscle mass and muscle strength were assessed at baseline and 24 weeks, using dual x-ray absorptiometry and dynamometer testing respectively. Mean changes were compared within and between groups.

Results: Of 93 participants randomized, 57 completed the 24-week intervention (24 in RT+S, 33 in RT+P). The mean age was 33.1 (SD 7.0), 67% were white and 47% female. The RT+S group had a significant increase in lean body mass (1.05 kg [SD 2.34], p=0.04), while the RT+P group did not (0.13 kg [SD 2.19], p=0.74). Mean change in handgrip strength also improved in the RT+S group (1.98 [SD 4.30], p=0.03); change approached significance in the RT+P group (1.49 [SD 4.60], p=0.07). All survivors significantly improved their strength over time (Table) as measured by one max repetition test at baseline and follow-up.

Exercise Testing 1RM (values in lbs)

| | RT + S | | | RT + P | | | |
	Baseline Mean (SD)	Follow-up Mean (SD)	P1	Baseline Mean (SD)	Follow-up Mean (SD)	P2	P3
Leg Press	180.2 (93.1)	388.0 (231.8)	<0.001	179.8 (85.1)	311.6 (177.3)	<0.001	0.64
Mean change		157.8 (176.5)			131.4 (148.3)		
Chest Press	106.0 (56.7)	141.5 (69.0)	<0.001	107.7 (51.9)	132.7 (58.1)	<0.001	0.25
Mean change		35.42 (33.97)			25.00 (31.07)		

P3: Comparison of change adjusted for age/sex.

Conclusions: Preliminary findings indicate that a supervised resistance training program among adult survivors of childhood cancer that includes protein supplementation is feasible and may increase total lean body mass and muscle strength.

P16. RISK OF SUBSEQUENT PRIMARY LEUKEMIAS AMONG 69,460 5-YEAR SURVIVORS OF CHILDHOOD CANCER IN EUROPE: A COHORT STUDY WITHIN PANCARESURFUP

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Background: Survivors of childhood cancers are at risk of developing subsequent primary leukemias (SPLs), but the long-term risks after 20 years following treatment are still unclear. We investigated the risk of SPLs in 5-year childhood cancer survivors using a large-scale pan-European (PanCareSurFup) cohort and evaluated variations in the risk by cancer and demographic factors.

Methods: This largest-ever assembled cohort comprises 69,460 5-year childhood cancer survivors from 12 European countries. Standardized incidence ratios (SIRs) and absolute excess risks (AERs) were calculated. Cumulative incidence was calculated accounting for competing risk of death.

Results: One hundred and fifteen survivors developed a SPL including 86 subsequent primary myeloid leukemias (SPML) and 17 subsequent primary lymphoid leukemias (SPLL); of these SPLs, 31 occurred beyond 20 years from first childhood cancer diagnosis. Compared with the general population, childhood cancer survivors had a 4-fold increased risk (SIR = 3.7; 95%CI: 3.1-4.5) of developing leukemia, and eight leukemias per 100,000 person-years (AER = 7.5; 95%CI: 6-9.2) occurred in excess of that expected. The risks remained significantly elevated beyond 20 years from first primary malignancy. Overall, the risk ratio for SPML (SIR = 5.8; 95%CI: 4.6-7.1) was higher than that for all other SPLs combined.

Conclusions: We demonstrate that beyond 20 years after childhood cancer diagnosis survivors experienced an increased risk for SPLs compared to that expected from the general population. Our findings show that alertness for symptoms potentially related to subsequent leukemias among long-term survivors of childhood cancer needs to continue well into middle age.

†Deceased 27th November 2018 to whom this research is dedicated.

P17. THE VALUE OF LEFT VENTRICULAR EJECTION FRACTION AT FIRST LONG-TERM FOLLOW-UP ECHOCARDIOGRAM IN THE SCREENING FOR CARDIOMYOPATHY IN LONG-TERM SURVIVORS OF CHILDHOOD CANCER

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Background: Echocardiography is currently used for cardiomyopathy surveillance in long-term childhood cancer survivors (survivors) with a frequency of at least once in 5-years depending on anthracycline and chest-directed radiotherapy dose. We assessed the value of the left ventricular ejection fraction (LVEF) at first follow-up echocardiogram as an additional predictor for cardiomyopathy in survivors treated with cardiotoxic cancer therapies.

Methods: Five-year survivors treated with anthracyclines and/or chest directed radiotherapy were selected from a larger Emma Children's Hospital cohort based on the following criteria: No previous diagnosis of cardiomyopathy and echocardiographic follow-up at least every five years. The endpoint was the development of cardiomyopathy (LVEF<40%) during screening. The additional predictive value of the first LVEF was evaluated with multivariable Cox regression models adjusted for time since cancer diagnosis, anthracycline and chest-directed radiotherapy dose.

Results: From a cohort of 690 survivors treated with cardiotoxic cancer therapies, 299 survivors (56% female) were included. The first LVEF was obtained at a median of 16.7 years (interquartile range (IQR) 11.8-23.2) after cancer diagnosis and a median age of 24.1 years (IQR 19.6-30.7). A mid-range first LVEF (EF 40-49%) was present in 41 (13.7%) survivors. The median time between the first and second echocardiogram was 3.8 years (range 1.1-5.0 years). During screening, 11 (3.7%) survivors developed cardiomyopathy after a median of 7.2 years (IQR 3.8-8.4). Cardiomyopathy was accompanied by heart failure symptoms in six survivors and 10/11 survivors were treated with heart failure medications. Addition of first LVEF on top of anthracycline and chest radiotherapy dose increased model discriminative performance (C-index increase of 0.79-0.86, likelihood ratio test P<0.01). The multivariable adjusted HR for developing cardiomyopathy in survivors with mid-range first LVEFs compared to those with preserved first LVEFs was 6.8 (P<0.01).

Table. Multivariable Cox regression model of potential risk factors for cardiomyopathy during follow-up	HR	Lower 95% CI	Upper 95% CI	P
Model without first LVEF				
Anthracycline dose (per 100 mg/m2 increment)	1.62	1.13	2.31	0.01
Chest directed radiotherapy dose (EQD2 per 10 Gy increment)	1.71	1.23	2.38	<0.01
Model with continuous first LVEF				
LVEF at first echocardiogram (per 10 points decrease)	8.26	2.49	27.4	<0.001
Anthracycline dose (per 100 mg/m2 increment)	1.39	0.99	1.95	0.05
Chest directed radiotherapy dose (EQD2 per 10 Gy increment)	1.75	1.23	2.48	<0.01
Model with categorical first LVEF				
Mid-range versus preserved LVEF at first echocardiogram	6.77	1.81	25.3	<0.01
Anthracycline dose (per 100 mg/m2 increment)	1.6	1.13	2.27	0.01
Chest directed radiotherapy dose (EQD2 per 10 Gy increment)	1.98	1.36	2.87	<0.001
Abbreviations: CI, confidence interval; LVEF, left ventricular ejection fraction; EQD2, equivalent dose in 2-Gy fractions; HR, Hazard ratio; Gy, Gray.				

Conclusions: Among long-term survivors of childhood cancer treated with cardiotoxic cancer therapies, those with a mid-range first LVEF are at higher risk for developing cardiomyopathy during follow-up.

P18. FERTILITY TREATMENT IN FEMALE SURVIVORS OF EARLY ONSET CANCER: A DANISH POPULATED-BASED COHORT STUDY

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Background: Despite the evidence of a decreased reproductive function after cancer treatment, little is known about the success of fertility treatment in female cancer survivors. Therefore, our aim was to assess the use of fertility treatment in a population-based cohort study using national register data on prescriptions on fertility drugs and fertility treatment.

Methods: The study included 23,331 women diagnosed with an early onset cancer (<39 years) in Denmark in 1948–2014 and 232,915 matched population comparisons. Information on fertility drugs (e.g. estrogens and progesterone) and fertility treatment (e.g. in vitro fertilization (IVF), frozen embryo replacements and egg donations) was ascertained from the Danish National Prescription Registry and IVF Registry in 1994–2016. Logistic regression models were used to estimate the odds ratio (OR) for prescription of fertility drugs or use of fertility treatment.

Results: Overall, 5,356 (23%) of the survivors had at least one prescription for a fertility drug and 925 (4%) survivors had undergone fertility treatment. Prescriptions were more common in both survivors of childhood cancer (21.9%) and cancer in adolescence and young adulthood (AYA) (23.3%) than in women in the background population (15.4% and 16.1%, P<0.0001); use of fertility treatment was also higher in survivors of childhood cancer (5.4%) than in the background population (4.6%), P=0.033. The OR for prescription of at least one fertility drug was 1.43 (95% CI 1.29–1.58) and 1.60 (1.54–1.66) for survivors of a childhood cancer and AYA cancer, respectively. The corresponding OR for use of fertility treatment was 1.21 (1.02–1.43) and 0.91 (0.84–0.98).

Conclusions: Survivors of a childhood cancer are more often prescribed fertility drugs and referred to fertility treatment than women in the background population. Further analyses will investigate parenthood probability after fertility treatment taking cancer type, radiation treatment and type of fertility treatment into account.

P19. POSITIVE PSYCHOLOGICAL OUTCOMES FOR PEDIATRIC CANCER SURVIVORS: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background: Happiness and positive emotional wellbeing can be operationalized in different ways, including with the PERMA model (Seligman, 2011): Positive emotions, Engagement, Relationship, Meaning, and Accomplishments. Neither this model nor others have been widely applied to pediatric cancer survivors. The goal of this study was to examine relationships between common measures of emotional wellbeing and happiness to determine whether these states represent a single or multiple construct(s) of positive psychological outcomes for childhood cancer survivors.

Methods: A sample of 1,460 young adult survivors of childhood cancer from CCSS who were diagnosed with cancer before the age of 10 (53% female, mean [range] 22 [19-24] years old, time since diagnosis 18 [14-19] years) completed the Posttraumatic Growth Inventory (PTGI, a measure of emotional wellbeing) and Cantril Ladder of Life (LOL, a measure of happiness). The PTGI has five subscales: Relating to Others, New Possibilities, Personal Strength, Spiritual Change, and Appreciation for Life. The LOL asks survivors to rate past, current, and future life satisfaction. A Confirmatory Factor Analysis was conducted to compare a one-factor solution that comprised subscales from the LOL and the PTGI with a two-factor solution of PTGI and LOL as distinct latent constructs.

Results: The result of the two-factor model showed a good fit ($\chi2$ (20)=134.66, p<0.001; SRMR= 0.05; RMSEA= 0.06, 95% CI= [0.05 0.07]; CFI= 0.98). The two factors were positively, though weakly, correlated (r=0.15, p<0.001). The life satisfaction construct had standardized factor loadings for the three indicators that ranged from 0.46 to 0.99,

and the factor loadings for PTG construct ranged from 0.70 to 0.93. The result of the one-factor model suggested that it was not a good fit ($\chi 2$ (21) = 973.01, p<0.001; SRMR = 0.13; RMSEA = 0.17, 95% CI = [0.17 0.18]; CFI = 0.83). When comparing the two models, model fit was significantly worse with the one-factor model, indicating that the life satisfaction and PTG constructs are distinct ($\chi 2D$ (1) = 838.25, dfD = 1, p<0.001).

Conclusions: Life satisfaction and posttraumatic growth are related but distinct constructs that have a weak, though statistically significant, association with each other. This pattern may explain why some cancer survivors are satisfied with their current life and explore life in a more positive way, while other may perceive positive growth but not be satisfied. Future surveys, enhanced with the PERMA model, should ask about the five pillars of happiness, with the goal to understanding why some survivors attain happiness and others do not.

P20. OBESITY AND WALKING EFFICIENCY IN SURVIVORS OF ACUTE LYMPHOBLASTIC LEUKEMIA: A REPORT FROM THE ST. JUDE LIFETIME COHORT

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Background: Treatment for childhood acute lymphoblastic leukemia (ALL) is associated with an increased risk of being overweight/obese, having neuromusculoskeletal impairment and mobility limitations. Obesity may contribute to mobility limitations by increasing the physiologic cost/effort associated with movement. We evaluated associations between obesity and walking efficiency in adult survivors of childhood ALL.

Methods: ALL survivors (N=351, mean±SD age: 28.5±6.0 years, 51.6% male) and 342 age-, sex- and race-matched controls (N=342, 29.0±7.5 years, 51.2% male) were assessed for body mass index (BMI: kg/m2), body fat percentage (%BF) using dual x-ray absorptiometry, and completed the six minute walk test. Walking efficiency was characterized with the physiological cost index (PCI). PCI is calculated using the formula: (Maximal heart rate (HR) during walking – HR at rest)/distance walked; expressed as beats per meter (normal range 0.13-0.49 in adults).

Results: ALL survivors with BMI =40 kg/m2 had higher PCI values compared with normal weight survivors (0.63±.040 vs. 0.50±0.019, p<.01), adjusting for age, sex, physical activity, and cranial radiation exposure. ALL survivors with excess %BF (defined as > 25% for men and > 33% for women) also had higher PCI values compared to survivors with normal %BF (0.54±.013 vs. 0.47±0.017, p<.01). No associations between obesity and PCI were evident among controls.

Conclusions: Obesity is associated with reduced walking efficiency in ALL survivors but not in healthy controls, suggesting that ALL survivors do not have the same capacity to compensate for excess body weight as their peers with no cancer history. Weight loss interventions may have a significant impact on daily activity in this population.

P21. PHYSICAL ACTIVITY AND NEUROCOGNITIVE OUTCOMES IN ADULT SURVIVORS OF CHILDHOOD CANCERS: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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Background: To investigate associations between physical activity (PA) and self-reported neurocognitive outcomes in adult survivors of childhood cancer.

Methods: 12,329 5-year survivors diagnosed between 1970-1999 and 727 siblings self-reported PA and neurocognitive concerns (Neurocognitive Questionnaire [NCQ] subscales Task Efficiency [TE], Emotion Regulation [ER], Organization [ORG] and Memory [MR]). PA was collected at baseline, and PA and NCQ data were obtained 7 [1-12] years later. 4,636 survivors completed another follow-up 12 [9-14] years later. PA consistency was defined as meeting the Centers for Disease Control and Prevention criteria (i.e., =75 min vigorous or 150 min moderate activity/week) across surveys. Associations of PA consistency with NCQ scores and their longitudinal changes were assessed using multiple linear regression. Potential mediating effects of body mass index (BMI) and severe chronic health conditions (CHCs) were explored.

Results: Survivors reported more neurocognitive problems than siblings in TE (NCQ T-scores, Mean±SD: Siblings=50.0±0.4, CNS=61.4±0.4, non-CNS=53.3±0.3), ORG (Siblings=49.9±0.4, CNS=52.8±0.3, non-CNS=50.4±0.2) and MR (Siblings=50.8±0.4, CNS=58.9±0.4, non-CNS=53.4±0.2), all p's <0.001. CNS survivors also reported more ER concerns than siblings (Siblings=51.4±0.4, CNS=54.6±0.3, p<0.001). Consistent PA over time was associated with fewer neurocognitive concerns compared to consistent inactivity for both CNS and non-CNS survivor groups in all neurocognitive domains (ß coefficient, a measure of effect size, ranged from -2.1 to -8.1) and larger improvements over time (ß's -2.2 to -6.4), all p's=0.009. Consistent PA was associated with neurocognitive problems to a greater degree in CNS survivors than siblings (TE: ßinteraction=-4.9, p<0.001; MR: ßinteraction=-3.5, p=0.004). Body mass index and severe chronic health conditions partially mediated the PA-NCQ associations, but the mediation effects were small (change in ß = 0.58, all p's < 0.001).

Conclusions: Adult survivors of childhood cancer who report more consistent PA have fewer neurocognitive problems and larger improvements in these concerns many years after treatment.

P22.   CORONARY ARTERY DISEASE SURVEILLANCE FOR CHILDHOOD, ADOLESCENT AND YOUNG ADULT CANCER SURVIVORS - RECOMMENDATIONS FROM THE INTERNATIONAL GUIDELINE HARMONIZATION GROUP

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Background: Childhood, adolescent and young adult (CAYA) cancer survivors are at risk for developing coronary artery disease (CAD). The International Guideline Harmonization Group (IGHG) and PanCareSurFup Consortium commissioned a taskforce to propose recommendations for CAD surveillance.

Methods: A guideline panel of 25 experts (pediatric/medical/radiation oncologists, pediatric/adult cardiologists, pediatricians, internists, epidemiologists) evaluated concordances/discordances between published international guidelines, developed focused clinical questions, conducted a systematic literature search (from 1/1990-11/2018), summarized and graded the evidence, and formulated recommendations according to IGHG evidence-based methods. Recommendations correlate to anticipated benefits and harms and the degree of uncertainty. Study selection criteria were: at least 20 eligible CAYA cancer survivors (diagnosed with cancer prior to age 35 years and off active treatment); CAD assessment any time after end of treatment; all study designs except case reports, case series and narrative reviews; published in English.

Results: We identified 30 eligible studies reporting the occurrence of CAD in CAYA cancer survivors including 8 studies providing results of multivariable analyses relevant to our clinical questions. We identified an increased risk of CAD in CAYA cancer survivors after radiotherapy involving the heart (low quality of evidence); no significant effect of chemotherapy was identified (very low to low quality of evidence). Male gender, older age at treatment and the presence of one or more cardiovascular disease risk factors (obesity, hypertension, dyslipidemia, (recent) smoking and diabetes) also increased the risk (very low to moderate quality of evidence). No studies assessing the diagnostic value of possible surveillance methods for asymptomatic CAD in CAYA cancer survivors were identified. Also, no studies were available on the treatment of asymptomatic CAD with lipid-lowering or anti-hypertensive agents or life style modifications in CAYA cancer survivors. We formulated preliminary recommendations for health care providers and CAYA cancer survivors (Table 1).

Conclusions: These recommendations aim to promote optimal care and preservation of cardiovascular health for CAYA cancer survivors at risk for CAD.

Table 1: Preliminary harmonized recommendations for surveillance of asymptomatic coronary artery disease in childhood, adolescent and young adult cancer survivors
General recommendation
Health care providers and childhood, adolescent and young adult cancer survivors treated with radiotherapy involving the heart should be aware of the increased risk of coronary artery disease (low level evidence and expert opinion, strong recommendation).
Who needs surveillance for asymptomatic CAD?
Surveillance of all childhood, adolescent and young adult cancer survivors for asymptomatic CAD is currently not recommended (no studies/expert opinion, strong recommendation).
What advice should be given regarding modifiable risk factors?
Surveillance for modifiable cardiovascular disease risk factors (i.e. overweight/obesity, hypertension, dyslipidemia, smoking, diabetes) is recommended with timing of initiation and frequency based on intensity of cardiotoxic treatment exposure(s), family history and presence of co-morbid conditions associated with CVD risk (low to moderate level evidence and expert opinion, strong recommendation).
Timely and aggressive management of modifiable cardiovascular disease risk factors (i.e. overweight/obesity, hypertension, dyslipidemia, smoking, diabetes) is reasonable due to the increased risk of coronary artery disease (existing guidelines and expert opinion, moderate recommendation).

P23.   ASSOCIATIONS BETWEEN CHEMOTHERAPY EXPOSURES, CHRONIC CONDITIONS AND NEUROCOGNITIVE IMPAIRMENTS IN PEDIATRIC ALL SURVIVORS TREATED WITH CHEMOTHERAPY ONLY VARY WITH SEX: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background: Prior research has identified neurocognitive impairments after treatment for childhood ALL with chemotherapy only; however, little is known about risk modifiers such as sex and chronic health conditions.

Methods: ALL survivors treated with chemotherapy only (N=1221; 55% female) and 728 siblings (56% female) in the CCSS study completed the Neurocognitive Questionnaire (CCSS-NCQ) to assess task efficiency, emotional regulation, organization, and memory. Cognitive impairments were defined as Z-scores = 1.28, corresponding to the 90th percentile of the sibling sample. Chemotherapy exposures were abstracted from medical records. Chronic health conditions were graded according to Common Terminology Criteria for Adverse Events v4.03. Multivariable logistic regression models compared survivors and siblings to identify associations with neurocognitive impairment, stratified by sex and adjusted for age at NCQ assessment and race.

Results: Female survivors had a higher prevalence of neurocognitive impairments related to task efficiency (adjusted proportion 20.9%) and memory (27.6%) compared to siblings (12.7% and 17.7% respectively), with adjusted odds ratio (OR) 1.8 (95% confidence interval [CI] 1.2 - 2.8) and 1.8 (95% CI 1.3 - 2.5), respectively. Male survivors endorsed more impairments related to task efficiency than did siblings (17.0% vs 11.8%; OR 1.5, 95% CI: 1.0 - 2.3), but not for memory. Chemotherapy exposures were not significantly associated with neurocognitive impairments, except for dexamethasone, which was associated with increased risk of memory impairments in males (OR = 2.1, 95% CI 1.2 – 4.0). Having a grade 2-4 neurological chronic condition increased the risk of all types of neurocognitive problems in both female and male ALL survivors. In males, grade 2-4 pulmonary conditions were associated with increased risk of impaired task efficiency (OR 5.0, 95% CI 1.4 – 17.1) compared to those with < grade 2. In females, grade 2-4 endocrine conditions were associated with increased risk for impaired task efficiency (OR 2.4, 95% CI 1.3 – 4.3), organization (OR 2.1, 95% CI 1.0 – 4.1) and memory (OR 2.3, 95% CI 1.4 – 4.1).

Conclusions: Significant variation in risk for neurocognitive impairments based on sex was identified, highlighting the need to investigate sex-related differences in pathophysiology and monitoring of survivors. Further evaluation of risk modifiers of neurocognitive impairments after childhood ALL is important to effectively address these problems.

P24. ULTRASOUND VERSUS PHYSICAL EXAM TO SCREEN FOR SECONDARY THYROID CANCER AMONG HIGH-RISK CHILDHOOD CANCER SURVIVORS

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Background: Thyroid cancer is a common secondary malignancy among childhood cancer survivors who have received radiation to the head, neck and/or upper thorax. The optimal strategy for surveillance for thyroid carcinoma in childhood cancer survivors remains controversial. Current Children's Oncology Group recommendations are limited to physical exam. The objective of this study was to determine the sensitivity and specificity of thyroid ultrasound versus neck exam by a pediatric endocrinologist in the diagnoses of thyroid cancer in a cohort of high-risk childhood cancer survivors.

Methods: Medical records of childhood cancer survivors who received radiotherapy to the head, neck and/or upper thorax were reviewed. These patients were seen in a comprehensive childhood cancer survivorship clinic from 01/01/2010 to 12/31/2017. Patient populations included oncology, bone marrow transplant and brain tumor patients.

Results: 226 patients that received radiation to the head, neck and/or upper thorax were identified. Of those, 129 patients were male (57%). Sixteen (7.1%) of patients developed a secondary thyroid malignancy including 4 patients previously treated for an oncological malignancy, 9 patients treated with bone marrow transplantation, and 3 patients with a CNS malignancy. Median radiation dose was 1800 cGy (range 400-5940 cGy). Time to thyroid carcinoma diagnosis occurred at a median of 12 years (range 4-19 years) from treatment with radiation. Screening ultrasounds were obtained in 146 (65%) patients while 226 (100%) had a physical exam. Two cases were identified by abnormalities on physical exam. The sensitivity of US was 100% (CI 80.6-100) compared to a sensitivity of 12.5% (CI 3.5-36) using physical exam (P < 0.0001). Screening ultrasound had a specificity of 73% (CI 65.1-80.1) while physical exam yielded a specificity of 100% (CI 98.2-100).

Conclusions: Regular screening with ultrasounds provide the greatest sensitivity for detection of secondary thyroid carcinomas after head, neck and upper thorax radiation in childhood cancer survivors. If screening ultrasounds were not routinely utilized in our clinic, 14 of the 16 patients (87.5%) would have had a delay in their diagnosis of a secondary thyroid malignancy. Screening ultrasounds may lead to earlier detection of thyroid carcinomas, with the potential to decrease the need for aggressive surgery, radioiodine therapy and, ultimately, to decrease recurrence risk.

P25. BODY MASS INDEX AT DIAGNOSIS AND HYPOTHALAMIC-PITUITARY DYSFUNCTION DURING FOLLOW-UP IN CHILDHOOD BRAIN TUMOR SURVIVORS

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Background: Childhood Brain Tumor Survivors (CBTS) are at increased risk of hypothalamic-pituitary (HP) dysfunction, which may be caused by radiotherapy or be a complication of the tumor itself or brain. Being overweighted or underweighted (body mass index (BMI) more than 2 SDS or lower than -2 SDS, respectively) at brain tumor diagnosis may reflect early hypothalamic dysfunction and may be a risk factor to develop HP dysfunction during follow-up. This has, to date, not been investigated. The objective of this study was to examine whether BMI at brain tumor diagnosis is associated with the development of HP dysfunction, independent of brain tumor treatment.

Methods: Children surviving a brain tumor, excluding craniopharyngioma or a pituitary tumor, for minimally two years, in whom BMI at diagnosis of their brain tumor had been recorded were selected from a previous reported nationwide cohort study of CBTS (n=685 of 718). Odds-ratios (OR) for developing HP dysfunction were calculated using multivariable logistic regression, including BMI at diagnosis, gender, age at follow-up, radiotherapy, histology, location of the primary tumor, hydrocephalus and state of disease.

Results: Of 685 CBTS, 10.8% (n=74) was overweighted and 5.0% (n=34) was underweighted at diagnosis. Median follow-up time was 7.1 years (5.0-9.6). Being overweighted or underweighted at diagnosis was significantly associated with the development of HP dysfunction during follow-up (OR 2.43, 95% CI 1.46-4.05) including anterior

pituitary deficiencies (OR 1.93, 95% CI 1.08-3.46), posterior pituitary deficiencies (OR 3.80, 95% CI 1.37-10.56), and central precocious puberty (CPP, OR 2.46, 95% CI 1.18-5.15). Underweight or overweight at brain tumor diagnosis was associated with high BMI at follow-up (OR 3.75, 95% CI 2.36-5.97). Development of HP dysfunction was also significantly associated with radiotherapy (OR 11.25, 95% CI 6.76-18.72) and location of primary tumor (OR 2.24, 95% CI 1.60-3.13). In children not treated with radiotherapy (n=430), underweight and overweight at brain tumor diagnosis were also both significantly associated with HP dysfunction and precocious puberty (OR 2.91, 95% CI 1.16-7.28 and 3.00, 95% CI 1.12-8.01, respectively). In this group, other significant risk factors for HP dysfunction included location of primary tumor (OR 8.90, 95% CI 4.11-19.24), hydrocephalus (2.27, 95% CI 1.06-4.88) and state of disease at follow-up (OR 6.38, 95% CI 1.37-29.58).

Conclusions: Being overweighted or underweighted at brain tumor diagnosis in childhood is associated with the development of anterior pituitary deficiencies, posterior pituitary deficiencies and CPP, independently of given treatment. This suggests that in these children hypothalamic dysfunction may already be present at brain tumor diagnosis. These findings may be used for future studies on hypothalamic dysfunction in CBTS and can be used to develop recommendations on monitoring the development of pituitary disorders in CBTS.

P26. FUNCTIONAL CONNECTIVITY OF THE CEREBELLO-THALAMO-CORTICAL PATHWAY IN SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA TREATED WITH CHEMOTHERAPY-ONLY

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Background: Contemporary chemotherapy for childhood acute lymphoblastic leukemia (ALL) may differentially impact brain regions with higher concentrations of glucocorticoid receptors and disrupt function and connectivity of the cerebello-thalamo-cortical network.

Methods: 176 survivors (49% male, mean [range] age at diagnosis 6.8 [1-18] years, 14.5 [8-27] years at evaluation) and 82 community controls (57% male, 13.8 [8-26] years at evaluation) completed functional brain imaging (fMRI) and neurocognitive testing. Multivariable generalized linear models were used to examine associations between brain morphology and neurocognitive function. Covariates included age at diagnosis, age at evaluation, intracranial volume, dexamethasone exposure, methotrexate exposure, and number of intrathecal injections. Associations were examined between fMRI global efficiency, where efficiency indicates network integration, within module z-scores [WMZ's], which informs how well connected a region is to its functional network, and neurocognitive outcomes. All analyses were stratified by sex.

Results: No significant difference was found in intracranial volume between survivors and controls. Volume and cortical thickness of the bilateral cerebellum, precuneus and dorsolateral prefrontal cortex were significantly smaller in survivors than controls (p's <0.05). Among survivors, smaller cerebellar volume was associated with poorer performance in working memory, organization and planning, and motor and visual processing speed (p's <0.05). Global efficiency was higher in survivors with executive dysfunction (p=0.01). In females, higher global efficiency was associated with poorer cognitive flexibility and visuo-motor processing speed (p's<0.05). Poorer organization/planning was associated with higher WMZ 's in the cerebellum and lower WMZ 's in the precuneus. (p's<0.05). In males, poorer executive function was associated with lower WMZ's in the dorsolateral prefrontal cortex and higher WMZ's in the cerebellum (p's <0.05).

Conclusions: Long-term survivors of childhood ALL treated with chemotherapy demonstrate a poorly differentiated and overly integrated cerebello-thalamo-cortical network, suggesting that treatment limits typical maturation of developing neural networks potentially making them more physiologically costly.

P27.   PRIMARY HEALTH CARE USE FOR CHILDHOOD CANCER SURVIVORS

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Background: Childhood cancer survivors are at risk of developing long-term morbidity, which is very likely to be presented to a primary care physician. Therefore, insight in primary care use in survivors is needed. We aimed to investigate the volume of primary care use among long-term childhood cancer survivors, underlying health problems and determinants.

Methods: Data from a Dutch nationwide cohort of five-year survivors was linked to the Nivel Primary Care database, which contains detailed data on primary care use from a representative sample of 10% of all Dutch primary care physicians. For every survivor included in the study, two matched controls were selected. Primary outcome was the number of contacts with the primary care physician per year of follow-up, secondary outcome was the reason for contact. We used negative binomial regression to compare the number of contacts between survivors and the reference population, and to identify determinants for having more contacts among survivors.

Results: A total of 602 survivors and 1,204 controls were included. Survivors were 1.3 times more likely to contact their primary care physician than controls (95% confidence interval (CI) 1.2-1.5), up to 1.5 times at an attained age over 40 years (95% CI 1.2-1.8). Compared to the reference population, survivors were 4.9 times more likely to seek contact for new types of malignancies, 3.1 times for hematological conditions and 2.8 times for endocrine conditions. Female sex, higher attained age and treatment with radiotherapy were determinants for having more contacts among survivors.

Conclusions: Childhood cancer survivors have a high health care use in the primary care practice as compared to matched controls. Especially females, those who are older and those treated with radiotherapy are at risk. Our results emphasize importance of disseminating the current knowledge on long-term morbidity in childhood cancer survivors among primary care physicians.

P28.   EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF SUBSEQUENT MENINGIOMAS AMONG LONG-TERM CHILDHOOD CANCER SURVIVORS: A DCOG LATER STUDY

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Background: Meningiomas are among the most frequent neoplasms diagnosed after cranial radiotherapy. Relatively limited information is available on the epidemiology and clinical characteristics of meningiomas in childhood cancer survivors. Meanwhile, such information is crucial for designing evidence-based follow-up guidelines. This study aims to describe clinical and therapeutic characteristics of survivors diagnosed with meningiomas after childhood cancer in the Netherlands.

Methods: Our case series is embedded in the DCOG LATER cohort study that includes over 6,000 5-year survivors diagnosed between 1963-2002, including 1277 survivors treated with cranial radiotherapy. We performed record linkage with the Dutch Pathology Registry (PALGA; 1990-2018) and abstracted details regarding diagnosis, treatment, and follow-up from patient records.

Results: Preliminary results include data on 102 survivors with subsequent meningiomas, 95% diagnosed after cranial radiotherapy. Mean age at diagnosis was 33 yrs (range 13-50 yrs). Four patients had a confirmed diagnosis of neurofibromatosis types 1 or 2. Multiple synchronous meningiomas were found at presentation in 31 patients. Fifty-seven patients presented with clinical symptoms, while 23 meningiomas were detected during imaging for other reasons, and for other patients detection mode was not reported. Mean follow-up after meningioma diagnosis spanned 8.7 yrs (range 0.2-21.8 yrs). The median interval between diagnosis and first surgery was 2,8 months (range 0-14 yrs). One third of the patients were initially followed by watchful waiting. Among 62 patients with a solitary meningioma at diagnosis, 23 (37%) developed new meningiomas and 13 (21%) developed recurrences during follow up. At the end of the study, 14 patients were deceased. Further details including comparisons with published case series of de novo meningiomas will be presented at the meeting.

Conclusions: Our preliminary results indicate that meningiomas in survivors treated with cranial radiotherapy occur at relatively young age. These patients often have multiple lesions and recurrent tumor after surgical resection is relatively frequent as well.

P29. EMERGENCY DEPARTMENT (ED) VISITS AND HOSPITALIZATIONS IN SURVIVORS OF CHILDHOOD CANCER IN THE CHILDHOOD CANCER SURVIVOR STUDY

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Background: Chronic health conditions are frequent among childhood cancer survivors and lead to increased health care resource utilization. We compared rates of ED visits and hospitalizations between survivors and siblings.

