ISLCCC

INTERNATIONAL SYMPOSIUM
ON LATE COMPLICATIONS
AFTER CHILDHOOD CANCER

2025

JUNE 19-21 2025, SEATTLE, USA

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Symposium Sponsors

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2025 4th International Symposium on Late Complications after Childhood Cancer

Schedule at a Glance

Thursday, June 19

3:00-3:45 pm	Welcome, Opening Remarks, Keynote 1 – Host: Scott Baker	
Keynote 1: Ann Mertens & Marilyn Stovall Memorial Lecture on Childhood Cancer Survivorship, Past, Present, and Future – Dr. Leslie Robison		
3:45-4:40 pm	Oral abstracts: *Accelerated Aging*	Moderators: Miranda Fidler-Benaoudia, Cindy Im
4:40-5:25 pm	Panel discussion: Transition of AYA Survivors to Adult Care	Moderators: Katie Devine & Jikke Wams Panelists: Jennifer Belle, Jeff Renner, Maggie Rogers, Dava Szalda
5:25-6:20 pm	Oral abstracts: *Health Services Session 1*	Moderators: I-Chan Huang, Stephanie Smith
6:20 pm	*Evening Reception / Poster viewing on your own*	

Friday, June 20

7:00 am	Dan Green Fun Run	Host: Eric Chow; meet at Edgewater lobby
7:15 am	Mentee Breakfast	Hosts: Monica Gramatges, Tara Henderson, Nina Kadan-Lottick, Paul Nathan: meet at Marriott lobby
8:30-9:15 am Keynote 2: Immune Reconstitution Following Cancer Therapy – Dr. Joshua Hill		
9:15-10:10 am	Oral abstracts: *Other Key Health Outcomes*	Moderators: Lillian Meacham, Satomi Sato
10:10-10:35 am	*Break*	
10:35-11:30 am	Oral abstracts - *Cardiovascular Health Session 1*	Moderators: Neel Bhatt, Lieke Feijen-Allenstein
11:30-1:00 pm	*Group Lunch / Poster viewing on your own*	
1:00-1:45pm Keynote 3: Bridging the Gap – Enhancing Genetic Testing Access for Childhood Cancer Survivors – Dr. Angela Bradbury		
1:45-2:40 pm	Oral abstracts:- *Subsequent Malignant Neoplasms*	Moderators: Monica Gramatges, Anna Holmqvist
2:40-3:10 pm	*Break*	
3:10-3:55 pm	Panel discussion: Development of Survivorship Care and Research in LMIC Settings	Moderator: Matthew Ehrhardt Panelists: Monica Cypriano, Maya Prasad, Anel VanZyl
4:00-5:00 pm	Highlighted Posters – Rapid Review	Moderators: Stephanie Dixon, Paul Nathan
5:00-6:00 pm	Poster Viewing with Poster Presenters On-Site	
6:30 pm	*Group Dinner*	

Saturday, June 21

8:30-9:15 am Keynote 4: Implementation and Issues around Multi-Cancer Detection Screening – Dr. Ruth Etzioni		
9:15-10:10 am	Oral abstracts: *Health Services Session 2*	Moderators: Wendy Landier, Monica Muraca
10:10-10:40 am	*Break*	
10:40-11:35 am	Oral abstracts: *Cardiovascular Health Session 2*	Moderators: Kevin Oeffinger, Christina Schindera
11:35-12:00pm	Closing Remarks, CME information, ISLCCC 2026 details	Host: Eric Chow

Oral Research Abstract Presentation Schedule in Detail

(Full text of each abstract can be found on subsequent pages of the Program Book)

Thursday, June 19 – 3:45 to 4:40 pm – Accelerated Aging

Presenter	Title
AnnaLynn Williams	Accelerated aging among long-term survivors of childhood cancer: a report from the Childhood Cancer Survivor Study
Neel Bhatt	Longitudinal changes in pulmonary function after treatment for childhood cancer: a report from the St. Jude Lifetime Cohort Study
Jennifer French	Genetic contributions to treatment-associated neurocognitive outcomes among childhood cancer survivors
Xiaoxi Meng	Mediating effects of epigenetic age acceleration on associations between cancer treatments and cardiometabolic and cardiovascular disease risk among survivors of childhood cancer: a Report from the St. Jude Lifetime Cohort

Thursday, June 19 – 5:25 to 6:20 pm – Health Services Session 1

Presenter	Title
Tamara Miller	Automating ascertainment of chemotherapy exposure for the Childhood Cancer Survivor Study with the ExtractEHR+ Toolkit
Cindy Im	Social determinants of health and late mortality among survivors of childhood cancer: a report from the Childhood Cancer Survivor Study
Matthew Ehrhardt	United States population level costs and cost-savings associated with long-term follow-up screening for survivors of childhood cancer
Jordan Marchak	Results from a hybrid effectiveness-implementation trial on return for survivorship care for pediatric cancer survivors*

*Top ranked abstract featuring a randomized trial

Friday, June 20 – 9:15 to 10:10 am – Other Key Health Outcomes

Presenter	Title
Joyce Claessens	Risk factors for azoospermia and testosterone deficiency among survivors of childhood cancer in the Netherlands: results of the DCCSS-LATER 2 study
Brooke Cherven	A sequential mixed-methods study of fertility assessment among female survivors of childhood cancer
Demi de Winter	Genetic susceptibility to changes in bone mineral density in long-term childhood cancer survivors: A trans-ancestry genome-wide meta-analysis in 4,031 survivors from the Dutch Childhood Cancer Survivor Study (DCCSS-LATER 2) and the St. Jude Lifetime Cohort Study
Tara Brinkman*	The Impact of Sleep Disturbances on Trajectories of Neurocognitive Functioning in Adult Survivors of Childhood Cancer: A report from the Childhood Cancer Survivor Study

*Presenting on behalf of Chiara Papini

Friday, June 20 – 10:35 to 11:30 am – Cardiovascular Health Session 1

Presenter	Title
Maya Prasad	Cardiac dysfunction in childhood cancer survivors : a retrospective cohort study from India*
Wendy Bottinor	Cardiovascular risk factor severity and adverse cardiovascular events: a report from the Childhood Cancer Survivor Study
Stephanie Dixon	Cardiovascular risk factor control associated with future cardiovascular events in survivors of childhood cancer: a report from the St. Jude Lifetime Cohort
Danielle Friedman	Cardiovascular risk factors in survivors of childhood hematopoietic cell transplantation and their role in development of cardiovascular disease: A CCSS-CIBMTR Analysis

*Top ranked abstract from a LMIC institution

Friday, June 20 – 1:45 to 2:40 pm – Subsequent Malignant Neoplasms

Presenter	Title
Jop Teepen	Temporal trends of subsequent malignant neoplasms in childhood cancer survivors and the impact of treatment changes: a DCCSS-LATER 3 Study
Chaya Moskowitz	International Study of Subsequent Colorectal Cancer Among Survivors of Childhood, Adolescent, and Young Adult Cancers (I-SCRY)*
Grit Sommer†	Sun exposure and sun protection behavior in survivors of childhood cancer – findings from the Swiss Childhood Cancer Survivor Study
Lucie Turcotte	Breast cancer recurrence and mortality among survivors of childhood cancer: a report from the Childhood Cancer Survivor Study

*Overall conference top ranked abstract; †Presenting on behalf of Carina Nigg

Saturday, June 21 – 9:15 to 10:10 am – Health Services Session 2

Presenter	Title
Daksha Marfatia	Education and employment outcomes in survivors of adolescents and young adults cancer in Ontario, Canada
I-Chan Huang*	Longitudinal associations between chronic health condition burden and financial hardship among adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study
Tim Ohlsen	Development of a pediatric oncology financial toxicity outcome measure with content and face validity: The Parent-Reported Instrument of Costs and Experiences with financial toxicity (PRICE) measure
Lisa Schwartz	Validation of the Transition Readiness Inventory for adolescent and young adult survivors of cancer

*Presenting on behalf of Tara Suntum

Saturday, June 21 – 10:40 to 11:35 am – Cardiovascular Health Session 2

Presenter	Title
Erin Mobley	Longitudinal change in cardiac function after doxorubicin and dexrazoxane: a report from COG ALTE11C2
Kateryna Petrykey	Risk prediction of coronary artery disease in long-term survivors of childhood cancer: findings from the St. Jude Lifetime Cohort and the Childhood Cancer Survivor Study
Daniel Mulrooney	Predicting valvular heart disease in adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study and St. Jude Lifetime Cohort
Jan Leerink	A diagnostic algorithm to triage childhood cancer survivors for a surveillance echocardiogram: a DCCSS LATER 2 study

BELL HARBOR INTERNATIONAL CONFERENCE CENTER – FACILITY MAP / LAYOUT

2211 Alaskan Way (Pier 66), Seattle, WA 98121 – telephone (206) 441-6666

*Note that ISLCCC is taking place on **Level 3** of the center. All scientific presentations will occur in the Bay Auditorium. Group lunch and dinner on Friday will be held in the Harbor Room. Posters will be displayed in the pre-function area along with the Sound Room from Friday afternoon through Saturday morning.*

The conference center is within easy walking distance from the two conference hotels (Marriott Waterfront & Edgewater). For those driving to the conference center, parking is available at the Bell Street Pier Garage at 2323 Elliott Ave. The garage connects directly to the conference center via a sky bridge that crosses Alaskan Way.

2025 ISLCCC PROGRAM COMMITTEE

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Emory University, Children's Healthcare of Atlanta, USA

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SickKids, University of Toronto, Canada

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University Children's Hospital, Zurich, Switzerland

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University Medicine at Johannes Gutenberg University, Mainz, Germany

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St. Luke's International University, Tokyo, Japan

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Children's Hospital of Eastern Switzerland, St. Gallen, Switzerland

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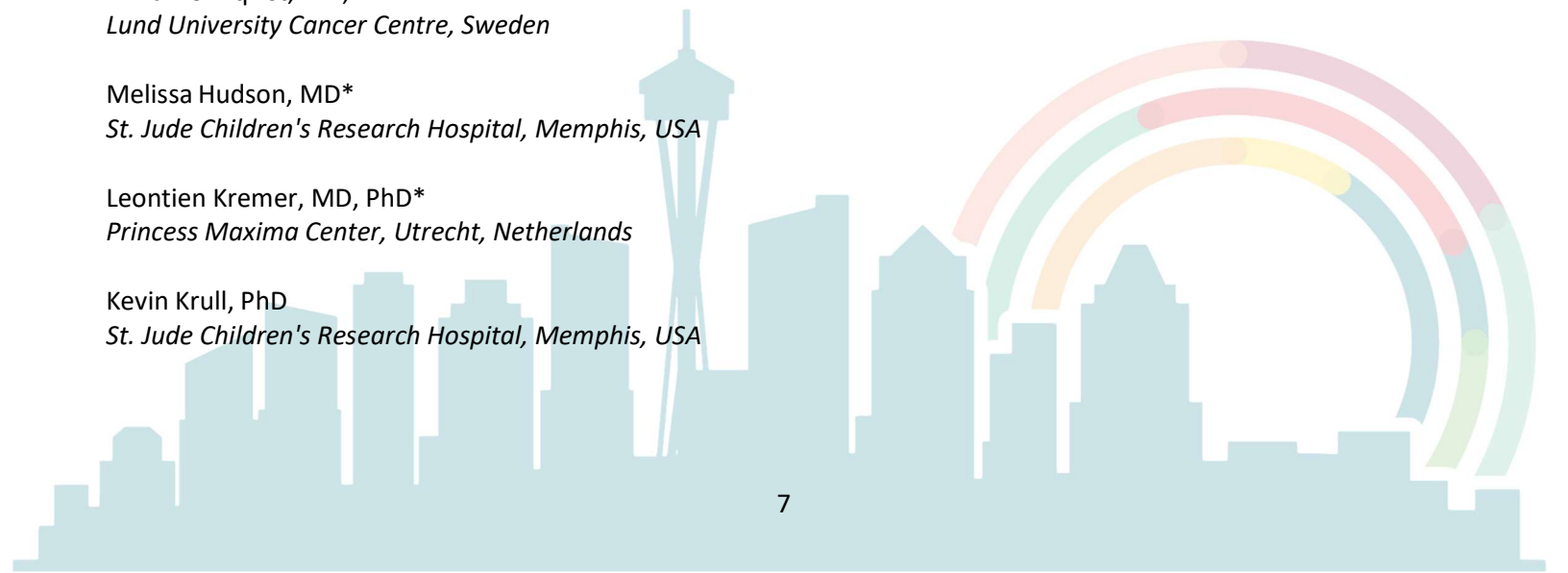
*Member of the Core Organizing Committee



In Memoriam – Two Pioneers in Understanding Survivorship Issues following Childhood Cancer

Ann Mertens, PhD

Marilyn Stovall, PhD

KEYNOTE LECTURE 1 – Thursday June 19, 3:00 pm
Ann Mertens & Marilyn Stovall Memorial Lecture on Childhood Cancer Survivorship, Past, Present, and Future

Leslie Robison, PhD
Chair Emeritus, Department of Epidemiology and Cancer Control
St. Jude Children's Research Hospital

KEYNOTE LECTURE 2 – Friday June 20, 8:30 am
Immune Reconstitution Following Cancer Therapy

Joshua Hill, MD
Associate Professor, Vaccine & Infectious Disease Division
Member, Immunotherapy Integrated Research Center
Fred Hutchinson Cancer Center, University of Washington

KEYNOTE LECTURE 3 – Friday June 20, 1:00 pm
Bridging the Gap: Enhancing Genetic Testing Access for Childhood Cancer Survivors

Angela Bradbury, MD
Professor of Medicine (Hematology-Oncology)
Member, Abramson Cancer Center
University of Pennsylvania

KEYNOTE LECTURE 4 – Saturday June 21, 8:30 am
Implementation and Issues around Multi-Cancer Detection Screening

Ruth Etzioni, PhD
Professor, Rosalie & Harold Rea Brown Endowed Chair
Public Health Sciences Division
Fred Hutchinson Cancer Center

PANEL 1 – Thursday June 19: Transition of AYA Survivors to Adult Care

Moderators:

Katie Devine, PhD, MPH
Associate Professor of Pediatrics
Rutgers Cancer Institute

Jikke Wams, MA
Pediatric Oncology
Princess Máxima Center

Panelists:

Jennifer Belle, MBA
Chair, Patient Advocate Committee
Children's Oncology Group

Jeff Renner, MHA
Division Administrator, Department of Pediatrics
University of Washington School of Medicine

Maggie Rogers, MPH
Director, Pediatric, Adolescent and Young Adult Cancer Support
American Cancer Society

Dava Szalda, MD, MSHP
Co-Director of the Transition to Adulthood Program
Children's Hospital of Philadelphia

PANEL 2 – Friday June 29: Development of Survivorship Care and Research in Lower- and Middle-Income Country Settings

Moderator:

Matthew Ehrhardt
Associate Member, St. Jude Children's Research Hospital, Memphis, USA

Panelists:

Monica Cypriano, MD
Chief Medical Officer of GRAACC/Pediatric Oncology Institute/UNIFESP
Sao Paolo, Brazil

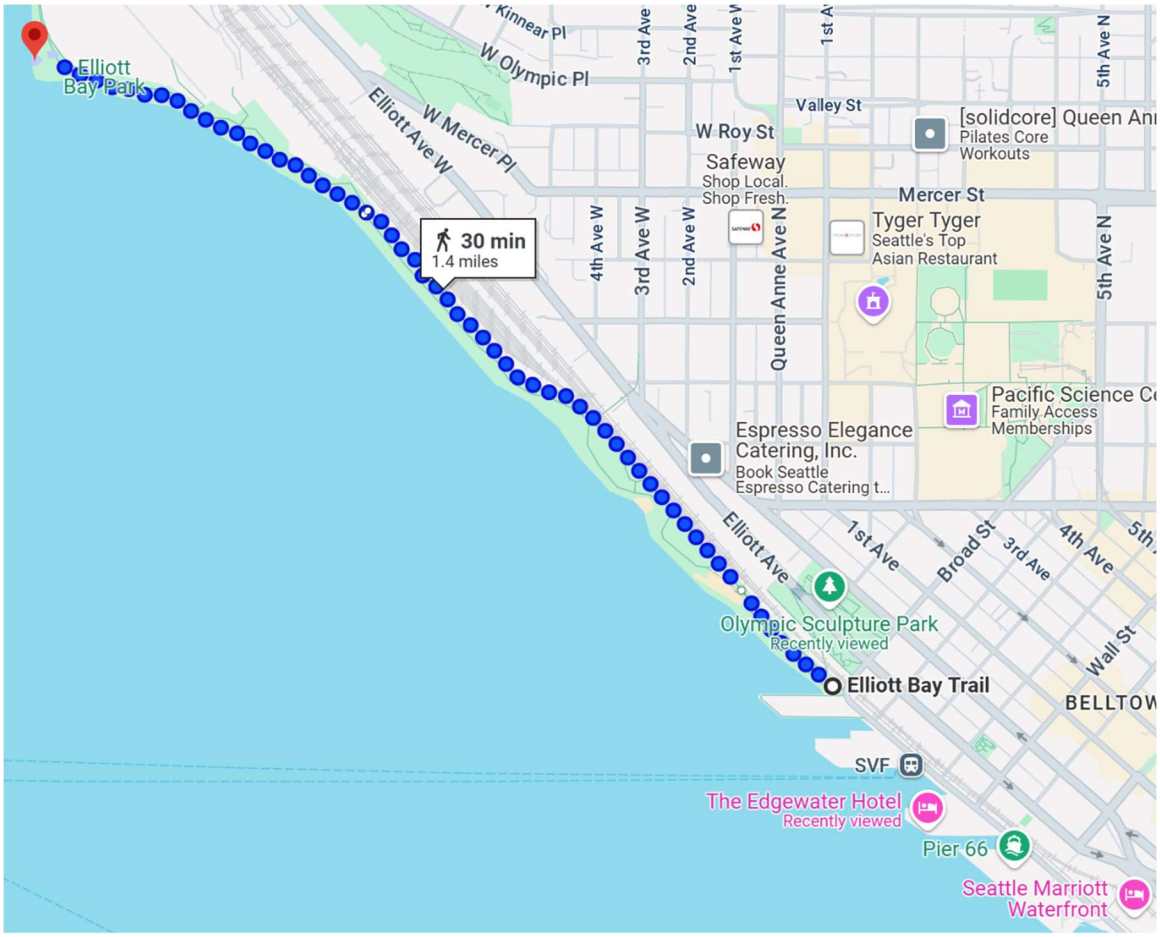
Maya Prasad, MD, MBBS
Professor, Division of Paediatric Oncology, Tata Memorial Hospital
Mumbai, India

Anel VanZyl, MBChB, FC, MMed, PhD
Head, Paediatric Haematology/Oncology, and Senior Lecturer
Stellenbosch University, Tygerberg Hospital, Cape Town, South Africa

Dan Green Fun Run/Walk

Friday June 20 at 7am – Meet at Edgewater Hotel Lobby (2411 Alaskan Way; contact: Eric Chow – 206-683-6097 cell)

Suggested route: run/walk along the Elliott Bay Trail ending at Elliott Bay Park / Beach at Expedia (around Pier 90) – distance is ~1.5 miles one-way (3 miles round trip). For those who have extra time, can also consider a detour to the Olympic Sculpture Park. First scientific session on Friday starts at 8:30am.



Elliott Bay Trail starts on the left side of the fountain (below left) while stairway on the right leads up to the Olympic Sculpture Park. Beach at Expedia Group marker (below right).

Mentee Breakfast

Friday June 20 at 7:15am – Location: Marriott Waterfront Lobby (2100 Alaskan Way)

Hosted by Drs. Monica Gramatges, Tara Henderson, Nina Kadan-Lottick, and Paul Nathan. Casual networking event open to all interested junior investigators (trainees, assistant professors). Bring your own breakfast.