Methods: Analyses included 10,762 =5-year survivors and 2,069 siblings who completed a questionnaire from 2014-2016. We calculated ED visits and non-obstetric hospitalizations in the last 12 months per 1,000 person-years (PY), and compared survivors to siblings with relative rates (RR). We evaluated cause-specific hospitalization rates among survivors using ICD-10 categories. Multivariable Poisson regression models evaluated predictors of survivor visits.

Results: Median age in survivors and siblings was 35.3 years (interquartile range [IQR] 29.0-43.1) and 42.9 years (IQR 35.6-50.2), respectively. Time from cancer diagnosis was 27.8 years (IQR 21.7-34.1). 24.2% of survivors and 16.2% of siblings had =1 ED visit (p<0.001); rates were 521/1,000 PY for survivors and 246/1,000 PY for siblings (age/sex-adjusted relative rate [RR] 2.0; 95% confidence interval [CI] 1.7 - 2.3). Factors associated with increased survivor ED visits were black race (RR 1.6, CI 1.2-2.0), being obese (RR 1.4, CI 1.2-1.7) or underweight (RR 1.9, CI 1.2-3.0), female sex (RR 1.3, CI 1.1-1.5), younger age (p=0.02) or abdomen/pelvis (RR 1.2, CI 1.1-1.4) or brain irradiation (RR 1.2, CI 1.0-1.4). 13.3% of survivors and 8.3% of siblings had =1 hospitalization (p<0.001); rates were 219/1,000 PY for survivors and 130/1,000 PY for siblings (RR 1.9; CI 1.3 - 2.9). Factors associated with increased survivor hospitalizations were female sex (RR 1.3, 1.1-1.5), younger age (p<0.0001), being obese (RR 1.3, CI 1.0-1.6) or underweight (RR 1.5, 95% CI 1.1-2.2) or platinum chemotherapy exposure (RR 1.6, CI 1.3-2.0). The most common indications for hospitalization were diseases of the digestive (21.9/1,000 PY; CI 18.7 - 25.7), circulatory (20.9/1,000 PY; CI 17.8 – 24.4) and genitourinary (19.5 1,000 PY; CI 16.6 – 23.0) systems. Leukemia survivors had the highest ED visit and hospitalization rates.

Conclusions: Childhood cancer survivors had a 2-fold increased likelihood of an ED visit or hospitalization compared with their siblings. This increases the economic burden on survivors and the health care system.

P30. LONG-TERM RISK OF SKIN CANCER AMONG CHILDHOOD CANCER SURVIVORS: A DCOG-LATER COHORT STUDY

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Background: Subsequent skin cancers, in particular basal cell carcinoma (BCC), are common after radiotherapy among childhood cancer survivors. Nonetheless, comparatively few studies address specific skin radiation exposure parameters. Also, most existing studies rely on self-reported BCC diagnoses. Based on pathology report data, we studied risks and risk factors for subsequent skin cancers with emphasis on radiation dose, skin surface area exposed to radiation, and chemotherapeutic agents.

Methods: The DCOG-LATER cohort study includes five-year survivors diagnosed between 1963 and 2001. Subsequent skin cancers were identified from record linkages with the Netherlands Cancer Registry and Dutch Pathology Registry (PALGA) (1990-2015). Incidence rates were compared to general population rates for all skin cancer types. For power reasons, we conducted multivariable Cox regression cohort analyses for BCC only, applying repeated case-control sampling that enables evaluation of radiotherapy exposure to the specific skin compartment where the BCC occurred.

Results: Among 5,843 survivors, 259 developed in total 1,061 BCCs (standardized incidence ratio (SIR): 29.8, 95% CI:26.3-33.6), 20 had melanoma (SIR=2.3, 95% CI:1.4-3.5), and 10 had squamous cell carcinoma (SIR=7.5, 95% CI:3.6-13.8). After a first BCC, 47% developed more BCCs. BCC risk was associated with any radiotherapy to the skin compartment of interest (HR=14.32, 95% CI:10.10-20.29) and with surface area of the skin compartment exposed to radiation (26-75%: HR=1.99, 95% CI:1.24-3.20; 76-100%: HR=2.16, 95% CI:1.33-3.53, versus 1-25% exposed; p-trend among exposed=0.002), but not with prescribed radiation dose. Of all chemotherapy groups examined, only vinca alkaloids increased BCC risk (HR=1.54, 95% CI:1.04-2.27).

Conclusions: Childhood cancer survivors have a strongly, 30-fold increased BCC risk, which appears to increase with greater skin surface area exposed. Survivors who received radiotherapy should be educated to seek medical advice for local skin changes. It is important that survivorship health care professionals will be trained by dermatology experts to recognize suspicious skin lesions.

P32. LATE HEALTH OUTCOMES FOLLOWING CONTEMPORARY LYMPHOME MALIN DE BURKITT THERAPY FOR MATURE B-CELL NON-HODGKIN LYMPHOMA: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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Background: The widely utilized, risk-based Lymphome Malin de Burkitt (LMB) chemotherapy regimen has improved survival rates for children with mature B-cell non-Hodgkin lymphoma (NHL), however associated late effects remain understudied. We assessed late health outcomes after LMB treatment in the Childhood Cancer Survivor Study.

Methods: Multivariable regression models compared chronic health conditions, health status, and socioeconomic and neurocognitive outcomes between NHL survivors treated with the LMB regimen (n=126), non-LMB regimens (n=444), and siblings (n=1,029).

Results: LMB survivors were a median age of 10.2 (range:2.5-20.5) years at diagnosis and 24.0 (10.3-35.3) years at evaluation. Compared to siblings, LMB survivors were at increased risk for adverse health outcomes. However, LMB and non-LMB survivors did not differ with regards to risk of having any chronic health condition, impaired health status, neurocognitive deficits, or poorer socioeconomic outcomes. Increased risk for specific neurologic conditions was observed in LMB compared to non-LMB survivors: epilepsy (RR 15.2, 95% CI:3.1-73.4), balance problems (RR 8.9, 95% CI:2.3-34.8), tremors (RR 7.5, 95% CI:1.9-29.9), weakness in legs (RR 8.1, 95% CI:2.5-26.4), severe headaches (RR 3.2, 95% CI:1.6-6.3), and prolonged arm, leg, or back pain (RR 4.0, 95% CI:2.2-7.1). LMB risk group Group C (n=50) survivors were at the highest risk for these conditions; however, except for worse functional status (OR 2.7, 95% CI:1.2-5.8), they were not at increased risk for other adverse health status or socioeconomic outcomes compared to non-LMB survivors.

Conclusions: Survivors treated with LMB and non-LMB regimens are largely comparable in late health outcomes except for excess neurotoxicity among LMB survivors. These data inform treatment efforts seeking to optimize disease control while minimizing toxicity.

P33. GENOME-WIDE ASSOCIATION STUDY USING WHOLE-GENOME SEQUENCING IDENTIFIES A NOVEL LOCUS ASSOCIATED WITH INCREASED RISK OF CARDIOMYOPATHY IN ADULT SURVIVORS OF CHILDHOOD CANCER: UTILITY OF A 2-STAGE ANALYTIC APPROACH

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Background: Survivors of childhood cancer are at increased risk of treatment-related cardiomyopathy, found to be modified by genetic factors. To further investigate genetic risks of cardiomyopathy, we utilized whole-genome sequencing (WGS) in a clinically phenotyped cohort of long-term survivors of pediatric cancer.

Methods: Utilizing a novel 2-stage analytic approach, we first performed association analysis for ejection fraction (EF) using WGS data in European-descent childhood cancer survivors from the St. Jude Lifetime Cohort (SJLIFE). EF was analyzed as a continuous variable to increase statistical power for genetic discovery. Common variants (minor allele frequency (MAF) > 0.05) were analyzed using linear regression, adjusting for age at diagnosis, sex, age at follow-up, doses of anthracycline and average radiation dose to the heart, and eigenvectors. Rare/low-frequency variants were aggregated by different functional annotations and agnostic 4-kb sliding windows, testing jointly using Burden/SKAT test. In the second stage, only the variant showing genome-wide significance with EF was tested for its association with cardiomyopathy risk.

Results: Among the 2,015 SJLIFE survivors with WGS data, a locus on 6p21.2 near KCNK17 achieved genome-wide significance with EF (rs2815063; MAF = 0.13; per allele beta = -0.016; P = 2.10×10^{-8}), which replicated in 320 SJLIFE African survivors (MAF = 0.48; beta = -0.015; P = 0.004). In SJLIFE Europeans, 282 had a CTCAE Grade 2-5 cardiomyopathy. rs2815063 was significantly associated with increased risk of cardiomyopathy [per allele odds ratio (OR) = 1.38; P = 0.02], which replicated in 3,957 European survivors from the Childhood Cancer Survivor Study (163 CTCAE Grade 3-5 self-reported cases; per allele OR = 1.39; P = 0.038). rs2815063 alters DNA binding motif of EWSR1-FLI1, whose expression was found to lead to cardiomyopathy and death due to chronic cardiac failure in mice.

Conclusions: Using a 2-stage approach, we report a novel locus for cardiomyopathy in childhood cancer survivors, which warrants additional work to gain mechanistic insights.

P34. PATIENT-REPORTED OUTCOMES (PROS) IN ADULT SURVIVORS OF CHILDHOOD HEMATOPOIETIC CELL TRANSPLANT (HCT): A REPORT FROM THE ST. JUDE LIFETIME COHORT STUDY

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Background: We examined PROs including symptom prevalence and quality of life (QOL) in adult survivors of childhood HCT compared to those treated with conventional therapy and non-cancer controls, and risk factors of impaired PROs.

Methods: Physical and psychological symptoms and QOL were reported by 112 survivors of hematologic malignancies treated with HCT, 1106 treated with conventional therapy, and 242 non-cancer controls. PROs were self-reported using a survey, which included demographics, Brief Symptom Inventory and 36-Item Short Form Survey. Each participant completed a clinical physical health assessment and chronic health conditions (CHCs) were graded using a modified Common Terminology Criteria for Adverse Events. Multivariable logistic regression was conducted to estimate odds ratios (OR) and 95% confidence intervals (CI) for PROs using demographics and CHCs as predictors.

Results: HCT and conventional therapy survivors' mean age at survey and time since diagnosis were 28 and 29 years, and 19 and 20 years, respectively. The mean age at survey for non-cancer controls was 35 years. HCT survivors reported high prevalence of pain (64%), sensory (39%) and memory problems (29%), anxiety (29%), and depression (24%), which was not significantly different from survivors treated with conventional therapy. Compared to non-cancer controls, HCT survivors had more sensory (OR 3.2; 95% CI 1.5-6.8), motor (OR 4.3; 95% CI 1.2-15.4), and memory (OR 3.7; 95% CI 1.5-8.9) problems, and worse physical QOL (OR 5.4; 95% CI 1.6-18.6). Presence of PROs were associated with organ-specific CHCs (grade 3-4 vs. grade 0-2) not receipt of HCT: cardiac symptoms with cardiovascular CHCs (OR 3; 95% CI 1.8-4.9), pulmonary symptoms with pulmonary CHCs (OR 2.5; 95% CI 1.4-4.3), nausea with gastrointestinal CHCs (OR 2; 95% CI 1.2-3.1), and sensory (OR 1.9; 95% CI 1.2-3.1) and motor (OR 3.3; 95% CI 2-5.5) problems with neurological CHCs.

Conclusions: Prevalence of symptoms and impaired QOL in HCT survivors is comparable to survivors treated with conventional therapy, but higher than non-cancer controls. PROs may have a role in facilitating identification of adverse events in survivors.

P35. NEUROPATHY AND FINE-MOTOR-FUNCTION IN SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: A REPORT FROM THE ST. JUDE LIFETIME COHORT STUDY

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Background: Up to 40% of survivors of childhood acute lymphoblastic leukemia (ALL) have persistent neuropathy, which interferes with general mobility and walking. Neuropathy may also interfere with fine motor skills, which potentially impacts activities of daily living and quality of life (QOL). These relationships have not been investigated in long-term survivors of childhood ALL. PURPOSE: To evaluate associations between peripheral neuropathy, fine motor skills, and QOL in adult survivors of childhood ALL.

Methods: Adult survivors of childhood ALL (N=365, 52% male; age 6.8±4.5 years at diagnosis and 28.6±5.9 years at evaluation) were evaluated using the modified total neuropathy score (mTNS), physical performance test (PPT), and Medical Outcomes Study Short Form Survey (SF-36). Neuropathy was defined as a total score =4 on the mTNS. Participants were identified as having fine motor impairments according to timed writing and eating PPT tasks (> 10 seconds). Vincristine and cranial radiation doses from childhood cancer treatment, abstracted from medical records, were included as covariates in logistic regression models.

Results: 39.7% of ALL survivors had neuropathy (N=145) and 44.1% had fine motor impairments (N=161). Survivors with neuropathy received a mean cumulative dose of vincristine of 47.4 mg/m2; those without neuropathy had a mean cumulative dose of 31.5 mg/m2 (p<0.001). Neuropathy was significantly associated with fine motor impairments (Odds ratio (OR): 1.5, 95% confidence interval (CI): 1.01-2.39), after controlling for current age, sex, and cranial radiation. Fine motor impairments were associated with a 2.20-fold (95% CI: 1.07-4.52) risk of a physical component summary T-score <40 on the SF-36.

Conclusions: Adult survivors of childhood ALL with neuropathy are at higher risk for fine motor impairment. In addition, survivors with fine motor impairment are at increased risk for reporting poor physical quality of life. Interventions designed to address loss of fine motor function may improve quality of life in this vulnerable population.

P36. FERTILITY TREATMENTS IN EARLY ONSET FEMALE CANCER SURVIVORS: A FINNISH REGISTER-BASED STUDY ON 8,929 SURVIVORS

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Background: Advances in multimodality cancer treatments have increased the risk of long-term complications in early onset cancer survivors. For female cancer survivors these include diminished reproductive function, often resulting in a narrowed fertile window. The aim of this study was to evaluate the use of fertility treatments in cancer survivors (aged 0-39 years at diagnosis) compared to siblings.

Methods: Data from Finnish registers on cancer, birth and prescribed medications were merged to identify 8,929 survivors and 9,495 siblings without previous deliveries. Fertility drug purchases from 1993 to 2012 at the age of 16-41 years were included. A Poisson regression model was used to estimate incidence rate ratios (IRR) for the use of fertility drugs, adjusting for age and calendar time at fertility drug purchase.

Results: Fertility treatments were more common in survivors compared to siblings, as 6.1% of survivors compared to 3.8% of siblings had bought fertility drugs (IRR 1.43, 95% confidence interval [CI] 1.25-1.65). A sub-classification of fertility treatments into ovulation inductions and assisted reproductive technology (ART), showed increased use of ART (IRR 2.41, 95 % CI 1.97-2.96), whereas the use of ovulation induction was similar in survivors and siblings. Analyses by calendar time periods showed the use of ART to be significantly higher in the most recent decade, from 2003 onwards.

Conclusions: Cancer survivors have an increased risk for subfertility, which is why fertility counselling is important. However, our results mirror a more active approach among clinicians towards fertility treatments in cancer survivors during the most recent years.

P37. LONG-TERM CAUSE-SPECIFIC MORTALITY IN HODGKIN LYMPHOMA PATIENTS

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Background: As most reports on late treatment effects in Hodgkin lymphoma (HL) patients include 5-year survivors, few studies could directly compare HL mortality and long-term mortality from adverse events across treatments. We compared survival from HL and all other causes between different primary treatments, ignoring treatment of relapsed/refractory HL, in order to estimate benefits and harms associated with initial treatment choice.

Methods: Our multicenter cohort includes 2,943 HL patients, diagnosed <31 years and treated 1965-2000. Cause of death was available for 95% of 1,118 deceased patients. Cause-specific Standardized Mortality Ratios (SMRs) and Absolute Excess Mortality (AEM) were calculated. Cumulative HL mortality by stage and primary treatment choice was estimated with other causes of death as competing risk, and vice versa.

Results: Median follow-up was 21.7 years. The SMR for any cause of death excluding HL was 6.6 (95%CI:5.6-7.6). Second malignancy (SMN) and cardiovascular disease (CVD) contributed most to the AEM (42 and 26/10,000 person-years); after 35 years, the overall SMR and AEM were 7.4 (95%CI:5.5-9.7) and 491/10,000 person-years. For stage I-II, 30-year cumulative HL mortality varied between 8-11% for initial treatment with chemotherapy (CT) alone, radiotherapy (RT) alone and CT+RT combined (no statistically significant differences). By contrast, 30-year mortality from all other causes varied much more, from 8% (95%CI=3-16%) for CT only to 20% (95%CI=17-24%) for CT+RT combined, and 27% (95%CI=24-31%) for RT only. Age- and calendar period-adjusted subdistribution Hazard Ratios [sHR] were 0.5 (95%CI=0.2-1.0) for CT only vs. CT+RT, and 1.3 (95%CI=1.1-1.6) for RT only vs. CT+RT. For stage III-IV, 30-year mortality from HL did not significantly differ between CT alone (31%) and CT+RT combined (27%), while 30-year mortality from other causes was 16% (95%CI=11-21%) and 23% (95%CI=18-28%), respectively; 35-year mortality rates were 22% (95% CI=16-28%) and 33% (95%CI=26-39%), respectively (sHR=0.6 (95% CI=0.4-0.9)) for CT only vs. CT+RT.

Conclusions: Excess mortality from adverse events persists >35 years after HL treatment. Primary treatment with CT alone was associated with lower long-term mortality from causes other than HL than RT only or CT+RT combined. It is important to consider that these long-term data are largely based on treatments used in the past, that treatment was not randomized and that stage migration may play a role.

P38. NEIGHBORHOOD EFFECTS AND OBESITY IN ADULT SURVIVORS OF PEDIATRIC CANCER: A REPORT FROM THE ST. JUDE LIFETIME COHORT STUDY

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Background: Survivors of childhood cancer are at risk for obesity and associated chronic health conditions - risks that are potentially modifiable if survivors adopt a lifestyle with adequate physical activity and a healthy diet. Neighborhoods where survivors reside may influence uptake of health behaviors. We examined associations between neighborhood factors and obesity in survivors.

Methods: Adult survivors participating in the St. Jude Lifetime cohort with addresses available for geocoding were eligible for analysis [N=2265, mean assessment age 32.5 (SD 9.1) years, 46% female, and 85% white]. Survivors completed questionnaires regarding individual behaviors; percent body fat was assessed via dual x-ray absorptiometry (obesity: =25% males; =35% females); and neighborhood effects were characterized using census tract of residence (e.g. neighborhood socioeconomic status (SES), rurality). Structural equation modeling (SEM) was used to determine associations between neighborhood effects, physical activity, diet, smoking, treatment exposures, and obesity.

Results: Obese survivors (n=1420, 62.7%) lived in neighborhoods with less access to exercise opportunities (63% vs 66%, p=0.01) and lower SES (22% vs 18%, p<0.001); and were more likely to live in small town/rural areas (14% vs 10%, p=0.04) compared to non-obese survivors. Obese survivors who lived in the lowest SES neighborhoods were more likely to be CNS tumor survivors (17% vs 12%, p=0.02) and received higher mean doses of cranial radiation (CRT) (15Gy vs 11Gy, p=0.02) than obese survivors living in higher SES neighborhoods. Resource poor neighborhoods (standardized effect: 0.09, p<0.001) and CRT (0.14, p<0.001) had direct effects on percent body fat. Associations between neighborhood of residence and percent body fat were attenuated (-0.02, p<0.001) among individuals with a better diet.

Conclusions: The neighborhood in which a childhood cancer survivor resides as an adult is associated with obesity, and obese survivors treated with CRT are more likely to live in neighborhoods with lower SES. Interventions targeting survivors should incorporate strategies that address environmental influences on obesity.

P39. RADIOTHERAPY EXPERIENCE OF LONG-TERM CHILDHOOD CANCER SURVIVORS IN THE NETHERLANDS: CHARACTERISTICS AND TEMPORAL TRENDS (1963-2001). DCOG-LATER COHORT

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Background: Radiotherapy is a traditional cornerstone of childhood cancer treatments. Numerous technical advances have changed clinical practice considerably in recent decades. We aim to describe pediatric radiotherapy characteristics and temporal changes based on four decades of treatment experience among Dutch five-year childhood cancer survivors (CCSs).

Methods: The Dutch Childhood Oncology Group – Late effects after childhood cancer (DCOG LATER) cohort study includes 6,013 five-year CCSs diagnosed 1963-2001 in one of seven academic centers. Radiotherapy characteristics were abstracted from medical notes/letters by trained data managers. We used descriptive analyses and join-point regression analysis to evaluate time-trends in radiotherapy treatment exposure.

Results: Overall, 2,403 (40%) five-year CCSs received any form of radiotherapy at primary tumor diagnosis and/or at the time of recurrence. Radiotherapy was most commonly part of protocols for medulloblastoma (98%) and Hodgkin lymphoma (57%), and least frequently for non-Hodgkin lymphoma (NHL; 25%) and neuroblastoma (21%). The proportion of all five-year CCSs treated with radiotherapy declined sharply over time; from 65% (N=1,279) to 31% (N= 663) to 24% (N=461) during respectively 1963-1984, 1985-1994, and 1995-2001.The most pronounced declines were seen among CCSs with a prior diagnosis of leukemia, NHL, central nervous system (CNS)-non medulloblastoma, and renal tumor, while fairly stable radiotherapy rates were seen for soft tissue tumors, medulloblastoma and germ cell tumors. Salvage radiotherapy among CCSs treated without frontline radiotherapy was mostly used for survivors of leukemia, NHL, and CNS-non medulloblastoma in the last two diagnoses periods.

Conclusions: Radiotherapy treatment exposure declined sharply in five-year CCSs since the 1960s. Survivorship studies benefit from incorporation of radiation exposure details and a full understanding of exposure time-trends. Although the contribution of radiotherapy in pediatric cancer declined, it is very likely that radiotherapy will play an important role in some childhood cancer types in the future.

P40. RISK FACTORS OF SMALL FINAL HEIGHT IN SURVIVORS OF CHILDHOOD CANCER, IMPORTANCE OF THE IRRADIATION DOSE AT THE HYPOPHYSIS GLAND

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Background: Growth failure concerns 10-20% of the survivors of childhood cancer. The present knowledge is insufficient to predict the risks, especially concerning chemo- and radiotherapy treatment details. Our study aimed to define the significant determinants of a small adult height.

Methods: Of the 7670 5-year solid childhood cancer survivors from the FCCSS, a French cohort, and treated before 2001, 2965 were included because they sent back a self-questionnaire between 2006 and 2013, of whose 2776 did not received Growth Hormone (GH). Complete clinical, chemotherapy and radiotherapy histories were collected from medical data at cancer diagnosis adapted to sex and age was calculated. Radiation dose to most organs, including

pituitary gland, and vertebras were reconstituted from technical records of radiotherapy using a homemade software. Small height was defined has < 2 Standard Deviation (SD). Univariable and multivariable logistic regression models were built.

Results: The incidence of small final height was 9.2% (254/2776), 9.3% among women and 9.0% among men (p = 0.8). In a multivariate analysis, being young at the time of the cancer, being already small (< 2DS) at this time, having received high (> 15 Gy) radiation dose to the pituitary or to a large volume of vertebra (>=15 Gy to more than 90% of the volume of > 7 vertebrae), or have received more than 300 mg/m² of CCNU, were independent risk factors of small adult size. Additionally, a late sequelae not related with radiotherapy nor a specific drug of chemotherapy was still significant in multivariable analysis: dialysis.

Conclusions: More studies are needed to validate CCNU impact on growth. Survivors treated with radiotherapy should have a growth monitoring and a research of GH deficiency when having received 15 Gy on 95% of the pituitary gland, and growth control should be done after CCNU when the cumulated dose is > 300 mg/m².

P41. CANCER SCREENING PRACTICES AMONG ADULT SURVIVORS OF RETINOBLASTOMA: RESULTS FROM THE RETINOBLASTOMA SURVIVOR STUDY

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Background: Adult survivors of hereditary retinoblastoma (Rb) are at lifelong increased risk for subsequent malignant neoplasms (SMN). This study aims to describe cancer screening practices of adult Rb survivors for common adult cancers.

Methods: Rb survivors treated between 1932-1994 and at least 18 years of age completed comprehensive questionnaires adapted from the Childhood Cancer Survivor Study (CCSS). We compared them to 2,271 CCSS siblings 18 years or older, without a history of cancer, who completed a CCSS follow-up survey in 2007 and served as non-RB controls. A Log-binomial regression model was used to evaluate differences in self-reported cancer screening patterns of mammography, Papanicolaou (Pap) test, and colonoscopy or sigmoidoscopy between Rb participants (overall and by laterality) and non-Rb controls.

Results: 470 Rb survivors participated (52% female; median age: 48 years (range, 18-77); 53% with bilateral disease; 71 with history of SMN). Among eligible females, there was no difference between the prevalence of screening mammogram (76.2% vs 73.3%, p=0.53) or pap test (82.9%, vs 84.1%, p=0.66) between Rb survivors and non-Rb controls, or between Rb survivors with unilateral vs bilateral disease (80% vs 72.2% for screening mammogram; 83.7% vs 82.3% for Pap test). Among eligible participants, Rb survivors were more likely than non-Rb controls to report a history of screening colonoscopy or sigmoidoscopy (70% vs 55%, p<0.01). However, after adjusting for attained age, the prevalence of colon cancer screening was similar between the two groups (Relative risk [RR]: 1.1, 95% confidence interval [CI]: 0.9-1.3, p=0.31); there was also no difference in colonoscopy uptake in survivors of bilateral vs unilateral disease (71.4% vs 68.6%, p=0.84). Among Rb survivors, females with health insurance were more likely to obtain screening mammograms (RR: 1.7: 95%CI: 1.02-2.8) and older age was associated with colonoscopy or sigmoidoscopy screening (RR: 1.3: 95%CI: 1.2-1.5). Survivors of bilateral disease were more likely to have had contact with a medical professional in the past 2 years, when compared to survivors of unilateral disease (90.0% vs 82.8%, p=0.01).

Conclusions: The majority of adult Rb survivors adhere to general cancer screening guidelines. Although bilateral survivors reported more contact with the medical system, there was no difference in the utilization of cancer screening services between those with unilateral and bilateral disease. Clinicians should continue educating Rb survivors about their future health risks and the importance of population-based cancer screening guidelines.

P42. EDUCATIONAL ATTAINMENT IN LONG-TERM SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background: Diagnosis and treatment of childhood cancer place survivors at risk for lower educational attainment, the increased burden of chronic conditions on attainment has not been examined.

Methods: Participants included 16724 survivors (48% female; mean diagnosis age 9.1 years, current age 36.2 years, time since diagnosis 26.6 years) and 4098 siblings (mean current age 39.3 years) Educational attainment was categorized as college graduation (yes/no) among survivors > age 25 years. Chronic conditions occurring before age 25 years of age were graded using Common Terminology for Adverse Events 4.3. Modified Poisson regression models estimated relative risks (RR) and 95% confidence intervals (CI) of treatment exposures and chronic conditions on education attainment, adjusting for age at diagnosis and sex.

Results: College graduation was reported by 8391 (51%) survivors and 2410 (59%) siblings. Survivors of all diagnoses were more likely to not graduate compared to siblings (all p's<0.05), with survivors of CNS tumor (RR1.36, CI 1.25-1.49), leukemia (RR 1.17, CI 1.07-1.28), and Hodgkin lymphoma (RR 1.17, CI 1.07-1.29) being at higher risk than survivors of neuroblastoma. Compared to survivors with no history of cranial radiation therapy (CRT), higher risk of not graduating college was seen in those who received 20-30Gy (RR 1.16, CI 1.09-1.25), 30-50Gy (RR 1.37, CI 1.26-1.49) and >50Gy (RR 1.35, CI 1.28-1.42). Among survivors not exposed to CRT, dexamethasone had a protective effect on college education (RR 0.88, CI 0.80-0.97) compared to no corticosteroid exposure. Male sex and older age (> 5 years) at diagnosis were associated with being more likely to not graduate college. survivors reporting any serious/life threatening chronic condition prior to age 25 years (grades 3-4) were more likely to not graduate college (RR 1.14, 95% CI 1.10-1.18) compared to no or mild/moderate conditions (grades <3).

Conclusions: Survivors reporting chronic conditions are less likely to complete a college education by age 25 years and may need additional early educational or vocational resources.

P43. IMPACT OF A NURSE NAVIGATOR WITHIN A PEDIATRIC SURVIVOR CLINIC ON SUBSPECIALTY CARE COMPLIANCE AND ANNUAL SURVEILLANCE

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Background: Pediatric cancer survivors are at risk for life-threatening chronic conditions that require management by multiple providers. The objective of this analysis was to describe the feasibility of using a nurse navigator within an established pediatric survivor clinic and determine the impact on survivors' compliance with subspecialty care and annual survivor clinic follow-up.

Methods: This was a two-arm randomized pilot study of parent proxies of pediatric cancer survivors <18 years old seen for their annual survivor clinic visit. Participants were randomized to standard of care (SOC) or Nurse Navigator (NN) follow-up. Those randomized to NN received two phone calls at 6-8 and 10-12 weeks following their visit. Up to 5 attempts were made to complete each call. During the calls, the NN would check the completion of clinic recommendations for subspecialty care and aid in ameliorating barriers identified. The proportion of patients who returned for their annual survivor visit within one year (±3 months) was compared between treatment arms using a chi-squared test. Preliminary review of the completion of clinic recommendations is also reported.

Results: Overall, 158 parent proxies enrolled – 83 NN and 75 SOC. Survivors were a mean 5.7±3.1 years from the completion of therapy and those randomized to NN were older at diagnosis (NN 5.1±3.9 vs. SOC 3.7±3.0 years; p=0.01). At 6-8 weeks, 90.4% of the phone calls were completed. On average, it took two attempts to reach the participant and the call lasted 7 minutes (range: 1-31). Similarly at 10-12 weeks the NN connected with 84.3% of the participants with calls lasting approximately 6 minutes (range: 1-33). Common barriers reported included: scheduling problems, parent/guardian health, insurance issues, and being too busy. At one year, similar return rates were seen for annual survivor clinic follow-up visits (NN 72.3% vs. SOC 81.3%; p=0.19). In a preliminary analysis of the completion of clinic recommendations, 32/35 NN participants and 17/26 SOC had subspecialty referrals. A higher proportion of those with NN follow-up completed cardiology (NN 71.4% vs. SOC 50.0%), psychology (NN 46.2% vs. SOC 37.5%), and dermatology referrals (NN 57.1% vs. SOC 42.9%).

Conclusions: Even in an established pediatric survivor clinic, a nurse navigator increased subspecialty care compliance. These findings contribute to our understanding of strategies to ensure needed care is received, ultimately decreasing complication-related healthcare costs.

P44. CLUSTERS OF HEALTH BEHAVIORS AND THEIR DETERMINANTS AMONG ADULT SURVIVORS OF CHILDHOOD CANCER

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Background: Health behaviors are generally studied separately, despite the existing evidence suggesting that health risk behaviors were not independent. To our knowledge, there are few studies have examined the clustering of healthy risk behaviors among childhood cancer survivors.

Methods: The present study focused on the 3149 patients treated in France for solid cancers in childhood who sent back the questionnaire. Latent class analysis was used to identify health behavior patterns using data regarding physical activity, unhealthy eating behaviors (current body mass index), smoking, cannabis use, and alcohol consumption. Multinomial logistic regression analysis was used to examine the associations between these latent health behavior patterns and demographic, social, health, and treatment-related risk factors.

Results: Three health behavior patterns emerged: 'Low-risk' (n = 1099, 34.90%), included the participants who exhibited the lowest probabilities for all risk behaviors; 'Insufficiently active' (n = 1459, 46.33%), and 'High-risk' (n = 591, 18.77%) for survivors who exhibited the highest probabilities for smoking (=10 cigarettes per day, 11 to 20 cigarettes per day, or = 21 cigarettes per day), cannabis use, and alcohol consumption (= 3 drinks per week). The multinomial logistic regression analysis revealed that males survivors, with beyond high school, age at first cancer from 12 years, and treated by radiation therapy alone or no radiotherapy and nor chemotherapy were significantly more likely to be in the high-risk group than the low-risk group.

Conclusions: As childhood cancer survivors remain a vulnerable population, to characterize survivor groups according to their health risk behaviors and to identify its potential predictors are important to motivate behavioral change. Ours findings are important for clinicians supervising this population's health care for targeted health interventions on modifiable behaviors for the high-risk group in particular.

P45. ASSESSING STRUCTURAL GROWTH PLATE ABNORMALITIES WITH DIFFUSION TENSOR IMAGING IN HIGH-RISK NEUROBLASTOMA SURVIVORS WITH GROWTH FAILURE

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Background: Survival of patients with high-risk neuroblastoma (HR-NBL) has increased with multimodal therapy. Most survivors demonstrate striking growth failure, yet no studies have examined the mechanism of growth failure in HR-NBL survivors. Cis-Retinoic acid (cis-RA), the cornerstone of HR-NBL therapy, can cause premature growth plate (physis) closure and is a potential explanation for growth failure. Skeletal growth is dependent on columnar chondrocyte proliferation within the physis. Diffusion tensor imaging (DTI) is a magnetic resonance technique that evaluates physeal structure, and a biomarker for growth. The objective of this study was to assess physeal structure in HR-NBL survivors compared to healthy controls by using DTI of the distal femoral physis.