Monica Gramatges, MD, PhD
Professor of Pediatrics
Associate Chief, Oncology
Texas Children's Hospital,
Baylor College of Medicine

Tara Henderson, MD, MPH
Chair, Department of Pediatrics
Lurie Children's Hospital
Northwestern University
Feinberg School of Medicine

Nina Kadan-Lottick, MD, MSPH,
Professor of Pediatrics
Director, Survivorship Research Initiative
Lombardi Cancer Center
Georgetown University

Paul Nathan, MD, MSc
Professor of Paediatrics
Head, Solid Tumor Section
Aftercare Program Director
SickKids, University of Toronto

Marriott Lobby Area *– more open seating area adjacent to the Hook & Plow restaurant*

LOCAL ACTIVITY SUGGESTIONS

Nearby the Conference Center (<15 minute walk)

- Pike Place Public Market and Waterfront Park, Seattle Aquarium, Seattle Art Museum, Olympic Sculpture Park
- The ferry to Bainbridge Island is also very close (Pier 50) and there are walk-on tickets available (no reservation needed) if you are interested in doing a beautiful 30 minute ride to this nearby island, with views of Seattle from the water and if the sky is clear, Mt. Rainier in the distance
    - Please check the sailing schedule at the Washington State Department of Transportation website: https://wsdot.com/ferries/schedule/scheduledetailbyroute.aspx?route=sea-bi
    - There is a small town square on the island immediately upon walking off the ferry with casual restaurants, a free art museum, coffee, beer, etc.

Slightly farther away, but still very walkable (20 minute walk)

- Space Needle, Seattle Center/Chihuly Garden & Glass exhibit, Pacific Science Center, Museum of Pop Culture

Other attractions in Seattle (need taxi* to reach):

- Seattle Asian Art Museum, Museum of Flight, National Nordic Museum
- Ballard Locks – akin to a very small version of the Panama Canal with locks that raise boats up and down so that they can traverse between Puget Sound [salt water] and Lake Union [fresh water] set amidst a garden and also with fish ladders and an underwater viewing area to view salmon returning from the sea to spawn in freshwater
- Kayak or stand-up paddleboard Lake Union – rentals available at Moss Bay, Northwest Outdoor Center, Agua Verde Paddle Club – recommend checking websites first and see if reservations are possible as availability can be limited on nice summer weekends

Performing arts:

- Seattle Symphony/ Benaroya Hall, Seattle Opera / McCaw Hall, 5th Avenue Theater, Seattle Rep (Theater), Paramount Theatre

Live sports:

- Mariners at T-Mobile Park (baseball), Sounders & Reign FCs at Lumen Field (soccer), Storm at Climate Pledge Arena (basketball); note that the FIFA Club World Cup is holding some games at Lumen field in late June as well

Nature close by (within Seattle; need taxi* to reach):

- Discovery Park, Washington Park Arboretum, Seward Park, Kubota Garden

Nature farther away (but still in Washington):

- Mt. Baker-Snoqualmie National Forest, Mt. Rainier National Park, Olympic National Park, North Cascades National Park, Mount St. Helens National Volcano Monument, San Juan Islands
- For hiking trail suggestions and conditions, please check wta.org

**Or if you are adventurous, could consider using a shared electric bike or scooter rental – Bird & Lime are the two companies that service Seattle. Please ride safely!*

SAVE THE DATE FOR 2026!

Dear Survivorship Community,

We are pleased to announce the 5th International Symposium on Late Complications after Childhood Cancer (ISLCCC), which will be held in Genoa, Italy on June 4-6, 2026 at the Porto Antico venue.

Similar to past meetings, the 2026 symposium will give you the opportunity of sharing worldwide experiences on emerging research results on clinical and epidemiologic survivorship issues. We are sure that the meeting will give the opportunity to promote research collaborations and to improve survivorship care throughout the world.

We are looking forward to welcome you all in Genoa with its mediaeval city center, its museums and several sightseeing opportunities in the nearby Riviera.

Registration and other related information will be soon available at the ISLCCC website: www.islccc.org

Sincerely,
Riccardo Haupt & Monica Muraca
Local Organizing Committee

ABSTRACTS SELECTED FOR ORAL PRESENTATIONS (listed in alphabetical order by first author)

The top 28 ranked abstracts as determined by the Program Committee were selected for oral presentation and are listed alphabetically by first author on the following pages. The Program Committee determined that each first author would only be able to present one oral abstract, and as a result, there are some top-ranking abstracts that are being presented as posters. The next 23 ranked posters are featured as highlighted posters on Day 2 of the symposium. Listings of all posters can be found in the second half of the Program Book.

To acknowledge a few specific outstanding abstracts:

- Overall, top scoring abstract: Moskowitz, et al. “International study of subsequent colorectal cancer among survivors of childhood, adolescent, and young adult cancers (I-SCRY)”
- Top abstract featuring a randomized trial: Marchak, et al. “Results from a hybrid effectiveness-implementation trial on return for survivorship care for pediatric cancer survivors”
- Top abstract from a low/middle-income region: Prasad, et al. “Cardiac dysfunction in childhood cancer survivors : a retrospective cohort study from India”

Longitudinal Changes in Pulmonary Function after Treatment for Childhood Cancer: a Report from the St. Jude Lifetime Cohort Study (SJLIFE)

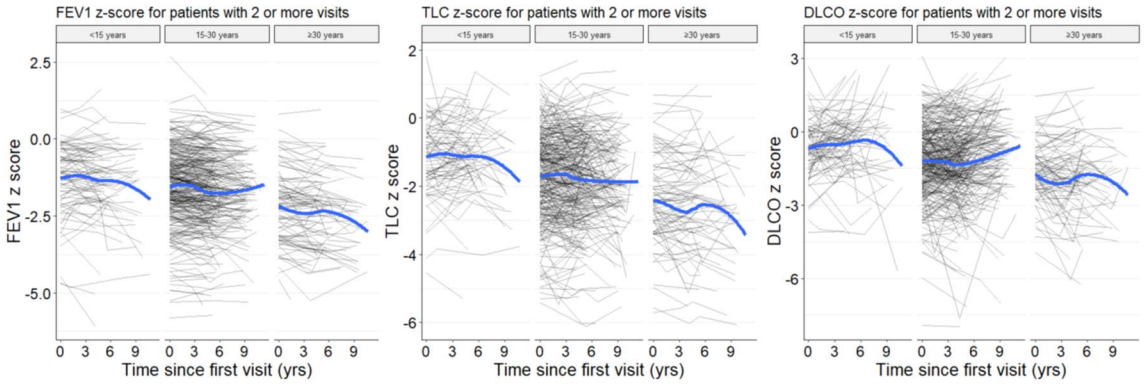
Neel Bhatt, Lu Xie, Kendrick Li, Deo Kumar Srivastava, Saumini Srinivasan, Kiri Ness, Daniel Mulrooney, Stephanie Dixon, Greg Armstrong, Melissa Hudson, Leslie Robison, Daniel Green, Dennis Stokes

Background: Longitudinal changes in pulmonary function in long-term survivors of childhood cancer have not been clearly defined.

Methods: We included adult survivors of childhood cancer enrolled in the SJLIFE study with longitudinal, clinical assessment of health outcomes. Participants who had ≥1 pulmonary function test (PFT) after completion of therapy and had available radiation dosimetry data were included. We aimed to 1) describe PFT deficits at the most recent assessment; 2) determine the changes in PFTs among those with ≥2 assessments, stratified by time from cancer diagnosis; and 3) evaluate risk-factors associated with changes in PFTs over time. Z-scores for FEV1, total lung capacity (TLC), and single breath diffusing capacity of the lung for carbon monoxide corrected for hemoglobin (DLCOcorr) were derived through the American Thoracic Society/ European Respiratory Society technical standard methodology. Z-score ≤-1.65 was considered abnormal. Associations between clinical and treatment-factors and persistently abnormal or worsening Z-scores were assessed using linear and logistic regression.

Results: Among 606 survivors with ≥1 PFT assessment, median age at last assessment and median time from diagnosis were 39.2 years (range 19.3-64.3) and 27.3 years (range 11.3-54.1), respectively. Overall, 49.5% had an FEV1 Z-score ≤-1.65, 50.5% had a restrictive defect (TLC Z-score ≤-1.65), and 37.4% had a diffusion defect (DLCOcorr Z-score ≤-1.65), Among survivors with ≥2 PFT assessments (n=481, median interval between first and last PFT of 5.3 years), FEV1, TLC, and DLCOcorr Z-scores declined, with most pronounced decline in those who were ≥30-year since diagnosis at their first PFT assessment (Figure 1). Each 10% increase in estimated percentage of lung tissue that received ≥10 Gy radiation (V10) was associated with higher risk of reduced FEV1 (odds ratio [OR] 1.14, 95% confidence interval [CI] 1.02-1.29), but not restrictive or diffusion defects. Exposure to chemotherapy or history of surgery did not predict changes in Z-scores. BMI ≥30 kg/m2 was associated with higher risk of reduced FEV1 (2.95, 1.37-6.59) and current or former smoker status was associated with higher risk of diffusion defect (2.31, 1.30-4.18). Higher elapsed time from diagnosis to first PFT was associated with increasing risk of obstructive, restrictive, and diffusion defects.

Figure 1: Pulmonary function test (PFT) Z-score changes according to time from diagnosis and first PFT assessment and time interval between PFT assessments



Conclusion: In adult survivors of childhood cancer, pulmonary function declined over time. Persistently abnormal or worsening pulmonary function was seen in those who were obese, smoked, or had an increasing proportion of lung exposed to ≥10 Gy radiation. Further work to study associations between PFT changes and participants' symptoms and functional status is ongoing. These findings will help identify survivors who might benefit from interventions to improve pulmonary function and inform revision of guidelines for pulmonary function surveillance after completion of cancer directed therapy.

Cardiovascular Risk Factor Severity and Adverse Cardiovascular Events: a Report from the Childhood Cancer Survivor Study (CCSS)

Wendy Bottinor, Haoxue Xiang, Yan Chen, Stephanie Dixon, Cindy Im, Scott Borinstein, Jonathan Soslow, Debra Friedman, Saro Armenian, Nirupa Raghunathan, Emily S. Tonorezos, Kevin Oeffinger, Wendy M Leisenring, Greg Armstrong, Yutaka Yasui, Eric Chow

Background: Among survivors of childhood cancer, more severe grades of CVRFs are associated with increased risk for adverse cardiovascular events (ACE). The impact of low severity CVRFs has not been defined.

Methods: Among 25,723 long-term survivors of childhood cancer, CVRF severity was graded using longitudinal self-report: Grade 1 conditions are reported but not on medications; Grade 2 are prescribed medications. Cumulative incidence of CVRFs were estimated into the 6th decade of life with death and Grade 2 CVRFs a competing risk event for Grade 1 CVRFs. Starting at 1st report of a CVRF, multivariable piecewise-exponential models were used to estimate relative rates (RR) of heart failure (HF), myocardial infarction (MI), valvular disease (VD), arrhythmia, and cardiac death relative to survivors without hypertension (HTN), diabetes (DM), and hyperlipidemia (HLD), all as time-dependent covariates.

Results: The median age of survivors was 35y (range 9-70) and 26y (range 7-52) from cancer diagnosis. Cumulative incidence by age 55 of Grade 1 HTN, DM, and HLD were 7.8% (CI 7.1-8.5%), 4.3% (CI 3.8-4.9%), and 10.8% (CI 9.9-11.6%), respectively. The cumulative incidences of Grade 2 HTN, DM, and HLD were 37.9% (CI 36.4-39.3%), 14.0% (13.0-15.0%), 31.3% (29.9-32.7%), respectively. Grade 2 CVRFs were significantly associated with an increased RR for nearly all ACE (Table). Grade 1 CVRFs were also significantly associated for most ACE; often with a similar magnitude as Grade 2 CVRFs. Grade 1 vs no HTN was associated with a 2 to 5-fold significantly increased RR of HF, MI, VD, arrhythmia, and cardiac death. Grade 1 vs no DM was associated with an increased RR of HF (1.9, CI 1.1-3.4). Grade 1 vs no HLD was associated with an increased RR of MI (2.9, 1.9-4.2) and arrhythmia 2.1 (1.2-3.5).

Table: Relative rates of ACE among survivors by CVRF severity

Individual models for each CVRF vs no respective CVRF (ref)	HF	MI	VD	Arrhythmia	Cardiac death
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
HTN Grade 1	2.9 (1.9-4.4)	3.6 (2.4-5.3)	4.7 (3.0-7.5)	2.8 (1.6-4.8)	1.9 (1.1-3.3)
HTN Grade 2	7.2 (6.1-8.6)*	7.1 (5.9-8.5)*	4.7 (3.7-6.1)	5.3 (4.2-6.7)	1.5 (1.1-2.0)
DM Grade 1	1.9 (1.1-3.4)	1.5 (0.7-3.0)	0.8 (0.3-2.5)	1.5 (0.6-3.7)	0.6 (0.1-2.2)
DM Grade 2	2.5 (1.9-3.2)	2.7 (2.2-3.5)	2.2 (1.6-3.1)	2.3 (1.6-3.2)	1.8 (1.3-2.6)
HLD Grade 1	1.5 (0.95-2.4)	2.9 (1.9-4.2)	1.5 (0.8-2.8)	2.1 (1.2-3.5)	1.2 (0.6-2.2)
HLD Grade 2	3.8 (3.2-4.7)*	6.5 (5.4-7.8)*	3.8 (2.9-4.8)*	3.1 (2.4-4.0)	1.1 (0.8-1.4)

Models adjusted for sex, race, current age, age at diagnosis, current smoking, obesity, sedentary lifestyle, anthracycline and heart radiation dose. Models fitted separately for each ACE. No respective CVRF as referent group. *Grade 2 vs Grade 1 condition above, $p<0.05$

Conclusions: Grade 1 CVRFs are associated with increased risk for ACE. These data suggest a role for more aggressive treatment of Grade 1 CVRFs among survivors.

A Sequential Mixed-Methods Study of Fertility Assessment among Female Survivors of Childhood Cancer

Brooke Cherven, Katie Liu, Scott Gillespie, Ebonee Harris, Shaheen Rana, Karen Burns, Jenna Demedis, Holly Hoefgen, Ann Mertens, James Klosky

Background/Purpose: Female survivors of childhood cancer may benefit from fertility status assessment (FSA) with discussion of ovarian reserve/fertility potential in consultation with reproductive specialist to elucidate options for parenthood/family-building. This sequential mixed-methods study explored psychosocial, decisional, and clinical factors associated with FSA.

Methods: Female survivors (18.00-29.99y, diagnosis <21y, >1y post-gonadotoxic treatment) were recruited from four U.S. cancer centers. Participants reported sociodemographics, developmental milestones (living/financial independence, employment), reproductive concerns, fertility-related knowledge, decisional factors, and history of FSA. Clinical characteristics (diagnosis, treatment-related infertility risk, hormonal testing, survivorship visit with pediatric reproductive subspecialist [gynecology/endocrinology/fertility preservation]) were abstracted from the medical record. Multivariable logistic regression models were used to identify factors associated with FSA. Maximum variation sampling (FSA completion/non-completion, participant site) was used to recruit a subset of participants (n=32) for qualitative interviews. Quantitative results and qualitative themes were integrated using joint display to expand understanding of factors associated with FSA in this population, develop meta-inferences, and draw overall conclusions.

Results: Of 325 participants, N=260 (aged 23.7±3.1 years, 74% non-Hispanic white) completed all survey items of interest; 96 (36.9%) reported FSA. FSA was associated with developmental milestones (Odds Ratio [OR] 2.20, 95% Confidence Interval [95%CI]:1.10-3.85, p=.027), survivorship reproductive subspecialist visit (OR 3.37, 95%CI:1.1-10.9, p=.032), fertility-information desire (OR 1.86, 95%CI:1.2-2.77, p=.001), informed decision for FSA (OR 1.82, 95%CI:1.30-2.59, p=.001), and several aspects of fertility-related knowledge (fertility-related procedures [OR 4.12, 95%CI:2.36-7.57, p<.001], fertility preservation [OR 1.76, 95%CI:1.31-2.44, p<.001], family-building options [OR 0.47, 95%CI:0.27-0.79, p=.006]). Diagnosis, infertility risk, and hormonal evaluation were not associated with FSA completion. Qualitative findings confirm that survivors want to accomplish life goals (education, financial, relationship) before family-building. Lack of understanding how to access FSA is a barrier and survivors identify providers/parents as primary influences on FSA decision-making. Survivors, both with and without prior FSA, describe benefits of completing FSA early to better prepare for future family-building.

Conclusions: During emerging adulthood, developmental milestone attainment is a natural prompt for survivors to pursue FSA. Psychoeducation and navigation assistance by clinicians with expertise in fertility could address knowledge gaps and serve as an intervention for FSA completion, thereby informing plans for future family-building.

Risk Factors for Azoospermia and Testosterone Deficiency among Survivors of Childhood Cancer in the Netherlands: Results of the DCCSS-LATER 2 Study

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Background/Purpose: Treatment with chemotherapy, radiotherapy, or surgery that involves reproductive organs can cause gonadal dysfunction, which may lead to fertility problems and testosterone deficiency. This study aimed to evaluate the risk factors for azoospermia and testosterone deficiency among adult childhood cancer survivors (CCSs).

Methods: A national cohort study was conducted as part of the Dutch Childhood Cancer Survivor Study (DCCSS) LATER cohort (1963-2001) part 2; clinical visit & questionnaire study. Male CCSs aged 18 years or older were eligible for this study (n = 2,596). Azoospermia was demonstrated by semen analysis. Testosterone deficiency was defined by use of testosterone replacement therapy or gonadotrophin therapy (as determined through the review of medical records and self-reported data), or, in the absence of medication use, a decreased testosterone concentration measured from an early morning blood sample: 1) total testosterone < 12 nmol/L, or 2) if total testosterone ≥ 12 nmol/L, a calculated free testosterone < 220 nmol/L. Cancer- and treatment-related and demographic risk factors of azoospermia and testosterone deficiency were identified using multivariable logistic regression.

Results: A total of 642 CCSs provided a semen sample and 1,132 CCSs provided a blood sample, at a median age of 32.1 and 33.8 years, respectively. The prevalence of azoospermia was 17% (n = 107/642). Time since diagnosis [year](OR, 1.09; 95% CI, 1.04-1.14; p <.001), total body irradiation (TBI) dose (OR, 2.17; 95% CI, 1.70-3.27; p < .001), alkylating agent (cyclophosphamide equivalent) dose per 1,000 mg/m2 (OR, 1.20; 95% CI, 1.14-1.27; p < .001), and epipodophyllotoxin [yes versus no](OR; 3.02; 95% CI, 1.38-6.46; p = .006) were associated with azoospermia. The prevalence of testosterone deficiency was 20% (n = 226/1,132). Time since diagnosis (OR, 1.06; 95% CI, 1.03-1.09; p < .001), TBI dose (OR, 1.33; 95% CI, 1.23-1.43; p < .001), radiotherapy exposing testes (OR, 5.15; 95% CI, 1.17-27.93; p = .037), and body mass index (BMI)(OR, 1.16; 95% CI, 1.11-1.21; p < .001) were associated with testosterone deficiency.

Table. Cancer- and treatment-related and demographic risk factors for azoospermia and testosterone deficiency, using multivariable logistic regression.

	Azoospermia (100 of 621 childhood cancer survivors)		Testosterone deficiency[a] (190 of 981 childhood cancer survivors)	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Cancer- and treatment-related risk factors				
Age at cancer diagnosis, years	0.99 (0.91, 1.06)	.707	1.02 (0.98, 1.07)	.283
Time since diagnosis, years	1.09 (1.04, 1.14)	<.001	1.06 (1.03,1.09)	<.001
TBI dose, Gy	2.17 (1.70, 3.27)	<.001	1.33 (1.23, 1.43)	<.001
Radiotherapy exposing testes (no radiotherapy exposing testes as reference)	-	-	5.15 (1.17, 27.93)	.037
Cranial radiotherapy (no cranial radiotherapy as reference)	0.72 (0.28, 1.67)	.456	1.21 (0.75, 1.94)	.423
Pelvic / abdominal radiotherapy (no pelvic / abdominal radiotherapy as reference)	2.80 (0.95, 7.94)	.056	1.23 (0.63, 2.31)	.529
Alkylating agent (cyclophosphamide equivalent[b]) dose, 1,000 mg/m^2	1.20 (1.14, 1.27)	<.001	1.01 (0.98, 1.03)	.459
Cisplatin dose, 100 mg/m^2	1.09 (0.87, 1.35)	.46	1.11 (0.94, 1.29)	.209
Carboplatin dose, 1,000 mg/m^2	0.78 (0.41, 1.29)	.392	1.33 (0.99, 1.77)	.061
Doxorubicin dose, 100 mg/m^2	1.12 (0.89, 1.39)	.322	1.09 (0.96, 1.23)	.197
Anthracycline (doxorubicin equivalent[c]) dose, 100 mg/m^2	1.16 (0.98, 1.34)	.055	1.08 (0.95, 1.20)	.220
Vinca alkaloids (no vinca-alkaloids as reference)	1.09 (0.39, 3.41)	.874	1.13 (0.58, 2.28)	.733
Antimetabolites (no anti-metabolites as reference)	0.69 (0.28, 1.64)	.401	0.62 (0.37, 1.05)	.080
Asparaginase (no asparaginase as reference)	1.16 (0.42, 3.28)	.778	1.59 (0.95, 2.68)	.079
Epipodophyllotoxin (no epipodophyllotoxin as reference)	3.02 (1.38, 6.64)	.006	0.66 (0.40, 1.07)	.103
Demographic risk factors				
BMI, kg/m^2	1.06 (0.97, 1.15)	.191	1.16 (1.11, 1.21)	<.001

Abbreviations: BMI, body mass index; TBI, total body irradiation; OR, odds ratio.