Methods: We prospectively obtained physeal DTI in 20 HR-NBL participants (mean age 12.4 years, 7 females) treated with cis-RA, and 20 age (±1 yr)- and sex-matched controls. We compared fractional anisotropy (FA), normalized tract volume (cm3/cm2), and tract concentration (tracts/cm2) between the groups, in relation to height Z-score and response to growth hormone (GH) therapy. FA is a constant value with respect to age and sex that increases with structural organization. Normalized tract volume and tract concentration reflect the abundance of parallel cartilage columns and new bone in the physis, and highest during the period of greatest growth.

Results: See Table 1 HR-NBL survivors responding to GH treatment compared to non-responders had higher FA (0.25±0.04 vs 0.18±0.03, P=0.02) and tract concentration (31.4±13.7 vs 14.8±7.9, P<0.05). All DTI parameters were linearly related to height Z-score (R2>0.31; P<0.001).

Table 1. DTI parameters (mean±SD) in HR-NBL and matched-control participants.

DTI Parameters	HR-NBL (n=20)	Matched controls (n=20)	P-value
Fractional Anisotropy	0.22 ± 0.05	0.26 ± 0.02	<0.01
Normalized tract volume (cm^3/cm^2)	0.44 ± 0.27	0.70 ± 0.21	<0.01
Tract concentration (tracts/cm^2)	23.2 ± 14.7	36.7 ± 10.5	<0.01

Conclusions: HR-NBL survivors treated with cis-RA demonstrate structural physeal abnormalities that correlate with short stature.

P46. SECOND MALIGNANT NEOPLASMS OCCURRING UNDER THE AGE OF 21 YEARS IN CHILDHOOD CANCER PATIENTS IN SWITZERLAND - A REPORT FROM THE SWISS CHILDHOOD CANCER REGISTRY

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Background: Second malignant neoplasms (SMNs) are among the leading causes of death in children diagnosed with cancer after their primary disease and acute treatment toxicities. We identified SMNs in childhood cancer patients in Switzerland up to the age of 21 years and analyzed their survival to identify risk factors for mortality.

Methods: We used data from the Swiss Childhood Cancer Registry (SCCR) to identify children with a primary childhood cancer (according to ICCC-3) diagnosed under the age of 16 years between 1976 and 2016. We identified those who had developed SMNs up to the age of 21 years and followed their survival until death or loss to follow-up. We used the Kaplan-Meier method to generate survival curves and Cox proportional hazards regression to estimate associations with risk factors.

Results: We identified 8,312 childhood cancer patients (median age at diagnosis 6.1 years, 44% females). Of those, up to the age of 21 years, 130 (1.6%) had developed one SMN and three (<0.1%) two SMNs. The most common primary tumors among those with SMNs were leukemias (n=49, 37%), central nervous system (CNS) tumors (n=22, 17%), and lymphomas (n=19, 14%). Median time from primary to SMN was 6.1 years (IQR 3-10.3y). The most common SMNs were CNS tumors (n=28, 21%), epithelial neoplasms/ melanomas (n=25, 19%), and leukemias (n=23, 17%). Five-year survival after one SMN was 60% (95%-CI 51 – 68%), which contrasted to 5-year survival in patients without SMN of 80% (95%-CI 79 – 81%). None of the patients with two SMNs survived 5 years. A latency from primary tumor to SMN of >5y was seen in 58% (n=78) and was associated with an increased hazard ratio of death (HR 2.4 [95%-CI 1.2-4.8]).

Conclusions: An important proportion of childhood cancer survivors develop SMNs before the age of 21 years which affects negatively their survival. Awareness of SMNs in this patient population is important and strategies for early detection of SMNs should be investigated with a particular focus on those who are later in their follow-up.

P47. ENDOCRINE OUTCOMES IN PEDIATRIC HODGKIN LYMPHOMA PATIENTS FOLLOWING MODERN THERAPY

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Background: Survival rates for pediatric Hodgkin lymphoma (HL) exceed 95% with modern therapy. Risk-adapted therapy was developed with the intent of reducing long-term morbidity while maintaining disease control; however, little is known about late effects associated with this therapy. We evaluated endocrine outcomes of patients treated with modern therapy.

Methods: We conducted a retrospective review of HL patients diagnosed from 2010-2014 at <21 years. Endocrine outcomes included: hypothyroidism requiring medication, thyroid nodules, low testosterone (<200 ng/dL), elevated follicle-stimulating hormone (FSH) in males (=12 mIU/ml), premature ovarian insufficiency (POI; FSH =30 mIU/ml), diminished ovarian reserve (DOR; anti-mullerian hormone (AMH) < normal range), and low bone mineral density (BMD; height-adjusted Z-score <-2). FSH, AMH, and testosterone levels were included if =1 year off-therapy. Censoring occurred on December 31, 2017. Percentage of outcomes in screened patients (based on COG/institutional guidelines) and event-free survival (EFS) using Kaplan Meier statistics were calculated using SAS 9.4.

Results: 163 patients (59% male; 46% non-Hispanic white) were 13.6±3.7 years at diagnosis and followed for 5.0±2.4 years. Initial therapy included: 51% chemotherapy only and 49% multimodality therapy. 5-year EFS was 91% (CI: 85-94%). Salvage therapy included chemotherapy only (n=1), multimodality therapy (n=1), or stem cell transplant (n=12). Overall, 153 patients (93%) received alkylating agents (median cyclophosphamide equivalent dose [CED] 4000mg/m2, IQR 3200-7200). 88 (54%) received radiation (51 supradiaphragmatic, 2 infradiaphragmatic, 35 both; median dose 21Gy). Overall, 29% (40/138) of screened patients developed =1 endocrine outcomes (1 in 21%, 2 in 6%, 3 in 2%). Hypothyroidism was present in 11% (12/110) and 3 patients had thyroid nodules (prevalent at diagnosis) with 1 undergoing malignant transformation. Elevated FSH was present in 14% (7/50) of males and none had low testosterone. 13% (5/40) of females had POI. DOR was present in 93% (14/15) of females who received CED =7000mg/m2 and 5% (1/19) of females who received CED <7000mg/m2. None of the 94 patients screened had low BMD.

Conclusions: In an era of risk-adapted therapy, pediatric HL survivors remain at risk for endocrine dysfunction. Females exposed to CED =7000mg/m2 are at increased risk for diminished ovarian reserve and should be prioritized for fertility preservation approaches prior to initiation of cancer therapy.

P48. PHYSICAL ACTIVITY AND SCREEN TIME IN CHILDREN AFTER CHILDHOOD CANCER ? A REPORT FROM THE SWISS CHILDHOOD CANCER SURVIVOR STUDY

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Background: A healthy lifestyle is important to reduce late effects in childhood cancer survivors (CCS). We described physical activity and screen times in a nationwide study of young CCS in Switzerland.

Methods: As part of the Swiss Childhood Cancer Survivor Study, we sent questionnaires to parents of all Swiss resident =5 year-survivors diagnosed 1995–2010, aged 5–15 years at study. We defined adherence to physical activity recommendations as =7 hours/week (World Health Organization) and screen time recommendations as =2 hours/day (American Academy of Pediatrics). A multivariable logistic regression model was used to assess characteristics associated with physical activity and screen time adherence.

Results: This study included 766 CCS (median [interquartile range/IQR] age at diagnosis 2.8 [1.4–5.0] years; median [IQR] age at study 12.5 [10.0–14.3] years; 56% male). 55% of children adhered to physical activity (median [IQR] 7.3 [4.8-10.0] hours/week) and 68% to screen time recommendations (median [IQR] 1.4 [0.8–2.0] hours/day). Compulsory school sport and walking or cycling to school contributed to more than half of the total physical activity time. CCS were physically less active when living in the French/Italian versus the German speaking region of Switzerland (OR 0.6, 95%CI 0.4–0.9; p=0.005), had a relapse (OR 0.6, 95%CI 0.4–0.9; p=0.03), or musculoskeletal/neurological late effects (OR 0.7, 95%CI 0.5–0.9; p=0.02). High screen times were associated with male sex (OR 0.6, 95%CI 0.4–0.9; p=0.006), lower parental education (OR 0.4, 95%CI 0.2–0.8; P=0.01), and migration background (OR 0.6, 95%CI 0.4–0.9; P=0.02). Brain tumor survivors had lower screen times (OR 2.2, 95%CI 1.1–4.7; P=0.04).

Conclusions: Swiss CCS are not very active. Pediatric oncologists should raise awareness of the importance of being physically active to prevent late effects in CCS. Community policies need to preserve school sports and assure safe ways to school.

P49. UPTAKE OF CLINICAL GENETICS SERVICES AMONG CHILDHOOD AND YOUNG ADULT CANCER SURVIVORS ON A REGISTRY TRIAL

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Background: Prior work suggests that a substantial proportion of childhood and young adult cancer survivors may harbor a heritable cancer susceptibility. Whether survivors will utilize clinical genetics services after participation in a genetic registry is unknown.

Methods: Survivors of childhood and young adult cancer were invited to participate in a genetics registry study. Each participant completed a detailed questionnaire including family cancer history, age at cancer diagnosis, ethnicity/race, and religion, and provided a saliva or blood sample. Using details from the questionnaire, a clinical genetics counselor created and reviewed pedigrees; if this assessment suggested that the participant harbored heritable cancer susceptibility, a referral letter from the study principal investigator for clinical genetics consultation was mailed to the participant.

Results: Of the 948 pedigrees reviewed by a clinical genetics counselor, 790 participants were enrolled in the Adult Long-Term Follow-Up Program (83%), 116 participants were enrolled in the Pediatric Long-Term Follow-Up Program (12%), and 42 in the Lymphoma Program (4%). 163 of the 948 pedigrees (17%) was suggestive of a heritable cancer susceptibility, resulting in 132 referral letters. 30 flagged participants did not receive a letter due to: lack of available relevant clinical testing (15/30; 50%), history of a clinical genetics appointment (9/30; 30%), request not to

be contacted (6/30; 20%). Following delivery of the referral letters, 14% of participants (18/132) completed clinical genetics counseling and five of 18 (28%) were found to have actionable results.

Conclusions: Most childhood and young adult cancer survivors who participated in a genetics registry did not pursue clinical genetics services following family history review and referral via mailed letter. Alternate methods of referral should be explored in this at-risk population.

P50. THE PROJECT FORWARD COHORT: A POPULATION-BASED STUDY OF CANCER-RELATED FOLLOW-UP CARE AMONG SURVIVORS OF CHILDHOOD CANCERS

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Background: Childhood cancer survivors (CCS) are at high risk for co-morbidities and late effects from their cancer treatments and are recommended to receive life-long cancer-related follow-up care. The Project Forward Cohort is a cancer-registry, population-based study examining patterns of long-term cancer-related follow-up care among young adult CCS.

Methods: Risk and protective factors for receiving cancer-related follow-up care were examined among 1,106 CCS diagnosed with any cancer (stage II or greater/all stages for brain) between ages 0-19 during 1996-2010 in Los Angeles County. Cancer registry data were linked with self-report data from surveys that assessed follow-up care and sociodemographic, clinical, and psychosocial factors. Multivariable logistic regression examined factors associated with cancer-related follow-up care within the prior 2 years.

Results: The characteristics of the sample were 50.8% female; 52.1% Hispanic; mean age at survey=25.1, SD=4.9, 18-39; mean age at diagnosis=11.7, SD=5.5; mean years since diagnosis=14.5, SD=4.4, 5-22; 35.4% Leukemia, 21.7% Lymphoma, Brain 15.3%. Overall, 58.1% of CCS reported a recent cancer follow-up visit, 51.7% discussed long-term follow-up care needs with their doctor, and 44.3% received a written treatment summary. Follow-up care steadily declined with greater years since diagnosis and attained age (74.2%, 65.5%, 52.4% and 42.9% among those ages 18-21, 21-25, 26-30, & 31-39 years, respectively; p<.001). In a multivariable logistic regression model (controlling for treatment intensity, socioeconomic status, race/ethnicity) follow-up care was inversely associated with time since diagnosis and attained age, and positively associated with having health insurance, health care self-efficacy, greater knowledge of needing lifetime follow-up care, having a regular (non-cancer) doctor, discussed follow-up care needs with their doctor(s), and having received a written treatment summary (all p's<0.05). The most common health care providers for cancer-related follow-up care included adult oncologists (41.8%), pediatric oncologists (29.9%), and primary care physicians (15.5%). CCS over the age of 26 (vs. younger) were more likely to have seen an adult (vs. pediatric) oncologist. Among those in care, the most commonly endorsed facilitators for their follow-up care included having health insurance (72.5%), ability to assess that their health has not worsened (64.8%), trust in their doctor/nurse (61.8%), early identification of potential health problems (60.7%), and ease of making appointments (58.0%).

Conclusions: Cancer-related follow-up care among CCS declines with attained age and time from diagnosis. Interventions targeting improving patient-provider communication regarding the need for long-term care, health insurance, and patient HCSE and knowledge, may improve follow-up care among CCS throughout young adulthood.

P51. BRAIN CONNECTIVITY AND ACTIVITY PATTERNS AND SOCIAL COMPETENCE IN PEDIATRIC BRAIN TUMOR SURVIVORS

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Background: Pediatric brain tumor survivors (PBTS) experience significant social competence difficulties, including fewer friends, lower peer acceptance and greater social isolation than peers. These challenges may be related to disruptions in the social brain that interfere with social information processing. Understanding the brain-related mechanisms for social impairments is essential to developing prevention and intervention efforts. This study used an MRI protocol to evaluate associations between brain connectivity and activity patterns and indices of social competence in PBTS.

Methods: PBTS (n=19; ages 8-17, > 5 years from diagnosis and 2 years from end of tumor-directed treatment) completed an MRI protocol that included diffusion weighted imaging (DWI) and functional neuroimaging during a Facial Identity Discrimination Task (FIDT). The FIDT consisted of determining if two faces presented side-by-side are the same person compared to a control task of determining if two houses are the same. For DWI data, probabilistic tractography was used to estimate mean brain connectivity using a whole brain parcellation scheme. For FIDT imaging data, GLM analyses compared participant statistical maps with parameter estimates corresponding to each condition (face/house). PBTS also completed a brief evaluation of indices of social competence, including facial affect recognition and social adjustment. Pearson correlations evaluated associations between imaging metrics and indices of social competence.

Results: In the DWI data, mean whole brain connectivity was associated with parent-rated social skills ($r = .57$, $p < .05$) with a trend association with social impairments ($r = .46$, $p = .06$). Activity strength in bilateral fusiform gyrus areas during a facial processing task (faces v. houses) was associated with facial affect recognition accuracy (r's = .52 to .56, $p < .05$). Additionally, activity strength in the right fusiform gyrus was associated with more social impairments ($r = .64$, $p < .01$) and poorer social relationships ($r = .57$, $p < .05$).

Conclusions: Findings highlight potential mechanisms for poor social outcomes in PBTS. Linking PBTS social deficits to brain-related processes may enhance intervention development based on the premise of neural plasticity. Expertise training in facial processing can enhance both facial processing and brain activity in facial processing regions and exercise has been shown to enhance structural connectivity in PBTS.

P52. FEMALE FERTILITY PRESERVATION (FP) AT PEDIATRIC CANCER CENTERS: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP (COG)

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Background: Preserved fertility after cancer is a priority for female survivors and their families. Embryo/oocyte cryopreservation are standard of care (SOC) for post-pubertal females. Experimental ovarian tissue cryopreservation (OTC) is the only current option for pre-pubertal girls. We surveyed COG sites about their FP infrastructure and practices.

Methods: A REDcap™ survey was emailed to one individual previously identified as knowledgeable about FP or the Principal Investigator at each COG site. Site specific factors associated with outcomes were determined using logistic regression. All study procedures were IRB-approved.

Results: Responses were received from 144 of 220 sites (65%). Discussions about fertility at diagnosis were reported as routinely held with all females "at risk" of infertility, all post pubertal females, and all females at 113 (78%), 94 (65%), and 65 (45%) of sites respectively. Embryo/oocyte cryopreservation was offered at 95 (70%) institutions and independently associated with large (>120 new patients/year) sites (OR 6.0 95%CI 1.6-22.8) and presence of a FP navigator/team (OR 4.7 95%CI 1.7-13.5). OTC was offered at 64 (48%) sites: 34 (25%) by referral to another institution, 18 (13%) under an IRB protocol, and 12 (9%) as a clinical service. OTC accessibility was associated with large sites (OR 3.2 95% CI 1.1-8.9) and a FP navigator/team (OR 3.2 95%CI 1.4-7.0). A total of 102/133 (77%) sites use gonadotropin releasing hormone analogues (GnRHa) for any indication; 90 (68%) for menstrual suppression, 75 (56%) with the goal of ovarian suppression for fertility preservation, and 27 (20%) for contraception.

Conclusions: Variation in FP services exists across COG. Discussion of infertility risk is not universal. The availability of OTC at treating institutions is limited. The presence of an FP navigator/team is a modifiable factor associated with greater likelihood of accessing SOC and experimental options. Despite conflicting evidence and lack of endorsement from professional societies, GnRHa's are commonly used for FP. These survey results suggest FP services remain inadequate but highlight opportunities for improvement and areas of needed research.

P53. P53 DELETION IN CARDIAC FIBROBLASTS MITIGATES DELETERIOUS CELLULAR CHANGES INDUCED BY DOX

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Background: Doxorubicin (DOX) exposure in pediatric cancer patients leads to progressive changes to the cellular milieu that comprises the heart, which over time results in congestive heart failure. The current study investigates the role of p53 in stress responses to DOX-induced damage in cardiac fibroblasts (CFs), which are the central mediators of the cardiac injury response.

Methods: Primary CFs were isolated from juvenile wild-type (WT) or p53-deficient mice and treated with 3 µM DOX for three hours. Cell health and function were assessed by evaluating proliferation, migration, and gene expression. Gene arrays focused on adhesion, extracellular matrix dynamics, and inflammation were selected to measure a total of 168 genes. Quantification of mitochondrial-specific reactive oxygen (mROS) species production and changes in mitochondrial membrane potential were used to evaluate mitochondrial stress.

Results: In DOX-treated WT cells proliferation and migration were both decreased. While p53 gene deletion had no impact on proliferation, it did restore migratory abilities to the CFs. DOX-induced inflammatory gene expression was attenuated in p53-/- cells. Fifty genes were differentially regulated between the WT control and DOX-treated cells. Only 13 genes were differentially regulated between p53-/- control and treated cells. Inflammatory genes, such as Ccl2 (MCP-1) and its ligand Ccr4 were upregulated 40- and 50-fold in DOX-exposed WT cells. In contrast, Ccr4 was only upregulated 3-fold in the DOX-treated p53-/-, while Ccl2 was not significantly different. Finally, DOX increased mROS and membrane potential in WT CFs.

Conclusions: The dual response in CFs to DNA damage and mitochondrial dysfunction induced by DOX is dependent on functional p53. An inability to adequately produce energy and increased mROS production could represent an early step in the progression to chronic myocardial changes that lead to heart failure. CFs are key mediators of injury response and cardiac remodeling. While significant changes in remodeling and inflammatory genes were noted in DOX-treated WT CFs, p53 deletion completely abrogated these changes. Collectively, these studies suggest that restoring normal CF function could improve overall heart health and inhibition of p53 in CFs may mitigate the detrimental effects of DOX. Future studies will focus on CF-restricted knockout of p53 in vivo, as means to evaluate the cardioprotective potential of blocking p53.

P54. AN INNOVATIVE METHOD FOR SENSOR-BASED FRAILTY ASSESSMENT IN SURVIVORS OF CHILDHOOD CANCER

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Background: Survivors of childhood cancer are at increased risk for premature, accelerated aging and early onset frailty, the decline in physiologic reserve and reduced resilience to stressors that typically occurs with physiologic aging. Frailty is determined by fulfillment of at least three of the five Fried criteria: loss of lean muscle mass, exhaustion, weakness, slowness, and decreased physical activity; however, this method is time-consuming and requires specialized training to administer. Alternatively, the upper extremity frailty meter (FM) leverages sensor technology to rapidly and accurately predict frailty and pre-frailty, with a sensitivity of 94% and a specificity of 98% when compared against the Fried criteria. The application of this technology has thus far been limited to geriatric populations. Our objective was to test feasibility of FM assessment in adolescent and young adult survivors of childhood cancer, and compare mean frailty index (MFI) in survivors to age-matched controls.

Methods: We recruited survivors >1 year off therapy from our Texas Children's Cancer Center Late Effects Clinic, and age-matched controls scheduled for a well visit, immunization, or non-systemic medical concern at the Texas Children's Family Medicine Clinic. All subjects were consented to an IRB-approved protocol (H-38994, PI: Najafi). The FM consists of a wrist sensor wirelessly linked to a tablet device (BioSensics). The seated participant rapidly and fully flexes and extends each arm at the elbow for 20 seconds. Outcome measures including speed, flexibility, power, rise time, moment of inertia, and smoothness are quantified and used to determine the MFI for each arm. Cut points for pre-frailty (0.2-0.34) and frailty (>0.34) were derived from the Fried criteria. Mean MFI was then compared between survivors and controls using a Student t test.

Results: Thirty-six survivors (44% female, mean age 19.2 years, range 13-47 years, median time off therapy 6 years, range 1-36 years) and 34 controls (62% female, mean age 21.2 years, range 13-37 years) participated. Survivors had a higher MFI compared with controls, a difference primarily driven by slowness and weakness (MFI controls: 0.14 +/- 0.05 compared with MFI survivors: 0.18 +/-0.06, p = 0.001). This difference was most pronounced within a subset of 11 survivors who had been exposed to cranial radiation (MFI: 0.22 +/-0.05, p<0.001) (Table 1). No participants met criteria for frailty, but 15/36 survivors and 5/34 controls met criteria for pre-frailty (p=0.013).

Table 1: Mean frailty index in survivors with and without history of cranial radiation compared with controls

Variable	Controls (n = 34)	Cancer Survivors (n = 25)	Survivors Exposed to CRT* (n = 11)	p-value Survivors vs. Controls	p-value CRT Survivors vs. Controls
Dominant Arm (Single task)					
Frailty Index	0.138 ± 0.050	0.168 ± 0.057	0.219±0.046	.034	<.001
Weakness	0.135 ± 0.130	0.234 ± 0.137	0.354±0.118	.006	<.001
Slowness	0.219 ± 0.222	0.404 ± 0.224	0.555±0.127	.002	<.001
Exhaustion	0.270 ± 0.137	0.230 ± 0.123	0.206±0.152	.270	.178
Non Dominant Arm (Single task)					
Frailty Index	0.130 ± 0.048	0.168 ± 0.053	0.182±0.062	.008	.006
Weakness	0.127 ± 0.117	0.202 ± 0.114	0.278±0.104	.017	<.001
Slowness	0.196 ± 0.196	0.354 ± 0.178	0.443±0.151	.002	<.001
Exhaustion	0.303 ± 0.122	0.287 ± 0.162	0.258±0.131	.663	.359

*CRT: cranial radiation

Conclusions: Consistent with expectations from clinical assessments of frailty in large childhood cancer survivor cohorts, we observed a higher mean frailty index among survivors compared with controls, especially among survivors exposed to cranial radiation. The FM is a feasible, time efficient method for assessing frailty in survivors of childhood cancer, requires minimal training, and is readily scalable for extension to larger survivor populations.

P55. LATE CHOLECYSTECTOMY IN SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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Background: Cholecystectomy (CCY) is among the most common operations performed in the developed world and is offered as a cure for symptomatic gallbladder disease. Whether survivors of childhood cancer undergo CCY at a higher rate than the general population is unknown.

Methods: We identified 5-year survivors diagnosed between 1970 and 1999 who self-reported late (>5 years after cancer diagnosis) CCY. Rates of CCY were determined among the entire cohort and in association with various risk factors and treatment exposures. Adjusted rate ratios (ARR) were estimated with multivariable piecewise exponential models.

Results: Among 24,248 survivors (median follow-up 22.3, interquartile range [IQR] 16.2-30.1 years) and 5,038 siblings (median follow-up 26.4, IQR 19.3-33.7 years), the unadjusted cumulative incidence of CCY at age 50 was 7.2% (n=757) in survivors and 6.5% (n=168) in siblings. After adjusting for age, sex and race/ethnicity, survivors underwent CCY at higher rates compared to siblings (ARR=1.3, 95% CI=1.1-1.5). Relative to siblings, acute lymphoblastic leukemia survivors underwent CCY at a higher rate (ARR=1.6, 95% CI=1.3-2.0), all other diagnoses were not independently associated with higher rates of CCY. Among survivors, risk factors for late CCY included female sex, increasing body mass index (BMI) class, exposure to platinum agents and total body irradiation (TBI) (Table).

Conclusions: CCY is performed more commonly among childhood cancer survivors relative to siblings. In addition to known risk factors for gallbladder disease, cancer treatment exposures may further enhance risk for CCY. Awareness and education regarding this observation may ensure timely diagnosis and treatment of symptomatic disease.

TABLE. Multivariable analysis of risk factors for late CCY among survivors.

Variable	ARR* (95% CI)
Female sex	4.0 (3.2-5.1)
Age at diagnosis (years)	
0-3	Referent
4-9	1.1 (0.8-1.5)
10-14	1.1 (0.8-1.4)
≥15	0.9 (0.6-1.2)
Race/ethnicity	
White, non-Hispanic	Referent
Black, non-Hispanic	0.7 (0.4-1.3)
Hispanic/Latino	0.8 (0.5-1.3)
Other	0.6 (0.3-1.1)
Insurance status	
Yes (referent no)	1.1 (0.8-1.5)
Decade of Diagnosis	
1970-1979	Referent
1980-1989	1.0 (0.8-1.2)
1990-1999	1.1 (0.8-1.6)
BMI (kg/m²; ref 18.5-24.9)	
<18.5	0.7 (0.4-1.3)
25-29.9	1.8 (1.4-2.3)
30-39.9	2.7 (2.1-3.5)
≥ 40	4.1 (2.7-6.1)
Cyclophosphamide equivalent dose (mg/m²)	
None	Referent
<4000	1.0 (0.7-1.5)
4000-7999	0.9 (0.7-1.3)
≥8000	1.0 (0.8-1.3)
Any platinum agent	1.5 (1.0-2.2)
Any anthracycline	1.0 (0.8-1.2)
Any antimetabolite	0.8 (0.6-1.1)
Any asparaginase	1.3 (0.9-1.8)
Any topoisomerase inhibitor	1.0 (0.7-1.4)
Any vinca alkaloid	1.3 (0.9-1.7)
TBI	3.2 (1.4-7.4)
Stem cell transplant	1.0 (0.5-2.2)
Abdominal radiotherapy (Gy)	
None	Referent
<10	0.5 (0.2-1.6)
10-29.9	1.0 (0.8-1.4)
≥30	0.8 (0.6-1.2)

*also adjusted for attained age (as cubic splines)

P56. GAPS AND OPPORTUNITIES IN SURVEILLANCE FOR LATE EFFECTS IN PEDIATRIC PATIENTS RECEIVING TYROSINE KINASE INHIBITOR THERAPY

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Background: While tyrosine kinase inhibitors (TKIs) have revolutionized the treatment of children with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ALL) and chronic myeloid leukemia (CML), screening recommendations for off-target late effects are lacking. Due to the potential TKI associated risk for endocrine and cardiac late effects among Ph+ALL and CML patients, we evaluated institutional screening practices among those who had received TKIs.

Methods: This is a retrospective analysis of patients with Ph+ALL/CML diagnosed between 2000-2015 who received TKIs for >6 months. Treatment details, echocardiograms (ECHO), electrocardiograms (EKG), dual-energy x-ray absorptiometry (DXA), thyroid function (TSH, Free T4), and gonadotropins (FSH, LH, AMH, estradiol, testosterone in those =13 years) following diagnosis to May 31, 2016, were abstracted. Patients were eligible for survivor clinic at two years post therapy completion. Descriptive results are presented by diagnosis and if recommended for screening by nonTKI therapy per Children's Oncology Group (COG) Survivorship guidelines.

Results: Ph+ALL (Table 1)(n=20): Patients initiated TKI therapy at age 9.6±5.2 years, had 2.7±1.7 years of TKI exposure and 4.4±2.8 years of follow-up. All patients received anthracyclines and steroids: 90% had an ECHO, 45% had an EKG, and 35% had a DXA. Among the 12 patients who also received cranial or total body irradiation, thyroid function was evaluated in 58.3%. Gonadotropins were checked in 57.1%. Of patients without exposure recommendations, thyroid function and gonadotropins were checked in 37.5% and 50%, respectively. Seven patients were eligible for survivor clinic, of which 5 had been seen. CML (Table 1)(n=28): Patients were diagnosed at 12.2±3.8 years, had 5.4±3.5 years of TKI exposure and 5.7±3.1 years of follow-up. Four patients had exposures with screening recommendations: 2/3 had an ECHO, 1/3 had an EKG, 1/4 had a DXA, 2/3 had thyroid function, and 1/4 had gonadotropin testing. Among the patients without screening recommendations, 44% had an ECHO, 44% had an EKG, 8.3% had a DXA, 40% had thyroid function and 19% had gonadotropins checked. Two patients were eligible for survivor clinic, of which 1 had been seen.

Table 1. Summary of Late Effects Surveillance by Diagnosis and Presence or Absence of non TKI Exposures with COG Guideline Screening Recommendations

	Ph+ALL (n=20)		CML (n=28)	
	Has Exposure Based Screening Recommendation	No Exposure Based Screening Recommendation	Has Exposure Based Screening Recommendation	No Exposure Based Screening Recommendation
Echocardiogram	90.0% (18 / 20)	---	66.7% (2 / 3)	44.0% (11 / 25)
Electrocardiogram (EKG)	45.0% (9 / 20)	---	33.3% (1 / 3)	44.0% (11 / 25)
Dual-energy X-ray Absorptiometry (DXA)	35.0% (7 / 20)	---	25.0% (1 / 4)	8.3% (2 / 24)
Thyroid Function Assessment	58.3% (7 / 12)	37.5% (3 / 8)	66.7% (2 / 3)	40.0% (10 / 25)
Gonadotropins**	57.1% (4 / 7)	50.0% (2 / 4)	25.0% (1 / 4)	19.0% (4 / 21)

Numerators are number of patients with screening completed. Denominators are total number of patients with or without an exposure with COG screening recommendations
** Only includes those ≥13 years old at last follow-up (CML n=25; Ph+ALL n=11)

Conclusions: There is a lack of screening guidelines for children with hematologic malignancies treated with a TKI and opportunities to standardize referrals to survivor clinic for these patients. We have established a prospective study to evaluate annual endocrine and cardiovascular screening to inform evidence-based monitoring guidelines.

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Background: By age 50, up to 81% of childhood cancer survivors (CCS) develop pulmonary dysfunction causing significant morbidity and mortality. However, due to a lack of longitudinal data on pulmonary function starting at diagnosis, lung function trajectory and its associated factors for CCS are not known. This study seeks to measure and understand changes in pulmonary function from diagnosis to survivorship in CCS who received pulmonary toxic therapy.

Methods: We included children <18 years old who were diagnosed with Wilm's Tumour (WT), Extracranial Germ Cell Tumour (GCT) or Hodgkin's Lymphoma (HL) between January 1994 and December 2014. They must have received pulmonary toxic therapy and at least two pulmonary function tests, including one within 90 days of treatment completion. Pulmonary toxic therapy included either chemotherapy agents or lung radiation. Outcomes included age- and sex-adjusted percent predicted values for spirometry, lung volumes, and diffusion capacity of the lungs for carbon monoxide. Patient characteristics were summarized using descriptive statistics. Statistical analysis was performed using interrupted time series analysis, where outcomes are summarized and compared at several time points before and after treatment completion.

Results: A total of 89 children met inclusion criteria, where 78 were diagnosed with HL and 11 with WT or GCT. Overall, preliminary results show that lung function declined immediately following treatment completion. However, a larger decline was observed in female CCS for all three primary outcomes, and this observed decline continued with poorer lung function outcomes and recovery within the 4-year post-treatment period.
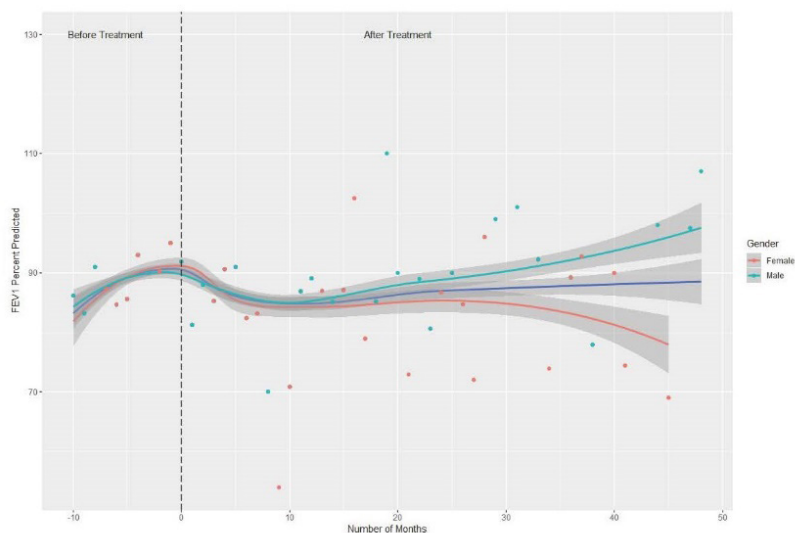
Figure 1. Trajectory of percent predicted forced expiratory volume in 1 second before and after treatment completion by gender.

Conclusions: Our results show that lung function declines immediately among CCS post-pulmonary toxic cancer treatment. The long-term lung function trajectory is variable, with some patients stabilizing or improving after about a year and others declining throughout the study period. These findings provide new elements of consideration in the treatment of childhood cancers with pulmonary toxic therapy. The findings also provide insights on potential risk factors associated with lung function trajectories and will help identify subsets of the population at a higher risk of respiratory dysfunction at an older age.

P58. PULMONARY LATE EFFECTS IN SWISS CHILDHOOD CANCER SURVIVORS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION: A REPORT FROM THE SWISS CHILDHOOD CANCER SURVIVOR STUDY

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Background: Childhood cancer survivors (CCS) treated with hematopoietic stem cell transplantation (HSCT) have an increased risk to develop pulmonary late effects. This study investigates prevalence and risk factors for self-reported pulmonary late effects in a national cohort of CCS treated with HSCT.

Methods: As part of the Swiss Childhood Cancer Survivor Study, we sent a questionnaire to all CCS diagnosed 1976 – 2010, aged <21 years at diagnosis, who had survived =5 years, and were treated with HSCT (autologous and allogeneic). Primary outcomes were self-reported pulmonary late effects (pulmonary fibrosis, emphysema, recurrent pneumonia, and chronic cough). We counted Bleomycin, Busulfan, Nitrosoureas, chest radiation, and thoracic surgery as lung toxic treatment modalities. We collected data on treatment and transplant characteristics, pulmonary infection and graft versus host disease from medical records. We used multivariable logistic regression to assess risk factors associated with pulmonary late effects.

Results: We included 157 CCS (53% male) with a median [interquartile range, IQR] age at diagnosis of 9 [4-14] years and a median time since diagnosis of 11 [8-16] years. Eighty-five CCS (53%) underwent allogeneic, 62 (38%) autologous, and 14 (9%) both types of HSCT. One third of CCS (n=54) was exposed to at least one lung toxic treatment modality in addition to HSCT. Thirty-four CCS (21%) reported at least one pulmonary symptom with recurrent pneumonia (12%) and chronic cough (8%) being the most common symptoms. We found that age at first HSCT >15 years was the strongest predictor to develop pulmonary problems (OR 7.7, 95%CI 1.9-30; P=0.004).

Conclusions: This cohort of CCS after HSCT has a high prevalence of self-reported pulmonary late effects. The burden might be even higher with longer follow-up times and objective pulmonary assessments. Clinicians need to follow and counsel this population at risk to minimize further pulmonary damage.

P59. INITIAL FEASIBILITY AND ACCEPTABILITY OF A DIGITAL HEALTH SELF-MANAGEMENT INTERVENTION FOR AYA SURVIVORS

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Background: We describe the feasibility and acceptability of a digital health intervention that includes electronic survivorship care plans (SCP) and a companion app for adolescent and young adult (AYA) survivor self-management being evaluated in a randomized control trial (RCT).

Methods: AYA survivors were randomized to receive an electronically created SCP and an app intended to enhance SCP uptake vs. SCP alone. SCPs were tailored by treatment and disease history. The app included daily tailored text messages related to SCP content as well as features to enhance health promotion. Feasibility was assessed via indices of time cost analysis and technology issues for both arms. Acceptability items common across both study arms (15 items) are described.

Results: Ongoing enrollment includes 224 AYA who have completed baseline; 176 (mean age=20.07, 80% White, and 47% female) completed follow-up measures. Feasibility is evidenced by mean minutes to: 1) complete treatment summary for SCP preparation (14.1), 2) create SCP (9.6), review SCP with AYA (5.7), and download and explain app (7.8). Difficulties accessing technology for 13 AYA, which were easily remedied, related to lost/new phone, app platform missing patient data, log-in issues, and the app crashing. Acceptability ratings were highest (=3.25/5) for 4 items related to the SCP (e.g., improving knowledge, impact quality of life) and 4 items on general impact (e.g., motivation to improve health behaviors, seek health-related information). AYA (50%) most commonly used the SCP to remind themselves of late effect risks and what they need to do to stay healthy. The group with the app were more likely to report having read the SCP after it was created (p=.012).

Conclusions: Creating and providing an individualized survivorship care plan and accompanying app is a feasible and acceptable mode of self-management intervention for AYA survivors.

P60.   INTERVENTION OUTCOMES AND EDUCATIONAL PREFERENCES FOR IMPROVING KNOWLEDGE OF INFERTILITY RISK IN YOUNG ADULT (YA) SURVIVORS OF CHILDHOOD CANCER

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Background: Many survivors of childhood cancer have misperceptions of their treatment-related risk for infertility. This study evaluates the effectiveness of an educational intervention designed to increase young adult (YA) survivors' knowledge of their risk for future infertility and describes their preferences for fertility-related education

Methods: Patients aged 18-21 were recruited during a survivor clinic visit. Using the PLISSIT model and teach back methods, participants received a one-on-one education session about their risk for infertility using a gender-specific laminated collateral; method 1 (M1). Results from M1 were evaluated, which informed modifications for method 2 (M2) including the addition of a personalized take-home handout. At baseline and one month post intervention, participants completed surveys assessing knowledge of their risk for infertility (Yes/No), level of risk (none, low, moderate, high), impact of cancer treatment on their fertility window, and the need to use protection during sexual activity. Educational preferences were also ascertained. Descriptive statistics were performed and changes in knowledge were assessed using McNemar's test.

Results: 44 survivors were educated using M1 (23 Males/21 Females) and 54 using M2 (22 Males/32 Females). There were no demographic, infertility risk, or baseline knowledge differences between the groups and a majority wanted to have a child one day (77.8% Males/75.5% Females). Among those who completed a follow-up survey in M1 (n=34), significant improvements in correct answers at follow-up were only seen on impact on the fertility window (69.7% vs. 90.9% (p=0.03)). Significant improvements were seen at follow-up in all areas using M2 (n=38): knowledge of overall fertility risk (68.4% vs. 93.1% (p=0.03)), risk level (39.5% vs. 86.8% (p<0.001)), impact on fertility window (55.3% vs. 86.8% (p=0.003)), and needing to use protection (62.2% vs. 81.1% (p=0.03)). Overall 94% of survivors found the intervention helpful and 78% preferred their parents not be included (97% Males/66% Females). In regard to additional resources, 53% would like a website and 54% would like additional discussions with a provider.

Conclusions: YA survivor's knowledge about their risk for future infertility improves with individual education sessions and personalized handouts. Additional communication strategies regarding use of protection to avoid pregnancy need to be developed.

P61. CLINICAL PRACTICE FOR THE SCREENING AND MANAGEMENT OF SUBSEQUENT ASYMPTOMATIC MENINGIOMAS IN CHILDHOOD, ADOLESCENT AND YOUNG ADULT (CAYA) CANCER SURVIVORS: AN INTERNATIONAL PHYSICIAN SURVEY FROM THE INTERNATIONAL LATE EFFECTS OF CHILDHOOD CANCER GUIDELINE HARMONIZATION GROUP (IGHG)

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Background: CAYA cancer survivors treated with cranial radiotherapy are at risk for developing subsequent meningiomas. The IGHG is developing a guideline for the surveillance of subsequent central nervous system neoplasms for this patient group. Data related to clinical decision-making is essential to formulate recommendations. The purpose of this study was to obtain expert opinions concerning management and screening of asymptomatic meningiomas in CAYA cancer survivors.

Methods: A survey consisting of 10 questions to identify the current international clinical practice for the management and screening of subsequent meningiomas among CAYA cancer survivors was created. Fifty-nine specialists from North America and Europe were invited to participate.

Results: Thirty-five out of 59 (59%) responded to the survey, representing expertise in neuro-oncology (n=11), oncology (n=8), radiation oncology (n=6), neurosurgery (n=5), late-effects (n=3), neurology (n=1), and neuroradiology (n=1). Growth (n=33, 97%), location (n=31, 91%) and size of the meningioma (n=29, 85%) were endorsed as the most important factors in the decision to intervene. Intention to treat with either surgery or radiotherapy increases when the meningioma is surgically accessible, large, has an effect on surrounding brain tissue or has a critical location close to vital structures, and perceived to have greater likelihood of adversely impacting health-related quality of life. Challenging locations (n=14, 52%) and indolent tumor growth pattern (n=13, 48%) were endorsed as the main reasons to monitor without intervention. Twelve (44%) physicians explicitly stated that the absence of symptoms (in combination with an uncritical location) influenced decision to not intervene. Physicians also expressed their concerns about harms from MRI screening, including risks of unnecessary investigations (n=25, 73%) and overdiagnosis (n=19, 56%). The reported number needed to screen to detect one meningioma in CAYA cancer survivors varied widely. Moreover, there appeared to be a difference between respondents from the US (median 50, range 0-500) and Europe (median 10, range 0-750). This means that, on average, in the opinion of US respondents, a risk of 2% is a reasonable threshold to justify screening whereas in Europe this is 10%.

Conclusions: There is a lack of international consensus regarding the management of subsequent asymptomatic meningiomas. Accessibility, size, location, and growth pattern are relevant factors in clinical decision-making. Physicians expressed their concerns about MRI screening.

P62. SURVIVOR/PARENT PERCEPTIONS OF CURRENT HEALTH AND CONCERNS REGARDING FUTURE HEALTH OUTCOMES

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Background: Childhood cancer survivors are at risk for late-onset treatment-related complications; however, survivor/parent perceptions regarding current health status and future health concerns are less understood.

Methods: We assessed survivor rating of current/future health concerns via cross-sectional survey administered at a survivorship clinic visit. Survivors (age >18y) or parents (if <18y) rated the following on 5-point Likert scales: current health status (excellent-poor); and concern (very-not at all) regarding: future health; fertility; risk of birth defects/cancer

in offspring; cancer relapse; and new cancers. Multivariable logistic regression models adjusting for relevant co-variates, determined the association between clinical, sociodemographic, and treatment-related variables and parent-/survivor-ratings of health status and concerns. Therapy-related risk for infertility and new cancers were included in relevant models.

Results: A total of 471 surveys were completed (65% parent/caregiver; 35% survivor); mean age at diagnosis: 6.3+5.1y; at visit: 16.4+7.2y; 50.5% male; 70.7% non-Hispanic white; 51.8% leukemia/lymphoma. Excellent/very good health status was endorsed by 68% of survivors; factors associated with being less likely to report excellent/very good health included: older age at diagnosis (OR 0.93/y; p=.02); longer time from diagnosis (OR 0.95/y; p=0.02); female sex (OR 0.77; p=0.02); CNS tumor (ref: solid tumor) (OR 0.45; p=0.03); and low household income (OR 0.38; p<0.0001). Concern regarding future health outcomes was endorsed by 45-54% of survivors

Proportion Very/Somewhat Concerned About...

(Figure). Survivors from low income households were more likely to endorse concerns about future health (OR 1.7; p=0.02), offspring health (OR 1.6; p=0.03); relapse (OR 2.3; p=0.0003); and new cancers OR 1.7; p=0.02). Parents were more likely to endorse concerns about future health (OR 3.0; p=0.0008); relapse (OR 2.9; p=0.001); and new cancers (OR 2.3; p=0.009).
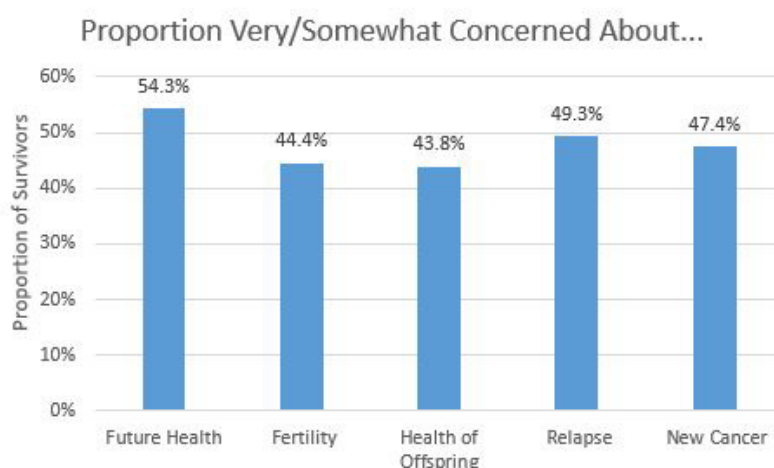
Conclusions: Findings suggest that those from households with lower income and parents (rather than survivors) have increased concern regarding survivor future health outcomes and may benefit from targeted interventions to address these concerns.

P63. ASSESSMENT OF OVARIAN FUNCTION IN ADOLESCENTS AND YOUNG ADULTS AFTER CHILDHOOD CANCER TREATMENT: HOW ACCURATE ARE YOUNG ADULT/PARENT PROXY-REPORTED OUTCOMES?

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Background: Providers treating adolescent and young adult (AYA)-aged survivors of childhood cancer who received gonadotoxic treatment often depend on self-report of survivor's ovarian health when making clinical decisions. The purpose of this study was to determine the agreement between young adult/parent proxy-reported premature ovarian insufficiency (POI) and biochemical POI in this population.

Methods: Data for this cross-sectional study were derived from female survivors (or their parent-proxy) aged 13 – 21.9 years who were participants in Children's Healthcare of Atlanta Childhood Adolescent and Young Adult Cancer Survivor Study (CHOA-CAYACSS), a longitudinal health status survey administered between 2008-2017. Survivors who received gonadotoxic treatment and had ≥1 FSH level were eligible for this study. Survivors who received >30 Gy cranial radiation, bilateral oophorectomy, or had a central nervous system tumor were excluded. Respondent-reported POI was defined as endorsement that the survivor had been told she had ovarian failure or was taking hormone replacement therapy (HRT) for ovarian failure. Biochemical POI was defined as FSH levels ≥40 mIU/ml. The agreement between respondent-reported and biochemical POI was determined using Cohen's kappa coefficient (κ) and analyzed by demographic and clinical factors.

Results: There were 130 eligible survivors included in this study (72.3% non-Hispanic white, 46.2% leukemia survivors, 46.2 % ≥ 18 years of age). Survivors chronicled a median of 4 survivor clinic visits (range 1-13 visits) and 1 endocrinologist visit (range 0-12 visits). Survey results showed that 17.7% reported POI and 18.5% had biochemical

POI (κ=0.66, sensitivity 70.8%, specificity 94.3%). Only 13 survivors (10%) had inaccurate self-reports. The highest agreement of respondent-reported and biochemical POI was with young adult (≥ 18 years of age) self-report (κ=0.78) and survivors with >5 survivor clinic visits (κ=0.83) and/or >5 endocrinologist visits (κ=1.00).

Conclusions: Respondents had increased accuracy of reported POI if the survivor had repeated survivor clinic or endocrinologist visits, highlighting the importance of continued education. AYA-aged survivors of childhood cancer must be well informed about their ovarian function to enable them to advocate for their reproductive health.

P64. CURRENT TRANSITION PRACTICES FOR SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP (COG)

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Background: Pediatric health care professionals and systems must support childhood cancer survivors to optimize their transition to adult care. An effective, coordinated transition does not always take place for survivors, leading to care that is fragmented, age- or developmentally inappropriate, and unable to address their specialized medical, informational, and psychosocial needs. The aim of this study was to assess the current state of healthcare transition services provided by Children's Oncology Group (COG) institutions.

Methods: A 190-question online survey was distributed to 221 COG institutions in 2017 to query current survivor services including transition practices, barriers, and implementation of the Six Core Elements of Health Care Transition 2.0 from the US Center for Health Care Transition Improvement. Descriptive statistics were used to describe transition services.

Results: Representatives from 153 (69.2%) institutions responded to the survey. Of these, 137 institutions (89.5%) reported information about their transition practices. 33.6% were able to see survivors at any age and did not transition survivors elsewhere, while 66.4% transition survivors outside of the treating institution for cancer-related follow up care in adulthood. Of COG institutions who transfer survivors, the age (years) criterion for transition was 18 (8.0%), 21 (13.9%), 25 (7.3%), =26 (11.7%), or based solely on transition readiness of the survivor (25.6%). The most prevalent reported barriers to transitioning survivors to adult care providers were perceived "Lack of knowledge about late effects by the clinician being referred to" (34.8%) and "Lack of survivor desire to leave the comfort of the treating institution or oncologist" (26.1%). Only a minority of institutions reported having an established process to match and communicate with survivors' adult providers (44.4%), incorporating transition readiness assessment into clinical practice (33.3%), having a written transition policy (24.4%), utilizing a transition readiness assessment tool (17.8%), and systematically obtaining feedback from young adults about the transition process (8.9%).

Conclusions: A minority of COG institutions report delivering survivor-focused care that specifically addresses the transition from childhood to adulthood. Therefore, there is no current benchmark for transitional survivorship care in the U.S. Development of best practices is needed, including transition readiness assessments, to guide program development for childhood cancer survivors.

P65. VACCINE PRACTICES OF PEDIATRIC ONCOLOGISTS FOR OFF-THERAPY CANCER PATIENTS

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Background: For pediatric cancer survivors, timely vaccination following treatment is vital for protecting against vaccine-preventable diseases. However, as patients transition into survivorship, it is unclear how pediatric oncologists perceive their role with respect to post-therapy vaccinations. We surveyed pediatric oncologists about their vaccine practices.

Methods: We surveyed pediatric oncologists across nine different states in the United States (N=112; response rate=67.8%). Descriptive statistics were used to summarize demographics, healthcare factors (e.g., access to vaccine records, provider recommendations, barriers), opinions of survivorship guidelines, and the importance of the HPV vaccine to prevent second cancers.

Results: Pediatric oncologists were evenly distributed between males and females. Most were in their first 15 years of practice (62.5%) and Non-Hispanic (83.9%). The majority (80.4%) stated that they recommended age-appropriate vaccines all of the time to their off-therapy patients. However, only 58% reported that they felt vaccine guidelines for pediatric cancer survivors were well-defined. In total, 56.3% of oncologists stated that they do not have previous vaccine records for their patients. Half (49.1%) reported being familiar with their state's vaccine registry and 33% stated they used the registry to obtain vaccine records. Of participants, 36.6% indicated that vaccines are not stocked at their clinic and 52.7% felt that primary care providers should be administering vaccines. Concerning the HPV vaccine, 89.3% of oncologists stated that the HPV vaccine is an important aspect of survivorship for pediatric cancer patients and 90.9% knew that the HPV vaccine prevents cancer.

Conclusions: Most pediatric oncologists do counsel their patients on getting appropriate vaccines after cancer therapy and view the HPV vaccine as an important aspect of survivorship care. Factors limiting pediatric oncologists' ability to manage post-therapy vaccination for cancer survivors include a lack of well-defined vaccine guidelines for survivors and access to previous vaccine records.

P66. MINERALOCORTICOID RECEPTOR ANTAGONIST THERAPY IMPROVES LEFT VENTRICULAR FUNCTION IN CHILDHOOD CANCER SURVIVORS WITH LATE CARDIAC EFFECTS OF ANTICANCER TREATMENT

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Background: Standard of care heart failure therapy fails to prevent progression of advanced anthracycline-induced cardiomyopathy. Recent studies have suggested cardioprotective effects of mineralocorticoid receptor antagonists (MRA) for primary prevention in patients receiving treatment with anthracycline chemotherapy. However, the role of MRA in secondary prevention of late cardiomyopathy is unknown. Therefore, this study tested the hypothesis that MRA treatment prevents progression of cardiomyopathy in childhood cancer survivors.

Methods: This retrospective cohort analysis on 377 adult survivors of childhood cancer in UT Southwestern's childhood cancer survivors' clinic included patients who had: 1) been exposed to anthracyclines, 2) an echocardiogram within the past 10 years, and 3) valid contact information. Clinical, laboratory, and imaging data were extracted from the electronic medical record and cross-sectional symptom questionnaires were administered. Longitudinal changes were analyzed in 3 groups of patients: A) MRA within the past year, B) an alternative cardiac-specific medication, and C) no cardiac-specific medication.

Results: 182 patients met inclusion criteria. Of these 67 completed the study (37%). Most frequent malignancies were leukemia (n=23) and Hodgkin's Lymphoma (n=14). Anthracycline exposure correlated inversely with left ventricular ejection fraction (LVEF) (p=0.005) and directly with end-systolic volume (ESV) (p=0.016). Group A consisted of 4

subjects on eplerenone and 4 on spironolactone. At baseline compared with group C, group A demonstrated lower LVEF (p<0.01) and higher ESV (p<0.05). Group A reported decreased current ability to walk one block compared with group B and C (p=0.013). Administration of MRA resulted in a significant improvement in LVEF (after vs. before administration, p=0.016) whereas there was no change during administration of other medications.

Conclusions: MRA administration as a single drug or in combination with standard of care heart failure therapy may reverse the left ventricular functional decline due to anthracycline induced cardiomyopathy in survivors of childhood cancer. Further prospective investigations are necessary to confirm this effect.

P67. QUALITY IMPROVEMENT INITIATIVE TO DECREASE VARIABILITY IN REPORTING LEFT VENTRICULAR FUNCTION IN PEDIATRIC CANCER PATIENTS: LESS IS MORE

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Background: Evaluation of left ventricular function (LV) to detect chemotherapy-induced cardiac dysfunction using 2D echocardiograms (ECHOs) may be limited by equipment and operator variability. Texas Children's Cancer and Hematology Centers (TCCHC) is one of the largest pediatric cancer programs in the United States, with over 1000 ECHOs performed each year in this patient population. For pediatric cancer patients undergoing serial ECHOs, any significant change in LV function from baseline may be suggestive of therapy-induced cardiotoxicity, therefore both accuracy and precision are essential. Our objective implementing this quality improvement initiative was to reduce reporting variability in ECHOs performed in this population, and also to increase communication between cardiology and oncology services.

Methods: A new standard operating procedure (SOP) was developed to standardize measurement and reporting of LV function in cancer patients at TCCHC. We established a limited team of 5 sonographers and 6 cardiologists to implement this SOP for all ECHOs beginning in January 2018. We performed consecutive ECHOs, including one at baseline, to measure LV end-diastolic dimension (LVEDD), posterior wall thickness (PW), shortening fraction (SF), and ejection fraction by Simpson's biplane (EF) as indicatives of LV function. Image quality was scored based on number of LV segments visualized as described next: score 1, 2 or more LV segments not imaged; score 2, 1 LV segment not imaged; score 3, all segments imaged; score 4, all segments imaged with optimal endocardial border detection. Adherence to the proposed SOP was evaluated every 3 months. A subset of 100 ECHOs pre-SOP and 100 ECHOs post-SOP were randomly selected, and reliability analysis conducted with intra-class correlation coefficient (alpha). Pre/post SOP variables were compared with t-test or Chi-square where appropriate.

Results: The 100 ECHOs reviewed prior to SOP implementation were performed by 27 sonographers and read by 27 cardiologists. Overall image quality was sub-optimal, with 13% scoring =3. Intra-operative variation (IOV) was excellent for measurement of LVEDD (alpha = 0.98) ,and good for PW (alpha = 0.84) and SF (alpha = 0.85). IOV for EF was poor (alpha = 0.65, p < 0.001). The 100 ECHOs reviewed post SOP implementation were performed by 13 sonographers (92 performed by 5) and read by 12 cardiologists (93 read by 6). Study quality of echocardiograms significantly improved, with 46% scoring =3 (p < 0.001). IOV for measurement of EF was significantly improved post-SOP (alpha = 0.87), while other measures were similar or marginally improved.

Conclusions: In the 12 months following the proposed SOP implementation, we were able to perform and interpret >90% of ECHOs in pediatric cancer patients using a limited set of sonographers and operators. The new SOP improved image quality and reduced IOV of LV EF, thereby facilitating improved detection of chemotherapy-induced cardiac dysfunction.

P68. MALE FERTILITY PRESERVATION (FP) AT PEDIATRIC CANCER CENTERS: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP (COG)

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Background: Preserved fertility after cancer is a priority for male survivors and their families. Sperm banking (SB) before initiation of treatment is standard of care for post-pubertal males. Experimental testicular tissue cryopreservation (TTC) is the only current option for pre-pubertal boys. ASCO recommends TTC be carried out under an experimental protocol. We surveyed COG sites about their FP infrastructure and practices.

Methods: A REDcap™ survey was emailed to one individual previously identified as knowledgeable about FP or the Principal Investigator at each COG site. Site specific factors associated with outcomes were determined using logistic regression. All study procedures were IRB-approved.

Results: Surveys were received from 144 of 220 institutions (65%). Discussions about fertility were reported as routinely held with all post-pubertal males, all males "at risk" of infertility, and all males at 108 (75%), 100 (69%), and 55 (38%) institutions, respectively. SB was available at 135 (94%) sites; 105 (73%) offer SB inpatient and outpatient, 88 (64%) offer SB to all post-pubertal males, and 39 (28%) offer SB after chemotherapy has started. TTC was accessible at 37 (27%) sites and was independently associated with large (>120 new patients/year) size (odds ratio [OR] 3.3 95% confidence interval [CI] 1.2-9.3), and the presence of a FP navigator/team [OR 3.3 CI 1.4-7.8). Seventeen sites (12%) offered TTC by referring elsewhere, 14 (10%) under an IRB protocol and 6 (4%) as a clinical service.

Conclusions: SB is widely available across participating COG sites, however only 2/3 of sites offer banking to all post-pubertal males. The availability of TTC at treating institutions is quite limited. This access may be modifiable given the association of an established FP navigator/team with the ability to offer and/or refer patients to outside institutions for TTC. There are practices, such as SB after the start of treatment and offering TTC as a clinical service, that do not align with guideline recommendations. These survey results suggest FP services remain inadequate in this patient population and highlight opportunities for research leading to interventions.

P69. PREDICTORS OF IRON OVERLOAD AND DECREASE IN FERRITIN VALUES OVER TIME IN CHILDHOOD CANCER SURVIVORS

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Background: Iron overload secondary to multiple packed red blood cell (PRBC) transfusions is a serious complication of treatment for childhood cancer that may lead to organ dysfunction and increased infectious risk. Screening for iron overload is done via checking a ferritin value, followed by liver MR for iron quantification. There is known association between volume of PRBC transfusion and increasing ferritin values, but little is known about the predictors of increased ferritins in childhood cancer survivors. In addition, the natural history of ferritin values over time in these patients has not been described.

Methods: Study patients had signed consent to participate in the Childhood Cancer Survivor Registry at Phoenix Children's Hospital. Cancer type, volume of PRBCs received, ferritin values, and demographic variables were recorded. A cutoff of 150 ml/kg was utilized to discriminate between low vs. high volume of PRBCs received. Univariate and multivariate modeling was utilized to determine predictors of high vs. low ferritin values (with a cutoff of 500 ng/ml [nl range 10-150]). For patients who had > 1 ferritin measurement, a rate of change over time was calculated.

Results: Among 505 childhood cancer survivors, 290 (57%) were recorded as having received =1 PRBC transfusion and had = 1 ferritin checked. Patients with lower PRBC volume had a lower mean baseline ferritin measurement (131.9±207.4 vs. 407.5±450.1, p<0.001). There was a moderate correlation between PRBC volume and ferritin value (Spearman's Rho = 0.38, p<0.001). Female gender and leukemia diagnosis but not race were significantly associated with higher ferritin values and PRBC volumes in univariate analysis. Only older age at diagnoses (OR 1.37, 95% CI 1.22-1.54, p<0.001) and PRBC volume (OR 149.1 for >150ml/kg PRBC volume, CI 12.3-1808.5, p<0.001) was significantly associated with ferritin of >500 in multivariate logistic regression analysis. 109 patients (37.6%) had =2 ferritin values checked over time, and ferritin levels did drop significantly over time (54% decrease in 107.2 months). A best-fit line was created with an equation of: y= -0.5013x-2.9223 (see Figure).
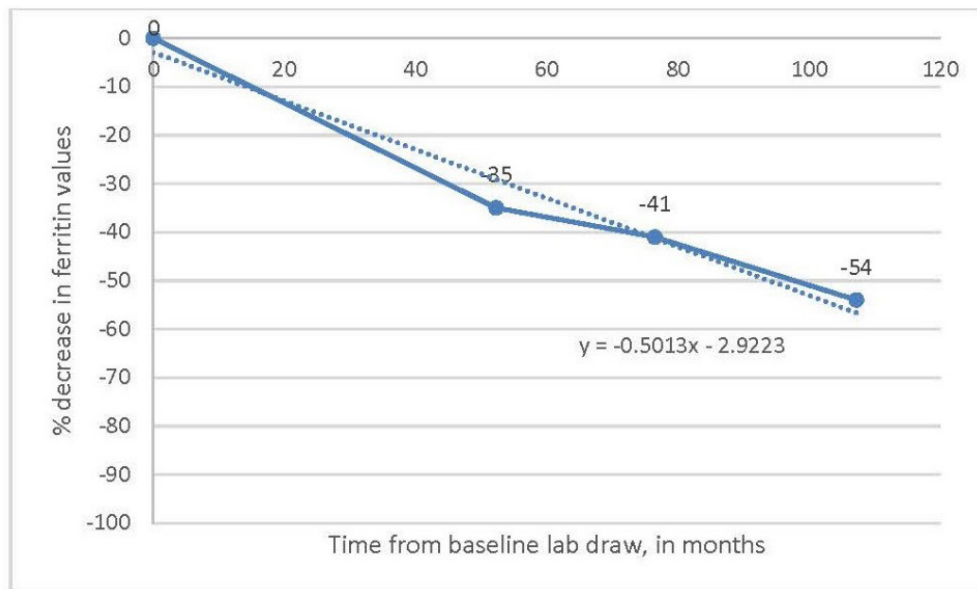
Conclusions: Our data confirms previous work showing ferritin values correlate modestly with PRBC transfusion volume. Older age at diagnosis and total volume/kg of PRBCs transfused were both associated with higher ferritin values. Ferritin values decrease modestly over time. Our modeling would predict that it would take a patient with an initial ferritin value of 1000 ng/ml 105.6 months (8.8 years) to decrease to 500 ng/ml.

P71. SECONDARY THYROID CANCER DETECTED BY SCREENING ULTRASOUND IN ALLOGENEIC STEM CELL TRANSPLANT SURVIVORS

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Background: Hematopoietic stem-cell transplantation (HSCT) is effective treatment for some hematologic malignancies, solid tumors, and non-malignant diseases in children. However, toxicities from chemotherapy and radiation utilized prior to and during transplant puts patients at increased risk for secondary cancers as adolescents and young adults (AYA).

Methods: Study participants protected under IRB approval for retrospective review of survivorship patients within our department for the time period studied. We reviewed data from 170 survivors who had undergone allogeneic HSCT. Since 2014, 7/56 patients exposed to > 400cGy of radiation (12.5%) developed thyroid cancer, all identified via screening ultrasound (U/S). Mean age at diagnosis was 17.2 years (10.9 to 22.6 years). Six of the patients (86%) were transplanted for malignant disease, and received = 800cGy of radiation. One thalassemia patient received only 400cGy of radiation.

Results: The median age at radiation exposure was 5.3 years (range 21-208 months). The median time between radiation exposure and the development of thyroid cancer was 10.3 years (64 to 216 mos). Two patients received radiation at > 10 years of age and developed thyroid cancer at a median of 73 months compared to 132 months for those < 10 years of age at time of exposure. Four of seven patients who underwent screening U/S every three years had lower stage disease. Of the three patients that had longer intervals between screening U/S, two had lymph node involvement. All but one patient required total thyroidectomy. Fifty percent required postsurgical radioactive iodine ablation (RAI) therapy. No patient had distant metastatic disease.

Conclusions: Children who receive radiation therapy are at risk for secondary thyroid cancer as an AYA. While we have small patient numbers, our screening U/S protocol detected thyroid cancer earlier in this patient cohort than previous reports which relied on physical exam findings or symptomology1,2. Additionally, 50% of our patients required RAI compared to > 90% reported in previous studies1. Early detection may limit interventions needed to treat thyroid cancer in this population.

P72. MULTI-ETHNIC SURVIVORS OF CHILDHOOD CANCER (MESCA) COHORT: DEVELOPMENT AND POSSIBILITIES

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Background: Childhood cancer survivors continue to experience substantial risks of life threatening conditions and premature mortality. Longitudinal childhood cancer survivorship cohorts have shaped current understanding of late effects. But research framework for multiethnic survivors using population-based approach and unbiased outcome assessment is lacking. Using individual-level linkages between California Department of Public Health administrative datasets, we aimed to build a population-based research source for multiethnic survivors and severe medical outcomes unrestricted by patient contacts and consents. This retrospective cohort, "Multi-ethnic Survivors of Childhood Cancer (MESCA)" will serve as a rich resource for childhood cancer survivorship research.

Methods: Patients diagnosed with cancer before age 20 from 1988 to 2010 and survived 5+ years were identified from the California Cancer Registry (CCR). Severe medical outcomes were defined as conditions that required hospitalization and those that led to premature mortality from 1993 to 2016. CCR data was individually linked to hospital discharge records from Office of Statewide Health Planning and Development and to vital statistics data from Center for Health Statistics and Informatics using state record numbers, names, date of birth and other personally identifiable data. Hospital discharge and mortality records of California population who have never been diagnosed with childhood cancer were used as comparison.