Notes:

Cancer- and treatment-related and demographic risk factors of azoospermia and testosterone deficiency were identified using multivariable logistic regression. Age at cancer diagnosis, time since diagnosis, and BMI were included as continuous variables after testing linearity. Radiotherapy exposing the testes was not included in the model of azoospermia because no odds ratio could be calculated as a result of low survivor numbers. As details regarding exposure of the hypothalamic-pituitary region and exposure to the testes are missing for the variables treatment with cranial radiotherapy and treatment with pelvic / abdominal radiotherapy, respectively, prescribed radiotherapy doses were not included, and these variables were dichotomized (yes vs. no). As haemopoietic stem cell transplantation (HSCT) was strongly correlated with TBI dose, HSCT was not included in both models. Orchidectomy was not included due to missing data in more than 20% of CCSs.

[a]Testosterone deficiency was defined by use of testosterone replacement therapy or gonadotrophin therapy (as determined through the review of medical records and self-reported data), or, in the absence of medication use, a decreased testosterone concentration measured from an early morning blood sample: 1) total testosterone < 12 nmol/L, or 2) if total testosterone ≥ 12 nmol/L, a calculated free testosterone < 220 nmol/L.

[b]A calculation formula for the cyclophosphamide equivalent dose can be found in Green et al. Pediatr Blood Cancer. 2014;61(1):53-67.

[c]A calculation formula for the doxorubicin equivalent dose can be found in Feijen et al. JAMA Oncol. 2019; 5:864-871.

Conclusions: This study provides valuable insights into knowledge gaps regarding male gonadotoxicity through its unique evaluation of semen analyses and serum testosterone levels in a national cohort of CCSs. Our findings highlight previously underexplored aspects of the influence of cyclophosphamide equivalent dose, TBI dose, and follow-up time on the risk of azoospermia, as well as the influence of TBI dose, radiotherapy exposing the testes, and follow-up time on the risk of testosterone deficiency. The association between epipodophyllotoxin and azoospermia has not been reported in previous studies. The results of this study can support guidelines for gonadotoxicity surveillance and fertility preservation, contributing to the survivors' health and quality of life.

Genetic Susceptibility to Changes in Bone Mineral Density in Long-Term Childhood Cancer Survivors: a Trans-Ancestry Genome-Wide Meta-Analysis in 4,031 Survivors from the Dutch Childhood Cancer Survivor Study (DCCSS-LATER 2) and the St. Jude Lifetime Cohort Study (SJLIFE)

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Background: Childhood cancer survivors are at risk for late adverse effects, including reduced bone mineral density (BMD). Inter-individual variability indicates a role for genetic susceptibility, though the exact role of genetic variation in BMD deficits in survivors remains to be fully explored.

Methods: We conducted genome-wide association study (GWAS) meta-analyses to identify genetic variants associated with lumbar spine (LS) and total body (TB) BMD in European ancestry (EA) survivors from the Dutch Childhood Cancer Survivor Study (DCCSS-LATER), as well as EA and African ancestry (AA) survivors from the St. Jude Lifetime Cohort Study (SJLIFE). BMD was assessed using dual-energy X-ray absorptiometry and expressed as continuous age and sex-standardized Z-scores. GWAS analyses were performed using linear regression models adjusted for attained age, sex, weight, height, cranial radiotherapy dose (CRT; categories 0, 0-24, ≥24Gy), corticosteroid dose, methotrexate (yes/no), and the first four ancestry-specific principal components. Results were pooled using inverse-variance meta-analysis in METAL. Genome-wide significant associations were defined at $p<5\times10^{-8}$. Treatment-stratified sensitivity analyses assessed potential treatment-differential associations for genome-wide significant variants identified in EA survivors. Additionally, we calculated a polygenic risk score (PRS) using summary statistics from a GWAS meta-analysis on TB BMD in the general population (n = 56,284 EA individuals), including 59 genome-wide significant loci, and assessed its association with BMD.

Results: Our meta-analyses identified multiple genetic variants associated with BMD. Notably, we found three genome-wide significant associations with LS BMD (n = 3,604, EA) and one with TB BMD (n = 3,472, EA). Preliminary functional annotation of these variants and corresponding regions highlighted biological pathways involved in bone metabolism, with most aligning to those reported in the general population, for example, rs2033345 in the WLS locus and rs11934731 near MEPE. Treatment-stratified analysis showed that rs2033345 had a stronger association with LS BMD in EA survivors not treated with CRT (n = 2,261; pooled meta-analysis: β = -0.231, 95%CI = -0.306, -0.156, p = 1.65x10-9), compared to those with CRT (n = 1,343: β = -0.152, 95%CI = -0.252, -0.052 , p = 0.003), which suggests that CRT may attenuate the effect of rs2033345 on BMD. The PRS was strongly associated with TB BMD in EA and AA survivors (n = 3,883; pooled meta-analysis: β = -0.260, 95%CI = -0.299, -0.221, p = 3.07x10-37).

Conclusions: This study provides insights into genetic variants contributing to changes in BMD in childhood cancer survivors and provides a foundation for using the PRS for risk stratification and personalized interventions to support long-term bone health in these individuals. Further investigation into the PRS and the potential role of survivor-specific (pharmacogenetic) variants is ongoing.

Cardiovascular Risk Factor Control Associated with Future Cardiovascular Events in Survivors of Childhood Cancer: a Report from the St. Jude Lifetime Cohort

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Background: Modifiable cardiovascular risk factors (CVRFs; hypertension, dyslipidemia, diabetes) contribute to the excess health-related death in long-term survivors of childhood cancer. However, whether control of CVRFs reduces the risk of major adverse cardiovascular events (MACE) in survivors is not known.

Methods: Prevalence of hypertension (HTN), diabetes (DM) and LDL cholesterol elevation (LDL) was assessed via in-person assessments in 5+ year survivors ≥13 years old in the St. Jude Lifetime Cohort. Based on ACC/AHA primary prevention guideline recommendations, sub-optimal CVRF control was defined as blood pressure ≥140/90 mmHg, hemoglobin A1c ≥7.0%, and LDL ≥130 mg/dl. MACE was defined as new onset cardiomyopathy, myocardial infarction, stroke and/or cardiovascular death. Piecewise exponential models estimated the multivariable adjusted relative risk (RR) with 95% confidence intervals (CI) for MACE among survivors according to degree of CVRF control. Models were adjusted for sociodemographic factors, physical activity, smoking status, chronic kidney disease, and cancer treatment exposures (anthracycline chemotherapy, chest and/or brain irradiation).

Results: Among 4876 survivors of childhood cancer, 36.1% had HTN, 8.4% DM and 56.5% elevated LDL at first assessment (mean age 28.6 years, standard deviation 9.1). One-third of survivors (33.5%) had at least one sub-optimally controlled CVRF. Among those with HTN, DM or LDL, 30%, 33% and 52% were sub-optimally controlled, respectively. In multivariable models, sub-optimal LDL control was associated with a > 8-fold higher risk of MACE compared to those with no LDL elevation (RR 8.4, CI 4.2 – 19.3; Table). This was more than twice the risk observed in those with well-controlled LDL compared to no LDL elevation (RR 4.0, CI 1.9 – 9.4; p-value <0.001). Similarly, sub-optimal DM control vs never having DM was associated with increased MACE risk (RR 3.4, CI 1.8 – 6.1) with twice the risk in those with sub-optimal control compared to well-controlled DM (p = 0.05; RR well-controlled DM vs no DM 1.6, CI 0.9 – 2.8). HTN, compared to no HTN, was associated with a 3 to 4-fold increase in risk of subsequent MACE, regardless of degree of control.

CVRF Control	RR of MACE (95% CI)	P-value comparing RR
LDL elevation		
Sub-optimal LDL vs no LDL elevation	**8.4 (4.2 – 19.3)**	**<0.001**
Controlled LDL vs no LDL elevation	**4.0 (1.9 – 9.4)**	
Diabetes		
Sub-optimal DM vs no DM	**3.4 (1.8 – 6.1)**	**0.05**
Controlled DM vs no DM	1.6 (0.9 – 2.8)	
Hypertension		
Sub-optimal HTN vs no HTN	**3.9 (2.2 – 7.0)**	0.28
Controlled HTN vs no HTN	**3.0 (1.9 – 4.8)**	

Conclusions: Survivors of childhood cancer had a high prevalence of sub-optimally controlled CVRFs that was associated with an increased MACE risk. Optimal control of CVRFs among survivors of childhood cancer may reduce the risk of MACE. These findings motivate an intervention trial in intensive CVRF control.

United States (US) Population Level Costs and Cost-Savings Associated with Long-Term Follow-Up (LTFU) Screening for Survivors of Childhood Cancer

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Background: Children's Oncology Group's (COG) LTFU Guideline adherence is poor. We evaluated the impact of universal payer coverage on patient costs associated with adherence to COG-directed cardiomyopathy (CM), breast (BC), and colorectal cancer (CRC) screening.

Methods: We reviewed coverage guidelines for Medicare, Medicaid, and commercial plans for COG screening for exposure-based CM (echocardiogram [echo] every 2-5 yrs based on cumulative chest radiation (RT) and anthracyclines), BC (yearly mammography [MAM] and magnetic resonance imaging [MRI] beginning at age 25 or 8 yrs from chest RT), and CRC (colonoscopy [COL] every 5 yrs or multitarget stool DNA [MTSD] every 3 yrs, starting 5 yrs from abdominopelvic RT or age 30). The eligible US population was estimated from SEER and American Cancer Society cancer survival rates. Cost of screening was derived from the Center for Medicare & Medicaid Services (CMS) and of lifetime treatment from published data. Net costs vs. benefits (in US $) were calculated, assuming 100% adherence, as the sum of cost-savings (i.e., treatment costs averted) and monetary value of quality-adjusted life-yrs (QALYs) gained minus costs (e.g., screening, false positives).

Results: Screening coverage varied by payer (Table). BC screening for all US survivors with prior chest RT (n = 42,847) yielded a net benefit ranging from $0.5 to $3.4 billion, with patients paying 19.3% of costs. Among 138,702 survivors at-risk of CRC, net benefit from COL and MTSD was $5.7 and 5.0 billion. Patients nationally bore 0% of MTSD but 60% of COL costs. Among 218,322 at-risk of CM, costs exceeded cost-savings by $1.7 billion when using the median echo cost by payer but yielded a $400 million benefit when using the average cost of CMS and the lowest commercial plan. Patients bore 90% of CM costs.

COG Screening		By Payer (Subset)			Cost Bearer, % (Aggregated across Payers)		Value of Cases Averted	Value of QALYs Gained	Total Cost	Net Costs (-) or Benefit (+)
		Medicare	Medicaid	Commercial	Patient (Pt)	Payer	Billion US $, Range			
BC	Coverage	Full, at physician's discretion	**MAM:** Full **MRI:** None	Full	19.3	80.7	NA*	2.6 - 5.9	2.1 - 2.5	0.5 - 3.4
MAM & MRI	Pt Cost	20% copay after Part B deductible	20% copay	**MAM:** 0% **MRI:** 15-30% copay after deductible						
CRC	Coverage	**COL:** None **MTSD:** Full	None Full	None Full						
COL or MTSD	Pt Cost	**COL:** 100% **MTSD:** 0%	100% 0%	100% 0%	**COL:** 60 **MTSD:** 0	40 100	3.7 2.9	4.4 4.0	2.4 1.9	5.7 5.0
CM	Coverage	None	None	≤2 covered after age 18	90.3	9.7	0.01	0.74	0.36 - 2.5	-1.7 - 0.4
Echo	Pt Cost	100%	100%	15%-30% copay after deductible						

* Not available in published models

Conclusions: Screening for CM, BC, and CRC per the COG guidelines results in substantial cost savings and benefits. However, as adherence is < 100% due to copay, inadequate coverage, and low provider awareness, interventions and policies focused on boosting adherence could yield cost savings to the health system and reduce disease burden in this population.

Genetic Contributions to Treatment-Associated Neurocognitive Outcomes among Childhood Cancer Survivors

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Background: Long-term survivors of childhood cancer experience heightened risk of late effects, with about 40% developing cognitive impairment. Established risk factors include cranial radiation and specific chemotherapies. Variability in treatment-related outcomes has been associated with genetic factors, though prior studies examined targeted pathways and not whole genome approaches.

Methods: Participants included 4,077 childhood cancer survivors with whole genome sequencing and direct neurocognitive testing from the St. Jude Lifetime Cohort Study (SJLIFE). The mean (standard deviation) age at primary cancer diagnosis was 7.8 (5.7) years, and 28.5 (10.3) years at neurocognitive testing; 52.3% were male; 78.9% were Non-Hispanic White. Linear regression evaluated associations between common genetic variants (minor allele frequency, MAF≥1%) and 20 neurocognitive measures (as age-adjusted Z-scores). Analyses were adjusted for sex, age at primary childhood cancer diagnosis, age at neurocognitive testing, cumulative doses of high-dose methotrexate, intrathecal methotrexate, anthracyclines and cranial radiation, and genetic ancestry. Loci with P≤5x10-8 were considered genome-wide significant and evaluated in stratified analysis by genetic ancestry and treatment exposures.

Results: 21 SNPs met genome-wide significance for associations with ≥1 neurocognitive measure, 9 SNPs with a MAF ≥1% in EUR (n=3,312) and AFR (n=636) survivors. All 9 SNPs had 1.1-3.6 times larger effect sizes in AFR compared to EUR. The biggest differences in ancestry groups were seen when stratifying analyses by anthracycline exposure. An intronic variant in ERG, rs1309269486, had a 2.0-times larger effect on motor speed in exposed EUR (β=-0.70; P=2.9x10-6) compared to unexposed EUR (β=-0.35; P=0.039). In AFR, rs1309269486 was only associated with motor speed in unexposed survivors (β=-1.33; P=2.9x10-3), with a 3.8-times greater effect size compared to unexposed EUR. ERG has been shown to play a role in neurogenesis. Another intronic variant in P2RY12, rs1755678683, also showed a 1.8-times larger effect on attention span in exposed EUR (β=-0.68; P=5.9x10-4) than unexposed EUR (β=-0.38; P=0.035). However, it was associated with attention span in only unexposed AFR (β=-1.28; P=2.1x10-3), showing 3.4-times greater effect than in unexposed EUR. P2RY12 plays a role in microglia function, neuroinflammation, and neurodegeneration. An intronic variant in COL15A1, rs1837227843, was associated with working memory in exposed EUR (β=-0.47; P=5.3x10-7) and unexposed AFR (β=-0.58; P=4.9x10-3). While COL15A1 is highly expressed in many brain tissues, previous associations with neurocognition have not been established.

Conclusions: These findings highlight the independent and combined role (with treatment) of genetics and genetic ancestry in adverse neurocognitive impairment among survivors of childhood cancer.

Cardiovascular Risk Factors in Survivors of Childhood Hematopoietic Cell Transplantation and Their Role in Development of Cardiovascular Disease: a CCSS-CIBMTR Analysis

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Background: Hematopoietic cell transplantation (HCT) is an important curative treatment for children with high-risk hematologic malignancies and solid tumors. Cardiovascular disease (CVD) remains a key cause of premature mortality among HCT survivors. CV risk factors (CVRF) potentiate these risks in adult HCT survivors but their incidence and impact in childhood HCT survivors are not well established.

Methods: Five-year survivors of childhood cancer in the Childhood Cancer Survivor Study (CCSS), diagnosed at age <21 years between 1970-1999, were linked to the Center for International Blood and Marrow Transplant Research (CIBMTR) registry, which captures HCT data. We assessed the cumulative incidence of diabetes mellitus (DM), hypertension (HTN), and dyslipidemia requiring treatment, collectively known as CVRF, and subsequent serious CVD (coronary artery disease, myocardial infarction, arrhythmia, cardiomyopathy) using time since cohort entry as the time scale. The risk of each CVRF among HCT survivors transplanted within 5-years of diagnosis (n=1,349) was compared to survivors treated with conventional chemotherapy (n=8,018) and siblings (n=5,045). Cause-specific Cox proportional hazard models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI).

Results: Among survivors treated with childhood HCT (49% allogeneic; 56% male; median age at HCT, 9 years [range, 0-26]; median age at last follow-up, 31 years [range, 6-64]), the 20-year cumulative incidence was 19.3% for HTN, 13.7% for DM, and 15.2% for dyslipidemia. When compared to siblings, HCT survivors were at 7.6-fold risk for HTN [95% CI, 6.5-9.0]; 18.7-fold risk for DM [14.7-23.8]; and 14.3-fold risk for dyslipidemia [12-18]. Risks of each CVRF were also higher in HCT survivors compared to survivors treated with conventional chemotherapy (HR HTN 2.3 [2.1-2.7]; HR DM 6.1 [5.0-7.3]; HR dyslipidemia 4.3 [3.7-5.1]). Among HCT survivors matched between CCSS and CIBMTR (n=712), multivariable analyses revealed that total body irradiation-based HCT was associated with risk of DM (HR 2.8 [1.2-6.6]) and dyslipidemia (HR 2.3 [1.02-5.1]). Obesity (BMI ≥30 kg/m2) was associated with increased risk for developing each CVRF. Full results of the multivariable analysis are shown in the Table. The 20-year cumulative incidence of CV disease among the HCT cohort was 12.3% [10.4-14.4] with no difference noted among those treated with allogeneic versus autologous HCT. The presence of any CVRF was independently associated with a 2.0-fold risk of developing CV disease [1.5-2.8], while ≥2 CVRF were associated with a 2.5-fold risk [1.5-4.0].

Conclusion: Childhood HCT survivors have a higher risk of developing CVRFs than siblings or survivors treated with conventional chemotherapy, which appear to confer an increased risk of developing subsequent CVD. Interventions to reduce risk of CVRFs should be prioritized in this population.

TABLE. Multivariable risk factor analysis for developing a CV risk factor (diabetes, hypertension, or dyslipidemia) after hematopoietic cell transplantation among CCSS survivors treated with HCT within the first five years after diagnosis and matched to CIBMTR*‡

	Diabetes			Hypertension			Dyslipidemia		
Characteristic	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Age at diagnosis, yr	0.90	0.77, 1.07	0.2	1.03	0.88, 1.19	0.7	0.97	0.83, 1.14	0.7
Age at first HCT, yr	1.07	0.91, 1.26	0.4	0.99	0.85, 1.14	0.9	1.04	0.89, 1.21	0.6
HCT type									
Autologous	Ref	Ref		Ref	Ref		Ref	Ref	
Allogenic, no cGvHD	1.76	0.66, 4.68	0.3	1.65	0.81, 3.38	0.2	1.53	0.68, 3.46	0.3
Allogenic, yes cGvHD	1.86	0.62, 5.55	0.3	1.68	0.75, 3.77	0.2	1.91	0.76, 4.82	0.2
Pre-HCT exposure‡									
Chemotherapy-based HCT; conventional chemo, no RT	Ref	Ref		Ref	Ref		Ref	Ref	
Chemotherapy-based HCT; conventional chemo + RT	1.22	0.42, 3.52	0.7	0.93	0.46, 1.87	0.8	1.38	0.57, 3.32	0.5
TBI-based HCT with conventional chemo +/- RT	2.75	1.15, 6.59	**0.02**	1.54	0.83, 2.84	0.2	2.28	1.02, 5.08	**0.046**
Ever obese (BMI ≥30 kg/m²)									
No/unknown	Ref	Ref		Ref	Ref		Ref	Ref	
Yes	2.01	1.10, 3.70	**0.02**	2.18	1.39, 3.42	**<0.001**	2.30	1.39, 3.80	**0.001**
Ever physically active**									
No/unknown	Ref	Ref		Ref	Ref		Ref	Ref	
Yes	0.75	0.47, 1.18	0.2	1.07	0.73, 1.57	0.7	0.78	0.51, 1.18	0.2
Ever smoker									
No/unknown	Ref	Ref		Ref	Ref		Ref	Ref	
Yes	0.81	0.47, 1.40	0.5	1.08	0.71, 1.65	0.7	0.70	0.42, 1.15	0.2

Abbreviations: HCT, hematopoietic cell transplantation; HR, hazard ratio; 95% CI, 95% Confidence Interval; cGVHD, chronic graft versus host disease; TBI, total body irradiation; RT, radiation therapy; BMI, body mass index. *The cause-specific hazard model was stratified by disease diagnosis (leukemia, neuroblastoma, lymphoma, all others), race (Non-Hispanic, White, other) and sex to allow for separate baseline hazard within each stratum and account for subpopulation differences. **Ever physically active refers to ever meeting CDC criteria for meeting moderate to vigorous physical activity recommendations. ‡ Chemotherapy and radiation therapies were received within the 1st five year of childhood cancer diagnosis.