Results: We identified 34,506 5-year survivors of childhood cancer (15,376 whites, 2,042 African Americans, 13,219 Hispanics, 2,899 Asians and 970 others). Of these, 22,111 were hospitalized at least once. The survivors were hospitalized more frequently for conditions relating to central nervous system, male reproductive systems, blood

disorders, eye/ear/nose/throat disorders and infections compared to non-cancer general population in California. They were less frequently hospitalized at psychiatric care or chemical dependency facilities compared to the general population. Linkage results to vital statistics records are currently undergoing data cleaning.

Conclusions: We report development of our MESCA cohort and demonstrate a great potential for population-based and ethnicity specific assessment of severe late effects. We will continue to explore this rich cohort and provide critical understanding of occurrence and timing of late effects, and contribute to relevant preventive and monitoring effort.

P73. CURRENT CANCER SURVIVORSHIP PRACTICES: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP (COG)

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Background: The 5-year overall survival rate for childhood cancer is >80%, leading to greater than 400,000 survivors of childhood cancer in the United States. These survivors require lifelong monitoring for chronic health conditions. A 2007 survey described the variability of survivor care within Children's Oncology Group (COG) institutions; however, little is known about the current delivery of survivor care. This study aimed to describe current survivor services provided by COG institutions.

Methods: A 190-question online survey was distributed to 221 COG institutions over a 3-month period in 2017. Descriptive statistics were used to describe survivor services.

Results: Of the 153 (69.2%) institutions that completed the survey, 96.7% reported they provide pediatric cancer survivor care either in a specialized late effects program (75.5%) or a general pediatric oncology clinic (24.5%). 88.1% of institutions provided survivors with a copy of their cancer treatment summary. The median time for treatment summary preparation ranged from 30 minutes (range 5-210) for survivors of low-grade Wilms tumor to 90 minutes (range 15-600 minutes) for patients with multiple relapses or stem cell transplant. Many institutions provided a multi-disciplinary approach to survivor care with a pediatric oncologist involved in survivor care at 89.0% of institutions and primary care physician involved at 11.9%. Other disciplines included social work (75.9%), nursing (71.5%), advanced practice providers (62.8%), psychology (49.0%), neuropsychology (44.1%) and nutrition (45.5%). The median face-to-face time for an initial late effects visit was 60 minutes (range 15-330) and 45 minutes (range 15-90) for follow-up visits. While a majority of institutions reported having a specialized late effects program, only 33.6% reported that >75% of eligible patients were seen in a late effects clinic. Philanthropic support was received by institutions to support personnel (41.0%) and enable clinical care (34.3%) for survivors. The most prevalent reported barriers to survivor care were lack of dedicated time for program development (51.6%) and insufficient funding for program support (36.6%).

Conclusions: The majority of responding COG institutions have dedicated care for survivors of childhood cancer; however, at most institutions <75% of eligible patients access this care. Research regarding more efficient technology-based strategies is needed to ensure all survivors have the opportunity to receive appropriate and equitable care.

P74. NURSE NAVIGATORS IMPROVE PARENT-PROXY USE OF AN ELECTRONIC PERSONAL HEALTH RECORD

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Background: Electronic personal health records (PHR) may aid in the self-management of late effects in pediatric cancer survivors. This analysis determines the impact of a nurse navigator on parent-proxy uptake and use of an electronic personal health record, Cancer SurvivorLink (www.cancersurvivorlink.org).

Methods: Parent proxies of pediatric cancer survivors <18 years old enrolled in a randomized pilot study of standard of care (SOC) or Nurse Navigator (NN) follow-up were invited to register for SurvivorLink. Those randomized to NN received two phone calls at 6-8 and 10-12 weeks following their cancer survivor clinic visit during which the nurse navigator provided individualized troubleshooting on SurvivorLink registration and use. Parent proxies who completed registration and the medical records release process for clinic to upload their survivor healthcare plan (SHP) were identified. Comparisons were made between groups using Fishers exact tests.

Results: Overall, 158 parent proxies enrolled – 83 NN and 75 SOC. Survivors were 5.7±3.1 years from the completion of treatment and 63.9% non-Hispanic white with no difference between the groups. Those randomized to NN were older at diagnosis (5.1±3.9 vs 3.7±3.0 years; p=0.01). At enrollment, 19 were SurvivorLink users with their SHPs uploaded, 28 were partial SurvivorLink users with only registration complete, and 111 were new users with no difference between the NN and SOC groups. There was no difference in the partial users who then completed the medical record process to have clinic upload their SHP during the study (NN: 38.5% vs SOC: 20.0% p=0.41). Among new users, those randomized to NN follow-up were more likely to complete registration as compared to SOC (70.5% vs 46.0%; p=0.01). Completion of the medical records release for clinic to upload the SHP was observed in 76.7% (33/43) of the new registrants with NN follow-up compared to 54.2% (13/24) of those with SOC follow-up (p=0.10).

Conclusions: Successful use of an electronic personal health record requires users to complete several steps; however, these steps are often automated after initial registration. Clinical endorsement with nurse navigator follow-up increases the likelihood of initial uptake of an electronic personal health record and in turn their overall use.

P75. HOLISTIC SUPPORT IN SURVIVORS OF CHILDHOOD CANCER IN A RESOURCE-LIMITED SETTING: INTERVENTIONS TO REMEDIATE FINANCIAL HARDSHIP

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Background: Financial hardship in long-term survivors of childhood cancer is increasingly recognized, especially in those with chronic late effects. Survivors of childhood cancer (CCSs) in countries like India which lack established universal healthcare coverage can incur significant out-of-pocket expenditures. Since survivorship care is still not established in most parts of the country, most of our survivors return to our center for surveillance of late effects and medical care. Travel and basic investigations are heavily subsidized by our public funded hospital, but survivors need funding for other medical costs, lodging during hospital visits etc. At our center, we established a paediatric foundation (ImPaCCT foundation) for holistic support of all pediatric patients in 2010, which now also supports CCSs of all ages.

Methods: The After Completion of Therapy (ACT) clinic at Tata Memorial Hospital, Mumbai has been catering to 5-year survivors of childhood cancer since 1991.The core medical team (paediatric oncologist and psycho-oncologist) is assisted by two CCSs who are now adults working for two different Non-governmental organizations (NGOs) to provide guidance and varied support to survivors. Since 2016, we have been receiving funding specifically for CCS from Corporate groups (as part of corporate social responsibility, CSR) and individual donors. Survivors from out of town are provided either lodging by our accommodation NGO partners or reimbursement for stay elsewhere.

Results: There are 2600 CCS registered with the ACT Clinic , of whom over 1800 undergo regular follow up. Of these, 526 (29%) have late effects of at least grade 2 (NCI CTCAE) requiring intervention. Generous funding for treatment of CCS to the tune of Indian rupees (INR) 20 million, the equivalent of 3,00,000 USD (2016- 5 million INR, 2017- 5 million INR, 2018-8.9 million INR, 2019 till date-2.2 million INR) has enabled us to fund 125 survivors of both genders and all ages , from 2016 to date. The large bulk of funds has been used for Growth hormone supplementation (approximate annual cost/person is INR 3,60,00 ie USD 5000) and assisted reproduction, which were both hitherto unaffordable to most survivors. Indian Cancer society is the main NGO partner providing education support, vocational guidance and other rehabilitation, as well as the peer support group, Ugam; their work will be presented separately.

Conclusions: Financial hardship experienced by survivors of childhood cancer in resource-limited settings is a barrier to appropriate follow-up care. It is possible to mitigate this barrier to an extent by providing them holistic care (including financial/ psychosocial) and constant motivation. This model can be replicated partially at other centers facing similar constraints.

P76. COMPARISON OF HEIGHT, WEIGHT AND BODY MASS INDEX AFTER CHEMOTHERAPY WITH AND WITHOUT 12 GY CRANIAL RADIATION THERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: It is unknown whether central nervous system prophylaxis with 12 Gy cranial radiotherapy (CRT) during treatment for childhood acute lymphoblastic leukemia (ALL) leads to shorter stature or higher body mass index (BMI) in survivors when compared to treatment with chemotherapy alone. Purpose: To compare height, weight and BMI trends among patients with ALL treated with chemotherapy with and without 12 Gy CRT.

Methods: We identified 30 children diagnosed with ALL who were treated with prophylactic CRT at our tertiary large children's hospital between 2000 and 2011. Using institutional databases, we then ascertained 35 patients, frequency matching by age at diagnosis and race/ethnicity (minimum 1:1) to the CRT group, treated with chemotherapy only. We obtained height, weight, and BMI values from diagnosis and most recent follow up and converted them into z-scores using the Centers for Disease Control growth charts. Changes in the two time-point Z-scores were then compared across the two treatment groups using ANOVA procedures, adjusting for sex. Additional 3-way ANOVA procedures were also performed to test for possible effects of age at diagnosis and corticosteroid use.

Results: The median age at diagnosis and median follow up since were 5.1 years (range, 1-13.9 years) and 5.4 years (range 3.8-12.5 years), respectively for the whole group with comparable values between the two groups. Thirty-two patients were male (49%) and 48 were Hispanic (71%).There was no statistically significant difference in the change in height, weight and BMI z-scores from initial diagnosis to last follow-up between the two treatment groups in univariate and multivariable analyses. Average z-score changes for height were -0.45 (SD 0.6) and -0.49 (SD 0.8) for CRT and chemotherapy groups, respectively. Corticosteroid type or cumulative doses were not associated with any changes in the study parameters.

Conclusions: There is no evidence that CRT with 12 Gy leads to shorter stature or higher rates of obesity compared to chemotherapy alone in children with ALL. ALL patients are at risk for short stature even when treated with chemotherapy alone.

P77.   METHYLPHENIDATE IMPROVES BMI CONTROL IN CHILDHOOD BRAIN TUMOR SURVIVORS WITH HYPOTHALAMIC OBESITY

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Background: Hypothalamic obesity remains an unrelenting cause of severe obesity for childhood brain tumor survivors. To date, no single therapy provides universal weight control for these patients. Stimulant therapy, such as methylphenidate, has been used to attempt weight regulation despite limited data of efficacy. We aimed to evaluate the impact of long-term methylphenidate therapy on BMI reduction or stabilization in children with hypothalamic obesity at Texas Children's Hospital.

Methods: We performed a retrospective analysis of all children with a history of brain tumor and resulting hypothalamic obesity who received methylphenidate from January 2010 until May 2018. Included subjects were evaluated for BMI trajectory. We collected data before and after methylphenidate start for height, weight, BMI and BMI percent of the 95th percentile for age and gender. We also included data collection of tumor diagnosis, tumor therapy received, endocrinopathies, and growth hormone treatment. Descriptive analysis for demographic data and Wilcoxon sign ranked test was used for comparison of BMI change using the slope of change in BMI percent of the 95th percentile before and after methylphenidate start.

Results: A total of 11 patients were identified with hypothalamic obesity on methylphenidate therapy for at least 6 months (median 1.8 years, range 0.3-4.6 years) with 3 of 11 (27%) completing up to 4 years of treatment. All subjects had a suprasellar tumor (7 [63%] with craniopharyngioma), with 10 (91%) having pituitary dysfunction. Pre-treatment median BMI percent of the 95th percentile was 129% (IQR 25-75: 117.9-139.8%) with BMI z-score of 2.42 (IQR 25-75: 2.19-2.64). Following methylphenidate treatment there was a 16 percent reduction in the slope of BMI change (p <0.05). At methylphenidate completion, median BMI percent of the 95th percentile decreased to 119.3% (IQR 25-75: 108-124.9%) with median BMI z-score of 2.16 (IQR 25-75: 1.91-2.26). Discontinuation of methylphenidate due to side effects was not reported. Of the 8 subjects receiving growth hormone therapy, only 2 patients had growth hormone started within 15 months of methylphenidate start.
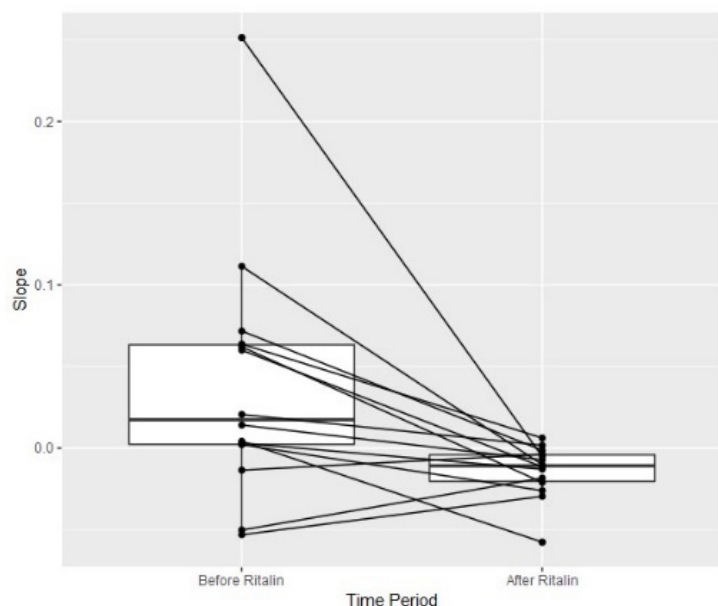
Conclusions: Methylphenidate effectively reduced BMI in children with hypothalamic obesity due to intracranial tumors, for up to 4 years in 27% of users. Stimulant therapy is an effective primary agent that may further reduce weight gain if added early in the course of hypothalamic obesity progression.

P78. TRANSITIONAL CARE POLICIES AND PROCEDURES IN CHILDHOOD CANCER SURVIVORSHIP: A SURVEY OF U.S. INSTITUTIONS

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Background: There are limited reports describing transition of young adult childhood cancer survivors (CCS) from pediatric to adult-focused survivorship care. The purpose of this study was to characterize current transitional care practices in the United States.

Methods: An online survey was sent to one pre-selected respondent at 163 Children's Oncology Group member institutions in the U.S. Data was collected on institutional policies and procedures for transitioning.

Results: The response rate was 60% (97/163). Thirty-nine percent (38/97) of programs delivered specialized care to adult CCS that included transitional care. Typical age of transition was 18-21 years for 42% (14/33) of programs and 22-25 years for 30% (10/33). Most programs "always" (39%, 15/38) or "sometimes" (39%, 15/38) introduced survivors or families to the idea of transitioning greater than 1 year prior to the actual transfer. Patient navigators or transition coordinators were used in 39% (15/38) of programs. Twelve (35%, 12/34) programs assessed if survivors were developmentally and logistically ready for transition; using either provider opinion or an internally developed scale. During the transition, patients were given a Survivor Care Plan (SCP) by 97% (33/34) of programs. Educational messages at the time of transition included insurance (61%, 23/38) and vocational (58%, 22/38) counseling. The accepting adult care provider was notified of the transition by email (34%, 12/35), by receipt of medical summary (31%, 11/35), and by telephone (23%, 8/35). However, 9 programs reported that at least one provider was in both settings and 7 programs reported that this communication occurred in person via a joint visit with both the pediatric- and adult-centered providers.

Conclusions: Our results suggest a need for validated and predictive readiness assessment tools that facilitate the transfer of CCS to adult-centered care. The delivery of SCPs at the time of transition provides a possible benchmark for transitional care of CCS.

P79. CARDIOVASCULAR RISK FACTORS IN ADULT CHILDHOOD CANCER SURVIVORS: PREVALENCES AND ASSOCIATIONS WITH ANAEROBIC CAPACITY

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Background: Cardiovascular disease (CVD) risk related to cancer therapy and an unfavorable lifestyle is common in childhood cancer survivors (CCS). We aimed to assess prevalence of CVD risk factors in a sample of adult CCS and their associations with anaerobic capacity.

Methods: We analyzed baseline data of an ongoing exercise intervention study including =5-year CCS, aged =16 years at study. Treatment exposure was categorized into low, moderate and high risk for CVD depending on anthracycline and radiation dose. We assessed anaerobic capacity by a 1-min sit-to-stand test (STS), overweight and obesity, high waist circumference, hypertriglyceridemia, insulin resistance, and hypertension. We estimated the association between anaerobic capacity and different CVD risk factors by logistic regression models adjusted for sex, age, and CVD risk group.

Results: We included 162 survivors, diagnosed 1976-2012 (56% male) with a median age of 6.7 years (interquartile range (IQR) 3.1-11.8) at diagnosis and 28.4 years (IQR 23.4-36.6) at study. Of the 162 survivors, 28% were at low, 40% at medium, and 32% at high risk for CVD. Median STS repetitions for females were 45 (IQR 38-54; predicted median of Swiss normal population 48, IQR 40-56), and for males 53 (IQR 45-62; predicted median 48, IQR 40-56). Survivors were overweight and obese in 25% and 9%, respectively, had high waist circumferences in 27%, hypertension in 18%, high triglycerides in 19%, and insulin resistance in 29%. Per 10 more repetitions in the STS, we found a decreased risk for high waist circumference (OR 0.62, 95%CI 0.44-0.87, P=0.006), high triglycerides (OR 0.58, 95%CI 0.41-0.82, P=0.002), and insulin resistance (OR 0.69, 95%CI 0.52-0.92, P=0.011). There was no statistically significant association with overweight/obesity and hypertension.

Conclusions: This cohort of CCS is at considerable risk for CVD with high prevalence of CVD risk factors. Increased anaerobic capacity was associated with reduced CVD risk. Our longitudinal data will show whether an exercise intervention improves CVD risk in CCS.

P80. LONG-TERM TOXICITIES IN ADULT SURVIVORS OF CHILDHOOD CANCER IN A RESOURCE-LIMITED SETTING: THE NEED TO FOCUS ON AGEING SURVIVORS

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Background: Adult survivors of childhood cancers are known to have an elevated risk of morbidity and mortality, especially beyond the fourth decade of life. Accelerated ageing seen in survivors of childhood cancer (CCSs) can significantly impact health status. Survivorship care is still developing in parts of world, and there is significant attrition to follow-up due to multiple reasons. There is limited data on late effects in adult CCSs from India.

Methods: After Completion of Therapy (ACT) clinic was established in 1991 at Tata Memorial Hospital, Mumbai and caters to 5-year CCSs. Data of all adult 10-year survivors of childhood cancer (<18 years at diagnosis, >18 years at last follow-up) was retrieved from database and medical records. Late Toxicities were clinically ascertained and graded as per National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI-CTCAE) v4.03 : grade 0- none, grade 1- mild, grade 2-moderate, grade 3-severe/ disabling, grade 4-life-threatening and grade 5-death. CCSs lost to long-term follow-up and with incomplete data were excluded.

Results: Of 2550 CCS (median age 17y, range 2-57y, M:F – 2.8:1) registered with the ACT Clinic since 1991, 937 (36.7%) are over 18y of age, and 228 (9%) over 30 y. Nearly half of adult CCSs have late effects at least grade 2 (NCI-CTCAE) requiring intervention(grade 2-15.5%, grade 3-24%, grade 4-6.4%, death -2%) . Of the 228 adult survivors above 30 y of age (median age 33y, range 31-57y ; ALL -19%, Hodgkin lymphoma-33.6%, M:F -4:1), over 75% had late toxicities requiring intervention (grade 2-22.7%,grade 3-40%, grade 4-12.5%, death-3.7%). This cohort had a median of 2 grade 2, 1 grade 3 and 1 grade 4 toxicity, which expectedly increased to 2,2 and 1.5 respectively in those over 50y. The most frequent toxicities were azoospermia (23%), hypothyroidism (15%), diabetes/ dyslipidemia (15%), viral hepatitis (12.3%), hypertension (8%) and second neoplasms (13%). Notably, in our entire cohort, over half of those diagnosed before 2000 are lost to follow-up, and we have no recent information on these survivors who would be adults if still alive.

Conclusions: The high prevalence of clinically ascertained grade 2-5 late effects in ageing survivors is of concern, especially in settings where a large proportion is lost to long-term follow-up. Our cohort maybe unrepresentative, but even so gives a fair idea. We are working hard to educate survivors and setting up various strategies to improve compliance.

P81. EVENT-RELATED P3B LATENCY TRAJECTORIES OVER 4 YEARS AFTER A DIAGNOSIS OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) ARE AFFECTED BY CRANIAL IRRADIATION AND GLUCOCORTICOID TOTAL DOSE

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Background: The P3b is an ERP component generated by the temporal-parietal junction, the medial temporal complex and the lateral frontal cortex. P3b generation is linked to a working memory updating process when a subject detects deviants in a series of standard stimuli. We used the P3b as a probe to assess brain functioning in children during and after cancer treatment.

Methods: 113 individual children (67 females, 46 males) diagnosed with ALL were recruited from 1993 to 1997, and treated with the Dana-Farber ALL Consortium Protocol 91 and 95 protocols. The mean age at diagnosis was 8.3 years [4.6-22.1 years]. A total of 351 ERP recordings were obtained over five measurement times using a visual oddball task. Time 1 was immediately after the diagnosis. Time 2, 3, 4 and 5 were every year post-diagnosis. In this task, we presented 160 black and white pictures of a moose (75%) or a raccoon (25%) during 100 ms on a computer screen. Participants responded to each stimulus by pressing a left/right button. The electro-encephalogram (EEG) was recorded using 14 electrodes, with a common reference (linked ear lobes). The horizontal and vertical electro-oculogram (EOG) was also recorded. EEG and EOG were sampled at 4 ms/channel (0.1–30 Hz bandpass, X 20,000 for EEG, X 5,000 for EOG) over 2,048 ms (including a 80 ms pre-stimulus baseline) for each trial. The P3b was identifiable across all participants. Latency and amplitude were measured on the left parietal lead where it peaked. Data were analyzed using Latent Growth Mixture Modeling, where the parameters of the individual growth curves are modeled as latent variables.

Results: P3b latency (but not amplitude) was influenced by treatment and subject characteristics. The best model showed that the typical P3b latency decrease across years was significantly influenced by age at assessment and treatment variables. Children treated with cranial irradiation had longer P3b latency, persistently across years, and this effect was stronger in older patients. On the other hand, children who received a total dose of prednisone-equivalent above the group median also had longer P3b latency, especially during treatment, but this effect was stronger in younger children.

Conclusions: P3b latency measured over time provides a reliable marker of treatment effects. We will use trajectories to predict the very late effects, more than 20 years after diagnoses, in the same subjects within the current PETALE study.

P82. DIETARY INTAKE AND DIET QUALITY OF ADULT CHILDHOOD CANCER SURVIVORS COMPARED TO THE GENERAL POPULATION: THE SWISS CHILDHOOD CANCER SURVIVOR STUDY

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Background: Childhood cancer survivors (CCSs) are at increased risk of developing chronic health conditions, which may be reduced by following a healthy lifestyle including a good diet. This study compared the dietary intake and quality of CCSs and the general population.

Methods: As part of the Swiss Childhood Cancer Survivor Study, we sent a food frequency questionnaire (FFQ) to CCSs who had a median age of 34 years (IQR: 29-40 years) and a median of 26 years (20-31 years) postdiagnosis at the time of survey. We compared dietary intake and quality of CCSs and three comparison groups representing the general adult population using FFQ and 24h recall data (24HDR). We evaluated whether mean individual intake met national dietary recommendations and used the Alternative Healthy Eating Index (AHEI) to estimate diet quality.

Results: The 774 CCSs in our study were compared to 8964 participants in the Bus Santé study, 1276 participants in the CoLaus study, and 1134 participants in the Swiss National Nutrition Survey. Dietary intake was equally poor in CCSs and the general Swiss population. CCSs consumed inadequate amounts of vitamin D, fiber, carbohydrates, iron, vitamin A, and calcium (12%, 41%, 72%, 72%, 79%, and 89% of the recommended intakes, respectively), and excessive amounts of saturated fat, protein, cholesterol, and total fat (137%, 126%, 114%, and 107% of the recommended intakes). The mean AHEI score in CCSs was low at 48.0 (men: 45.0, women: 50.9) out of a maximum score of 100. The general population, assessed by 24HDR, scored lower overall than CCSs (41.5; men: 38.7, women: 43.8). Clinical characteristics were not associated with diet quality in CCSs.

Conclusions: Long-term CCSs and the general adult population have similarly poor dietary intake and quality in Switzerland, which suggests population-based interventions for everyone.

P83. PREFERENCE-BASED QUALITY OF LIFE IN PEDIATRIC CANCER PATIENTS AND SURVIVORS: EVIDENCE FROM META-ANALYSES

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Background: Preference-based quality of life (a.k.a. health utility) is a useful metric for comparing effectiveness of cancer therapies. It ranges between 0 and 1 with a higher score indicating better health. However, preference-based quality of life in pediatric oncology has not been summarized systematically. This study aims to conduct a meta-analysis to compare preference-based quality of life between pediatric cancer patients/survivors and general populations by focusing on the effects of diagnoses and treatment modalities.

Methods: Studies published in the PubMed, Embase, Web of Science, and Cochrane Library until October 31, 2018, were included. Meta-analyses were conducted to estimate the weighted means of quality of life associated with cancer diagnoses and treatment modalities by self- and proxy-responses. Mixed-effects meta-regressions were applied to compare differences in quality of life between patients/survivors and general populations (the reference group).

Results: Among 69,538 studies identified, 115 were included. Quality of life was measured by Health Utility Index version 2 and 3. Among patients undergoing active therapies, acute lymphoblastic leukemia (ALL) had 0.129 (95% CI: -0.183, -0.075) and brain tumor had 0.257 (95% CI: -0.354, -0.160) poorer proxy-reported quality of life compared to general populations. Less intensive therapeutic strategies were associated with better quality of life for ALL patients. Among survivors, ALL had 0.062 (95% CI: -0.104, -0.021), brain tumor had 0.179 (95% CI: -0.230, -0.128), and neuroblastoma had 0.084 (95% CI: -0.016, -0.011) poorer proxy-reported quality of life compared to general populations. As the increase in the length of survivorship, quality of life for ALL and brain tumor survivors was improved significantly. Similar findings were observed in self-reports, which however had smaller effects than proxy-reports.

Conclusions: Pediatric cancer patients/survivors had poorer preference-based quality of life than general populations. Our findings highlight the importance of offering interventions to manage quality of life issues for this population.

P84. A PILOT STUDY OF SLEEP-RELATED BREATHING DISORDERS AND HYPERSOMNIA IN ADULT SURVIVORS OF CHILDHOOD HODGKIN LYMPHOMA TREATED WITH THORACIC RADIATION

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Background: Survivors of childhood Hodgkin lymphoma (HL) often report fatigue and daytime sleepiness. The presence of sleep disorders, such as obstructive sleep apnea (OSA), could further increase cardiovascular and cerebrovascular morbidity and mortality in these patients. The purpose of this pilot study was to assess for the presence of sleep-related breathing disorders and hypersomnia in adult survivors of childhood HL treated with thoracic radiation.

Methods: Survivors, =18 years of age and =10 years from diagnosis, were randomly selected from the St. Jude Lifetime Cohort (SJLIFE) study and assessed with nocturnal polysomnography (PSG) and the multiple sleep latency test (MSLT). Enrollment was stratified by body mass index (BMI) to include an equal number of normal weight and overweight/obese survivors. Survivors with a history of neurotoxicity related to cancer therapies, and neurological, genetic, or neurodevelopmental conditions associated with neurocognitive impairment were excluded.

Results: Thirty adult survivors of childhood HL (60% male; 73% white; mean age 35.8 years [range,19.9-52.8]; BMI 28.6 [range, 18.2-43.5]) enrolled, and 14 (47%) met PSG criteria for mild or moderate OSA (OSA; apnea-hypopnea index 5-30). Of those with OSA, 11 had concurrent hypersomnia using the MSLT criteria and 3 of these 11 met diagnostic criteria for narcolepsy. Twelve (40%) had hypersomnia without OSA and 3 of these 12 met diagnostic criteria for narcolepsy. Within the cohort, 86% had objective evidence of OSA and/or hypersomnia/narcolepsy.

Conclusions: Findings suggest adult survivors of childhood HL may be at increased risk for OSA, which when concurrent with treatment-related cardiopulmonary and cerebrovascular risk may further increase morbidity and mortality. Future studies are warranted to compare the prevalence of OSA in this population with a matched community control group and examine whether and how the mechanism for OSA might differ from that in the general population.

Table 1. Demographics and Clinical Characteristics of Participants According to Sleep Disturbance

Variable	Full Sample (n=30)	No Sleep Disorder (n=4)	Hypersomnia (n = 12)	Obstructive Sleep Apnea ± Hypersomnia (n = 14)
Age, years (range)	35.8 (19.9-52.8)	29.4 (25.8-32.1)	32.4 (19.9-43.1)	40.8 (26.2-52.7)
Age at radiation	13.4 (3.3-19.4)	12.9 (9.5-17.8)	13.0 (3.1-18.4)	13.7 (9.3-19.4)
Years since diagnosis	20.3 (11.3-36.6)	14.9 (11.3-22.0)	20.1 (11.4-27.7)	26.0 (12.9-36.6)
Body mass index	28.6 (18.2-43.5)	24.5 (20.9-28.4)	28.2 (18.2-43.5)	30.1 (21.7-43.0)
Gender	18 males	1 male	6 males	11 males
Neck circumference	32.5 (25.5-40.3)	31.1 (28-32.5)	32.4 (25.5-40.3)	33.3 (27.9-38.3)
Neck radiation	24.6 (.2-40) Gy	26 Gy	25.3 (.2-40) Gy	23.6 (21-33) Gy
Chest radiation	25.8 (20-45) Gy	26 Gy	28.1 (26-45) Gy	23.8 (20-36) Gy
Abdominal radiation	14.7 (.2-40) Gy	10 (0-26) Gy	11.8 (2-40) Gy	18 (2-36) Gy
Apnea-hypopnea index	6.9 (0.2 − 29.6)	2.7 (.7-4.7)	2 (0.2-3.7)	12.4 (5.2-29.6)
Minimal O_2 saturation	87 (71 − 95)	92.5 (91-94)	89 (81-95)	85 (71-94)
Spontaneous respiratory arousal	18.7 (0-64)	12.5 (4-22)	5.8 (1-28)	31.5 (0-64)
Fatigue	40.7 (19-52)	43 (32-59)	42.8 (27-52)	38.2 (23-50)
Epworth Sleepiness Scale	7.1 (0-17)	8 (3-13)	7 (1-17)	6.9 (0-13)
Pittsburg Sleep Quality Index	7.6 (2-14)	6.8 (4-10)	6.5 (2-10)	8.7 (4-14)

P85. THE FUNCTIONAL IMPACT OF EXECUTIVE DYSFUNCTION IN BRAIN TUMOR SURVIVORS

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Background: Brain tumors account for appropriately 26% of all childhood cancers and are the second most common cancer diagnosis. While treatment advances have improved five-year survival rates, long-term late effects following treatment completion continue to be prevalent. Neurocognitive sequalae, particularly executive functioning (EF) deficits, are well-documented; however, the impact of these deficits on health related quality of life (HRQOL) in childhood brain tumor survivors is not yet fully understood. Literature in healthy populations recommends using a multi-modal approach to assess EF that utilizes both objective and subjective measures; exclusive reliance on intellectual functioning (IF) measures may not capture the degree of functional impact of EF deficits and associated behaviors on HRQOL. Thus, the use of self and collateral report measures are important components to comprehensive assessment. The primary aim of the current retrospective study was to identify the degree of relationship between IF and parent- and teacher-report measures of EF on HRQOL. It was hypothesized that measures of both IF and EF would be significantly related to functional impact captured by a measure of HRQOL.

Methods: Neuropsychological testing, HRQOL, and medical data were abstracted via systematic medical chart review. In total, 90 brain tumor survivors [61.1% female] followed in a comprehensive brain tumor program were previously administered IF measures (i.e., WISC-V; WISC-IV), collateral report measures of EF (BRIEF-Parent, Teacher), and HRQOL measures (Pediatric Quality of Life™ Inventory, Version 4.0-Self, Parent [PEDSQL]).

Results: Preliminary analyses revealed statistically significant correlations between EF reports and HRQOL (BRIEF– Parent Global Score and PEDSQL–Parent Total Score, $r=-.341$, $p==.001$; BRIEF–Parent Global Score and PEDSQL– Self School Scale, $r=-.240$, $p==.005$; BRIEF–Teacher Total Score and PEDSQL–Self School Scale, $r=-.279$; $p==.005$). No clinically significant relationships were found between measures of IF and HRQOL. Additional analyses will examine the unique contribution of variables of interest in multivariate models.

Conclusions: Initial results suggest HRQOL has the strongest relationship with collateral reports of EF when compared to measures of IF. These findings are consistent with the literature in healthy populations, which suggests that self and collateral measures best capture the functional impact and behaviors consistent with executive dysfunction. Such measures should be used as a part of a multi-method assessment of neurocognitive functioning in survivors. Future prospective research will identify the longitudinal impact of executive functioning on HRQOL and determine how best existing EF interventions can be utilized to improve overall HRQOL of brain tumor survivors.

P88. HOW TO INFORM PATIENTS ABOUT LATE EFFECTS OF CHILDHOOD CANCER: LESSONS FROM A PEER-RESEARCH STUDY

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Background: Childhood cancer survivors (CCS) may face various late effects because of cancer treatment. Because former patients who have been lost to follow-up are a hard-to-reach population, e-health interventions are extremely relevant. However, given the diversity of risks and their probabilistic nature, informing childhood cancer survivors about iatrogenic effects represents a challenge. The aim of this study was to understand how informing former patients, by exploring their beliefs and expectations on this issue, in order to develop an e-health intervention. Based on the hypothesis that talking about the illness and the perceptions of risks would be easier with a peer, a peer-based research was set up.

Methods: A qualitative peer-research was conducted by 7 members of the French Organization of CCS ("Les Aguerris"), in collaboration with social scientists and clinicians. Social scientists taught qualitative methods to peer-researchers during several workshops. Then the 7 peer-researchers conducted and analyzed 28 in-depth interviews made with subjects of the FCCSS (French Childhood Cancer Survivors Study). An additional inductive analysis was conducted by the social scientists, using Nvivo software, based on the thematic analysis framework identified by the peer-researchers.

Results: Former patients who were interviewed were treated for diverse diagnoses (leukaemia, lymphoma, bone tumour, Wilm's tumour, brain tumour, other). Half of them had late effects related to cancer treatment. A familial "taboo" about cancer was reported in many cases (7/28). Overall, many CCS were not fully informed about their medical history and possible late effects. Most of the survivors who had not experienced late effects saw themselves as cured of cancer and thus healthy individuals who did not need to adopt specific health behaviors. Survivors who had experienced a medical condition related to prior treatment wanted to know more about late effects, because they wanted to understand the origin of their current medical conditions rather than to anticipate future additional risks. In addition, several interviewees had a fatalistic perception of adult cancer based on their conception of childhood cancer as an unpredictable and unpreventable disease. Diverse practical implications were proposed by the peer-researchers.

Conclusions: The study shows the importance to take into account the beliefs and expectations of CCS in order to develop effective patient-centered strategies.

P89.   EFFECTS OF METHOTREXATE AND CYTARABINE ON COGNITIVE FUNCTION IN JUVENILE MICE

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Background: Survivors of childhood acute lymphoblastic leukemia (ALL) often experience long-term cognitive deficits, though mechanisms of cognitive decline are not well understood. We measured cognitive function and brain anatomy in juvenile murine models exposed to methotrexate and cytarabine.

Methods: Twenty-one-day old (human age equivalent [HAE] = 6 years old) male mice (C57BL/6J) were administered a combination of methotrexate (10 mg/kg) and cytarabine (5 mg/kg) or 0.9% saline solution intrathecally once per week for three weeks ([HAE] = 9 years). Five weeks following final injection (HAE = 13 years), animals underwent behavioral assessment, including Morris water maze (MWM) to measure spatial learning and memory. Blood was collected to measure circulating leukocytes. Animals were then sacrificed and brains were harvested. Golgi staining was performed on brain sections (200μm) and dendritic complexity, morphology and spine morphology was analyzed across hippocampal regions.

Results: Hippocampal dependent spatial memory was impaired in chemotherapy-treated mice compared to controls (Saline $p < 0.05$; MTX+AraC: $p = 0.32$); treated mice did not prefer the target quadrant in probe trials while controls showed preference for the target quadrant. Golgi staining revealed decreased mushroom spine density across hippocampal regions (DG: $p < 0.0005$, CA1 apical: $p < 0.05$, basal: $p < 0.05$). In addition, dendritic complexity (DG: $p < 0.005$; CA1 apical: $p < 0.05$; CA3 apical: $p < 0.05$) and morphology were altered throughout the hippocampus (DG, CA1, CA3: $p < 0.05$). Elevated circulating leukocytes were detected in serum of chemotherapy-treated mice ($p < 0.05$).

Conclusions: Juvenile mice treated with intrathecal methotrexate and cytarabine demonstrated cognitive deficits similar to human children. These deficits occur in conjunction with anatomical changes in the hippocampus and increased systemic inflammation.

P90. DEVELOPMENTAL DIFFERENCES IN HEALTH RELATED QUALITY (HRQL) IN ADOLESCENT AND YOUNG ADULT (AYA) SURVIVORS OF CHILDHOOD CANCER

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Background: AYAs experience many distinct periods of developmental transition within this life stage. AYA survivors of childhood cancer are at risk for chronic physical and psychosocial health conditions due to treatment-related exposures. Few studies have evaluated HRQL differences that may exist among developmental subgroups of AYA cancer survivors. This study examined HRQL differences across AYA developmental subgroups (early teens 12-14 years; late teens 15-17; emerging adults 18-24; young adults 25-39) of long term childhood cancer survivors.

Methods: Cancer survivors ages 12-39 years who were seen in a long term follow up clinic at time of survey completion (as part of larger HRQL study) and completed therapy >2 years ago were included. HRQL was assessed using PedsQL (<18) and FACT-G (>18) measures. Demographic and treatment data were obtained from EMR. Analyses compared HRQL measure scores among AYA age subgroups and investigated predictors of HRQL outcomes.

Results: A total of 155 patients were included in analysis. Mean age at survey completion was 17.9 [range 12-33] years. PedsQL school functioning was significantly lower for 15-17 year-old compared to 12-14 year-old survivors (M= 77.60, p= 0.01). There were no differences between 18-24 and 25-39 year-old survivors on the FACT-G. PedsQL school functioning was significantly lower for survivors (<18) compared to normative data (p=0.004). FACT-G scores for survivors were significantly higher compared to population norms in all domains (p<0.001) except emotional well-being. Regression CART analysis indicated survivors who were <15 years-old and had not relapsed and survivors who were >15 years old and had >2 late effects had lower PedsQL scores. Survivors who were >21 years-old had lower FACT-G scores compared to <21 years. Survivors who were <21 years-old, >7 years-old at diagnosis, and >6 years from end of treatment had lower FACT-G scores.

Conclusions: Adolescent survivors may be at risk for school problems years after cancer treatment. Young adult survivors may be at greater risk of poor HRQL. This study highlights potential developmental differences in HRQL predictors and outcomes in long term AYA cancer survivors.

P91. MAPPING EARLY VOLUME LOSS IN THE BRAIN FOLLOWING CRANIAL IRRADIATION IN A MOUSE MODEL

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Background: Cranial radiotherapy (CRT) is an important component of treatment for pediatric brain tumours and high risk leukemias but is associated with lasting cognitive impairments in survivors. MRI studies in a C57BL6 mouse model have characterized CRT-induced changes in brain structure which include: (a) early volume loss in the week following treatment, and (b) decreased growth, resulting in progressive deficits. The early volume losses are most widespread; however, their evolution over the days post-treatment have not been characterized. To address this gap, we aimed to characterize changes in volume loss over the first week post-CRT in a mouse model of pediatric CRT.

Methods: C57BL/6J mice were imaged using in-vivo, manganese-enhanced magnetic resonance imaging. Mice were imaged at postnatal day (p) 14, received 7Gy CRT (or sham) at p16, and were subsequently imaged 2-3 times longitudinally over approximately one week. An automated image processing pipeline was used to measure the volume of 159 different brain regions in each image. A linear mixed effects model was used to detect differences in volume trajectory over the whole brain, accounting for both sex and age in the time course.

Results: In most affected regions, volume loss was already evident by p18. Most notable were the dentate gyrus (p = 0.02), the middle cerebral peduncle (p = 0.02), and the fimbria (p = 0.04) which showed a 5% volume loss by p18. The olfactory bulbs did not exhibit volume loss on p18, but did show volume loss by p19, a trend also present in the white matter of the anterior commissure (pars anterior). Volume loss was evident in both gray and white matter structures.

Conclusions: CRT resulted in widespread volume losses over the brain. The pattern of volume loss varied by structure, but was largely observed in the first 1-2 days post treatment. Gray and white matter regions exhibited different patterns of CRT-induced volume change.
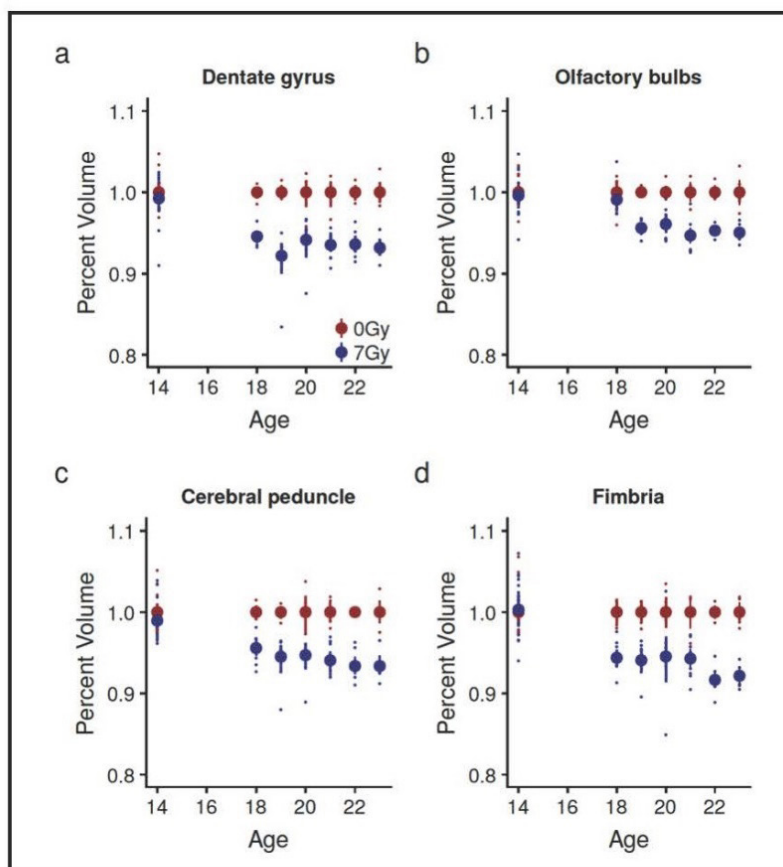
Fig. 1 MEMRI captures volumetric changes in brain structure following 7Gy whole brain CRT (or sham). **a-d** volume change over the course of 10-days. Volumes of each structure for mice receiving sham radiation were normalized, with a mean of 1.0. Mice treated were CRT were plotted relative to sham treated mice, demonstrating percent volume change. Larger points represent means per time point for each group, while smaller points represent a time point for individual mice. Error bars represent bootstrapped confidence intervals. We see that volume loss varied by structure, but the majority of brain regions demonstrated volume losses by p18. Olfactory bulbs did not exhibit volume loss at p18, but instead volume losses were present at p19.

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Background: Over a million survivors of childhood, adolescent, and young adult cancer live in the US; many were treated with radiation therapy (RT). RT to the coronary arteries is a risk factor for cardiovascular disease (CVD). Survivors may be unaware of their high CVD risk or how to mitigate it; tools are needed to improve understanding. The Institute of Medicine recommends decision aids to optimize patient discussions of therapies. We developed and pilot-tested a risk communication tool to improve shared decision making with survivors regarding CVD risk reduction with statin therapy. We included a qualitative arm to further tool development and testing.

Methods: The statin risk communication tool was adapted from a previously validated tool. Participants were recruited from Memorial Sloan Kettering Cancer Center into two arms: control discussion vs. tool-facilitated discussion. All patients were at increased risk for CVD due to history of chest RT. The post-visit survey used Likert-like scales to explore patient perceptions of statins and included knowledge questions and a decisional conflict scale. This pilot study used descriptive statistics and was not powered for significance. Semi-structured interviews with participants in the intervention arm explored the shared decision-making process.

Results: Median participant (n= 46) age was 45. Most intervention patients (22/24, 92%) and 50% (11/22) of controls found statin information acceptable while 31% (7/22) of the control arm selected "not applicable" regarding information acceptability. Most participants were unaware of their personal CVD risk or potential statin side effects. In semi-structured interviews participants found the tool helpful to visualize risk and aid physician conversations; they expressed apprehension at starting a statin.

What is a statin?

A statin is a medication that lowers cholesterol. This can reduce your risk of having a heart attack. Statins may also help your body reabsorb the cholesterol that has built up in your blood vessels. They can also stop more fat from blocking your blood vessels.

For the average 40-year old person with no known cardiovascular risk factors, the chance of having a heart attack in the next 10 years is 1%. This means that out of 100 people, 1 person will have a heart attack in the next 10 years, and 99 will not.

However, people who have been treated with radiation for their cancer are at an increased risk of having a heart attack, even if it's been years since they completed treatment.

Diet and exercise are important tools to improve your cardiovascular risk. Statins may also reduce your chance of having a heart attack.

Memorial Sloan Kettering Cancer Center

Statins reduce the chance of a heart attack in the next 10 years

12 out of 100 who were treated with more than 35 Gy of radiation 10 years ago may have a heart attack.

7 out of 100 people with the same heart and blood vessel problems who took a statin may have had a heart attack.

Things to know when taking a statin

Cost: If you do not have insurance, high-dose statins can cost about $100 per month.

Daily Routine: You will always need to take 1 pill every day.

Possible Side Effects:
Common Side Effects:
• Nausea, diarrhea, or constipation. Most people are okay with these side effects.
Less Common Side Effects:
• Muscle aches and stiffness (affects 1 in 20 people)
• Higher than normal blood liver levels (affects 1 in 50 people, no permanent liver damage).
Very Rare Side Effects:
• Muscle and kidney damage (affects 1 in 20,000 people) and the statin would be stopped.

Pregnancy: If you are pregnant, or trying to become pregnant, you should stop taking statins. If you are not trying to become pregnant, use a reliable form of birth control.

Conclusions: This risk communication tool was acceptable. Many receiving usual care did not recall a conversation, suggesting an absent or forgettable discussion. Knowledge of CVD risk and statins was poor. Qualitative data suggested the tool improved decisional clarity and comfort.

P93. RECALL AND LATE EFFECTS SCREENING FOR ADULT CHILDHOOD CANCER SURVIVORS OF HODGKIN LYMPHOMA PREVIOUSLY LOST TO FOLLOW-UP

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Background: Adult childhood cancer survivors (ACCS) previously treated for Hodgkin lymphoma (HL) are at high risk for late effects (LEs). Many of these patients followed in the community may not have appropriate follow-up and LEs screening. The aim of this project was to determine if patient recall and screening reveals previously unidentified LEs in a population of ACCS previously treated for HL.

Methods: Eligible patients were treated with radiation therapy (RT) for HL in British Columbia at =17 years of age from 1969-2010 and had been lost to follow-up by BC Cancer for at least 5 years. Patients were recalled for clinical assessment (history, physical examination and investigations). Results of their assessments were prospectively recorded. Data on patients' original disease and treatment details were abstracted from their medical chart

Results: 37 ACCS were recalled and assessed (12 males and 25 females). Median age was 16 years (SD=3.61) at diagnosis and 47 years (SD=9.42) at initial reassessment. 28 (75%) received chemotherapy in addition to RT. Of the 37 recalled survivors, 18 had either had a splenectomy or received splenic RT, of whom 14 were unaware of the risk of asplenism and had not received appropriate vaccinations. In total, 19 (51.3%) patients had heart valve disease; 14 were mild to moderate (of which 13 were previously unidentified), and 4 were severe (of which one was previously unidentified). In total 8 (21%) patients had mild to moderate left ventricular dysfunction (5 identified prior to recall and 3 after recall). 10 (27%) patients had coronary artery disease (5 identified prior to recall and 5 after recall with 1 requiring urgent CABG and another refusing surgical intervention). 6 new cases of mild to moderately severe carotid artery stenosis were identified after recall and no surgical intervention was recommended in any cases. 18 (72%) of 25 female patients who had not had mastectomies, were not followed with a high risk breast screening protocol at the time of recall. 7 female survivors (28%) were found to have breast cancer (5 detected prior to recall and 2 detected after recall). 12 (32.4%) patients had colon polyps (4 found prior to recall and 8 after recall). One patient was found to have recurrent lymphocyte predominant HL after recall (34 years after last treatment at BC Cancer). 22 patients (59.4%) became hypothyroid prior to recall and no new cases of hypothyroidism were identified after recall. 5 (13.5%) patients developed thyroid cancer, (3 detected prior to and 2 detected after recall).

Conclusions: ACCS previously treated for HL are at high risk for late-effects. Multiple health issues were identified in many survivors. Recall and reassessment of ACCS lost to follow-up by an oncology center revealed a significant number of previously unidentified health risks and LEs, many of which were amenable to intervention.

P94. BARRIERS, PREFERENCES, AND BELIEFS ABOUT CHILDHOOD CANCER SURVIVORSHIP CARE IN PARENTS AND YOUNG ADULT SURVIVORS

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Background: As few as 20% of childhood cancer survivors receive recommended survivorship care. This study aimed to assess barriers, preferences, and beliefs about survivorship care in parents and young adult survivors.

Methods: Childhood cancer survivors diagnosed with cancer at <18 years at a regional cancer center, cancer free, =1 year off treatment, and without prior survivorship clinic attendance were enrolled on a trial randomizing patients to survivorship care with their PCP or a survivorship clinic. At 12 months post-randomization, patients (or parents of patients <18 years) completed a web-based survey about barriers, preferences, and beliefs regarding survivorship care. Frequencies of barriers, preferences, and beliefs endorsed were described and Fisher's exact tests were used to examine differences between parents and patients.

Results: Thirty-seven parents and 44 young adult survivors completed the survey. When asked about barriers to attending survivorship clinic prior to the study, 99% of respondents reported lack of knowledge (e.g. unaware of risk of late effects), 76% reported avoidance, and 53% reported inconvenience (e.g. time). Young adult survivors were more likely to report inconvenience compared to parents (66% vs. 35%; p=0.01). Regarding preferences, overall, 83% of respondents were willing to be contacted by email or text message by their health care providers. Parents were more willing to be contacted by email/text message compared to young adult survivors (95% vs. 73%; p=0.02). Overall, 41% of respondents would prefer care at a survivorship clinic, 36% with their primary oncologist with a survivorship care plan (SCP), 17% with their PCP with an SCP, and 6% no survivorship care. Overall, 91% of respondents planned to transition to an adult treatment center for survivorship care at some point. Overall, 90% of respondents believed in the utility of survivorship care, 86% felt confident managing their care, 82% planned to get survivorship care in the future, and 62% believed there was a risk of late effects. Parents were more likely to believe in a risk of late effects compared to young adult survivors (76% vs. 50%, p=0.02).

Conclusions: Findings suggest significant differences in barriers, preferences, and beliefs regarding survivorship care between parents and young adult survivors. Understanding similarities and differences can help design and tailor interventions to encourage survivorship care.

P95. PARTNERSHIP IN CANCER SURVIVORSHIP OPTIMIZATION (PICASSO) PROJECT: AN INDIAN CANCER SOCIETY (ICS) INITIATIVE FOR CANCER SURVIVORSHIP PROGRAM IN INDIA

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Background: Indian Cancer Society (ICS) through its project PICASSO has developed a holistic module for survivorship (Ref- ASCO Survivorship symposium 2018 Abstract #208119) The objective is to facilitate the Pediatric Cancer Unit (PCU) to start After Completion of therapy (ACT) Clinic for holistic (Medical & Psychosocial) care of survivors of childhood cancer to improve their quality of life and standardize the survivorship care in India.

Methods: A survey was conducted for identifying survivorship practices in PCUs in Mumbai based hospitals to identify the partners willing to setup the ACT clinic. Hospital provides the infrastructure for ACT clinic as well as dedicated pediatric oncologist. ICS provides professional and technical assistance to PCU & survivors to enable them to live a productive life. The childhood cancer survivors (>two years post treatment & disease free) are registered in a dedicated ACT Clinic wherein late effect evaluation is being done by pediatric oncologist and the clinical psychologist who document treatment details, organs at risk, medical & psychosocial concerns. Survivorship care plan (SCP) is outlined and therapeutic interventions for both medical & psychosocial issues are implemented as per the plan. Medical surveillance & issues are managed by PCU while psychosocial intervention which includes psycho social testing& counseling, career counseling / aptitude tests, registering them as support group members, funding for education, facilitating job placements, is being done by ICS.

Results: Among five Mumbai based PCUs who participated in survey, ICS has partnered with three PCUs during 2018. Total 147 survivors have been registered in all three ACT Clinics. All (100%) have gone through psychosocial assessments. Common psychosocial issues identified and counseled were impairment in task efficiency and memory, deficit in attention and concentration, fear of relapse, presence of why me cognition, recall of unpleasant memories of cancer, & denial of health insurance for future cancer unrelated medical needs. Most common parental issues which needed attention was dilemma in disclosing the diagnosis to the young adult survivor who experienced cancer as child & future uncertainties of life. Twenty survivors received financial support from education fund.

Conclusions: A comprehensive model of survivorship care through partnership of PCU based ACT Clinics with Not for Profit Organization such as ICS will ensure holistic care of survivors & improved quality of life. The module will be implemented across India in the next phase to bring cancer survivorship issues at forefront.

P96. EXPLORING THE PSYCHOSOCIAL LATE-EFFECTS FACED BY ADULT SURVIVORS OF CHILDHOOD CANCER

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Background: Adult survivors of childhood cancer are at an increased risk of developing psychosocial late-effects like depression, anxiety; health related pre-occupations and PTSD (Post Traumatic Stress Disorder) as well as scholastic issues like cognitive impairments and learning disabilities. Together, these can impact the overall quality of life for the adult survivors of childhood cancer. Ugam, a childhood cancer survivors support group of Indian Cancer Society was established in 2009. The current study aims to explore the psychosocial issues faced by Ugam members.

Methods: A psychosocial pro-forma was created in line with various survivorship models established across the world. All Ugam members were contacted by Ugam administrator& those who agreed to undergo the psychosocial assessment were assessed for their psychosocial needs and issues using the pro-forma.The reported concerns were correlated with previous cancer experience.

Results: Of 135 survivors who were assessed on the psychosocial pro-formato address their late effects concern, M: F 102:33, 35% did not report any significant issue which could be attributed directly or indirectly to their cancer experience. However, 65% reported to have various issues which could be linked to their past cancer experience. Five significant concerns reported were in the area of career establishment and guidance (13%), presence of high family stressors (12%), adjustment issues arising out of changes in physical appearance (9%), non-compliance towards follow-up inAfter Completion of Therapy(ACT) Clinic (8%) and health related anxiety (8%).6% had marriage related issues, 4% had fertility concerns. Supportive counseling and need based therapeutic models are being developed& used for those members who have reported these concerns.

Conclusions: Identifying the psychosocial late effects by including them as an integral part of follow up care is essential. Timely, appropriate intervention is recommended in order to ensure a better quality of life for the childhood cancer survivors.

P98. SETTING UP A PAEDIATRIC CANCER SURVIVORSHIP PROGRAMME IN SINGAPORE: THE EARLY YEARS

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Background: KK Women's and Children's Hospital is the only integrated children's hospital in Singapore and provides pediatric oncology care for about 70% of local children. The Paediatric Cancer Survivorship Programme was established in 2017 with philanthropic funding from the Children's Cancer Foundation. The team consists of paediatric oncologists, nurse coordinators, clinical psychologist and a data manager. We describe our journey in setting up, developing and running this programme in its early years.

Methods: Paediatric cancer survivors were identified from the Singapore Childhood Cancer Registry (SCCR), which captures epidemiology, treatment as well as outcomes for paediatric oncology patients seen in public hospitals since 1997.

Results: Survivors were defined as patients who were in complete remission at five years from diagnosis. Therapy details as well as complications were entered into Passport for Care ®, an Internet based tool developed by the Baylor College of Medicine with the Children's Oncology Group (COG) to generate an anonymous, individualized treatment summary and care plan.

Conclusions: Our survivorship programme is in its infancy. We are constantly learning to further the scope of our services to provide holistic care to our survivors. Our initial focus has been on setting up clinical services but we plan on expanding our research horizons with pilot projects to determine incidence and prevalence of chronic health conditions in our survivors in the coming year.

P99. HYPERTHYROIDISM AFTER BONE MARROW TRANSPLANTATION: A REPORT OF TWO CASES

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Background: The thyroid dysfunction is one of the frequently seen complications after bone marrow transplantation (BMT). Although hypothyroidism is the most common endocrine late effect after BMT, hyperthyroidism is a rare condition. Herein, we report a series of 2 patients who were euthyroid before BMT but developed hyperthyroidism after transplantation. Objective: Case reports and the frequency of hyperthyroidism after BMT in our institute.

Methods: Case 1: A 10-year-old boy was diagnosed with adrenoleukodystrophy and underwent transplantation twice from his HLA-unmatched sister when 10 years of age. Conditioning regimens consisted of thoracoabdominal irradiation + Busulfan (Bu) + Cyclophosphamide (CY) + Antithymocyte globulin (ATG) for the first BMT and Bu + CY + ATG for the second BMT due to a rejection of the first BMT. At the time of both BMTs, his thyroid function tests were normal, respectively, and his donor had no history of thyroid disease. Prophylaxis against graft-versus-host disease (GVHD) was used short-term methotrexate (sMTX) and cyclosporine (CyA). He had acute GVHD presenting with nodular rash and prednisolone was initiated. Although subclinical compensated hypothyroidism was demonstrated after the first BMT, hyperthyroidism occurred 3 years after the first BMT. He was treated with methimazole. Case 2: A 15-year-old boy was diagnosed with severe aplastic anemia and underwent transplantation from his HLA-matched sister when 15 years of age. Conditioning regimens consisted of CY + ATG. Prophylaxis against GVHD was used sMTX and CyA. He had no acute and chronic GVHD. Hyperthyroidism occurred 3 years after BMT. After he was followed without treatment for 9 months, we started to treat with methimazole.

Results: Systematic evaluation of thyroid function tests in 156 who underwent BMT and are follow-up at our institute gave a rate of hyperthyroidism at 1.3% in this study.

Conclusions: The clinician should be alert to hyperthyroidism as a possible endocrine late effect after BMT.

P100. DIAGNOSTIC TOOLS FOR EARLY DETECTION OF CARDIAC DYSFUNCTION IN CHILDHOOD CANCER SURVIVORS: METHODOLOGICAL ASPECTS OF THE CROSS-SECTIONAL CARDIAC DCOG-LATER STUDY

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Background: Cancer therapy-related cardiac dysfunction and heart failure are major problems in long-term childhood cancer survivors. To identify survivors at risk who might benefit from early treatment, more evidence on early diagnosis is needed. We hypothesize that assessment of more sensitive echo- and electrocardiographic measurements, and/or biomarkers will allow for earlier recognition of cardiac dysfunction and stratification of patients at risk for developing heart failure. We describe the methodology of the Dutch Childhood Oncology Group LATER cardiology study (DCOG-LATER CARD). Aim of the study is to investigate 1) the magnitude of and risk factors for asymptomatic cardiac dysfunction compared to healthy siblings; 2) the single and joint diagnostic value of echocardiographic and electrocardiographic parameters and blood biomarkers in detecting (asymptomatic) cardiac dysfunction.

Methods: The DCOG-LATER CARD study is a cross-sectional study in 5-year childhood cancer survivors and part of the DCOG LATER study. Data on diagnosis and treatment are collected conform a uniform protocol. Echocardiography will include conventional parameters and strain analysis by speckle tracking. From 2017 to 2020 we expect to include 1,900 survivors (1600 treated with anthracyclines, radiotherapy on the heart region or mitoxantrone and 100 each treated with vincristine only, ifosfamide only or cyclophosphamide only, so without anthracyclines, radiotherapy or mitoxantrone) and 500 siblings.

Results: The eligible CARD study cohort includes 3,608 childhood cancer survivors and 1,066 siblings. The majority of survivors had a primary diagnosis of leukemia, lymphoma, renal tumors, bone or soft tissue sarcomas. Currently (February 2019), we have included 1102 survivors and 129 siblings. Data of echo- and electrocardiographic parameters, biomarkers en clinical parameters are currently collected and analyzed.

Conclusions: The DCOG-LATER CARD study will provide knowledge on different screening modalities for detection of asymptomatic cardiac dysfunction in long-term childhood cancer survivors. The results of the study will enable us to improve long-term follow-up screening guidelines for those at risk for heart failure.
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P101. PATIENT AND PARENT DECISION MAKING IN THE SETTING OF CHEMOTHERAPY-INDUCED SENSORINEURAL HEARING LOSS

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Background: Children with malignancies may be exposed to ototoxic therapies resulting in sensorineural hearing loss (SNHL). There is no consensus whether intervention with amplification is necessary due to a variety of factors such as disease status, speech and language development, and perceived difficulty with communication. The decision to proceed with amplification after cancer can be difficult for patients and families. The purpose of this study is 1) to understand the decision-making (DM) process of childhood cancer survivors (CCS) with SNHL and their parents, and 2) to identify their decisional needs.

Methods: Inclusion criteria were CCS ages 8-30 with a Chang grade >1b SNHL and off-therapy; parents of this group were also eligible. Patients with active disease were excluded. Semi-structure interviews guided by the Ottawa's decision support framework were recorded and transcribed verbatim. Prompts inquired of sources of decisional conflict, role in DM, and DM behaviors. Inductive content analysis of the narrative qualitative data was used.

Results: Seven parents of CCS and five CCS participated. Themes in both groups included: 1) Desire for information specific to cancer-related SNHL; 2) Need for decisional support from both their oncologist and hearing loss specialists; 3) Acknowledgement of SNHL is difficult; and 4) Fear of wearing hearing amplification. Parents more often framed their DM within the context of already experiencing the trauma of cancer, whereas CCS did not. One parent said, "You see all the rubble and you've lived through the devastation of the storm, but now you got to figure out what's broken." Parents also expressed financial concerns. CCS expressed bodily concerns regarding amplification, such as discomfort to the ear and difficulty adjusting to the volume. The following needs were identified: early, re-enforced education regarding late effects risks; open communication between providers, CCS, and parents; and audiogram result interpretations in patient- and parent-friendly language.

Conclusions: Understanding the DM process from the CCS and parent perspectives should be considered when providing counseling for hearing amplification in the setting cancer-related SNHL. Earlier and consistent delivery of late effects education, open communication regarding risk for SNHL, and improved delivery of audiogram results should be targets for meeting unmet needs. These findings should inform the development of decision aids to reduce decisional conflict in this population.

P102. STANDARDIZED MANAGEMENT OF IRON OVERLOAD DECREASES TIME TO COMPLETION OF PHLEBOTOMY IN SURVIVORS OF CHILDHOOD CANCER AND BONE MARROW TRANSPLANT

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Background: Intensive treatment regimens utilized for attaining a cure in childhood cancer and bone marrow transplantation (BMT) patients require aggressive supportive care measures including blood transfusions. Multiple packed red blood cell (PRBC) transfusions may result in iron overload, which, in turn, may lead to liver damage and increased infectious complications. Phlebotomy was initiated for patients with iron overload at Phoenix Children's Hospital in 2013. In January 2017, a multidisciplinary Iron Overload Team was created to develop treatment algorithms and individualize therapy. We hypothesize that the creation of this team decreased time to phlebotomy completion.

Methods: Patients who had undergone phlebotomy at our institution from 2013 to 2019 were identified. Demographic variables, amount of PRBCs transfused, T2* MRI and ferritin data were collected. Start and stop dates for phlebotomy were recorded. Patients were divided into 2 groups: those who started phlebotomy pre-standardization (1/13-12/16) and those who started post-standardization (1/17-1/19). The two groups were compared via chi-squared or paired t-tests.

Results: 25 patients underwent phlebotomy from 1/2013 to 1/2018. Six patients (24%) were diagnosed with AML, 10 (40%) with B-cell ALL, 3 (12%) with T-cell ALL, 3 (12%) with Severe Aplastic Anemia, 2 (8%) with brain tumors, and 1 (4%) with Ewing sarcoma. Ten patients (40%) had undergone BMT. 28% were female, phlebotomy starting age was 14.4±5.8 years, mean PRBC volume received was 316.5±188.2 ml/kg, and mean T2* liver iron was 10.5±4.4 mg/g dry tissue pre-phlebotomy vs. 4.7 ±2.7 post-phlebotomy. 14 patients underwent phlebotomy pre-standardization and 11 post-standardization. There were no significant differences between the groups in terms of gender, age, PRBC volume or liver iron pre- or post-standardization. The pre-standardization group completed phlebotomy in a mean of 610±118.2 days vs. 276±143 days in the post-standardization group (p<0.0001).

Conclusions: The creation of an Iron Overload team to manage and standardize phlebotomy in childhood cancer and BMT survivors significantly decreased time to phlebotomy completion.

P103. EXPLORATION OF ASSOCIATIONS BETWEEN TREATMENT HISTORY AND COGNITIVE OUTCOMES IN SURVIVORS OF ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Previous studies have established cognitive deficits in long-term survivors of childhood acute lymphoblastic leukemia (ALL). However, few have examined cognitive abilities shortly after treatment completion, or potential associations between cognitive performance and treatment history, such as age at diagnosis and cumulative chemotherapy exposures.

Methods: A retrospective chart review was conducted to identify 298 eligible patients diagnosed with ALL between January 2000 and December 2017 at the University of Iowa Hospital & Clinics. Scores from clinical psychological evaluations were pulled from medical records and treatment parameters were extracted from Passport for Care. Psychological assessments included measures of verbal comprehension, visual-spatial abilities, working memory and processing speed. Preliminary analyses were conducted on a sample of 36 ALL survivors (21 females, 15 males) who had neuropsychological assessments and treatment information recorded in our database. One sample t-tests were used to establish if performance of ALL survivors in the sample was significantly different from the normed mean. Participants were categorized based on age of diagnosis at age 10 or younger or older than 10. Cumulative treatment exposures were categorized into low vs. high based on the median split. Linear regression models were run separately for each agent with cognitive performance as the dependent variable and age at diagnosis and chemotherapy exposure as the independent variables.