Social Determinants of Health (SDOH) and Late Mortality among Survivors of Childhood Cancer: a Report from the Childhood Cancer Survivor Study (CCSS)

Cindy Im, Fang Wang, Yan Chen, Jaesung Choi, Carrie R. Howell, Kristine Karvonen, Vikki Nolan, Aaron McDonald, Lucie Turcotte, Eric Chow, Yutaka Yasui, Paul Nathan, Claire Snyder, Greg Armstrong, I-Chan Huang

Background: Neighborhood-level SDOH may increase disparities in adverse cancer-related outcomes. The US CDC-constructed Social Vulnerability Index (SVI) reflects 4 neighborhood-level SDOH domains (socioeconomic status [SES]; household composition; minority status/language; housing/transportation) and captures the vulnerability of underserved communities. Comprehensive investigations of the impact of neighborhood-level SDOH on late mortality among survivors of childhood cancer are needed.

Methods: Analyses included 5-year survivors in the US diagnosed in 1970-1999 participating in the CCSS, a multi-institutional retrospective cohort study. We evaluated geocoded SVI quintiles (Q1 to Q5, from least to most vulnerable) based on residential addresses and personal SES factors including income, education level, and health insurance status collected at CCSS baseline. The impact of SVI and personal-level SES on all-cause and cause-specific mortality rates were evaluated using cumulative incidence and relative rates (RRs) from piecewise exponential regression models adjusted for attained age, sex, age at primary cancer diagnosis, and treatments (any radiation therapy and any chemotherapy). Associations further adjusting for reported life-threatening or disabling chronic health conditions (CHCs with CTCAE grades 3-4, treated as time-varying) were also assessed.

Results: Among 20,261 survivors with geocode data (mean age at cancer diagnosis and baseline evaluation, 7 years and 24 years respectively, with a mean follow up of 17 years), 2,439 survivors died. All-cause late mortality was greater in survivors living in more vulnerable areas (Q5 vs. Q1, at 20y: 14.7% vs. 10.8%, P<0.001). We observed a dose-response relationship between worsening SVI and the all-cause mortality rate (Q5 vs. Q1 RR 1.52, 95% CI 1.32-1.76, Ptrend<0.001) as well as for mortality rates due to specific health causes (Table). Among the SVI SDOH domains, neighborhood SES (Q5 vs. Q1 RR 1.68, 95% CI 1.45-1.95) showed the strongest association with all-cause mortality followed by household composition (RR 1.43, 95% CI 1.24-1.66). Notably, the associations between SVI and all-cause mortality remained largely consistent after adjusting for personal-level SES as well as in analyses stratified by individual income, education level, and health insurance coverage. The magnitude of these associations also remained unchanged after further adjusting for reported life-threatening or disabling CHCs.

Table: Adjusted RRs and 95% confidence intervals for overall and cause-specific mortality

SVI	All cause	Subsequent neoplasm cause	Cardiovascular cause	Other health causes
Q1	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Q2	1.00 (0.88 - 1.14)	0.90 (0.74 - 1.11)	1.09 (0.76 - 1.55)	1.09 (0.85 - 1.39)
Q3	1.16 (1.02 - 1.32)	1.03 (0.84 - 1.27)	1.18 (0.82 - 1.70)	1.24 (0.97 - 1.59)
Q4	1.24 (1.08 - 1.42)	1.12 (0.90 - 1.39)	1.29 (0.88 - 1.90)	1.44 (1.11 - 1.86)
Q5	1.52 (1.32 - 1.76)	1.35 (1.07 - 1.69)	1.54 (1.02 - 2.33)	1.83 (1.38 - 2.42)

SVI Q1 (least vulnerable) is the referent.

Conclusions: Living in the most socially vulnerable neighborhoods during young adulthood is associated with an approximately 50% increased risk for late mortality among survivors of childhood cancer and is largely unaffected by favorable personal-level SES and persists even after accounting for serious CHCs. Policies and interventions targeting neighborhood-level SDOH during the transition to survivorship care are needed to reduce mortality risk in this population.

A Diagnostic Algorithm to Triage Childhood Cancer Survivors for a Surveillance Echocardiogram: a DCCSS LATER 2 Study

Jan Leerink, Remy Merkx, Esmee De Baat, Helena Van Der Pal, Marloes Louwerens, Marry M. Van Den Heuvel-Eibrink, Elvira Van Dalen, Margriet Van Der Heiden, Dorine Bresters, Andrica De Vries, Livia Kapusta, Annelies Mavinkurve, Wouter Kok, Leontien Kremer, Elizabeth Feijen

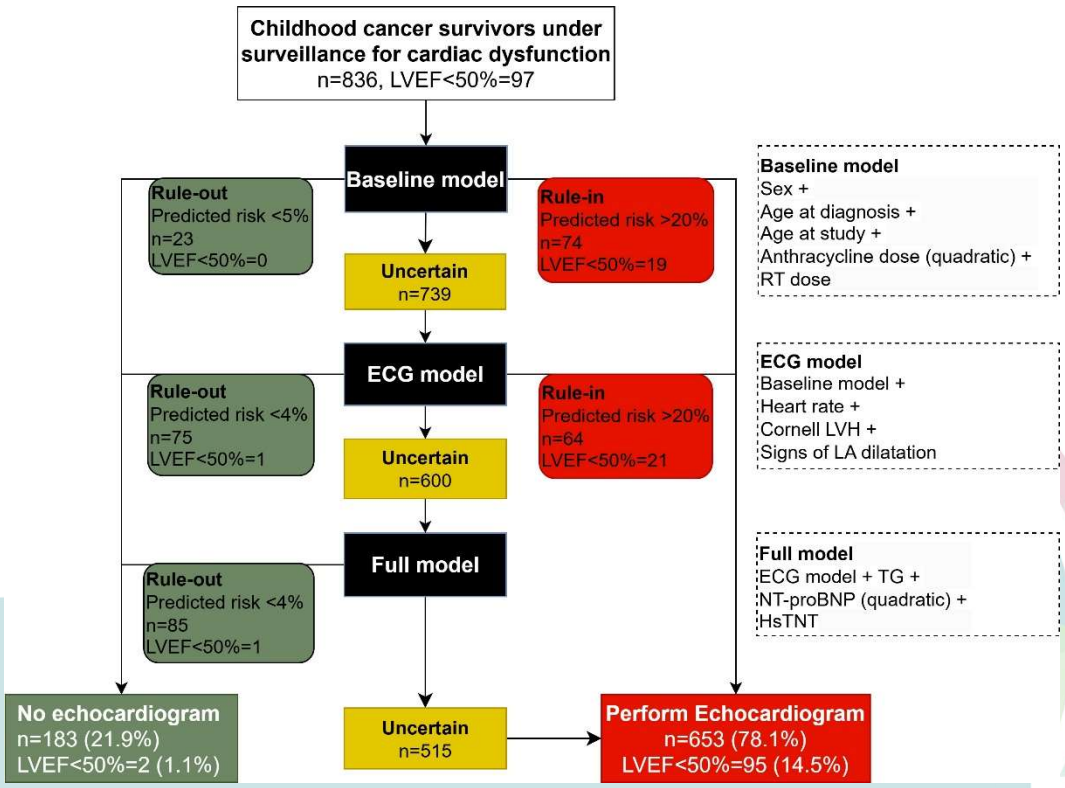
Background: A diagnostic algorithm based on clinical characteristics, electrocardiographic (ECG) parameters and blood biomarkers may be useful to exclude cardiac dysfunction in a subset of childhood cancer survivors in whom a surveillance echocardiogram can be deferred.

Objective: To develop a diagnostic algorithm for the rule-out and rule-in of cardiac dysfunction, defined as a left ventricular ejection fraction (LVEF)<50% on an echocardiogram.

Methods: We cross-sectionally obtained clinical variables, an echocardiogram, blood biomarkers and an ECG in 836 asymptomatic childhood cancer survivors treated with an anthracycline dose ≥100 mg/m2 and/or a chest-directed radiotherapy dose ≥15Gy included in the DCCSS LATER2 study. The diagnostic algorithm consisted of 3 sequentially placed logistic regression models (Figure). The optimal predicted probability for rule-out and rule-in of LVEF<50% was determined using receiver operating characteristic curve analysis.

Results: A LVEF<50% was present in 97 (11.6%) of survivors. The diagnostic algorithm started with a baseline model which included only patient demographics and treatment characteristics that are known without seeing a survivors at the outpatient clinic (Figure). This baseline model classified 23 (2.8%) survivors as ruled-out, 74 (8.9%) survivors as ruled-in and 739 survivors as uncertain. In survivors classified as uncertain by the baseline model, a model which additionally included heart rate and ECG parameters was used. This ECG-based model classified 75 (9.2%) survivors as ruled-out, 64 (8.7%) survivors as ruled-in and 600 survivors as uncertain. Finally, in survivors that were classified as uncertain by the ECG-based model, the full model was used which additionally included blood biomarkers (N-terminal pro-B-type natriuretic peptide, high-sensitivity cardiac troponin T and lipids). This full model classified an additional 85 (11.5%) survivors as ruled-out. Overall, the algorithm ruled-out LVEF<50% in 183 (21.9%) survivors with only 2 (1.1%) false negatives. These 2 false negatives had borderline LVEF.

Conclusions: The diagnostic algorithm was able to accurately rule-out cardiac dysfunction in around 20% of childhood cancer survivors who are currently recommended to receive life-long echocardiographic surveillance. Using the algorithm as a triage test before echocardiography may substantially reduce cardiomyopathy surveillance costs and burden to survivors and echocardiography laboratories.



Results from a Hybrid Effectiveness-Implementation Trial on Return for Survivorship Care for Pediatric Cancer Survivors

Jordan Marchak, Cam Escoffery, Regine Haardoerfer, Rebecca Williamson Lewis, Lillian Meacham, Victoria Krauss, Ana Arana, Swathi Sekar, Kenneth Cruz, Ann Mertens

Purpose: Pediatric cancer survivors face significant health risks, yet many do not seek recommended follow-up care. This study's objective was to evaluate the implementation of Cancer SurvivorLinkTM (https://cancersurvivorlink.org) in pediatric survivor clinics and its impact on survivor care. SurvivorLink is an electronic personal health record designed to promote survivor care and share health records across care providers.

Methods: This hybrid effectiveness-implementation trial randomized Children's Oncology Group (COG) survivor clinics to distribute survivorship care plans via SurvivorLink (intervention group) or standard care (waitlist control group). Each site enrolled up to 75 survivors (18-21 years) or their caregiver proxies (survivors <18 years). At 12-month follow-up (±3 months), clinic staff validated return for survivor care and other recommended health visits. Afterward, the waitlist (WL) group implemented SurvivorLink. Multilevel analyses on the impact of SurvivorLink on return to clinic and engagement in recommended care are underway. Clinic staff completed surveys on the ease, appropriateness, acceptability, and sustainability of SurvivorLink implementation.

Results: Twelve COG sites were matched and randomized to the SurvivorLink intervention (n=6 sites) or WL group (n=6 sites). A total of 542 survivors (56% male, 84% White, 17% Hispanic/Latinx, M=14.8 years [SD=4.1]) were enrolled. Across sites, 93.5% of survivors (200/214) in the SurvivorLink intervention group returned for survivor clinic visits compared to 84.5% of survivors (277/328) in the WL group (Intervention range: 76%-100%; WL range: 71%-99%). Both caregivers and young adult survivors rated SurvivorLink as useful and easy to understand (Caregivers= 83.9%, 83.4%; Survivors= 72.8%, 74.8%, respectively). Clinic staff mostly agreed that their clinic could implement SurvivorLink with ease (Intervention M= 3.5; WL M=3.3) on a scale of 1-strongly disagree to 5-strongly agree. Results on the Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM) indicated moderate to high acceptability, appropriateness, and feasibility of SurvivorLink implementation among clinic staff (AIM M: Intervention=4.2; WL=3.8; IAM M: Intervention=3.9; WL=3.8; FIM M: Intervention=4.1; WL=3.7). Using the Clinical Sustainability Assessment Tool (CSAT), both groups' highest sustainability capacity domains after implementation were Engaged Staff and Leadership, Implementation and Training, and Outcomes and Effectiveness.

Conclusions: SurvivorLink is acceptable, appropriate, and feasible as an intervention and shows promise in improving return to survivorship care in pediatric oncology programs. Ongoing effectiveness analyses will further inform its potential for broader implementation and integration into care models for pediatric cancer survivors.

Education and Employment Outcomes in Survivors of Adolescents and Young Adults (AYA) Cancer in Ontario, Canada

Daksha Marfatia, Sumit Gupta, Victoria Kirsh, Sho Podolsky, Andrew Calzavara, Paul Nathan

Background: AYA with cancer face unique challenges as their transition into adulthood is disrupted. This period includes critical milestones such as completing education, entering the workforce, and achieving financial independence. Using data from a provincial health study, we examined whether survivors of AYA cancer survivors experience delays or reductions in these outcomes.

Methods: This cross-sectional study utilized data from the Ontario Health Study (OHS), a population-based self-report questionnaire, linked to administrative health data, with participants recruited between 2011-2018. AYA cancer survivors were identified as individuals who self-reported a cancer diagnosis between the ages of 15 and 39 years. Each survivor was matched to five OHS controls without a reported cancer diagnosis before age 40 years, based on age, sex, and year of questionnaire completion. Education was categorized as the highest degree obtained and employment status as currently employed vs. unemployed. Students, retirees, and unpaid workers were excluded from employment analyses. Outcomes were compared between survivors and controls using multivariable logistic regression. The impact of cancer diagnosis, treatment, age at cancer diagnosis and other risk factors were assessed in survivors.

Results: Among 225,620 respondents, 3,197 AYA cancer survivors were identified and matched to 15,985 controls. Among those who completed a post-secondary degree, there was no difference between groups in obtaining an undergraduate or graduate compared to other post-secondary degrees [adjusted odds ratio (OR): 0.87, 95% confidence interval (95% CI): 0.74-1.01, p=0.07). However, among university graduates, survivors were more likely than controls to attain a graduate degree rather than an undergraduate degree (OR: 2.12, 95% CI: 1.71-2.64, p <0.0001). AYA cancer survivors were significantly less likely to report being employed compared to controls, with 2,060 survivors and 10,553 controls reporting employment (OR: 0.57, 95% CI: 0.50-0.65, p<0.0001). Additionally, AYA cancer survivors were significantly more likely to report being unable to work due to sickness or disability compared to controls with 305 survivors and 636 controls experiencing this limitation (OR: 2.29, 95% CI: 1.97-2.66, p <0.0001). Among those employed, there were no significant differences observed regarding full-time versus part-time work (OR: 1.08, 95% CI: 0.95-1.23, p= 0.23).

Conclusions: AYA cancer survivors achieved similar levels of education as their peers and were even more likely to attain graduate degrees. While some survivors faced employment challenges, the ability to work full-time or part-time was comparable to controls. These findings underscore the resilience of AYA cancer survivors in achieving educational milestones and highlight the importance of providing targeted support to help those facing workforce participation barriers to achieve long-term career stability.

Mediating Effects of Epigenetic Age Acceleration on Associations Between Cancer Treatments and Cardiometabolic and Cardiovascular Disease Risk among Survivors of Childhood Cancer: a Report from the St. Jude Lifetime Cohort

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Background: Childhood cancer survivors experience greater epigenetic age acceleration (EAA) due to genotoxic cancer treatments. Cardiometabolic risk factors (CMRFs: abnormal glucose metabolism, hypercholesterolemia, hypertriglyceridemia, hypertension, obesity) and cardiovascular diseases (CVDs: cardiomyopathy, myocardial infarction [MI]) are the most common types of adverse health outcomes among long-term survivors of childhood cancer. In this study, we systematically evaluated the mediating role of EAA in association between cancer treatment exposures and increased risks of CMRFs or CVDs.

Methods: Five-year childhood cancer survivors (n=2,052) from the St. Jude Lifetime Cohort underwent DNA methylation (DNAm) profiling using DNA derived from peripheral blood mononuclear cells. Multivariable linear regression evaluated associations between cancer treatment exposures and EAA based on Levine's clock. Multivariable logistic regression evaluated associations of EAA with the five CMRFs and two CVDs. Mediation analysis was conducted with EAA as the mediator and specific cancer treatment as the exposure to evaluate to what extent each treatment indirectly influenced each condition through EAA.

Results: Greater epigenetic age acceleration (EAA) was associated with exposure to radiotherapy (RT) directed to the chest, abdomen, or pelvis (i.e., body-trunk-RT), alkylating agents, and glucocorticoids. Specifically, body-trunk-RT was associated with an estimated 4.24-year (95% CI: 3.58–4.90) increase in EAA, alkylating agents with a 2.37-year (95% CI: 1.76–2.98 years) increase, and glucocorticoids with a 1.38-year (95% CI: 0.78–1.98 years) increase. Each standard deviation increase in EAA was also associated with a 24% higher risk of abnormal glucose metabolism (OR=1.24, 95% CI: 1.07–1.42), 22% higher risk of hypertension (OR=1.22, 95% CI: 1.10–1.35), 20% higher risk of obesity (OR=1.20, 95% CI: 1.09–1.32), 30% higher risk of cardiomyopathy (OR=1.30, 95% CI: 1.05–1.61), and 46% higher risk of myocardial infarction (MI) (OR=1.46, 95% CI: 1.18–1.81). Mediation analysis revealed that EAA mediated a significant proportion of the associations between cancer treatment exposures and cardiometabolic outcomes. Specifically, EAA accounted for 32.9% of the association between body-trunk-RT and risk of abnormal glucose metabolism, 23.1% between alkylating agents and risk of hypertension, 6.2% between glucocorticoid exposure and risk of obesity, 23.8% between heart-RT and cardiomyopathy risk, and 22.2% between heart-RT and MI risk.

Conclusions: The mediating effect of EAA for multiple exposure-outcome pairs provides novel insights into the underlying mechanism linking cancer treatment exposures to long-term cardiometabolic toxicity. Intervention strategies targeting accelerated aging may ameliorate long-term cancer treatment toxicities and hence the disease burden in this high-risk population.

Automating Ascertainment of Chemotherapy Exposure for the Childhood Cancer Survivor Study with the ExtractEHR+ Toolkit

Tamara Miller, Vikki Nolan, Edward Krause, Yang Xie, Gregory Joseph, Yun Gun Jo, Yimei Li, Maria Gramatges, Jennifer Wilkes, Greg Armstrong, Richard Aplenc

Background/Purpose: Since the National Cancer Institute established a pediatric cancer survivor cohort in 1971, manual chart abstraction has identified chemotherapy exposures. While many teams, including the Childhood Cancer Survivor Cohort (CCSS), have performed transformative research using manual abstraction, it is time intensive. The ExtractEHR+ toolkit, an R-based software package that includes ExtractEHR and MedCleanEHR, automatically extracts and curates electronic health record (EHR) data. We sought to test concordance between manually and ExtractEHR+ ascertained chemotherapy data for medications in the CCSS medical record abstraction form (MRAF) at 3 sites.

Methods: MRAF specified medications, including novel therapies and supportive care, were manually abstracted by trained staff using CCSS abstraction guidance for 50 patients across 14 diagnoses at Children's Healthcare of Atlanta, Children's Hospital of Philadelphia, and Texas Children's Hospital. Included patients were aged 0-20 years at diagnosis, English or Spanish speaking, and diagnosed with de novo cancer after EHR implementation at each site. ExtractEHR extracted all medication orders and administrations, including outpatient prescriptions. MedCleanEHR centrally cleaned and identified unique MRAF exposures. For 146 medications on the MRAF, presence (yes) or absence (no) in the medical record was ascertained manually and by ExtractEHR+. Concordance between manual and ExtractEHR+ MRAF medication exposure (yes/no) was tabulated and discrepancies were evaluated. Ascertainment time was estimated for both methods.

Results: Of 12,752 identified survivors, 11,818 had EHR data available. A total of 27,709,224 MRAF medication actions were extracted by ExtractEHR; after MedCleanEHR processing, there were 8,523,729 unique medication administrations. The 150 patients with manual chart abstraction data had 21,900 possible MRAF defined medication exposures (150*146). Overall concordance for yes/no exposure between manual and ExtractEHR+ was high at 98.3% with 20,633 no/no (94.1%) and 902 yes/yes (4.1%) concordance. 278 exposures were identified only by ExtractEHR (1.3%) and 87 were identified only in manual review (0.4%). Of 1,267 total MRAF exposures, 21.9% (278) were not identified by manual abstraction and 6.9% (87) were not identified by ExtractEHR+. The average time required for manual exposure ascertainment was 3 hours per patient while MedCleanEHR ascertainment required 0.001 seconds per patient.

Conclusions: ExtractEHR+ accurately and efficiently ascertains chemotherapy exposures for the CCSS MRAF. Manual abstraction had larger medication identification errors and ExtractEHR+ provides a 15% absolute gain in identification of chemotherapy exposures among patients with an exposure. Work is ongoing to complete planned analyses at 5 centers, understand intra/inter center level manual abstraction variability, analyze concordance of cumulative dose data, and complete a cost analysis.

Longitudinal Change in Cardiac Function after Doxorubicin and Dexrazoxane: a Report from COG ALTE11C2

Erin Mobley, David Doody, Steven Colan, Sanjeev Aggarwal, Richard Aplenc, Saro Armenian, Scott Baker, Smita Bhatia, Louis S Constine, David Freyer, Lisa Kopp, Wendy Leisenring, Nao Sasaki, Lynda Vrooman, Barbara Asselin, Cindy Schwartz, Eric Chow, Steven Lipshultz

Background/Purpose: Dexrazoxane (DRZ) has been associated with reduced adverse left ventricular (LV) remodeling shortly after doxorubicin (DOX) treatment (<5y) and preserved LV function in long-term (>15y) survivors of childhood cancer. What remains less clear are longitudinal changes in echocardiographic (echo) measures in this population.

Methods: ALTE11C2 analyzed participants who received DOX treatment and were enrolled on COG protocols P9404, P9425, P9426, P9754, and Dana Farber Cancer Institute 95-01. Except for P9754, all other protocols featured upfront 1:1 randomization with DRZ (10:1mg/m2 DRZ:DOX dose). Central echo remeasurements were used when possible, otherwise we used data from abstracted echo reports. Echo values were converted to age- or BSA-specific z-scores. Differences in z-scores by ±DRZ were estimated as a function of time using generalized estimating equations, adjusting for age, sex, DOX dose, chest radiotherapy, and data type (directly remeasured vs. report).

Results: 895 patients (67% male; 67% white non-Hispanic; mean age at diagnosis 11.4y; median DOX dose 360 mg/m2; 32% chest radiotherapy) had evaluable echo data (n=2279 echos; 1581 centrally remeasured; 698 report only; mean of 1.0-1.7 echos per patient per time period, with an average of 1.4 echos per patient ≥15y). In multivariable analysis, DRZ was overall associated with more normal LV fractional shortening and less LV end-diastolic and end-systolic dilation, a pattern consistent with less subclinical dilated cardiomyopathy directionality. These cardioprotective changes associated with DRZ were seen most clearly in patients treated with DOX ≥250 mg/m2 with this length of follow-up.

Z-score difference by ±DRZ as a function of time, adjusted for sex, age, echo type, DOX dose, chest radiotherapy

LV measure	Overall	Pre-treatment	<2 years post-treatment	2-4 years post-treatment	5-9 years post-treatment	≥10 years post-treatment
Fractional shortening	0.4 (0.2, 0.5) *	0.1 (-0.2, 0.5)	0.1 (-0.2, 0.5)	0.7 (0.4, 0.9) *	0.5 (0.2, 0.9) *	0.4 (0.2, 0.7) *
End-diastolic dimension	-0.2 (-0.4, -0.1) *	-0.2 (-0.4, 0.0)	-0.0 (-0.3, 0.2)	-0.4 (-0.6, -0.2) *	-0.2 (-0.5, 0.1)	-0.3 (-0.6, 0.0) *
End-systolic dimension	-0.3 (-0.5, -0.2) *	-0.2 (-0.5, 0.0)	-0.1 (-0.3, 0.1)	-0.5 (-0.7, -0.3) *	-0.4 (-0.7, -0.1) *	-0.4 (-0.7, -0.2) *
End-diastolic posterior wall thickness	0.0 (-0.1, 0.2)	-0.4 (-0.7, -0.2) *	-0.1 (-0.3, 0.2)	0.4 (0.2, 0.6) *	0.1 (-0.3, 0.5)	0.0 (-0.2, 0.3)
End-diastolic septal wall thickness	0.1 (-0.1, 0.2)	-0.2 (-0.5, 0.1)	-0.1 (-0.3, 0.2)	0.3 (0.1, 0.5) *	0.2 (-0.1, 0.5)	0.2 (-0.1, 0.4)
Thickness-to-dimension ratio (adverse remodeling=negative)	0.1 (-0.1, 0.2)	-0.3 (-0.5, 0.0)	-0.1 (-0.3, 0.2)	0.4 (0.2, 0.7) *	0.1 (-0.3, 0.6)	0.1 (-0.2, 0.4)
Mass	-0.1 (-0.2, 0.1)	-0.4 (-0.6, -0.1) *	-0.0 (-0.3, 0.2)	0.1 (-0.2, 0.3)	-0.3 (-0.9, 0.3)	0.2 (-0.1, 0.6)

** p<0.05*

Conclusions: DRZ exerts significant DOX cardioprotective effects on cardiac function and remodeling, detectable within 5y and persisting beyond 10y of follow-up.

International Study of Subsequent Colorectal Cancer among Survivors of Childhood, Adolescent, and Young Adult Cancers (I-SCRY)

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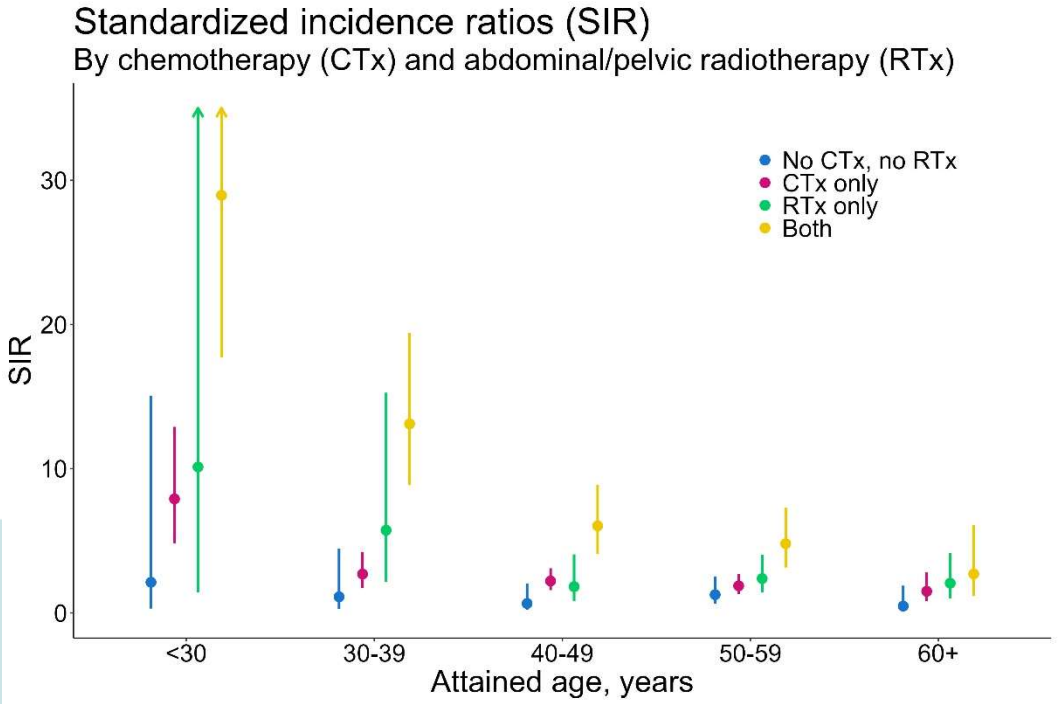
Background: Subsequent colorectal cancer (CRC) has one of the highest absolute excess risks of any subsequent malignant neoplasm among childhood, adolescent, and young adult cancer survivors. Characterizing CRC risk in survivors is important for understanding who might benefit from CRC screening. We describe an individual patient pooled analysis representing 8 cohorts across the U.S. and Europe.

Methods: I-SCRY is a pooled cohort with data on 56,391 5-year survivors of a cancer diagnosed 1953-2012 < 40 years of age. Country-, age-, sex-, race-, and calendar year-specific rates of CRC were obtained from population-based cancer registries and used to estimate standardized incidence ratios (SIR) and absolute excess risk (AER) per 10,000 individuals with 95% confidence intervals (95%CI).

Results: After a median of 24 years (range 5-60) at a median attained age of 39 years (range 5-88), 290 survivors had incident CRC, a 2.6-fold increased CRC risk compared to the general population (SIR=2.6, 95%CI 1.8–3.8). CRC diagnosis median age was 47 years (range 10-77). With 36 survivors (12%) diagnosed under age 30 years, compared to the general population this age group had an increased relative risk of CRC (SIR=10.6, 95%CI 6.4–16.3; AER=0.5, 95%CI 0.3–0.7). Survivors not exposed to abdominal/pelvic radiotherapy nor to chemotherapy (n=8,733) did not have a significantly increased CRC risk (SIR=0.9, 95%CI 0.7–1.5; AER=0.0, 95%CI -0.6–0.4), while survivors treated with chemotherapy alone (n=29,445) or abdominal/pelvic radiotherapy alone (n=2,790) had 2-fold increased relative risks (SIR=2.3, 95%CI 1.9–2.8 and SIR=2.4, 1.7–3.3; AER=1.0, 95%CI 0.7–1.3 and AER=3.1, 1.2–4.9, respectively), and survivors treated with both chemotherapy and abdominal/pelvic radiotherapy (n=8,263) had about a 7-fold increased relative risk (SIR=6.9, 95%CI 5.7-8.4; AER=4.7, 95%CI 3.6–5.9), a pattern also observed within attained age subgroups (Figure). Exposure to individual classes of drugs in the absence of abdominal/pelvic radiotherapy was associated with about a 2-fold increased relative risk: (a) alkylating agents alone: SIR=2.9, 95%CI 2.2–3.9; AER=2.2, 95%CI 1.1–3.3; (b) anthracyclines alone: SIR=2.5, 95%CI 1.2–5.5; AER=0.7, 95%CI -0.2–1.6; and (c) platinating agents alone SIR=1.7, 95% CI 1.1–2.5; AER=1.6, 95%CI -0.2–2.9. By primary diagnosis, excess risk was greatest among Hodgkin lymphoma (AER=3.3, 95%CI 2.4–4.1), Wilms tumor (AER=2.7, 95%CI 1.4–4.0), and Non-Hodgkin lymphoma (AER=2.1, 95%CI 0.9–3.3) survivors.

Conclusions: Risk of subsequent CRC is high in survivors of a childhood, adolescent, and young adult cancer. Risk of early onset CRC is particularly elevated with many cancers occurring before the age at which most guidelines recommend screening. Risk appears to be primarily concentrated among survivors treated with either chemotherapy or abdominal/pelvic radiation. More detailed dissection of CRC risk levels within this high-risk population is in progress.



Predicting Valvular Heart Disease in Adult Survivors of Childhood Cancer: a Report from the Childhood Cancer Survivor Study (CCSS) and St. Jude Lifetime Cohort (SJLIFE)

Daniel. Mulrooney, Qi Liu, Farideh Bagherzadeh-Khiabani, James Bates, Susan Smith, Suman Shreshta, Greg Armstrong, Louis Constine, Kiri Ness, Melissa Hudson, Yutaka Yasui, Rebecca Howell

Background: Radiotherapy (RT)-related valvular heart disease (VHD) is an understudied late toxicity of childhood cancer therapy. We aimed to define the risk of VHD with clinical data available at 5 and 20 years from cancer diagnosis.

Methods: Mean heart RT doses were estimated for participants of the CCSS and SJLIFE cohorts treated with RT. Two piecewise exponential regression prediction models were developed in the CCSS, from entry into survivorship (5 years post cancer diagnosis) and 20 years post diagnosis (inclusive of age- and lifestyle-acquired risk factors), to assess subsequent risk of developing severe/life-threatening/fatal VHD (≥ grade 3 Common Terminology Criteria for Adverse Events [CTCAE]) by age 50 years. Models were validated among clinically assessed SJLIFE survivors.

Results: Among 18,807 CCSS participants [mean age (±standard deviation) at diagnosis=8.1 (5.8) years and 40 (11.1) at assessment] including 9,998 treated with RT, 164 (0.9%) reported VHD after cohort entry. Of those ≥20 years post diagnosis (n=16,618) [7.9 (5.8) years at diagnosis; 42.5 (9.6) at assessment], 138 (0.8%) reported VHD. In SJLIFE, 44 (1.0%) of 4,388 survivors, including 2,103 treated with RT, and 35 (1.4%) of 2,423 ≥20-year survivors had VHD (mean ages at diagnosis and assessment: 7.8 [5.7] and 32 [12] years; 7.6 (5.5) and 38.7 (9.2) years, respectively). Prediction performance at age 50 years was good for both models [areas under the receiver operating characteristic curves 0.84 (95% CI 0.79-0.89) and 0.87 (95% CI 0.81-0.91)]. For each 10 Gy of heart RT, the rate of VHD increased approximately 2.5-fold (Table). Acquired risk factors, except glucose intolerance, further increased the risk, marginally for hypertension, significantly ($p<0.05$) for obesity (RR 1.7 95% CI 1.0-2.8) and dyslipidemia (RR 2.3 95% CI 1.3-4.0).

	Rate ratios (RR) of VHD			
	From entry into survivorship		From 20-year post diagnosis	
	RR	(95% CI)	RR	(95% CI)
Mean heart RT dose (per 10 Gy)	2.4	(2.2-2.7)	2.5	(2.2-2.9)
Age at diagnosis (years)				
<5		referent		referent
5-9	1.1	(0.6-2.1)	1.2	(0.6-2.5)
10-15	1.1	(0.6-2.1)	1.3	(0.6-2.6)
≥15	1.1	(0.6-2.1)	1.2	(0.6-2.6)
Female sex	1.1	(0.8-1.5)	1.3	(0.9-1.9)
Race/Ethnicity				
non-Hispanic White		referent		referent
non-Hispanic Black	1.3	(0.5-2.8)	0.8	(0.2-2.3)
Other	1.1	(0.6-1.6)	1.0	(0.6-1.7)
Anthracycline dose (mg/m^2)				
None		referent		referent
<100	0.6	0.1-1.6	0.8	(0.2-2.2)
100-249	0.9	0.5-1.4	0.9	(0.5-1.5)
≥250	1.5	1.0-2.2	1.3	(0.8-2.1)
Acquired risk factors*				
Glucose intolerance			0.3	(0.02-1.3)
Smoking (Y/N)			1.1	(0.8-1.5)
Hypertension		N/A	1.6	(0.9-2.7)
Obesity			1.7	(1.0-2.8)
Dyslipidemia			2.3	(1.3-4.0)

*≥grade 2 CTCAE

Conclusions: In the first study to develop validated risk prediction models for VHD in survivors of childhood cancer, mean heart RT dose and acquired factors significantly increased the risk, suggesting opportunities for intervention.

Sun Exposure and Sun Protection Behavior in Survivors of Childhood Cancer – Findings from the Swiss Childhood Cancer Survivor Study

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*Presenting author

Background/Purpose: Childhood cancer survivors (CCS) are at increased risk for skin cancers, with sun exposure and medical skin examinations being the strongest modifiable fac-tors. Yet, we know little about prevalence and risk factors of sun protection, sun exposure, and recommended skin examinations among CCS, which this study evaluates.

Methods: For the Swiss Childhood Cancer Survivor Study, we surveyed CCS diagnosed prior age 21 years who survived ≥5 years after diagnosis. The questionnaire covered sun protection behaviors, sunburn incidence during last summer, and yearly skin exams as recommended by the Children's Oncology Group. We obtained cancer-related information from the Swiss Childhood Cancer Registry. We stratified all analyses by age group (children/adolescents/adults) and used multivariable regression to explore risk factors.

Results: Out of 5,457 survivors contacted, 3,579 (66%) participated, including 1,048 children (5-15 years), 572 adolescents (16-19 years), and 1,959 adults (≥20 years). Median age at diagnosis was 7 years (IQR 3-13). Parents applied sun protection to children regularly (89%), compared to 65% of adolescents and 77% of adults (p<0.001). Twenty-three percent of children, 49% of adolescents, and 43% of adults reported sunburn (p<0.001). Thirteen percent of children, 16% of adolescents, and 17% of adults had a skin examination the previous year (p=0.267). With increasing age, children were less likely to protect from the sun (Odds ratios [OR]=0.77, 95%CI 0.70-0.84) and more likely to report sunburns (1.13; 1.06-1.20). Conversely, with increasing age, adults were more likely to protect from the sun (1.04; 1.02-1.07), less likely to report sunburn (0.95; 0.94-0.97), and more likely to attend skin examinations (1.02; 1.01-1.04). Children whose parents had completed higher education were more likely to protect from the sun (2.27; 1.10-4.58) and attend skin examinations (2.98; 1.08-9.89); higher parental education was also associated with skin examinations among adults (1.31; 1.00-1.71). Girls were less likely to protect from the sun (0.39; 0.25-0.58); adult women were also less likely to protect from the sun (0.49; 0.38-0.62) and attend skin examinations (0.63; 0.49-0.82). Across age groups, CCS treated with radiotherapy were less likely to report sunburns (OR: 0.64-0.69). Children treated with HSCT were less likely to report sunburns (0.48; 0.21-0.95). Children (4.66; 1.69-12.49) and adults (2.12; 1.31-3.93) treated with HSCT were more likely to attend skin examinations. Radiotherapy was unrelated to sun protection behavior and skin examinations across age groups.

Conclusion: Sunburns are frequent among CCS and recommended skin examinations highly insufficient, even among CCS who had received radiotherapy or HSCT. Skin cancer prevention strategies for CCS should target especially survivors who received photosensitizing therapies, adolescents and young adults, as well as those with less education and women

Development of a Pediatric Oncology Financial Toxicity Outcome Measure with Content and Face Validity: the Parent-Reported Instrument of Costs and Experiences with Financial Toxicity (PRICE) Measure

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Background: Cancer treatment often leads to adverse financial consequences for patients and families (i.e., financial toxicity, FT). There is no validated measure to quantify FT in pediatric cancer settings, limiting research in this area.

Methods: We applied a stepwise approach to measure development consistent with ISPOR guidelines. First, we conducted qualitative concept elicitation interviews with family caregivers of children treated for cancer, 3-24 months following diagnosis. Second, we drafted de novo survey items guided by salient domains and aspects of FT from the interviews. Items were reviewed by a multi-institutional panel of experts in oncology and/or FT-related research, who provided numeric ratings of item relevance for aggregation into content validity index (CVI) scores. Experts also provided free text feedback on clarity and content. Items with CVI <0.75 were removed or revised by a consensus-based process. The revised item list was organized into a preliminary measure and forward and back translated into Spanish. Finally, we pretested items with a new cohort of caregivers in English and Spanish, through iterative rounds of language-concordant cognitive interviews (3-4 per round). Between each round, we reviewed and revised the survey to optimize comprehension, decision and response processes, and flow.