Results: On average, cognitive performance was evaluated within 2 years after completing treated (SD = 4.0). Working memory and processing speed were significantly lower than population normed IQ scores (M=100, SD=15); WMI (t(20)= -2.90 p < 0.01), PSI (t(23)= -3.45, p < 0.005). However, neither age at diagnosis nor cumulative treatment exposures were associated cognitive performance. Note that few individuals were older than 10 at diagnosis (n=6).

Conclusions: Neurocognitive difficulties in working memory and processing speed were already evident shortly after treatment, suggesting that these problems emerge over the course of ALL treatment. Our preliminary analyses suggest that age at diagnosis and cumulative treatment exposures had limited impact on cognitive outcomes. However, we continue to gather more data to address if and how demographic factors (e.g., sex, age at diagnosis) and treatment may affect cognitive functions in ALL survivors.

P104. THE EXPERIENCE OF HEARING LOSS AND BARRIERS TO HEARING AID ACQUISITION IN ADULT SURVIVORS OF CHILDHOOD AND YOUNG ADULT CANCER: A QUALITATIVE STUDY

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Background: Despite the prevalence of hearing loss after cancer treatment and increasing awareness of associated treatment exposures, little is known about the psychosocial impact of hearing loss and potential barriers to hearing aid acquisition in survivors of childhood and young adult cancers. In this study, we aim to describe the phenomenological experience of hearing loss and explain the disparity between hearing loss and hearing aid use.

Methods: In a phenomenological qualitative study, we conducted in-depth interviews with adult survivors of childhood and young adult cancer who experienced hearing loss after cancer treatment. Included survivors had a history of platinum therapy, cranial radiotherapy, or both, as well as a history of hearing loss determined by audiogram and clinic notes. The study was exempt from IRB; no protected health information was collected or recorded. A single author (AK) interviewed all participants by telephone. Interviews were recorded and transcribed.

Results: Twenty-four survivors with hearing loss were interviewed. Themes characterizing the experience of hearing loss include social isolation, academic and professional challenges, use of adaptive behaviors such as lip-reading, the link between hearing loss and cancer treatment history, and the severity of hearing loss as compared with other late effects and other survivors. Barriers to hearing aid acquisition included cost and perceived lack of benefit. Factors associated with hearing aid acquisition included a preventive mindset, positive relationship with an audiologist, and perceived potential benefit.

Conclusions: Survivors with hearing loss have adapted to social settings but acknowledge isolation as well as academic and professional challenges. Interventions to lower the cost of aids may result in better uptake, but other barriers should be considered. Clinicians and audiologists should engage the preventive mindset and potential benefit when recommending hearing aids.

P105. OBESITY IN CHILDHOOD CANCER SURVIVORS

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Background: Previous studies have shown that childhood cancer survivors (CCS) face an increased risk of obesity and metabolic disorders. The purpose of this study is to determine the risk factors and incidence of obesity before and after treatment in cancer patients treated at UCSF Benioff Children's Hospital.

Methods: Using the Northern California Cancer Registry, a retrospective review was performed of patients under 21 years of age when diagnosed between 2013-2015 with a malignancy, including leukemia, lymphoma, thyroid or endocrine tumor, brain tumor, osteosarcoma, retinoblastoma, neuroblastoma or other cancer. Body Mass Index (BMI) was calculated using pre and post therapy heights and weights and defined as overweight or obese based on standardized age parameters used by the CDC. Age, sex, tumor type, treatment received (chemotherapy, radiation, surgery, or transplant), and ethnicity were also collected to assess risk factors.

Results: A total of 210 CCS were identified in this study, 33 of which were excluded due to insufficient follow up time (<1 year from diagnosis). Of the 177 included in this study 29 (16%) were overweight, 35 (20%) were obese and 18 (10%) were underweight at diagnosis. The prevalence of obesity at baseline did not differ statistically to population norms from 2015-2016 National Health and Nutrition Examination Study (NHANES) data. The mean time between diagnosis and post-treatment BMI was 30 +/-10 mo. Following therapy, 39 (22%) were overweight, 38 (21%) obese, and 12 (7%) underweight. There was no significant difference in obesity incidence based on gender. Using a paired T-test, change in BMI z-scores was not statistically significant pre and post therapy. Nor was there a significant change in BMI from baseline in the 37 patients who received any kind of radiation. Those with leukemia or lymphoma had the highest incidence of overweight and obesity post-therapy (57%), with 37 out of 59 receiving steroids as part of their treatment.

Conclusions: The incidence of overweight and obesity in CCS continues to be significant both pre and post therapy, though the risk may start even before cancer therapy is initiated. While our study did not show a significant change in overall BMI scores from diagnosis to treatment end, radiation and chemotherapy may later add further insult to an already metabolically at-risk population. This study indicates the need for patient education on obesity risks starting at the time of cancer diagnosis.

P106. PREDICTORS FOR OBESITY IN PEDIATRIC CANCER SURVIVORS

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Background: It is well documented that childhood cancer survivors are at increased risk for obesity, cardiovascular disease, endocrinopathies, secondary cancers and other long term sequelae. Our study aimed to explore the strongest predictors and risk factors of obesity in survivors of childhood cancer. We focused on specific chemotherapies, dosages, cancer types, radiation treatments and locations and other variations in treatment that place some cancer survivors at higher risk for obesity than others.

Methods: This study was a retrospective chart review of childhood cancer survivors being followed in a specialized survivorship program called HOPE. 430 charts of children aged 6 years to 21 years who had a visit to the cancer survivors' clinic anytime between 01/01/2000 – 06/01/2018 were reviewed. Inclusion criteria were: two years post therapy or five years from diagnosis whichever is later, and followed in the survivors' clinic. Exclusion criteria were: pregnant adolescents, children with a concurrent diagnosis that could impact weight such as diabetes or other endocrine disorders prior to cancer diagnosis. Logistic regression models were used to identify the strongest predictors of obesity

Results: Odds of being overweight/obese at first HOPE visit are 2.18 times higher for females compared to males (95% CI: 1.18, 4.07). A one percent increase in BMI percentile at diagnosis results in 1.03 times greater odds of being overweight/obese at first HOPE visit (95% CI: 1.02, 1.04). A one year increase in treatment duration results in 1.62 times greater odds of being overweight/obese at first HOPE visit (95% CI: 1.03, 2.61). Odds of being overweight/

obese at first HOPE visit are 2.29 times higher for Hispanics compared to non-Hispanic whites (95% CI: 1.23, 4.3). For the global test of cancer diagnosis influence on developing obesity, we found significant influence, pvalue=0.03, giving evidence that at least 2 cancer types may increase or decrease the odds of obesity.

Conclusions: Based on our results, we see that females, those of Hispanic race and those with increased BMI at cancer diagnosis are at highest risk of having high BMI in survivorship. We also found there is a positive correlation between cancer treatment duration and increased BMI. We identified that cancer diagnoses may have an increased or decreased risk of obesity but unfortunately need a greater number of subjects to determine specifically which cancer types increase the risk.

P107. SURVIVORCONNECT™: MAKING THE DIFFERENCE IN THE LIVES OF PEDIATRIC CANCER SURVIVORS

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Background: UPMC Children's Hospital of Pittsburgh Survivorship program was established in 2009. Survivors have unique stories, which may include physical, social and/or emotional challenges. SurvivorConnect™ was established to enhance annual face-to-face visits, enabled by a grant from the Hyundai Hope on Wheels Foundation. SurvivorConnect™ enables us to "connect" with survivors to improve education and communication with the Survivorship Clinical team. The program optimizes information exchange with our young adult, mobile population, providing resources aiding in transition to adult care. The program continues through generous support from the Mario Lemieux Foundation.

Methods: Survivorship clinic visits continue to increase annually due to increased referral from primary oncologists and increased survival due to advancements in care. SurvivorConnect™ uses a database, events, web technology, email, a quarterly newsletter, social media, texting, written communication and Passport for Care® to improve and make critical resource material accessible to our young adult survivors. The database tracks key demographic information used in reporting, fundraising and presentations. Events offered by SurvivorConnect™ include awareness, educational, celebration and fundraising. The website is used to provide education, link to resources and set expectations for what to expect at a visit. Email allows us to communicate with the population about upcoming events, topics of interest and our quarterly newsletter. Survivors share stories in the newsletter, supporting one another. Social media, in a closed setting, allows survivors to support one another and find common ground. Texting allows us to confirm appointments and missed appointments or indicate that lab results are available. Survivors are given a written welcome brochure at their first visit which details the program and answers questions about what to expect. Passport for Care®, developed at the Texas Children's Cancer Center, empowers pediatric cancer survivors, putting them in charge of their own care and ultimately improving their quality of life.

Results: The Survivorship program population is growing at a rate of ~100 survivors per year, congruent with the expected referral rate based on number of new patients per year. SurvivorConnect™ resources are provided to each patient and resource documents are shared with primary care physicians. Attrition rate is low and survivors remain engaged. Survivors report feeling "connected" through the SurvivorConnect™ program.
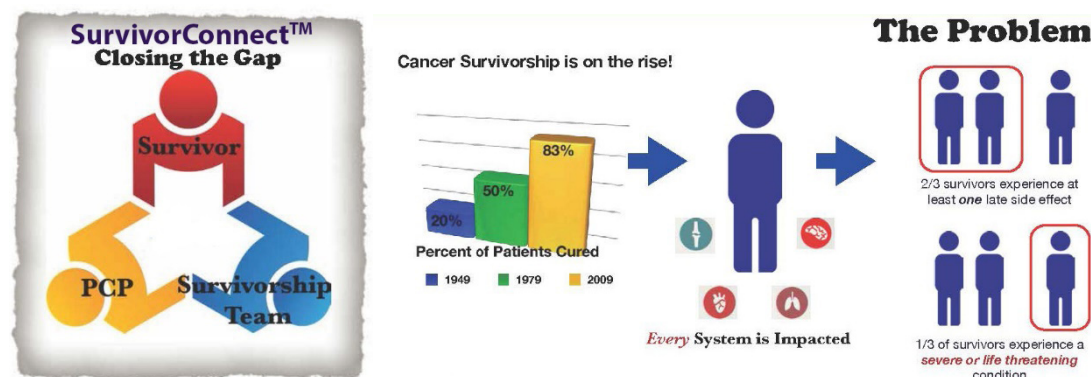
Conclusions: SurvivorConnect™ serves to connect, educate and empower this heterogeneous patient population. In this highly mobile, young adult population, the program provides tools and resources that will aid in transition to adult care. Additional study is needed to quantify impact of such tools.

P109. SAME SAME BUT DIFFERENT

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Background: Improvements in treatment of childhood cancer have brought about a remarkable increase in overall survival. With a growing number of childhood cancer survivors reaching adulthood, their Health-Related Quality of Life (HRQOL) has come to the fore. Age-group-specific questionnaires exist for HRQOL assessments in children and adults. In principle, an instrument´s age-specificity is beneficial to its construct validity. However, particularly when conducting research that bridges the existing gap between HRQOL assessments in clinical studies and long-term follow-up, the use of distinct instruments limits comparability. Our aim was thus to devise a method which overcomes this problem.

Methods: We used HRQOL data from the EURAMOS-1 trial, the EWING 2008 study and the EU-funded PanCareLIFE study. Pooled HRQOL data were assessed at up to five time points including PanCareLIFE data from long-term-follow-up. During childhood and adolescence, PedQOL and PedsQL inventories were used, while the EORTC QLQ-C30 inventory was employed once participants had reached adulthood. We restricted our study to sub-scales pertaining to physical functioning (PF), given the importance of this construct for well-being and a putatively substantial conceptual overlap between instruments. We performed score linking based on the results of a sub-set of study participants who had either completed both PedsQL and EORTC QLQ-C30 (n = 34) or both PedQOL and EORTC QLQ-C-30 (n = 20) at the same time of assessment. To ascertain agreement between instruments, we created Bland-Altman plots. Additionally, we calculated Lin´s concordance correlation coefficient (CCC) and Liao's improved CCC (ICCC). To map PedsQL and PedQOL to EORTC QLQ-C30 PF scores, we used the circle-arc linking method for small samples.

Results: Visual inspection of Bland-Altman plots, as well as Lin's CCC and Liao's ICCC indicated fair to moderate agreement between PF sub-scales. The sub-set of study participants who had completed two distinct instruments permitted score linking for the whole cohort (n = 124) and a complete analysis of PF scores over time.

Conclusions: With score linking, it is possible to directly compare physical functioning scores obtained with distinct age-group-specific inventories. We consider score linking a promising tool for assuring comparability of intra-individual HRQOL assessments in studies over time and extending across different stages of life and, sufficient concordance provided, beyond the physical functioning domain.

P110. HYPERTENSION IN CHILDHOOD CANCER SURVIVORS TREATED WITH POTENTIALLY NEPHROTOXIC THERAPY: EVALUATION OF PREVALENCE, RISK FACTORS AND THE USE OF 24-HOUR AMBULATORY BLOOD PRESSURE MEASUREMENT, A DCOG-LATER STUDY

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Background: Hypertension is a known late effect in childhood cancer survivors (CCS) after nephrotoxic treatment. Still, literature is inconclusive about the prevalence of, and risk factors for hypertension in CCS. Ambulatory blood pressure monitoring (ABPM) might be a valuable screening modality for CCS. The DCOG LATER RENA study aims to examine the prevalence of, and risk factors for hypertension in CCS treated with potentially nephrotoxic therapy as part of the DCOG LATER study. In addition, we evaluate the diagnostic value of 24-hour ABPM to detect abnormal blood pressure (BP) in CCS.

Methods: The DCOG-LATER RENA study is a nationwide cross-sectional cohort study in which 2000 CCS (= 5 years post diagnosis), aged = 18 years at time of study, treated between 1963–2002 with potentially nephrotoxic chemotherapy (ifosfamide, cisplatin, carboplatin, high-dose cyclophosphamide), abdominal radiotherapy, total body irradiation, and nephrectomy, are eligible. Renal function and BP are measured at study visit. For office BP, hypertension is defined as systolic =140 and/or diastolic =90 mmHg or the use of antihypertensive medication. A pilot study with 24-hour ABPM is performed in a subgroup. CCS using antihypertensive medication are excluded for ABPM. For ABPM, hypertension is defined as daytime: systolic = 135 and/or diastolic = 85 mmHg, nighttime: systolic = 120 and/or diastolic = 70 mmHg, 24 hour: systolic = 130 and/or diastolic = 80 mmHg. Masked hypertension is detected when hypertension is found according to ABPM, but not according to office BP. Abnormal nocturnal dipping of BP is defined as night-day BP ratio > 0.9. Logistic regression will be used to determine the relationship between GFR (CKD-EPI Scr-cys 2012 equation) and office hypertension. Multivariable logistic regression analysis will be performed to examine treatment related risk factors for hypertension. We will adjust for sex, BMI, and follow-up duration.

Results: In January 2019, we have collected data for 671 CCS and ABPM was performed in 43 CCS. Data are currently collected and analyzed.

Conclusions: This study will provide knowledge on the prevalence of, and risk factors for hypertension in long-term CCS treated with potentially nephrotoxic treatment. In addition, we will gain knowledge on the diagnostic value of ABPM for early detection of abnormal BP. These results are relevant for future treatment protocols and surveillance guidelines for survivors.

P111. A PILOT STUDY OF THE GUT MICROBIOME AND METABOLIC SYNDROME IN SURVIVORS OF CHILDHOOD AND YOUNG ADULT MALIGNANCIES

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Background: Long-term survivors of childhood cancer are at an elevated risk of metabolic syndrome which includes central obesity, dyslipidemia, impaired blood sugar, and hypertension. Chemotherapy and antibiotics have been demonstrated to alter the microbiome during and soon after treatment in cancer patients. In the general population, multiple studies have shown that an insult to gut organisms from antibiotics can lead to long-term changes in the microbiome. It is unknown whether alterations in the microbiome persist many years after treatment of childhood cancer and if these potential alterations may be associated with metabolic syndrome.

Methods: We conducted a pilot study with the primary aim of determining the feasibility of collecting clinical information, blood and stool samples from childhood cancer survivors and controls at Cleveland Clinic Children's Hospital. Survivors were recruited from our comprehensive survivorship clinic and controls were recruited among hospital staff and unaffected patient family members. Subjects had data collected on basic demographics, treatment exposures, diet, exercise, sleep, and measurements of the components of metabolic syndrome. Differences in groups for continuous variable were examined using the Mann-Whitney test and for categorical variables using the Chi-square test. Microbiota will be categorized by 16s rRNA gene sequencing and we will determine individual participant samples' alpha diversity (Shannon index) and relative abundance of bacterial taxa. We have subsequently begun enrolling subjects in a cross sectional study with the aim of determining clinically significant perturbations in the microbiome. For the cross-sectional portion, we will recruit 80 cases and 40 controls and have a power of 87% power to detect a 0.5 point difference in Shannon index.

Results: 12 Childhood cancer survivors and 13 controls were recruited for the feasibility study. Survivors had initial diagnoses of Hodgkin Lymphoma (4), ALL (4), AML/MDS (2), Astrocytoma (1), and Ewing Sarcoma (1). Controls had a greater median age than survivors (Table 1). DNA extraction has been performed on pilot study participants and samples are presently undergoing gene sequencing, with data available prior to the 2019 NASLCCC meeting.

Table 1	Survivors (N=12)	Controls (N=13)	P-Value
Demographics			
Age (years)	22.3 (16.4-31.5)	29.6 (10.4-40.0)	0.01
Female (%)	50%	85%	0.08
Treatment Exposures			
Year of Diagnosis	2008 (1994-2014)	-	
Years since Diagnosis	10 (4-24)	-	
Received XRT	50%	-	
Received Cranial XRT	33%	-	
Received Broad Spectrum Antibiotics	75%	-	
Total Days of Broad Spectrum Antibiotics (median, range)	32 (8-127)	-	
Metabolic Markers			
Body Mass Index	25 (18.1-28.8)	23.4 (18.1-33.3)	0.98
Systolic Blood Pressure (mm Hg)	119 (105-138)	115 (96-129)	0.17
Diastolic Blood Pressure (mm Hg)	66 (58-83)	70 (50-74)	0.47
HbA1c (%)	5.0 % (4.7%-5.4%)	-	
Triglyceride (mg/dL)	106 (62-239)	-	
HDL (mg/dL)	47 (41-61)	-	

Table 1. Numbers displayed as median (range).

Conclusions: Enrollment of study participants and controls is feasible at our center and results of the pilot sequencing data will be available soon. A similar consent and collection strategy will be used for the future cross-sectional study.

P112. "WE'RE OK, BUT…": A QUALITATIVE STUDY OF CHILDHOOD CANCER PATIENTS AND THEIR FAMILIES RECENTLY TRANSITIONED FROM TREATMENT TO SURVEILLANCE

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Background: For pediatric cancer patients and their families, transitioning from active treatment to surveillance brings many changes. Limited studies of childhood cancer survivors show concerns of patients/caregivers are not always identified by standard measures. In order to better understand these concerns, this qualitative study sought to learn more about the difficulties faced during this transition.

Methods: Patients were identified at University of Wisconsin-Madison survivorship clinic. Eligible patients/families had completed oncology treatment within the past 6 months. Qualitative descriptive design was used. Interviews occurred with patients and/or caregivers as available/appropriate. Six open-ended questions designed to introduce the concepts of mood, adjustment, educational achievement, social functioning, and re-integration into community life were asked. Interviews were conducted by the same interviewer and the patients/caregivers were encouraged to share additional thoughts/concerns. Data were transcribed verbatim and analyzed using qualitative content analysis to identify salient categories. A single researcher (AG) coded the first 5 interviews and then brought the codebook to the group for discussion. Two researchers (AG and CA) coded each additional interview separately using the established code book and brought coding to the group for consensus. The research team addressed discrepancies and confirmed the final analysis.

Results: 19 interviews were conducted (with patients and/or their caregivers as available and appropriate). Ten primary categories were identified with sub-categories under each. Expected content included anxiety about decreased medical visits, worry about relapse, and side effects of treatment. A significant desire to return to normalcy was identified by both patients and families throughout these interviews. Social side effects of treatment were explored, including difficulty returning to socially normed activities and challenges with relationships in and outside the family. The importance of a strong support network was also a key finding.

Conclusions: The desire to return to a sense of normalcy, importance of a support network, and social difficulties experienced by both patients and families led to a common, shared experience: the sense that they are doing ok… but they could be doing better.

P113. SEXUAL DIMORPHISM OF DOXORUBICIN-INDUCED CARDIAC ATROPHY IN YOUNG MICE

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Background: Nearly half of childhood cancer survivors have reduced left ventricular (LV) mass which has been shown to predict adverse cardiac outcomes and worsening heart failure symptoms. Although the mechanisms of anthracycline-induced cardiac dysfunction and heart failure have been extensively studied in animal models, the mechanisms of anthracycline-induced cardiac atrophy are still poorly understood. In addition, it is still not understood why young female cancer patients are at higher risk of anthracycline-induced cardiotoxicity than males. Therefore, the objectives of the current study are: (1) To design a juvenile mouse model of anthracycline-induced cardiac atrophy without significant cardiac dysfunction, (2) To identify sex-related differences in anthracycline-induced cardiac atrophy in young mice, (3) To determine the effect of sex hormone deprivation on anthracycline-induced cardiac atrophy.

Methods: Five-week old male and female mice were injected with doxorubicin (DOX) 4 mg/kg/week for 3 to 6 weeks. A cohort of gonadectomized and sham-operated male and female mice were injected with DOX 4 mg/kg/week for 5 weeks. Cardiac function and morphometry were measured by trans-thoracic echocardiography 1 and 5 weeks after the last DOX injection. Thereafter, the mice were euthanized and the hearts were harvested and analyzed for molecular markers of cardiotoxicity.

Results: In male mice only, DOX 4 mg/kg/week for 3 to 5 weeks caused significant cardiac atrophy without decline in cardiac function, whereas DOX administration for 6 weeks caused significant cardiac atrophy and dysfunction. Female mice were protected from cardiac atrophy at the 3 to 5 weeks regimen and from cardiac atrophy and dysfunction at the 6 weeks regimen. Intriguingly, castration of male mice exacerbated DOX-induced cardiac atrophy, while ovariectomy had no significant effect.

Conclusions: DOX-induced cardiac atrophy can be studied separately from cardiac dysfunction in animal models. In contrast to humans, young female mice are protected against DOX-induced cardiac atrophy and dysfunction. Deprivation of sex hormones by gonadectomy did not reverse this sexual dimorphism, suggesting that other mechanisms are implicated.

S114. ADVOCATING A NEW MODEL F SURVIVORSHIP CARE: A CASE STUDY

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Background: The survivorship phase of cancer care encompasses multiple domains. Bone sarcoma survivors have among the highest risk of any pediatric or adolescent cancer of premature development of chronic illnesses often associated with premature aging, including coronary artery disease. These chronic conditions manifest after therapy ends, often coinciding with the patients' transition from pediatric late-effects programs to medicine. The Sarcoma Survivorship Program (SSP) advocates locating long-term survivorship care within specialty medical oncology model for high-risk adult survivors of pediatric and adolescent cancers.

Methods: We present the case study of a survivor diagnosed with PNET at age 4. The complexity of this case demonstrates the need to develop long-term survivorship care for survivors of high risk pediatric cancers within specialty medical oncology settings.

Results: The patient received adjuvant chemotherapy and radiation to the chest wall. She was diagnosed with mild cardiomegaly and cardiomyopathy at age 9. She was followed by pediatric oncology and pediatric late effects, until age 18 when she transferred to the SSP in October 2017. She presented with chronic anxiety and depression, and concerns about fertility. In 2018 she suffered a stroke. Medications include: apitaxaban, carveditilol, losartan, spirolactone. Upon evaluation, her BP was 77/49; the mild cardiomegaly unchanged. Dosimetry review of her chest irradiation showed 96-100% of her heart received 10-12 Gy; one third of her heart received between 30-40 Gy including the left ventricle. Total dose of Adriamycin was 375 mg/m2.

Conclusions: This case study presents a complex and high risk patient who successfully transitioned from pediatric to medical care. Coordinated specialty medical oncology survivorship care is essential for high-risk adult survivors of pediatric and young adult cancers.

S115. INCREASING KNOWLEDGE REGARDING THE NECESSITY OF LONG-TERM FOLLOW UP CARE AMONG PEDIATRIC CANCER SURVIVORS: A QUALITY IMPROVEMENT INTERVENTION

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Background: Advancements in therapy have led to an approximately eighty percent survival rate of pediatric cancer patients, leading to more than 400,000 LTS patients in the United States today. This population is at increased risk for late effects of cancer therapy, including potentially life threatening conditions. Unfortunately more than fifty percent of LTS patients do not continue long term follow up care. Interventions aimed toward improving adherence to long term follow up care are needed.

Methods: The project SMART Aim was the following: By implementing an educational intervention we will increase knowledge about the need for long term follow up to more than 75% of the off-therapy acute leukemia patients followed at Texas Children's Hospital - West Campus Oncology Clinic by June 2019. Patients who were diagnosed and treated for acute leukemia (ALL/AML) who are 1 to 12 months off therapy will be targeted. During an office visit, patients and guardians will first receive a short questionnaire to evaluate baseline knowledge of pertinent late effects and need for long term follow up. The oncology provider will then provide an informational handout on cancer survivorship and need for long term follow up and review the answers for the questionnaire. At the subsequent appointment, patients and guardians will receive the same questionnaire to evaluate learning retention. Procedures will be regularly analyzed and tracked by utilizing checklists for each step to monitor and continue to develop and identify areas of improvement with appropriate modifications through multiple four-week rapid plan do study act (PDSA) cycles.

Results: Implementation of the project began in February 2019 and results from four PDSA cycles will be presented at the meeting.

Conclusions: Utilizing quality improvement methodology we will use a framework to measure and increase knowledge about the importance of long-term follow up in acute leukemia patients who recently completed therapy. Implementation of these processes is anticipated to increase awareness and improve adherence to follow up in the LTS patient population.

S116. PATIENT AND CAREGIVER PERSPECTIVES OF BARRIERS AND FACILITATORS TO RECEIVING FOLLOW-UP CARE AMONG PEDIATRIC CANCER PATIENTS

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Background: The Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors (COG LTFU) recommends lifelong screening and surveillance for potential late effects related to cancer and its treatment. Adherence to these guidelines is less than optimal for reasons that are not well understood. The primary objective of this study was to gain a better understanding of the barriers and facilitators to receiving follow-up care among pediatric cancer patients at a large children's hospital in the Southwestern United States.

Methods: Ten pediatric cancer patients and/or their caregivers participated in a semi-structured interview that explored what makes it easier or more difficult to access follow-up care. Patients were between the ages of 8-24 years (median = 6.5 years), previously treated for acute lymphoblastic leukemia (n=5), brain tumors (n=3), and bone tumors (n=2), and currently off therapy (median = 6.5 years, range = 0.4-13 years). Interviews were analyzed using Framework Analysis that included the following steps: familiarization with the data, identification of a thematic framework, indexing, charting, mapping and interpretation. Response statements were coded using emerging and a priori categorical themes to describe institutional attributes, patient/family context, provider/staff attributes, patient/family attributes, and interpersonal processes. Response statements were also coded as barriers or facilitators and incorporated into an illustrative model.

Results: Expensive parking, long distance to the clinic, and difficulty coordinating appointments were the most frequently reported barriers to receiving care. Friendly and responsive hospital personnel, recreational activities in the clinic waiting area, and support from family members were the most frequently reported facilitators to receiving care. A contextual model describing the interpersonal processes between patient/family and provider/staff was developed.

Conclusions: It is important to identify barriers and facilitators to improve follow-up among pediatric cancer patients. Challenges in getting to the clinic and accessing care were identified as major barriers while interpersonal processes and relationships were identified as major facilitators. These findings can help inform the development of interventions to improve long-term follow-up.

S117. PILOT STUDY CORRELATING NEUROTROPHIN LEVELS WITH COGNITIVE TRAINING TO PROMOTE NEUROPLASTICITY AND NEURAL RE-CIRCUITRY IN CHEMOTHERAPY ASSOCIATED COGNITIVE IMPAIRMENT

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Background: Cognitive deficits associated with chemotherapy exposure are well described. 15-50% of cancer survivors develop deficits in memory, attention and executive function which are multi-factorial and involve acute and sustained insult to neuronal structures. Various neuropsychiatric testing measures have been used to define cognitive abilities in survivors. Cognitive rehabilitation restores impaired function and promotes compensation for an area of deficit. Neurotrophins regulate survival, development, and function of the nervous system. Stimulation of brain derived neurotrophic factor (BDNF) correlates with synaptic plasticity and cognition. The primary study objective is to determine correlation in serum BDNF levels, cognitive rehabilitation training, and cognitive function.

Methods: Fourteen English-speaking participants ages 12-25 years with a de novo cancer diagnosis requiring front-line chemotherapy treatment were recruited via informed consent. All participants completed cognitive function assessment and serum BDNF analysis at 3 timepoints (time of enrollment, 16 weeks, and 24 weeks post-enrollment). Each participant was randomized to receive intervention (computer-based neurocognitive training) using an odd/even method. Patients diagnosed with brain tumors, brain metastases, or previous cognitive/developmental deficits were excluded.

Results:
Ten out of fourteen participants completed the study with even distribution between the intervention and non-intervention arms. Three of the five patients on the intervention arm had sustained if not improved BDNF levels as compared to the non-intervention arm. Preliminary results indicated that 100% of those receiving intervention improved in one-card learning, which measures visual memory. 75% improved in detection, which measures processing speed as well as in identification, which measures attention. Although 50% improved on one-back accuracy, which measures visual working memory, only 25% improved in ability to respond quickly. Only 25% demonstrated decreased errors in the maze task.
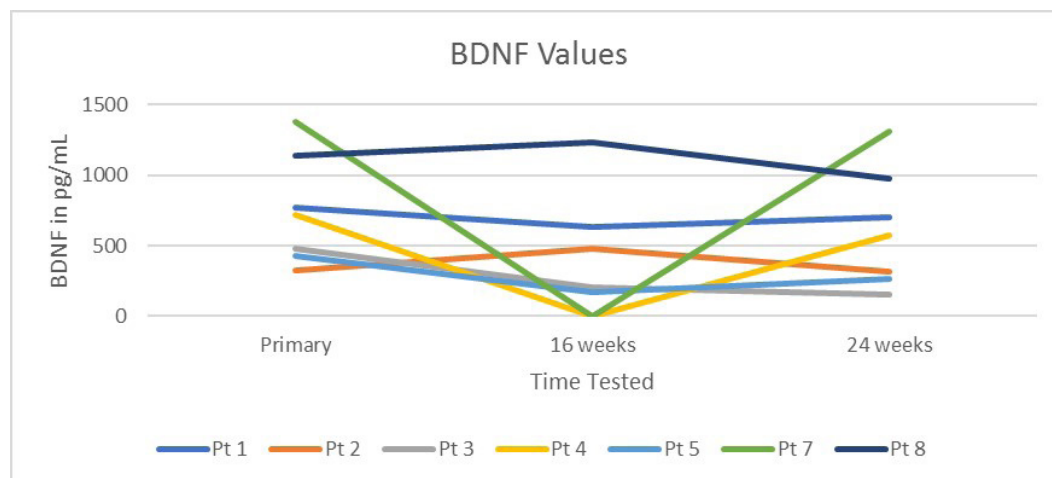
Conclusions:
Preliminary data correlating BDNF levels and cognitive rehabilitation with neurocognitive function is premature but promising. Limitations to the study included small numbers, lack of compliance with computer-based cognitive training, and timeliness of BDNF levels. However, we plan to complete evaluations of patients currently enrolled and analyze the data for consideration of future studies.

S118. DEVELOPING AN OUTDOOR EXERCISE INTERVENTION FOR ADOLESCENT AND YOUNG ADULT SURVIVORS OF CANCER: A COMMUNITY-CLINIC PARTNERSHIP

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Background: Exercise is protective against late effects of cancer treatment, including fatigue and heart disease. Yet, survivors of cancer, similar to the general adolescent and young adult (AYA) US population, do not participate in recommended amounts of exercise. Long-term support of healthy exercise behavior may require collaboration between clinicians and community partners. The purpose of this study is to describe the development of a community-clinic partnership to promote outdoor exercise in AYA cancer survivors and to present the design of a novel exercise intervention that resulted from this partnership.

Methods: A childhood cancer survivor clinic partnered with a non-profit outdoor exercise-focused community organization in Minneapolis, Minnesota under a community-based participatory research framework to develop an exercise intervention for survivors. Specific inputs to the initial design of the exercise intervention included a self-determination theory based conceptual model and 3 focus groups with young adult (n=3) and adolescent (n=5) survivors and parents of survivors (n=5).

Results: Partners from the clinic and the non-profit collaborated through monthly meetings in organizing formative focus groups with survivors. Findings from the focus groups indicated that employing survivors as lay health workers to implement an exercise intervention may be a desirable way to motivate survivors. A curriculum consisting of 6 exercise sessions was developed, each designed to encourage exercise motivation by supporting the Self-Determination Theory constructs of autonomy, competence and relatedness.

Conclusions: This study shows the feasibility of a community-clinical partnership in developing an exercise intervention for AYA survivors of cancer. Findings from these focus groups indicated that survivors should be included as equal partners both in an advisory role and as lay health workers implementing the exercise intervention. This partnership is currently in the next phase of hiring survivors as lay health workers and recruiting AYA survivors to participate in the pilot exercise intervention.