Results: Concept elicitation with 21 caregivers (86% mothers, 47% college-educated, 14% in Spanish) led to the creation of 56 initial survey items across 5 domains of FT: increased household spending, diminished income, household material hardship, psychological distress related to finances, and behaviors in response to FT. The expert panel (n=11) consisted of 5 providers, 2 clinical social workers, 2 nurse researchers, and 2 non-clinician researchers, with 6 members external to the study institution. CVI was <0.75 for 13 items; 11 of these were removed and 2 were revised based on free text feedback. Of 43 items with CVI ≥0.75, 9 were removed based on feedback and/or overlap with more highly rated items. Cognitive interviews were held with 19 caregivers (15 in English, 4 in Spanish; 74% mothers, 53% college educated) over 5 iterative rounds. The 36 remaining items were revised and/or removed, and ultimately organized into 16 questions, one of which was added during this phase based on caregiver feedback. In the final round of interviews, participants reported no concerns with content, clarity, or organization in either language.

Conclusions: We developed a novel outcome measure with content and face validity to assess FT specifically in pediatric oncology settings. Next steps consist of field testing to evaluate the measure's psychometric properties and other dimensions of validity. Potential future applications include use as a study endpoint and/or clinical screening tool.

The Impact of Sleep Disturbances on Trajectories of Neurocognitive Functioning in Adult Survivors of Childhood Cancer: a Report from the Childhood Cancer Survivor Study (CCSS)

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Background: Adult survivors of childhood cancer are at risk for neurocognitive impairment and sleep problems related to early cancer treatment and late-onset morbidities. The contribution of sleep disturbances to neurocognitive trajectories over time remains unknown.

Methods: CCSS participants (N=7333, 55.2% female, median [min-max] 8 [0-20] years at diagnosis; 37 [18-65] years at baseline evaluation) completed the CCSS Neurocognitive Questionnaire at two timepoints (follow-up interval: 5 [2-7] years) and the Pittsburgh Sleep Quality Index (PSQI) at an interim timepoint. Trajectories of neurocognitive impairment (score > 90th %ile of sibling controls) were defined as: persistent impairment, impaired at both timepoints; new-onset impairment, unimpaired to impaired; resolved impairment, impaired to unimpaired; stable non-impairment, unimpaired at both timepoints. Multivariable logistic models examined associations between poor sleep quality (PSQI total score >5) and sleep components (separately) and trajectories of neurocognitive impairment. Stratified analyses examined differences by CNS-directed therapy exposure or grade 3-4 (severe to life-threatening) chronic conditions using the Common Terminology Criteria for Adverse Events v4.03. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported.

Results: Survivors with poor sleep quality had 3-fold increased risk of new-onset and persistent neurocognitive impairment in all domains including task efficiency (OR [95% CI] 2.55 [2.17-2.99] and 3.40 [2.91-3.96]) and memory (OR [95% CI] 3.05 [2.57-3.61] and 3.35 [2.88-3.91]). Sleep medication was associated with 76-94% and 106-129% increased risk of new-onset and persistent impairment in any domain, respectively. Sleep problems due to pain were also associated with new-onset and persistent impairment (e.g., memory: OR [95% CI] 1.67 [1.23-2.27] and 2.23 [1.72-2.88]). Further associations were observed for all sleep components except sleep efficiency (Table, next page). Snoring was associated with new-onset and persistent impairment mostly in the CNS-directed therapy group (e.g., memory: OR [95% CI] 1.54 [1.08-2.21] and 1.59 [1.15-2.21]), whereas sleep medication and sleep problems due to pain were associated with adverse neurocognitive trajectories in both CNS- and non-CNS-directed therapy groups. Among survivors with grade 3-4 chronic conditions, sleep medication and sleep problems due to pain were the only significant predictors of new-onset (OR [95% CI] 2.27 [1.49-3.46] and 1.68 [1.03-2.72]) and persistent (OR [95% CI] 1.58 [1.07-2.32] and 1.87 [1.25-2.79]) memory impairment.

Conclusions: Sleep disturbances confer an increased risk of new-onset and persistent neurocognitive impairment over time for childhood cancer survivors. Behavioral treatments for sleep, pain and sleep-disordered breathing are potential interventions to mitigate or prevent deterioration of neurocognitive functioning in long-term survivors of childhood cancer.

Table: Associations between sleep problems and trajectories of neurocognitive functioning, adjusted for demographic characteristics.

	Neurocognitive functioning trajectories							
	New-onset impairment (unimpaired to impaired)				Persistent impairment (impaired at both timepoints)			
	Task Efficiency	Emotional Regulation	Organization	Memory	Task Efficiency	Emotional Regulation	Organization	Memory
Sleep problems	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Model 1: overall sleep quality								
Poor sleep quality	**2.55 (2.17-2.99)**	**2.53 (2.15-2.99)**	**2.61 (2.17-3.13)**	**3.05 (2.57-3.61)**	**3.40 (2.91-3.96)**	**3.80 (3.18-4.54)**	**3.63 (3.02-4.36)**	**3.35 (2.88-3.91)**
Model 2: specific components								
Sleep duration	0.99 (0.68-1.42)	0.98 (0.68-1.41)	0.85 (0.57-1.28)	1.20 (0.83-1.73)	1.34 (0.97-1.87)	**1.44 (1.02-2.03)**	1.40 (0.97-2.02)	1.25 (0.91-1.71)
Long sleep onset latency	**1.34 (1.07-1.67)**	1.24 (0.99-1.56)	1.19 (0.92-1.54)	**1.73 (1.38-2.17)**	**1.44 (1.15-1.80)**	**1.59 (1.26-2.01)**	**1.30 (1.02-1.67)**	**1.36 (1.10-1.68)**
Poor sleep efficiency	1.13 (0.88-1.44)	1.27 (0.99-1.63)	1.26 (0.95-1.66)	0.91 (0.71-1.18)	1.03 (0.80-1.32)	0.96 (0.74-1.25)	0.89 (0.67-1.18)	1.11 (0.88-1.40)
Night/early morning awakening	**1.32 (1.05-1.64)**	**1.58 (1.26-1.98)**	1.25 (0.97-1.62)	1.13 (0.90-1.43)	1.10 (0.88-1.38)	1.27 (1.00-1.61)	1.26 (0.98-1.62)	**1.42 (1.15-1.75)**
Snoring	**1.36 (1.05-1.76)**	1.15 (0.88-1.50)	1.31 (0.99-1.75)	**1.31 (1.01-1.70)**	**1.38 (1.08-1.77)**	**1.47 (1.13-1.89)**	**1.32 (1.00-1.73)**	**1.41 (1.11-1.78)**
Pauses in breathing	1.24 (0.79-1.96)	1.03 (0.62-1.69)	**1.93 (1.23-3.03)**	1.14 (0.71-1.84)	0.79 (0.49-1.28)	0.79 (0.48-1.29)	1.42 (0.89-2.26)	1.07 (0.70-1.64)
Delayed sleep timing	1.52 (0.81-2.87)	1.39 (0.72-2.68)	**2.61 (1.44-4.72)**	1.08 (0.58-2.04)	**2.27 (1.34-3.85)**	1.35 (0.77-2.36)	**2.65 (1.51-4.66)**	1.61 (0.96-2.70)
Delayed wake timing	0.78 (0.39-1.57)	0.66 (0.31-1.42)	1.26 (0.67-2.38)	1.76 (0.93-3.33)	0.96 (0.53-1.74)	**2.18 (1.24-3.82)**	1.24 (0.66-2.31)	1.71 (1.00-2.92)
Sleep medication	**1.94 (1.48-2.54)**	**1.80 (1.36-2.39)**	**1.83 (1.35-2.48)**	**1.76 (1.33-2.34)**	**2.08 (1.60-2.69)**	**2.29 (1.75-3.01)**	**2.26 (1.71-3.00)**	**2.06 (1.61-2.64)**
Sleep problems due to pain	1.28 (0.94-1.76)	1.32 (0.97-1.81)	**1.96 (1.43-2.69)**	**1.67 (1.23-2.27)**	**2.49 (1.92-3.24)**	**1.71 (1.27-2.30)**	**1.76 (1.30-2.40)**	**2.23 (1.72-2.88)**

Separate models were used for each neurocognitive outcome, adjusted for sex, race/ethnicity, age and BMI at baseline. Neurocognitive impairment was assessed at two timepoints, and sleep problems were assessed at an interim timepoint. Resolved (impaired to unimpaired) and stable non-impaired (unimpaired at both timepoints) neurocognitive functioning trajectories were combined as reference group. Bold font indicates statistically significant results.
Abbreviations: CI, confidence interval; OR, odds ratio.

Risk Prediction of Coronary Artery Disease in Long-Term Survivors of Childhood Cancer: Findings from the St. Jude Lifetime Cohort (SJLIFE) and the Childhood Cancer Survivor Study (CCSS)

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Background: Childhood cancer survivors face a 10-fold increased risk for coronary artery disease (CAD) compared to the general population. Current models to estimate CAD risk in this population rely on self-reported outcomes and exclude genetic predisposition which may limit predictive ability.

Methods: Childhood cancer survivors from the St. Jude Lifetime Cohort (SJLIFE; discovery, n=4,145; median age at diagnosis: 6.3 years) and Childhood Cancer Survivor Study (CCSS; validation, n=7,065; median age at diagnosis: 7.5 years) were evaluated for demographics, treatment exposures previously associated with CAD, cardiometabolic risk factors, and the most recent multi-ancestry polygenic risk score (PRS; PGS003725) for CAD from the general population at the time of cohort entry (5-years post-cancer diagnosis). Cox proportional hazards regression-was performed to predict the risk of CAD (CTCAE grade≥3) over the next 25 years, with predictors selected by elastic net with a hyperparameter selected by 10-fold cross-validation. Time-dependent area under the receiver operating characteristic curve (AUC) evaluated model performance. Based on the predicted risk score for CAD from the final model, survivors were categorized into low (<15th percentile), moderate (15-85th percentiles), and high (≥85th percentile) risk groups. The cumulative incidence of CAD over the next 25 years from the time of cohort entry was then estimated by group.

Results: CAD was clinically diagnosed in 71 (1.7%, SJLIFE; median age at CAD diagnosis: 34.9 years) and self-reported as diagnosed by a care provider in 181 survivors (2.6%, CCSS; median age at CAD diagnosis: 40.5 years) within 25 years of cohort entry. The AUC of a clinical model including older age at childhood cancer diagnosis, male sex, cardiomyopathy (CTCAE grade≥3), dyslipidemia (CTCAE grade≥2), and exposure to cisplatin, chest irradiation, and cranial irradiation was 0.872 (95% CI=0.829-0.916) in SJLIFE and 0.761 (95% CI=0.720-0.803) in CCSS. Incorporating the PRS into the clinical model led to a modest improvement in performance, with an AUC of 0.877 (95% CI=0.834-0.920; P=0.094; SJLIFE) and 0.775 (95% CI=0.735-0.815; P=0.0013; CCSS). With the inclusion of PRS, the 25-year cumulative incidence of CAD in the high-risk group increased from 16.8% (95% CI=12.5-20.9) to 17.7% (95% CI=13.1-22.1) in SJLIFE and from 10.8% (95% CI=8.7-12.9) to 12.7% (95% CI=10.2-15.2) in CCSS. The cumulative incidences in the moderate- and low-risk groups were similar regardless of the inclusion of the PRS.

Conclusions: We developed a prediction model using clinically assessed outcomes and genetic predictors to estimate the 25-year CAD risk in 5-year childhood cancer survivors. Validated in an independent cohort, our model showed substantially improved accuracy over current models based on self-reported data. The early onset of CAD in this population highlights the need for more precise models to enable personalized screening and interventions

Cardiac Dysfunction in Childhood Cancer Survivors: a Retrospective Cohort Study from India

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Background: We evaluated the burden and determinants of cardiac dysfunction in our cohort of 5-year survivors of childhood cancers as well as the relevance of the IGHG risk stratification in our cohort.

Methods: This retrospective study included survivors of children aged 0-18 years at diagnosis and at least 5 years from diagnosis treated at our center. Cardiac dysfunction (CD) was defined as left ventricular systolic dysfunction (left ventricular ejection fraction <50%), any diastolic dysfunction, valvular thickening, fibrosis or calcification and/or arrhythmia. Risk stratification was done as per the International Guidelines harmonization group (IGHG).

Results: The cohort consisted of 5465 survivors, median age at diagnosis 6 years, median follow-up 14 years and median current age 22 years. 1722 (31.5%) were high risk as per IGHG criteria, 1813 (33.2%) were moderate risk, 1675 (30.6%) had received doxorubicin dose >250 mg/m2 and 86 (1.6%) had received chest-directed radiotherapy (chest RT). 1345 (24.6%) had received neither anthracycline nor chest RT. Of 4437 children with available data, 2892 (65%) were undernourished at diagnosis. Cardiac dysfunction as defined was seen in 166 (3%) -13 (0.2%) symptomatic - and CD not meeting defined criteria in 42 (0.8%). As per IGHG risk- 137 (7.9%) high risk, 23 (1.3%) moderate risk and 3 (0.5%) low risk had CD. 3 (0.02%) survivors who had received neither chest RT nor anthracyclines developed CD.
IGHG risk (OR 10.2, 95% CI 3.6-28.8, p<0.001) and chest RT (OR 2.4, 95% CI 1.2 -4.7, p= 0.01), but not age, diagnosis, doxorubicin dose or undernutrition at diagnosis were predictive of developing CD.

Conclusions: The IGHG risk stratification is valid in our cohort. Surveillance for cardiac toxicity should be as per risk to balance resources and optimal care of survivors. The small subset of survivors with CD, without therapeutic risk factors underlines the need for genetic risk prediction.

Validation of the Transition Readiness Inventory for Adolescent and Young Adult Survivors of Cancer

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Background: Young adult survivors demonstrate significant decline in engagement in follow-up care, especially after the transfer to adult-focused follow-up care. Lack of transition readiness may be a significant contributor to the disengagement, yet there are no survivor specific measures of transition readiness to assess this. Guided by our SMART (Social-ecological Model of AYA Readiness to Transition) framework and rigorous patient-reported outcomes measurement development methods, we developed the TRI (Transition Readiness Inventory). Here, we provide psychometric results in a large multisite cohort of AYA survivors and discuss implications of TRI.

Methods: 840 AYA (Mage = 20, 18% Hispanic, 72% White, 50% female, 54% liquid) completed the TRI item pool of 61 items. A subsample of 587 completed additional measures for concurrent validity analysis. Confirmatory factor analyses based on 6 preliminary factors identified in earlier work was performed using the “fa” function in R. Tucker-Lewis indices (TLI), comparative fit index (CFI) and Root Mean Square Error of Approximation (RMSEA) were calculated for factor fit indices. Items were assigned to factors based on highest factor loading. Items with factor loadings <0.400 were deleted.

Results: Six factors (28 items) were retained that were consistent with concepts in the SMART conceptual model, although one was split into two factors to optimize fit, resulting in 7 final factors: Health Knowledge/Health Literacy (3 items), Skills/Self-Efficacy-Tasks (3 items), Skills/Self-Efficacy-Communication (3 items), Beliefs/Expectations (3 items), Goals/Motivation (3 items), Relationships/Communication (6 items), and Psychosocial/Emotions (5 items). The final measure yields a profile score of 26 items with 2 additional items (medication knowledge and global transition readiness). All factors have adequate to good fit indices (i.e., RMSEA , CFI, TLI) and high test-retest reliability within 10 days for 60 AYA. Cronbach’s alpha is high for all (0.73-0.95) with the exception of 0.57 for Knowledge. Correlations with extant measures demonstrated concurrent validity. Specifically, TRI scores related to transition readiness on the Transition Readiness Questionnaire subscales, as well as measures of health knowledge, self-management skills, health competence, health care trust, expectations cancer worries, patient maturity, depression, and anxiety. Based on subsequent item response theory analyses, most individual subdomains demonstrate acceptable precision (> 0.7) across a moderate range of the total score.

Conclusions: Analysis yields the definitive psychometric validation of TRI. The TRI is composed of 7 distinct factors consistent with SMART framework components. The TRI can be used to support the transition process over time via longitudinal evaluation that reveals targets of intervention and support needed. Next steps are to evaluate TRI as a predictor of survivorship care engagement in the adult care system.

Longitudinal Associations Between Chronic Health Condition Burden and Financial Hardship among Adult Survivors of Childhood Cancer: a Report from the Childhood Cancer Survivor Study (CCSS)

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Background: Childhood cancer survivors experience a large burden of chronic health conditions (CHCs) with the progression of these conditions facilitating potential economic burden. This study examined the association between CHC progression and financial hardship in adult survivors of childhood cancer.

Methods: The study included CCSS participants diagnosed with pediatric cancer (1970–1999) who survived >5 years post-diagnosis and were ≥26 years old at the assessment of financial burden. Participants completed surveys (2017-2019) assessing three financial hardship domains: behavioral, material, and psychological. CHCs were self-reported at baseline and on up to 4 follow-ups. CHC severity was graded using CTCAE v4.03. To estimate the impact of multiple CHCs, a severity score was calculated based on published methods (PMID: 17595271) accounting for the frequency and grade of conditions. Notable CHC burden was defined as any CHC above low severity grade. Multivariable logistic regression evaluated associations of CHC burden with financial hardship adjusting for age at diagnosis, attained age, sex, insurance, personal income, education, marital status, smoking status, and body mass index. Additional analyses examined whether neighborhood deprivation using the Area Deprivation Index (ADI) (range 0-100) modified the relationship between CHC burden and financial hardship.

Results: Among 3,638 evaluable participants, the prevalence of notable CHC burden was 66%, material hardship 16%, psychological hardship 26%, and behavioral hardship 21%. Survivors with very high CHC burden had 2.6-fold (95%CI 1.6-4.1) higher odds of material and 1.6-fold (95%CI 1.0-2.4) higher odds of psychological hardship vs. those with low CHC burden. Survivors who progressed to moderate, high, or very high CHC burden had 1.7-fold (95%CI 1.2-2.5) higher odds of material hardship and 1.6-fold (95%CI 1.1-2.2) higher odds of psychological hardship vs. those with persistent low CHC burden. For survivors living in more deprived neighborhoods (ADI≥50), having notable CHC burden was associated with 2.5-fold (95%CI 1.5-4.3) higher odds of material hardship vs. those without notable CHC burden. For survivors living in less deprived neighborhoods (ADI<50), having notable CHC burden was associated with 1.5-fold (95%CI 1.1-2.2) higher odds of psychological hardship and 1.6-fold (95%CI 1.1-2.1) higher odds of behavioral hardship vs. those without notable CHC burden.

Conclusions: Longitudinal CHC burden shows strong temporal associations with material and psychological financial hardship. Neighborhood deprivation is associated with financial hardship, beyond individual sociodemographic factors. Multi-level interventions will be crucial to address financial hardship in survivors who develop CHCs earlier than peers.

Temporal Trends of Subsequent Malignant Neoplasms in Childhood Cancer Survivors and the Impact of Treatment Changes: a DCCSS-LATER 3 Study

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Background/Purpose: The growing population of childhood cancer survivors face an elevated risk of developing subsequent malignant neoplasms (SMNs), contributing to excess mortality. Over the past decades treatment has been modified to decrease this risk. It is essential to evaluate whether these changes have effectively reduced the risk of SMNs over time. Therefore, we aimed to evaluate the temporal trends in the risk of developing SMNs among five-year childhood cancer survivors, and relate these to changes in radiotherapy and chemotherapy over the past five decades. In addition, we examined treatment-related risk factors for developing any SMN.

Methods: We assessed the risk of SMNs, temporal trends, and the impact of treatment among 11,548 five-year childhood cancer survivors from the Dutch Childhood Cancer Survivor Study (DCCSS)-LATER cohort (1963-2014). We calculated standardized incidence ratios (SIRs) and cumulative incidences. Multivariable Cox proportional hazard regression was used to estimate SMN risks, and mediation analysis to evaluate effects of treatment changes over time.

Results: After a median follow-up of 21.2 years, 550 survivors developed at least one SMN (SIR: 3.5, 95% CI: 3.2-3.8), with a 25-year cumulative incidence of 3.6% (95% CI: 3.2%-4.0%) for any SMN. Overall, the risk for SMN declined over period of diagnosis with hazard ratios (HRs) of 0.9 (95% CI: 0.7-1.2) , 0.8 (95% CI: 0.6-1.1), and 0.7 (95% CI: 0.5-0.99) for periods 1980-1989, 1990-1999, 2000-2014, respectively, vs. 1963-1979 (p-trend=0.04, Figure 1). Mediation analysis indicated that the decline in SMN risk was primarily associated with a decreased use of radiotherapy (p-trend after radiotherapy adjustment=0.51). Chemotherapy seemed to have the opposite effect, mainly due to the use of anthracyclines and/or epipodophyllotoxins (p-trend after chemotherapy adjustment<0.001). Survivors treated with anthracyclines (HR: 1.3, 95% CI: 1.0-1.6), epipodophyllotoxins (HR: 1.3, 95% CI: 1.0-1.7), or radiotherapy (HR: 2.3, 95% CI: 1.9-2.8) had a significantly increased risk of SMN.

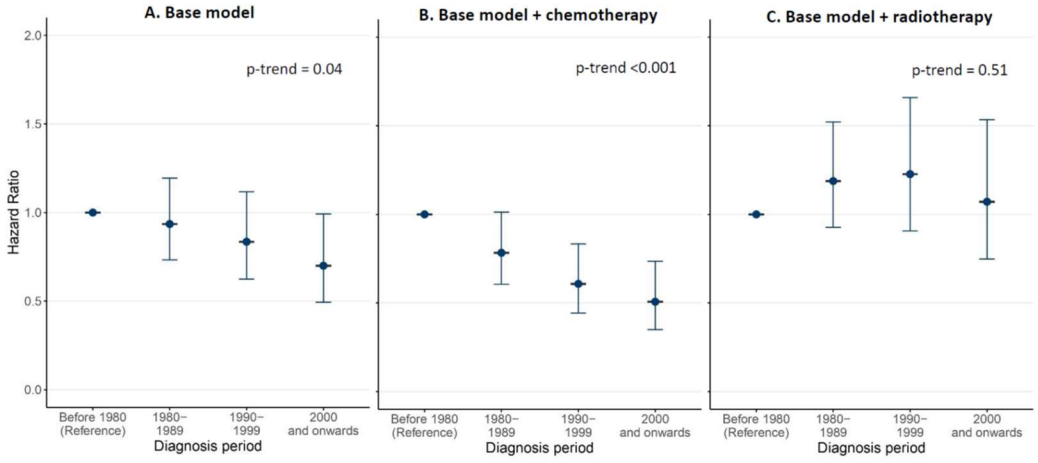


Figure 1. Hazard Ratios and their 95% confidence interval for overall SMN risk in the DCCSS-LATER cohort, by period of childhood cancer diagnosis, with diagnosis <1980 as reference group. Calculated by multivariable Cox proportional hazard regression, all models were adjusted for sex and age at diagnosis. **A.** Base model, without adjusting for treatment-related factors **B.** Model adjusted for yes/no variables for alkylating agents, anthracyclines, epipodophyllotoxins, platinum agents, and vinca alkaloids **C.** Model adjusted for radiotherapy yes/no.

Conclusions: While reductions in radiotherapy have lowered the risk of SMN throughout periods of diagnosis, the increased use of chemotherapy, especially anthracyclines and epipodophyllotoxins, increased the SMN risk. Furthermore, survivors treated with radiotherapy, anthracyclines, or epipodophyllotoxins have an elevated risk of developing any SMN. This highlights the need to reassess chemotherapy protocols for childhood cancer and to identify survivors at risk.

Breast Cancer Recurrence and Mortality among Survivors of Childhood Cancer: a Report from the Childhood Cancer Survivor Study (CCSS)

Lucie Turcotte, Hasibul Hasan, Emily Stene, Aaron McDonald, Chaya Moskowitz, Tara Henderson, Gregory Armstrong, Yutaka Yasui, Rita Nanda, Kevin Oeffinger, Joseph Neglia, Anne Blaes, Cindy Im

Background: Survivors of childhood cancer are at high risk for developing subsequent breast cancer (BC) and face excess mortality despite receiving therapeutic tradeoffs intended to lessen risk for long-term toxicities. Recurrence among women with first primary BC is well-studied, but knowledge surrounding survivors' risks for and survival after BC recurrence is limited.

Methods: Analyses included female 5-year survivors participating in CCSS with pathology-ascertained breast carcinomas (in situ or invasive) diagnosed from 1981-2016 at age ≥18y. BC treatment was evaluated against chronological period-specific National Comprehensive Cancer Network guidelines for primary BC. Recurrent BC cumulative incidence curves were estimated treating death as a competing risk among survivors and females with first primary BC (controls) matched one-to-one by demographics and first BC clinical characteristics including diagnosis age/year, histology and race/ethnicity. All-cause mortality rates among survivors and controls with recurrent BC were compared in multivariable Cox regression models adjusted for race/ethnicity, first BC diagnosis age and year, histology, and receipt of guideline-concordant treatment.

Results: Among the 431 childhood cancer survivors with subsequent BC (median diagnosis age: 40 years, IQR: 35-44), 68 developed recurrent BC. Compared with matched controls (N=206 pairs), survivors had similar 10-year BC recurrence risk (survivors: 14%, 95% CI: 9-20% versus controls: 12%, 95% CI: 9-18%; P=0.52). Among survivors with BC recurrence, Hodgkin lymphoma was the predominant primary cancer diagnosis (63%) and first subsequent BCs were largely early stage (stage 0: 8%; stage I/II: 69%) and estrogen (71%) or progesterone (80%) receptor positive. Most (84%) received first BC treatment following national guidelines for primary BC. However, nearly half (47%) underwent bilateral mastectomies (81% occurring before recurrence) and most received chest radiotherapy (86%) or anthracycline chemotherapy (69%) for either their primary childhood cancer or first subsequent BC. A total of 48 survivors died after BC recurrence, mostly related to BC (83%) or cardiovascular causes (11%). Following recurrence, the 10-year overall mortality probability was significantly higher among survivors (89%, 95% CI: 61-97%) than controls (42%, 95% CI: 18-58%; P=0.0025) and survivors had an adjusted 3.1-fold (95% CI: 1.24-7.94) greater risk of death.

Conclusions: Although the risk for BC recurrence among childhood cancer survivors with subsequent BC is similar to females with primary BC, this vulnerable population faces diminished treatment options and substantially greater mortality risk after recurrence. Future studies to identify early predictors of subsequent BC and BC recurrence among survivors are needed to reduce mortality risk.

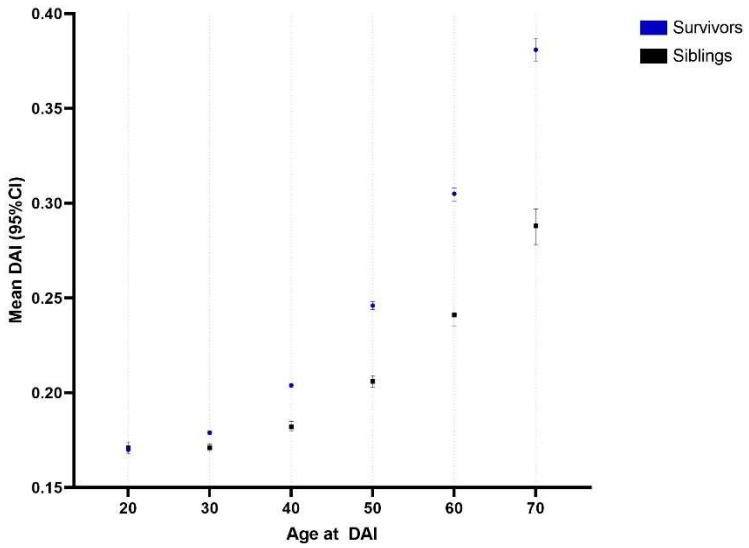
Accelerated Aging among Long-Term Survivors of Childhood Cancer: a Report from the Childhood Cancer Survivor Study (CCSS)

Annalynn Williams, Brent Small, Mingjuan Wang, Jeanne Mandelblatt, Kiri Ness, Harvey Cohen, Melissa Hudson, Tara Brinkman, Rebecca Howell, Eric Chow, Yutaka Yasui, Deo Kumar Srivastava, Greg Armstrong, Kevin Krull

Background: Cross-sectional studies have suggested childhood cancer survivors demonstrate a pattern of functional limitations and morbidity consistent with premature aging, but cannot confirm if aging is accelerated relative to peers without cancer. We used longitudinal data to characterize aging using a Deficit Accumulation Index (DAI) which examines the accumulation of multiple aging-related deficits.

Methods: We included 5+ year survivors of childhood cancer (N=21,856; at entry mean age 26.7 [SD 6.1], 18.7 [4.7] years post diagnosis) and siblings (N=4,628, mean age 29.1 [7.1]) from the CCSS, a longitudinal prospective cohort study. Participants completed questionnaires at up to five timepoints (mean [SD] follow-up 9.5[8.9] years), with DAI scores generated as the proportion of deficits out of 30 items related to aging, including chronic conditions (e.g. hearing loss, hypertension), psychosocial and physical function, and activities of daily living. The total score range is 0 to 1; and a moderate clinically meaningful difference is 0.02. As survivors completed multiple surveys at varying intervals, attained age was used as the time scale. Linear mixed models with random subject-specific intercept and age slope compared DAI in survivors to siblings with an attained age x survivor/sibling interaction term to determine if DAI was increasing faster in survivors, adjusted for the first DAI score, age at first DAI and sex. Similar models examined DAI changes associated with treatments among survivors.

Results: Across all time points, the adjusted mean [95%CI] DAI was 0.195[0.195, 0.196] for survivors and 0.180[0.178,0.182] for siblings (p<0.001). Survivors experienced more rapid increase in DAI over time compared to siblings (p<0.001). For example, at age 20 there was no difference in DAI between survivors and siblings, however the mean difference [95%CI] in DAI between survivors and siblings steadily increased with age to 0.008[0.006, 0.010] at 30 years, 0.021[0.019, 0.024] at 40 years, 0.040[0.037, 0.044] at 50 years, 0.064[0.058, 0.071] at 60 years, and 0.093[0.082, 0.105] at 70 years; all p's<0.001 (Figure). Survivors who received abdominal, cranial, or chest radiation experienced more rapid increase in DAI over time compared to those who did not (p's<0.001). Survivors who received platinum agents also experienced a more rapid increase in DAI over time (p's<0.001).



Conclusions: Our data confirm survivors of childhood cancer experience significant age acceleration relative to peers. Given the ease of measuring DAI using self-reported data, this tool may be used to routinely monitor survivors and identify those at risk for adverse aging-related outcomes so that we may intervene and mitigate their accelerated aging trajectory.

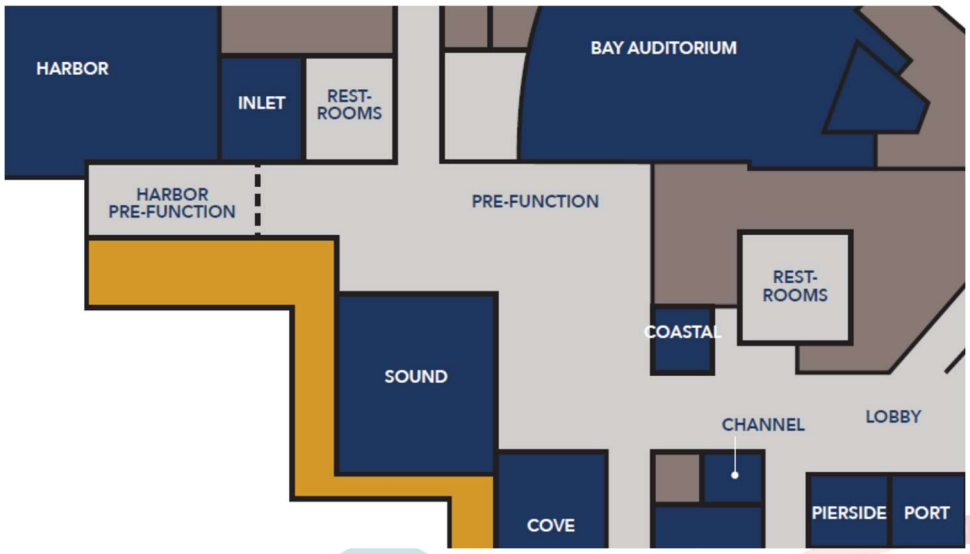
ABSTRACTS SELECTED FOR POSTER PRESENTATIONS (listed in alphabetical order by first author)

Poster Categories [number of abstracts]

- Cardiovascular (CV) Health [1-9]
- Endocrine Outcomes [1-7]
- Genetics/Genomics [1-8]
- Health Services Research [1-36]
- Intervention Research [1-9]
- Neurocognitive Outcomes [1-9]
- Other Late Effects [1-12]
- Quality of Life/Behaviors [1-12]
- Research Methods [1-11]
- Subsequent Malignant Neoplasms (SMN) [1-5]

The Poster Category-Number is noted in the first line of each abstract on the subsequent pages.

Posters will be displayed throughout the Pre-Function space and the Sound room (see conference center layout below). Categories will be grouped together to the extent possible. Poster presenters are encouraged to display their posters beginning on Day 1 of the symposium prior to the symposium reception when poster viewing is possible. Please pin your poster on the poster board (pins will be provided) based on your assigned poster category and number. *Poster presenters are asked to stand next to their posters at the end of Day 2 in the dedicated poster viewing hour prior to the symposium dinner.* Posters can remain hanging until the symposium adjourns at noon on Day 3. Posters not removed by Day 3 afternoon will be discarded.



Two abstracts being presented as posters were among the top scoring abstracts and are featured as posters due to the first author having another top scoring abstract. These two submissions are:

- Ohlsen, et al. "Treatment and Lifestyle Profiles of Healthy Aging Survivors: A Report from the Childhood Cancer Survivor Study"
- Petrykey, et al. "Risk prediction of dyslipidemia in long-term survivors of childhood cancer: a report from the St. Jude Lifetime Cohort (SJLIFE) and the Childhood Cancer Survivor Study (CCSS)"

Highlighted posters being featured on Day 2 of the symposium include:

- Barnea, et al. “Mortality in survivors of childhood cancer diagnosed with subsequent thyroid cancer: A report from the Childhood Cancer Survivor Study”
- Beccaria, et al. “Persistent cytopenia and hypogammaglobulinemia after cancer treatment reveals underlying Inborn Errors of Immunity in childhood cancer survivors: a monocentric Italian case series”
- Berkman, et al. “Cardiometabolic outcomes after bariatric surgery in adult survivors of childhood cancer in the St. Jude Lifetime Cohort Study”
- Fankhauser, et al. “Prevalence and risk factors of diastolic dysfunction among adult Swiss childhood cancer survivors – Results of the CardioOnco Study”
- Greber, et al. “Prevalence of endocrine conditions among Swiss childhood cancer survivors and their association with health-related quality of life”
- Hernandez, et al. “Childhood cancer survivors and their caregivers are amenable to survivorship surveillance with community-based primary care providers"
- Kapoor, et al. “Impact of Multidisciplinary Intervention on overweight and obese childhood cancer survivors and its psychosocial determinants”
- Kim, et al. “Epigenetic Impact of Social Vulnerability in Adult Survivors of Childhood Cancer with African Ancestry: An Epigenome-Wide Association Study from the St. Jude Lifetime Cohort”
- Lucas, et al. “A Phase IV Surveillance Trial of Pencil Beam Scanning Proton Therapy in Children”
- McNickle, et al. “Feasibility of Measuring Heart Rate Variability Using a Wearable Device: A report from the St. Jude Lifetime Cohort Study (SJLIFE)”
- Nissen, et al. “Lifestyle and metabolic late effects in long-term survivors of pediatric hematopoietic stem cell transplantation”
- O'Neil, et al. “Fitness and cardiometabolic risk factors in young childhood cancer survivors: A report from the St. Jude Lifetime Cohort Study (SJLIFE)”
- Pearson, et al. “Focal Nodular Hyperplasia in Childhood Cancer Survivors“
- Pollock, et al. “Reduced Beta Cell Function in Childhood Cancer Survivors: Impact of Total Body Irradiation and Abdominal Radiation”
- Ramsey, et al. “Outcomes of local control procedures in peri-articular bone sarcomas of the knee – a report from the Childhood Cancer Survivor Study
- Ross, et al. “Knowledge and Self-Efficacy for Survivorship Care Early Post-therapy among Childhood Cancer Survivors and their Parents
- Schindera, et al. “Physical fitness and clinically assessed disease burden in long-term childhood cancer survivors – the SURfit Study
- Srinivasan, et al. “Clinical utility of 99 breast cancer polygenic risk scores (PRSs) in female survivors of childhood cancer: a report from the Childhood Cancer Survivor Study (CCSS) and St. Jude Lifetime Cohort (SJLIFE)
- Studaway, et al. “Olfactory Function and Associated Neurocognitive Impairment among Adult Survivors of Childhood Cancer
- Svendsen, et al. “Concordance of Six Minute Walk Test and Cardiopulmonary Exercise Testing: A report from the St. Jude Lifetime Cohort Study (SJLIFE)
- Tallone, et al. “Cancer predisposition/congenital syndromes with increased cancer risk in Childhood Cancer Survivors Cohort: a monocentric case series
- Tark, et al. “Improved Early Referral in Long-Term Survivor Care with Institutional Standardized Practice Among Childhood Leukemia Survivors
- Wang, et al. “Identification of childhood cancer survivors at highest risk of developing subsequent thyroid cancer: A report from the Childhood Cancer Survivor Study

Health Services Research-15

Transition of Care Practices and Outcomes in Adult Survivors of Childhood Cancer

Melissa Acquazzino, Rachael Schmidt, Dana Verhoeven, Cassie Adams, Marsha Fuemmeler

Background: Transition to adult care continues to be a significant challenge for adult survivors of childhood cancer. Although risk of developing late effects from childhood cancer treatment increases as survivors age, adherence to evidence-based screening guidelines decreases the further survivors get from care at their pediatric center. Our Survivorship program consists of a pediatric survivorship clinic at the children's hospital and an adult survivors of childhood cancer clinic at the adult hospital. As part of ongoing quality improvement, we evaluated both our transition practices and the adherence to the COG Long-Term Follow-up (LTFU) guidelines for our adult survivors of childhood cancer.

Methods: A retrospective chart review was conducted from June 1, 2019 (start of the pediatric survivorship clinic) to February 1, 2025 to evaluate transition for survivors of childhood cancer to adult care. Diagnoses and treatment data were abstracted for each survivor from the medical record. Transition outcome is recorded prospectively by the pediatric survivorship clinic nurse case manager. Adherence to COG LTFU guidelines for echocardiogram, colon cancer, and breast cancer screening was determined based on medical record review.

Results: The pediatric survivorship clinic has transitioned 60 patients to adult care due to age. Thirty-eight percent of patients were transitioned to the adult survivorship clinic, 59% to a primary care provider (PCP), and 3% to a local adult oncologist. Table 1 shows the transition outcome by oncology diagnosis. For patients with a history of ALL, 57% transitioned to a PCP and 43% to the adult survivorship clinic. Although small numbers, 100% of survivors of CNS tumors and 75% of bone tumors transitioned to the adult survivorship clinic. The adult survivorship clinic has 64 adult survivors of childhood cancer, referred by the pediatric survivorship clinic, PCP, pediatric oncologist, or self. COG LTFU screening guidelines for secondary malignancy are being recommended appropriately for applicable survivors 100% of the time for breast cancer (n=7) and colon cancer (n=14) screening. Fifty nine adult survivors of childhood cancer required echocardiogram screening and the recommendations made in the survivorship clinic matched COG LTFU guidelines 90% of the time; 7% (n=4) of patients had screening every 2 years when the guidelines recommend every 5 years and only 3% (n=2) of patients had screening every 5 years when the guidelines recommend every 2 years.

Table 1: Transition Outcome by Cancer Diagnosis

	Patients transitioned to Primary Care Provider (n=35)	Patients transitioned to Adult Survivorship Clinic (n=23)
Oncology Diagnosis		
ALL	57% (n=12)	43% (n=9)
AML	0%	100% (n=1)
Hodgkin lymphoma	62% (n=5)	38% (n=3)
Non-Hodgkin lymphoma	71% (n=5)	29% (n=2)
Bone tumors	25% (n=1)	75% (n=3)
CNS tumors	0%	100% (n=3)
Solid tumors	75% (n=6)	25% (n=2)
Misc (APML, LCH, RBL)	100% (n=6)	0%

Abbreviations: Acute lymphoblastic leukemia (ALL); Acute promyelocytic leukemia (APML); Acute myeloid leukemia (AML); Central nervous system (CNS); Langerhans cell histiocytosis (LCH); Retinoblastoma (RBL)

Conclusion: Transition from the pediatric survivorship clinic is split between PCPs and the adult survivorship clinic and is often driven by patient preference. Adult survivors of childhood cancer followed in the adult survivorship clinic are receiving excellent care with near uniform adherence to the COG LTFU guidelines. Future work is needed to track screening adherence in survivors transitioned to a PCP.