S119. FOOD AND BEVERAGE INTAKE DURING CANCER THERAPY: A SYSTEMATIC REVIEW

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Background: Despite nutrition guidelines for cancer patients being available through various organizations, little research is available on the interactions between specific dietary intake and cancer treatment toxicities and effectiveness. This systematic review of the literature sought to determine what food or beverages consumed during cancer treatment might prevent recurrence, subsequent malignancies, or treatment-related toxicities.

Methods: With the help of a research informationist, a literature search of MEDLINE (Pubmed), Embase (Elsevier) and the Cochrane Central Register of Controlled trials was conducted on July 2018, following the PRISMA guidelines for systematic reviews. The following terms and concepts were used in the search strategy: neoplasms, patients, therapeutics, food, diet, diet therapy, eating, consume, ingest, intake, feed, recurrence, disease progression, second/ primary neoplasms, mucositis, nausea, and vomiting. Only studies published in English from January 2008 through July 2018 were included; animal studies and studies focusing solely on nutrient supplementation rather than food consumption were excluded. Risk for bias for the included studies was assessed independently by two review authors using the Cochran risk of bias tool.

Results: 19 studies were selected from 1,551 potential studies. All study participants were adults. Nine of the included studies were randomized controlled trials analyzing either different diets (high-protein; short-term fasting; low-fat; Fermentable Oligo-, Di-, Mono-saccharides And Polyols [FODMAP]) or comparing the consumption of one specific food or nutrient (Concord grape juice; onions; fiber). The remaining ten studies were either observational or retrospective; they tracked treatment symptoms, general dietary intake, and weight status, as well as the consumption of specific foods (nuts, coffee, and sugar-sweetened beverages). Heterogeneity of study populations, outcomes, and study designs precluded summary statistics.

Conclusions: Available evidence suggests that food can be effective at ameliorating cancer treatment related-toxicities and improving prognosis; however, caution is needed in interpreting findings since many outcomes are modest. There is an ongoing need for future research focusing on rigorously designed trials.

S120. THE YOUNG ADULT LIFESTYLE OF PEDIATRIC CANCER SURVIVORS: YIKES!

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Background: Obesity is a national concern. Childhood obesity has more than doubled in kids and quadrupled in adolescents over the past 30 years. Though weight gain occurs commonly throughout adulthood, adolescents and young adults (AYA) appear to gain weight the fastest and they exhibit some of the poorest dietary patterns of all age groups. Childhood cancer survivors are at a high risk of becoming overweight and obese along with an increased risk of cardiovascular disease, osteoporosis and obesity. Self-esteem, stress and depression problems are associated with low physical activity and AYAs with cancer are less physically active than their siblings or peers. Should Pediatric Long-term Clinics help address lifestyle issues?

Methods: To determine the clinical needs of our pediatric cancer survivors, we evaluated the diet and activity levels of new AYAs seen in our long-term survivorship clinic. We reviewed information on our "New Patient Intake Questionnaire" on 25 AYA survivors who were diagnosed at age <18 years.

Results: Fifty-six percent of survivors had a history of leukemia or lymphoma. 56% were female and mean age at time of visit was 18.1 years (15 - 26 years) and average of 9.1 years from diagnosis (5 - 16 years). Twenty percent ate 3 or more fast food meals per week. Only 36% reported vigorous activity every week and 12% reported zero physical activity. 56% spend 3-4 hours on tv/video/computer daily while 8% spend 5 or more hours per day.

Conclusions: Diet and exercise are modifiable factors that can prevent or delay the early onset of many chronic conditions. AYA age range is an influential period of development whereby a healthy lifestyle can be promoted for a long-term benefit. By addressing lifestyle issues, long term survivorship clinics may have a positive impact on pediatric cancer survivors transitioning through their AYA years. There remains much to learn about AYA cancer patients' and survivors' nutrition and lifestyle habits.

S121. PRECISION CLINICAL RESEARCH: SURVIVOR AND PARENT PREFERENCES FOR RESEARCH PARTICIPATION

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Background: There is minimal information on research participation preferences of childhood cancer survivors (CCS) and their parents. This information may have implications for research recruitment and enrollment. The purpose of this program evaluation project was to characterize the clinical research participation preferences of a single institution cohort of CCS and their parents.

Methods: Over a 12 month period, an online survey was administered to all patients receiving care in a childhood cancer survivor program. Data was collected on respondent preferences for 1) timing of research participation, 2)

participation in intervention research and 3) research participation incentives. Respondents were presented with a variety of research opportunities and they selected if they were "very willing," "willing," "not willing" or "undecided" in terms of participation.

Results: Data collection is ongoing and thus far 236 participants have completed the survey. This represents 80% of the patient volume receiving care over this time period. Survivors were 71% (167/236) of the respondents. They were "very willing" or "willing" to participate in research if it took place in their home through an online survey (92%, 216/236), while waiting to see their provider (92%, 216/236) and in their home through a mailed paper survey (84%, 199/236). If the research opportunity involved taking a medication orally, 41% (98/236) were "very willing" or "willing." Incentives were "not important" to 65% (153/236) of respondents and 78% (185/236) thought it was "very important" or "important" that providers share results of any research that they participated in with them.

Conclusions: While most CCS prefer survey-based research, there is a substantial group that is willing to participate in intervention research. Considering participant preferences may allow for more effective and efficient recruitment and initial enrollment of CCS in intervention research.

S122. IDENTIFYING METRICS OF SUCCESS FOR TRANSITIONAL CARE PRACTICES IN CHILDHOOD CANCER SURVIVORSHIP: A QUALITATIVE STUDY OF PARENTS OF SURVIVORS

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Background: Parents of childhood cancer survivors (CCS) play a critical role in the continuation of survivor-focused care as patients transition from pediatric to adult care-settings. Their input may provide valuable insight to inform the creation of transitional care models. This study determined what best practices look like from the vantage point of the parent of a survivor by identifying indicators of success in transitional care practices. We asked parents to define the key characteristics of a successful transition to adult care-settings and to identify physician behaviors and clinic attributes that contributed to transitions they would define as successful.

Methods: A qualitative study was conducted with a single institution cohort of parents of CCS as key informants. We approached a total of 30 eligible parents. Data was collected using structured phone interviews with parents of CCS receiving survivor-focused transitional care. Interviews lasted between 30-60 minutes and were transcribed and subsequently coded using directed content analysis to identify major themes.

Results: The final sample size was 27 parents. Our coding revealed two major themes with multiple subthemes. The first major theme was that providers need to be effective communicators. This included communication between providers but also communication between providers and survivors as well as between survivors and parents. The second major theme was that models of care must include both medical and non-medical counselling. Parents highlighted the importance of providers counselling survivors on topics such as insurance and social networking.

Conclusions: From the perspective of parents of CCS, programs and providers that excel in communication will provide optimal survivor-focused care through clear communication and multifaceted counselling. Non-medical counselling should address specific topics of highest relevance to both parents and patients. The optimal model of transitional care must be built on the input of multiple key stakeholders, including parents of CCS.

S123. IDENTIFYING METRICS OF SUCCESS FOR TRANSITIONAL CARE PRACTICES IN CHILDHOOD CANCER SURVIVORSHIP: A QUALITATIVE STUDY OF ADOLESCENT AND YOUNG ADULT SURVIVORS

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Background: Limited data exists to inform the creation of transitional care models for childhood cancer survivors (CCS) as they progress from pediatric to adult ages. For many CCS, life-long survivor-focused care is needed but only 18% report receiving such care as adolescents and young adults (AYA). Transition from pediatric to adult care

is a key point where patients may be lost to follow-up. This study determined what best practices look like from the vantage point of the survivor by identifying indicators of success in transitional care practices as reported by AYA-aged CCS.

Methods: A qualitative study was conducted with a single institution cohort of CCS as key informants. Our goal was to interview 25 participants, per standard requirements to achieve informational redundancy and theoretical saturation of the desired content. To account for attrition, a total of 30 eligible survivors were approached. Data was collected in structured phone interviews with survivors that were receiving survivor-focused care as adolescents and young adults. Interviews generally lasted between 30-60 minutes and were transcribed then coded using directed content analysis to identify major themes.

Results: Our final sample consisted of 29 pediatric survivors, 11 of whom were still in pediatric care settings, 18 who had already transferred to adult care settings. We identified two major themes with multiple subthemes. The first major theme was that providers must deliver consistent care between the pediatric and adult care-settings. Consistency in communication and familiarity with patient preferences was emphasized by survivors. The second major theme was that models of care must include age-appropriate services and providers from multiple subspecialties; that promote survivor independence while also providing psychosocial support.

Conclusions: From the perspective of CCS, the optimal model of care must be built around consistent providers and communication that offers AYA-focused comprehensive survivorship care.

S124. THE DEVELOPMENT OF DATA CAPTURE METHODOLOGIES IN PEDIATRIC CANCER PATIENTS TREATED WITH TARGETED AGENTS AND IMMUNOTHERAPIES: LEVERAGING THE RESEARCH INFRASTRUCTURE OF A CHILDHOOD CANCER SURVIVOR PROGRAM

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Background: For pediatric/adolescent/young adult patients treated with targeted agents and those agents that activate the immune system, optimal surveillance for long-term adverse events has not been determined. The primary objective of this study is to develop and test the feasibility and acceptability of a data capture methodology for longitudinal clinical surveillance in pediatric/adolescent/young adult patients treated with targeted agents and agents that activate the immune system.

Methods: An exploratory prospective cohort study was designed using a mixed method approach to assess the feasibility and acceptability of a proposed data capture methodology that was based on the current research infrastructure of the University of Minnesota Childhood Cancer Survivor Program (cCSP). Feasibility and acceptability were defined as 1) the number of patients that complete the consent discussion and the number of patients successfully recruited for enrollment, 2) patient or caregiver satisfaction throughout the study including the recruitment/enrollment process and follow-up, 3) provider satisfaction with the recruitment/enrollment process and 4) key informant interviews after the recruitment/enrollment process (patient/caregiver/provider) and throughout the follow-up period (patient/caregiver).

Results: All approached participants have enrolled (n=24), 22 were long-term survivors receiving care in the cCSP and 2 were receiving care for acute oncology diagnoses. The most common diagnoses were leukemia (7/24), non-malignant hematologic disorders (6/24), neuroblastoma (5/24), and osteosarcoma (3/24). The most common targeted agents were tyrosine kinase inhibitors (4/24). The most common immunotherapies were related to high risk neuroblastoma therapies (5/24). All participants expressed high satisfaction with the consent discussion. Data collection through provider satisfaction assessments and key informant interviews are ongoing.

Conclusions: Our results suggest that childhood cancer patients treated with targeted agents and immunotherapies are interested in participating in long-term follow-up studies but 92% of participants were already in survivorship care and not actively receiving oncologic treatment representing a very specific cohort of patients.

S125. ONE-STOP SHOPPING FOR CHILDHOOD CANCER SURVIVOR CARE: THE PATIENT PERSPECTIVE ON MULTIDISCIPLINARY CLINICS

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Background: Long-term follow-up (LTFU) care for childhood cancer survivors ((CCS) is often delivered through specialized multidisciplinary clinics by providers from multiple subspecialties in one extended clinic encounter. This model is often termed "one-stop shopping." The purpose of this program evaluation project was to determine CCS' preferences for "one-stop shopping" models of care including access to subspecialists and duration of visits.

Methods: In an Upper Midwest U.S. academic medical center with a NCI designated comprehensive cancer center, 250 CCS receiving structured LFTU care were queried on 1) the top 3 subspecialties that they would want to see in clinic as part of their LTFU care and 2) whether they preferred a "one-stop shopping" model of care or multiple shorter visits over several days.

Results: The most frequently selected subspecialties were endocrinology (38%), cardiology (25%), psychiatry (15%), nutrition (14%) and ophthalmology (14%). When queried on duration of visit preference, 25% preferred multiple shorter 1-2 hour visits, 14% preferred longer 2-5 hour multidisciplinary visits and 59% reported having no preference as long as the necessary LTFU care was being delivered.

Conclusions: For program development purposes, providing structured discussion and/or education on endocrinology and cardiology topics may be most aligned with survivor preferences. However, patient preferences may not align with the reality of referrals needed as deemed by the survivor-focused care provider. There are likely multiple models of care that adequately provide comprehensive LTFU care to CCS. The quality of this care appears more important to survivors than the associated appointment scheduling.

S126. REFERRAL PATTERNS OF A CHILDHOOD CANCER SURVIVOR PROGRAM: IMPLICATIONS ON PROGRAM DEVELOPMENT

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Background: There are benefits and challenges to offering multidisciplinary survivor-focused care that incorporates multiple subspecialists as part of single clinic visit or encounter for childhood cancer survivors (CCS). Several models of care exist but there is no consensus in the literature or in general practice on which subspecialists should be included. This project describes the subspecialty referral patterns of a large risk-based childhood cancer survivor program (CCSP) housed within an academic center and NCI-designated cancer center.

Methods: Data was collected as part of routine care on all referrals made by providers delivering care to patients in the CCSP over a 5 year period (2012-2017). This included over 1000 patient visits. As part of a program evaluation initiative, overall referrals, pediatric subspecialty referrals, adult subspecialty referrals, other specialty referrals and ancillary service referrals were tracked.

Results: The most common referrals are summarized in Table 1. Data was de-identified and reported in aggregate as ranked lists as per standard quality improvement protocols.

Ranking	Overall	Pediatric Subspecialties	Adult Subspecialties	Other specialties	Ancillary specialties
1	Neuropsychology	Endocrinology	Endocrinology	Dermatology	Neuropsychology
2	Endocrinology	Nephrology	Cardiology	Ophthalmology	Physical Therapy
3	Dermatology	Cardiology/ Gastroenterology	Neurology	OB/Gyn	Psychology
4	Primary Care Provider	Cardiology/ Gastroenterology	Gastroenterology	Orthopedics	Dentistry
5	Ophthalmology	Neurology	Hematology	Pain Clinic	Genetics

Table 1: Most common referrals for childhood cancer survivors receiving survivor-focused care.

Conclusions: Referral patterns from a single institution CCSP indicate that partnerships with providers in neuropsychology, endocrinology and dermatology would be most aligned with survivor subspecialty care needs. The identification of primary care providers both knowledgeable and interested in caring for CCS would be critically important as many CCS are in need of a medical home with a primary care provider.

S127. NEUROCOGNITIVE LATE EFFECTS IN PEDIATRIC ACUTE LEUKEMIA SURVIVORS WITH DOWN SYNDROME

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Background: Children with Down syndrome (DS) are at increased risk for developing acute leukemia (AL) and experience higher rates of treatment-induced toxicities. While there is some evidence that children with DS-acute leukemia (AL) may experience greater than expected neurocognitive late effects (NCLE) compared with children with DS and no history of cancer (Roncadin 2015), these findings have not yet been confirmed in larger and more diverse populations. Here, we present interim results from an ongoing study describing feasibility of assessing NCLE in a multi-ethnic population of children with DS and ALL or AML (DS-AL).

Methods: DS-AL survivors treated at Texas Children's Cancer and Hematology Center Clinics and older than 6 years, >1 year off therapy, and in first remission are eligible. DS-Controls are recruited from the Texas Children's DS Clinic and must be older than 6 years, without a history of cancer, and not have a history of brain trauma, seizures, uncorrected hearing or vision loss, or premature birth. All consenting subjects are enrolled to an IRB-approved research protocol, and complete a NC battery developed at Emory University and St. Jude Children's Research Hospital and conducted by trained personnel to measure intelligence, working memory, executive function, attention, verbal processing, behavioral inhibition, and fine motor skills. For this study, floor effects are defined as the lowest raw score possible for each task. Parents also provide a detailed medical history and complete standardized ratings of their child's executive function, adaptive function, behavior, communication skills, and quality of life.

Results: Forty-nine children with DS have been enrolled to date (n=49; DS-AL=21, DS-Control=28; 51% Hispanic/ Latino). Participation rates are 66% for DS-AL (21 out of 32 eligible) and 61% for DS-Controls (28 out of 46 eligible). NC assessments have been completed for 28 out of 49 English or Spanish-speaking parents (57%) and for 29 out of 44 English speaking children with DS (66%). Twelve out of 16 nonverbal children with DS completed the nonverbal portion of the battery, and all 13 verbal children with DS completed the entire battery. Of the 25 children with DS who completed the NC battery, floor effects ranged between 16% and 40%.

Conclusions: Contemporary leukemia treatment protocols reduce the risk of NCLE compared with historical protocols in children without DS, but the impact of modern therapy on NCLE in DS-AL survivors is unclear. This interim review of ongoing research in DS-AL outcomes demonstrates feasibility of assessing NCLE in this patient population, and also identifies potential challenges related to the sensitivity of these measures when applied to intellectually disabled populations.

S128. A STANDARD OPERATING PROCEDURE FOR IMPLEMENTING PASSPORT FOR CARE: A WEB-BASED CLINICAL DECISION TOOL FOR SURVIVORSHIP CARE

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Background: The Texas Children's Cancer and Hematology Centers (TXCH) Long Term Survivor (LTS) Clinic follows ~1,500 survivors of childhood cancer, leveraging Passport for Care (PFC) to deliver quality survivorship care. The PFC translates exposure-based risks derived from the Children's Oncology Group Long Term Follow Up Guidelines into user-friendly, personally-tailored recommendations for survivors. The TXCH LTS Clinic standard operating procedure (SOP) is for the LTS Program Coordinator to abstract survivor demographics, diagnosis, and treatment and related complications data at time of LTS Clinic referral for entry into PFC; however, there are intrinsic challenges with updating the PFC record once survivors have transitioned to LTS Clinic, particularly with respect to geographic relocation and optional PFC components such as late complications of treatment. Therefore, we implemented a revised SOP to address this challenge.

Methods: The revised SOP includes the following steps 1) Program Coordinator abstracts and enters data into PFC, 2) Survivor is given a copy of their PFC treatment summary on arrival to LTS Clinic and asked to review demographics and complications for accuracy (new), 3) Survivor modifies PFC treatment summary and reviews changes with medical provider during the clinic visit (new), 4) Medical provider updates PFC during the visit, 5) Modified PFC treatment summary undergoes secondary physician review, and any remaining discrepancies between complications and the electronic medical record (EMR) problem list are resolved (new) 6) Coordinator makes updates to the PFC record (new).

Results: 534 records were reviewed between May 25, 2018 and January 17, 2019. A total of 484 records required PFC record modification to either demographics (n=91) or late complications (n=321) or both (n=72). Survivors and/ or their parents suggested modifications to 118/495 records, with the remainder of modifications suggested by the medical provider or secondary physician reviewer.

Conclusions: The PFC plays a valuable role in survivorship care and survivor education. Limited data entry, specifically demographics, diagnosis, and treatment data, is sufficient to generate a comprehensive survivorship care plan. However, some PFC users may choose to leverage optional PFC components, such as 'treatment complications,' for clinical care or research purposes. At our site, integrating survivor review and secondary provider review into our SOP has improved the accuracy of both demographics and complications captured by PFC. We recommend that PFC sites electing to track survivor complications post-therapy establish an SOP that ensures fidelity between PFC and the EMR.

S129. LATE HEALTH OUTCOMES FOLLOWING CONTEMPORARY LYMPHOME MALIN DE BURKITT THERAPY FOR MATURE B-CELL NON-HODGKIN LYMPHOMA: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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Background: The widely utilized, risk-based Lymphome Malin de Burkitt (LMB) chemotherapy regimen has improved survival rates for children with mature B-cell non-Hodgkin lymphoma (NHL), however associated late effects remain understudied. We assessed late health outcomes after LMB treatment in the Childhood Cancer Survivor Study.

Methods: Multivariable regression models compared chronic health conditions, health status, and socioeconomic and neurocognitive outcomes between NHL survivors treated with the LMB regimen (n=126), non-LMB regimens (n=444), and siblings (n=1,029).

Results: LMB survivors were a median age of 10.2 (range:2.5-20.5) years at diagnosis and 24.0 (10.3-35.3) years at evaluation. Compared to siblings, LMB survivors were at increased risk for adverse health outcomes. However, LMB and non-LMB survivors did not differ with regards to risk of having any chronic health condition, impaired health status, neurocognitive deficits, or poorer socioeconomic outcomes. Increased risk for specific neurologic conditions was observed in LMB compared to non-LMB survivors: epilepsy (RR 15.2, 95% CI:3.1-73.4), balance problems (RR 8.9, 95% CI:2.3-34.8), tremors (RR 7.5, 95% CI:1.9-29.9), weakness in legs (RR 8.1, 95% CI:2.5-26.4), severe headaches (RR 3.2, 95% CI:1.6-6.3), and prolonged arm, leg, or back pain (RR 4.0, 95% CI:2.2-7.1). LMB risk group Group C (n=50) survivors were at the highest risk for these conditions; however, except for worse functional status (OR 2.7, 95% CI:1.2-5.8), they were not at increased risk for other adverse health status or socioeconomic outcomes compared to non-LMB survivors.

Conclusions: Survivors treated with LMB and non-LMB regimens are largely comparable in late health outcomes except for excess neurotoxicity among LMB survivors. These data inform treatment efforts seeking to optimize disease control while minimizing toxicity.

S130. UPDATE OF LATE EFFECTS AFTER HODGKIN LYMPHOMA IN CHILDHOOD AND ADOLESCENCE - THE GERMAN SURVIVOR COHORT AFTER 23 YEARS OF FOLLOW-UP

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Background: Overall survival after Hodgkin lymphoma (HL) in childhood and adolescence is 94% after 10 years, but decreases to 88% after 30 years due to long term effects. Treatment related late effects such as radiotherapy (RT)-induced malignant neoplasms, cardiovascular diseases, thyroid gland disorders, impaired fertility, and pulmonary fibrosis have so far been identified

Methods: Starting in 1999, questionnaires were sent every 3-4 years to all survivors of the first seven consecutive German-Austrian pediatric HL-treatment-studies (treatment in 1999-2002) for information on their health status by the former chairpersons (G. Schellong and W. Doerffel) and late effects data was analyzed. In 2016, after obtaining the survivors written consent the late effect registry was moved to the current HL-study-center (D. Körholz, U. Hennewig). In 10/2018 to 3/2019, questionnaires were sent out again and the original cohort was enlarged by including survivors treated in 2002-2005.

Results: Data on cumulative incidence of secondary malignancies, cardiovascular disease and fertility in respect to treatment exposition will be available by May 2019.

Conclusions: Findings on treatment related late effects have been used to design past and recent German Pediatric HL/EuroNet-PHL trials. Furthermore, these results translate into immediate improvements in long term follow-up care, i.e. implementation of breast cancer screening programs after chest irradiation. The long term follow-up of the German HL survivor cohort will be continued and extended to patients = 10 years after treatment. Long term follow-up of young HL survivors is essential for improving long term survival and follow-up care.

S131. SURVIVORS EMPOWERING SURVIVORS: CREATING A SURVIVOR LIFELINE

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Background: Long-term survivors (LTS) of childhood cancer who are young adults frequently have difficulty "fitting in" and adjusting to life after cancer. The Periwinkle Foundation has served our patients for 35 years by providing programming including camps, arts programs and in recent years, a robust LTS program. LTS over the age of 18, with no upper age limit, are invited to participate. Designed to provide a strong support network through positive peer interactions, LTS can participate in monthly socials, weekend retreats and volunteer opportunities.

Methods: 46 LTS ages 19-43 years old (median 27 years) participated in the program in 2018. Survivor diagnoses included central nervous system tumors (16); leukemia (14); lymphoma (4); neuroblastoma (3); Ewings and Wilm's (2 each); miscellaneous (5). Of these, 13 had significant physical and/or neurologic sequela. LTS activities included attending sporting events, crafting, participation in Periwinkle fundraising events, competing as teammates in the annual kickball classic, as counselors at Periwinkle camps and a variety of other volunteer activities. LTS were also invited to attend a weekend retreat designed to provide comradery and access to educational, financial, and employment resources.

Results: Participants in the 2018 Periwinkle LTS Program had 366 combined years of survivorship; 420 LTS program encounters; and logged 1237 volunteer hours with the Periwinkle Foundation. In LTS program surveys, survivor comments included "I would not be here without the support of the Periwinkle LTS program" (28 yo ALL survivor); "The LTS program provides a safe zone to talk about my experience without worrying about my medical issues" (25 yo brain tumor survivor); "I receive courage and a reminder that I am not alone. Most importantly, I get a reminder to appreciate love and life" (22 yo lymphoma survivor); "This program makes me feel included" (26 yo ALL survivor); "This is a safe place where people 'get me' without requiring explanation" (27 yo brain tumor survivor); "This program is my family – these are my siblings" (34 yo brain tumor survivor); "The program is as much a blessing as camp was as a child" (34 yo ALL survivor).

Conclusions: Establishing a social network of LTS in a non-medical environment provides critically important peer support which enhances the survivors' overall psychological health. Survivors who participate in such programming may find a lifeline would otherwise be inaccessible to them. Social programming directed at older LTS is a key intervention in creating and maintaining survivor mental health and wellbeing.

S132. USE OF INTEGRATED CLINICAL PATHWAY FOR IDENTIFICATION OF PEDIATRIC PATIENTS WITH CANCER THERAPEUTIC RELATED CARDIAC DYSFUNCTION (CTRCD)

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Background: Cancer therapy related cardiac dysfunction (CTRCD) is a major contributing factor to morbidity/mortality in pediatric oncology patients exposed to cardiotoxic medications.1 We previously demonstrated that Anthracycline-treated patients with a history of impaired left ventricular function have decreased cumulative survival of 54% at 25 years.2 With the goal of improving outcomes, we developed a clinical pathway in which interventions are defined and mapped over time based on risk stratification. We have assembled an interdisciplinary team of oncologists, cardiologists and nurses to work together in a clinic to implement primary, secondary, and tertiary heart failure prevention strategies.3

Methods: Our monthly pediatric cardio-oncology clinic started in September of 2018. Patients undergo risk stratification based on the known clinical and metabolic risk factors of cardiotoxicity and are given a composite score to categorize them in low, moderate, and high risk.1, 2 Extraction of oncology and cardiac history is performed utilizing multiple modalities (i.e. Passport for Care, EPIC, Roadmaps).

Results: Table 1 demonstrates the demographic characteristics of our first 23 consecutive patients. Six (26%) were categorized as low, 5(22%) moderate, and 12(52%) high risk (HR). All patients in the HR category had evidence of myocardial dysfunction with EF<55% (Range 22-54%) and are being treated. The HR group had an average of 7.3 risk factors compared to the low risk group with an average of 3.3 risk factors. The low and moderate risk groups had normal myocardial function and didn't require clinical intervention.

Conclusions: Risk stratification provides a reliable tool to identify patients with cardiotoxicity and help strategize interventions in this patient population. HR group patients require multiple clinic visits to titrate cardiac medications, while patients in the low and moderate risk groups may follow up on a yearly or bi-yearly basis.

Table 1. Demographics

	n=23
Current age (yr; mean ± SD; range)	11.7 ± 7.5 (1 - 26)
Age at diagnosis (yr; mean ± SD; range)	8 ± 6.2 (0 - 23)
Gender	
Male	15 (65.2%)
Female	8 (34.8%)
Diagnosis	
AML	3 (13.0%)
ALL	5 (21.7%)
Lymphoma	2 (8.7%)
Sarcoma	8 (34.8%)
Other	5 (21.7%)
RT to chest	
Yes	5 (21.7%)
No	18 (78.3%)
Vincristine	
Yes	18 (78.3%)
No	5 (21.7%)
Anthracycline dose (mg/m^2; mean ± SD; range)	229.1 ± 137.0 (0 - 375)
High dose cyclophosphamide	
Yes	17 (73.9%)
No	6 (26.1%)
Heart disease at Diagnosis	
Yes	1 (4.4%)
No	22 (95.7%)
BMT	
Yes	5 (21.7%)
No	18 (78.3%)
SF < 29 % or EF < 55%	
Yes	13 (56.5%)
No	10 (43.5%)
BMI (mean ± SD; range)	19.8 ± 4.8 (13.3 − 33.6)
Score (mean ± SD; range)	6.4 ± 2.8 (3 − 15)
Risk	
Low	6 (26.1%)
Moderate	5 (21.7%)
High	12 (52.2%)
Current 3D EF (mean ± SD; range)	57.7 ± 5.4 (45 − 72)
Current GLS (mean ± SD; range)	-20.5 ± 4.3 (-29 - -11)

†Other: medulloblastoma, neuroblastoma, and atypical teratoid rhabdoid tumor

P133. ALL IN THE FAMILY: IDENTIFYING HEREDITARY CANCER RISK IN ADULTS WITH A HISTORY OF CHILDHOOD CANCER

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Background: The excess risk for subsequent malignant neoplasms (SMNs) in adult survivors of pediatric cancer may be elevated based on treatment received, lifestyle factors and/or hereditary mutations. Prevalence of germline mutations in children with cancer is unknown but estimated at about 8.5 %. Given that SMNs may not present for years after treatment is complete, ongoing reassessment to identify those at highest risk based on less common hereditary cancer syndromes is crucial so that appropriate referrals can be made, as highlighted in this clinical vignette.

Methods: Setting: TACTIC (Thriving After Cancer Treatment is Complete) clinic in the Internal Medicine clinic at the University of Colorado Hospital. TACTIC visits include consultation with pediatric oncologist, general internist, clinical health psychologist and oncology nurse educator/coordinator. Eligibility criteria: Diagnosis and treatment for cancer prior to age 18; diagnosis > 5 years prior to visit; at least 2 years off of active therapy; age 21 or older

Results: 27 year old Hispanic female with a history of Acute Lymphoblastic Leukemia (ALL) at age 3. No regular source of primary care. HPI: chronic abdominal pain; occasional hematemesis; panic attacks; syncope; chronic hip and knee pain PMH: ALL, migraine headaches, benign breast cyst, cholecystectomy Social history: divorced, employed full time (night shift work), never smoker, rare alcohol use, no IV or other drug use. Family history: sister—"kidney" cancer (age 5); father and paternal grandfather—colorectal cancer (both at age 40+); paternal uncle—colorectal cancer, died age 62; 2 paternal aunts—breast cancer (unknown ages); paternal great-grandmother—brain cancer. Patient's sister with kidney cancer did have testing done and was told she was at increased risk for future

cancer, no further details known. Exam: BMI 26.34 kg/m2, BP 111/70 Labs: CBC, TSH, iron, ferritin, creatinine, liver panel, vitamin D, HgbA1c all normal. Referral to the Hereditary Cancer Clinic was made based on personal and family history of cancer.

Conclusions: Because SMNs are a significant cause of morbidity and mortality in childhood cancer survivors, it is important to obtain a thorough family history and to update family history over time. About 29% of survivors are deemed to be eligible for genetic counseling/screening, with most of those eligible based on family history of cancer. Adult primary care providers (PCPs) need to be prepared to identify those individuals at highest risk for SMNs and manage their surveillance, as recommendations for routine screening and prevention may be significantly altered.

S134. TREATMENT OF STEROID-REFRACTORY ACUTE AND CHRONIC GRAFT-VERSUS-HOST DISEASE WITH RUXOLITINIB IN CHILDREN

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Background: Steroid-refractory graft-versus-host disease (srGVHD) is a life-threatening complication of allogeneic stem cell transplantation. Currently there is no standard of care for this complication and with existing modalities the survival remains relatively low. The study was conducted children with steroid-refractory or steroid-dependent acute and chronic GVHD.

Methods: The prospective study (NCT02997280) included 30 patients (age 1-18 years, median – 5,5 y.o.). EBMT/ELN criteria were used for steroid refractory disease (T. Ruutu et al., 2014). 16 had acute srGVHD and 14 had moderate or severe chronic srGVHD. Eight (27%) had acute myeloid leukemia, 7 (23%) acute lymphoblastic leukemia, 12 (40%) - non-malignant diseases, 3 (10%) - other malignant diseases and. Donor type was: unrelated – 18 (60%), matched related donor – 1 (3%), haploidentical – 11 (37%). Patients with acute GVHD had a median of 2 prior lines of therapy (range 1-2), patients with chronic GVHD had a median of 3 prior lines (range 1-6). 13/16 acute GVHD patients had grade III-IV disease, and 12/14 chronic GVHD patients had severe (NIH) disease. Ruxolinib was administered at the starting dose of 0.3 mg/kg/day. Dose modifications were performed in patients with grade 4 hematologic toxicities. Ruxolinib was continued until complete response or absence of response in 28 days for acute GVHD and six months for chronic GVHD.

Results: Median follow-up for alive patients was 20 months (range 6-37). Overall response for acute GVHD was 81%. Complete response (CR) was observed in 11/16 patients with median time to CR 38 days (range 7-122). Three patients were in continued partial response (PR) and two had progressive disease. Overall response for chronic GVHD was 100%. 4/14 patients achieved CR after median 10,5 months of treatment (range 5-14 months). 10/14 achieved PR after median 1,3 months of treatment (range 0,2-6,5). Non-relapse mortality occurred in 6/30 patients, the cause of death were progression of GVHD in 3 cases, multidrug-resistant sepsis in 3 cases and two died due to progression of underlying malignancy. Overall survival for patients with aGVHD was – 62,5%, for cGVHD – 86%. Dose reduction/drug interruption due to cytopenia was required in 5/16 acute GVHD and 3/14 chronic GVHD patients.

Conclusions: Despite the small group size, our preliminary results indicate that ruxolitinib is a promising agent for srGVHD. Randomized prospective studies are required to confirm that ruxolitinib is superior to the other approaches.

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