Health Services Research-1

"To Prevent Any Recur or Side Effects…the Food is Very Important": a Qualitative Exploration of Factors Motivating Food Choice among Families of Childhood Cancer Survivors

Rahela Aziz-Bose, Lucille Lokko, Morgan Paul, Jane Roberts, Brett Nava-Coulter, Katelyn Fox, Colleen Kelly, Maimouna Sy, Fang Fang Zhang, Kira Bona

Background: High-quality diets reduce the risk of cardiovascular late effects among childhood cancer survivors (CCS); conversely, food insecurity is a known risk factor for poor cardiovascular health and diet quality. Limited data exist to describe factors motivating food choice among families in survivorship; no such data exist in the context of food insecurity. Within a mixed-methods study on nutrition and food insecurity in the early post-treatment period, we qualitatively explored the prioritization of nutrition and factors influencing food choice among families of CCS.

Methods: Parents of children (<18 years) less than 12 months post-cancer treatment at a large pediatric cancer center were purposively sampled from a survey cohort based on self-reported household food insecurity and chart-abstracted child cardiovascular risk factors (treatment exposure [anthracycline, chest radiation] or clinical condition [elevated body mass index, elevated systolic or diastolic blood pressure, dyslipidemia, or impaired glucose tolerance]). One-time semi-structured interviews in English or Spanish were audio-recorded, translated where applicable, and transcribed. We conducted a qualitative thematic analysis with a combined deductive and inductive coding approach.

Results: Twenty-five parents were approached for interview participation; 23 (92%) consented to participation and 20 (87%) completed interviews. Among 20 interview participants (3 Spanish-speaking), 14 (70%) reported household-level food insecurity; 18 (90%) had a CCS with at least 1 clinical or treatment-exposure cardiovascular risk factor. We identified 3 key themes around nutrition and food choice in early survivorship: 1) high importance of nutrition in supporting long-term health, including a perceived reduction in the risk of cancer recurrence; 2) tension between food costs and health value as drivers of food choice; and 3) nutrition as a means for parents to re-establish their parenting values after treatment disruptions to both parenting and child eating patterns. In the context of financial barriers, parents reported utilizing a variety of strategies and trade-offs (store selection, family and community support, deprioritizing other bills) to achieve their nutritional goals.

Conclusions: Parents of CCS report that prioritizing nutrition in the early post-treatment period is central both to supporting CCS' long-term health and to regaining a sense of parental control. However, parents concurrently identify financial challenges as a primary barrier to achieving nutritional goals. Given established associations between food insecurity, poor dietary quality and cardiovascular risk, interventions to mitigate financial barriers for CCS with food insecurity—e.g. "food is medicine" programs, nutrition assistance benefits navigation—represent an immediate opportunity to align with parental goals, improve dietary quality, and reduce late effects in survivorship.

Table 1. Key themes around nutrition and food choice in early survivorship, with exemplar quotes.	
Theme	**Exemplar Quotes**
Importance of nutrition in supporting long-term health	"I think to prevent any recur or side effects from the chemotherapy and radiation, I think the food is very important." (parent of 16-year-old with nasopharyngeal carcinoma) "Oh my god, it's like number one. It's our battle every day. Food is like all we do all day…That's my main goal, like less side effects after treatment. Because in reality, it's more than just secondary cancers, it's diabetes and the risk of being overweight because of all of the steroids." (parent of 6-year-old with acute lymphoblastic leukemia) "The eating, I think it's one of the top of priority. Like make sure he keeps his nutrition, like getting all the nutrition…All the nutrients that keep him as healthy as he can, all the vitamin that he needs." (parent of 14-year-old with Ewing sarcoma) "Everybody has to do better. It's not easy, but shoot, it's worth it. At least you're not getting diabetes and all these other bad things, and cancer still can come from foods, like you gotta be careful. So I think long term." (parent of 9-year-old with acute myeloid leukemia) "I am concerned because I am afraid he will relapse again because he is not eating the way he is supposed to." (parent of 10-year-old with acute lymphoblastic leukemia)
Tension between food costs and health value as drivers of food choice	"You could go to the store and you could fill your cart with all these fresh fruits and all these fresh vegetables, but they're so expensive. Do I buy all of these fresh fruits and vegetables and the really good healthy stuff, or do I buy steak for dinner?...When you go from having the two incomes and a pretty comfortable budget for food down to one, and then without that grocery card, I'm pretty sure that there would've been times that we couldn't have put stuff – we would've had to have gone to, oh, well, let's buy this processed, processed, processed because it's cheap. And we can get it with a gift card versus getting the better quality, healthier choice." (parent of 17-year-old with Ewing sarcoma) "It depends on the paycheck that week, and if I can afford fresh eggs over store-bought eggs, or fresh meat over store-bought meat. Sometimes I have to make the decision of not getting fresh meat, and just going to a grocery store and picking it up, which I hate because there's a big difference. And even organic milks and everything organic is more expensive, and so, there's a big increase in your grocery bill. And I can't afford it all the time, so I can't always buy it, which – but I try to get the best option that I can afford." (parent of 5-year-old with medulloblastoma) "Just financially we haven't been able to afford us the healthiest foods that I was giving her before. She's definitely eating more, which is great. And I'm really happy about that. It's just the quality of food is probably not the same as before…I've definitely had to choose less healthier options than I would normally choose because of the financial aspect." (parent of 5-year-old with rhabdomyosarcoma)
Nutrition as a means to re-establish parenting values after treatment disruptions	"After getting out, I'm like I want to cook better…[After child's diagnosis] I had a mental breakdown and I kind of lost my way. So when I came here, it was like I was forced to get these things back. I have a son to feed for and provide for, these are things that I have to build back within myself, my skills…Once we got out the hospital, this is what I want to do. This is what I need to do. I wanna take care of my child better. I want to connect with that." (parent of 9-year-old with acute myeloid leukemia) "I think that as a parent you want your kid to have the best life that they can, the best chance they can at life and being healthy. And I think that with all that she's gone through in her childhood, I want her adulthood to be easier. I want her to not have to worry about her body and just smooth sailing from this point forward." (parent of 6-year-old with acute lymphoblastic leukemia) "I'm worried about, you know, diabetes and being overweight. It's totally unfair for kids to start out their life that way if it's preventable, so I feel like it's something that I have to protect her from." (parent of 6-year-old with acute lymphoblastic leukemia) "But when she was going through treatment, she just wouldn't eat anything. So at that point, it didn't matter what she ate, as long as she was eating. So I wasn't strict at all there, there was no limits. But afterwards, for sure. I tried to eliminate as much as I could…It's a struggle, but it feels good to know that she's not eating all the cancer-causing ingredients." (parent of 5-year-old with acute lymphoblastic leukemia)

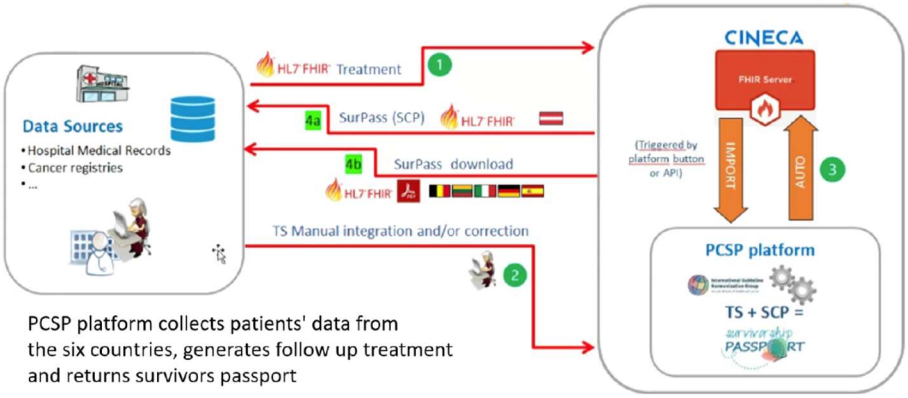
Health Services Research-16

Security and Privacy Support Measures for the Implementation of a Digital Survivorship Passport for Childhood Cancer Survivors: SurPass v2.0

Julia Balaguer Guill, Antonio Orduña Galán, Maria Teresa Tormo Alcañiz, Marisa Correcher Palau, Lucas Cervero, Celia Lucas Jimenez, Jose Vergara Pérez, Adela Cañete Nieto, Riccardo Haupt, Monica Muraca, Roberta Gazzarata, Giacomo Cavalca, Desiree Grabow, Anna-Liesa Filbert, Ruth Ladenstein, Monique Van Helvoirt, Anne Uyttebroeck, Jelena Jascon, Justas Trinkünas, Thorsten Langer, Anke Neumann, Ismay Beijer, Catherine Chronaki, Edit Bardi, Güenter Schreier, Stefan Beyer, Davide Saraceno

Background: Childhood cancer survivors (CCS) often need personalized screenings, but access to prior treatment data is limited. The Survivorship Passport (SurPass) is a platform developed through EU-funded projects. It provides a standardized summary of diagnoses and treatments, and produces a personalized Care Plan using IGHG and PanCare guidelines, tailoring recommendations for long-term follow up.

General Security Requirements
1. Privacy by Design
2. Data Privacy Impact Assessment
3. Local Training Calendar.
4. Software/System Audits.
5. Security Tools.



GDPR - Software/Systems Requirements
Data Protection Principles:
•Fair and Lawful Processing
•Specified Legitimate Purposes.
•Adequate, Relevant, and Limited Data.
•Accurate and Up-to-Date Data.
•Limited Data Retention period.
•Technical and organizational security measures.
Data Subject Rights:
•Inform individuals about data processing activities.
•Allow individuals to access their personal data.
•Allow Portability.
•Delete personal data upon request.
•Correct inaccurate personal data.
•Restrict processing upon request.
•Allow objections to data processing or automation
Accountability: Maintain documented evidences of data breaches, subject access requests, and audits.
International Transfers: Avoid it or ensure secure data transfers outside the UE.
Data Breaches: Implement data breach reporting procedures.

Methods: As it handles sensitive data, compliance with privacy regulations has been assessed, with emphasis on privacy by design, applying appropriate security, accountability and data protection measures.

A multi-step approach strengthened security measures:
•Questionnaire: Evaluated system security measures.
•GDPR Common Framework: Ensured compliance with data protection laws.
•Meetings: Aligned security strategies with development teams
•Privacy Impact Assessment (DPIA): Identified and mitigated system risks.

Key security requirements included privacy by design, DPIAs, structured training, pre-implementation audits, and advanced security tools.

Results: Security measures were successfully integrated into the PCSP-Central platform (CINECA-Italy) and six partner clinics. A compliance assessment showed nearly 100% adherence.
Recommended improvements:
•Data Retention & Removal: Clear policies for secure deletion and archiving. Addition of a form for revoking patient consent.
•Data Encryption: Encrypt or pseudonymize transferred personal data. For stored data: Addition of encryption of sensitive data, logs and generated Passports, implementation of secure access procedures with double authentication.
•Security Enhancements: Strengthen cryptographic protocols, training, operational security, and supplier compliance.

Conclusion: This initiative establishes security and privacy guidelines, ensuring full compliance with European regulations. SurPass v2.0 integrates these standards, providing a secure and transparent solution.

SMN-1

Mortality in Survivors of Childhood Cancer Diagnosed with Subsequent Thyroid Cancer: a Report from the Childhood Cancer Survivor Study

Dana Barnea, Qi Liu, Emily S. Tonorezos, Paul Nathan, Sogol Mostoufi-Moab, Shizue Izumi, Joseph P. Neglia, Greg Armstrong, Kevin Oeffinger, Yutaka Yasui, Lucie Turcotte

Background: Childhood cancer survivors are at increased risk of developing a subsequent thyroid cancer, particularly following radiotherapy. In the general population, thyroid cancer has a very low mortality rate. Mortality after a diagnosis of subsequent thyroid cancer in survivors is unknown.

Methods: We calculated the standardized mortality ratio (SMR) following the development of subsequent thyroid cancer in a cohort of 24,683 5-year survivors of childhood cancer diagnosed between 1970 and 1999 using the age-sex-calendar-year-specific general population all-cause mortality rates from the CDC as the reference rates. We estimated all-cause mortality post the diagnosis of thyroid cancer (time-dependent covariate), adjusting for development of other subsequent malignant neoplasms (SMN) and chronic health conditions (CHC), using a piecewise exponential model. Thyroid cancer-specific mortality among survivors was compared to SEER cases with thyroid cancer, adjusting for age, sex, race and calendar-year. SEER data was also used to compare thyroid cancer characteristics in childhood cancer survivors with thyroid cancer patients without a history of childhood cancer.

Results: Among 397 survivors with subsequent thyroid cancer, 63% were female, 83% had received radiotherapy for treatment of their primary childhood cancer with fields that included the thyroid gland, and 92% had at least one severe or life-threatening chronic condition. Thyroid tumor size was significantly smaller in survivors, with 33% of cases in survivors and 24% in SEER being less than 1 cm ($p<0.001$). There were 82 deaths with 7 deaths due to thyroid cancer. Within the cohort of survivors of childhood cancer, the rate of all-cause mortality did not increase with a diagnosis of thyroid cancer, adjusting for development of other SMNs and CHCs (RR=1.0, P=0.96), but it was 7 times higher than that of the general population (SMR=6.9, 95% CI 5.5-8.5). Compared to adults diagnosed with thyroid cancer in the general population, survivors with subsequent thyroid cancer did not have an increased risk of thyroid-cancer-specific death (RR=0.9, 95% CI 0.4-1.9). Mortality risk was higher among those with older age at subsequent thyroid cancer diagnosis, male sex, Black and Hispanic race and ethnicity and tumor size > 1 cm.

Conclusions: The rate of all-cause mortality does not increase with a diagnosis of subsequent thyroid cancer in childhood cancer survivors. This finding suggests that thyroid cancer screening in this population should be based on reducing morbidity since it likely will not provide survival benefit. Enhanced attention to CHC management may be critical for long-term survival.

Genetics/Genomics-1

Persistent Cytopenia and Hypogammaglobulinemia after Cancer Treatment Reveals Underlying Inborn Errors of Immunity in Childhood Cancer Survivors: a Monocentric Italian Case Series

Andrea Beccaria, Michela Di Filippo, Julia Lasagna, Ramona Tallone, Francesca Bagnasco, Alice Grossi, Isabella Ceccherini, Gianluca Dell'Orso, Marina Lanciotti, Paola Terranova, Michela Lupia, Lisa Pelanconi, Monica Muraca, Riccardo Haupt, Francesca Fioredda, Carlo Dufour, Maurizio Miano

Background: Inborn Errors of Immunity (IEIs) are linked to higher cancer risks, mainly lymphoma, and genetic predispositions underlie many hematologic malignancies. Cytopenias and acquired hypogammaglobulinemia (AHG) following cancer treatment may be transient or persist due to incomplete immune reconstitution. Recent findings suggest these abnormalities may indicate an undiagnosed IEI. Data on cytopenias and AHG in Childhood Cancer Survivors (CCSs) are very limited.

Aim: To evaluate the prevalence and long-term follow-up (LTFU) of persistent cytopenias (PC) and AHG in CCSs after care at the DOPO clinic (IRCCS Giannina Gaslini Children's Institute), describing their clinical, immunologic and genetic characteristics.

Materials and methods: PC is defined as lasting >12 months post-treatment or starting 6-12 months post-treatment and lasting over a year. AHG is defined as persisting >2 years after treatment. CCSs with brain tumor and marrow transplantation recipient were excluded. Immunological and genetic analysis (Next Generation Sequencing of 162 IEI genes or Whole Exome Sequencing) were performed.

Results: Among 755 eligible CCSs (308 with hematologic malignancies), 24 (3%, 75% male, median age at diagnosis 8.7 years, median follow-up 7 years) presented with isolated PC (19) or AHG (3) or coexistence of PC/AHG (2). PC were mainly neutropenia (14/21, 67% and never resolved), more common in hematologic malignancies than solid cancer ($p=0.02$). All AHGs had IgA deficiency and prior Rituximab exposure; 2/5 had opso-myoclonus syndrome and 3/5 required immunoglobulin replacement. Peripheral lymphocyte subpopulations showed in all cohort decreased B memory (mostly switched memory and marginal zone B cells) and T regulatory cells, increased activated δγ+ and HLADR+ T cells and B naïve cells, and a shift to memory T cells compartment. Over follow-up, 6 patients developed autoimmune signs (8.3% incidence at 5 years, median onset 6.0 years post-treatment), 3 had benign lymphoproliferation (one EBV-related). Among 16 CCSs screened for IEI, 9 showed pathogenic mutations in the following genes: TNFRSF13B (2 patients), MAGT1, ITK, GATA2, CEBPA, AIRE, SAMD9, RTEL1; 3/9 developed subsequent malignant tumors (lymphoma, sarcoma, giant-cell carcinoma). Of the 5 CCSs with AHG, 4 (80%) had genetic abnormalities, rising 100% for whom with concomitant PC.

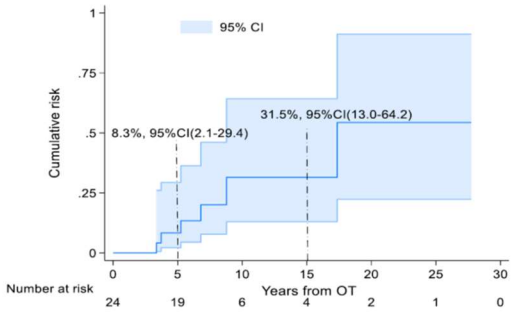
Conclusions: The prevalence of PC/AHG following cancer treatment although low is higher in hematologic malignancies ($p=0.03$). Based on its strong association with genetic abnormalities, AHG alone should raise suspicion of an underlying IEI. PC may suggest underlying IEI, especially in cases with unremitting cytopenia, autoimmunity, lymphoproliferation and a specific immunophenotype. LTFU is recommended for the potential development of autoimmunity and secondary malignancies.

Figure: Features of the cohort (A), cumulative incidence of autoimmune phenomena (B), and lymphocyte subpopulations (C).

A

Gender, n (%)	
Male	18 (75)
Age at cancer diagnosis, years, median (IQR)	8.7 (2.8-11.5)
Cancer diagnosis, n (%)	
Hematological malignancies	15 (63)
Lymphoblastic Leukemia	4
Myeloid Leukemia	1
Hodgkin Lymphoma	4
Non Hodgkin Lymphoma	5
Histiocytosis	1
Non-Hematological malignancies	9 (37)
Neuroblastoma	6
Ewing Sarcoma	1
Schwannoma	1
Nefroma	1
Treatment, n (%)	
Only Chemotherapy	14 (58)
Radiotherapy	5 (20)
Only Surgery	4 (17)
Rituximab	6 (25)
Haematology abnormalities, n (%)	
Cytopenia	21 (88)
with concomitant ipogammaglobulinemia	2
Ipogammaglobulinemia	5 (21)
Cytopenia, n (%)	
Persistent since EoT	9 (42)
Onset after EoT	12 (57)*
Type of cytopenia, n	
Leukopenia	9
Neutropenia	14
Autoimmune (AIN)	3
Idiopathic (IN)	6
AIN/IN diagnosis in progress	5
Lymphocytopenia	7
Monocytopenia	6
Trombocytopenia	8
Anemia	0
*Median time after EoT years (min-max)	2.6 (1.3-8.2)
Median follow-up time after EoT, years (IQR) (min-max)	7.0 (5.2-11.8) (3.7-27.7)
Family history, n (%)	
Relatives with autoimmune disease	11 (46)
1st degree	7
Relatives with cancer	14 (58)
1st degree	1

B



C

	% Low values*	% Normal values*	% High values*
CD3+ (T cells)	22	74	4
CD3+CD4+ (Helper)	26	74	0
CD3+CD4+CD45RA (Naive T Helper)	72	28	0
CD3+CD4+CD45RO (Memory T Helper)	0	33	67
CD3+CD8+ (Suppressor)	26	65	9
CD3CD4CD25brCD45RA+ (T regulatory)	96	4	0
gamma/delta T lymphocytes	13	26	61
CD3HLADR+	9	39	52
CD19+ (B cells)	17	74	9
CD3-CD56+CD16+ (NK cells)	9	87	4
CD19CD27+ (Memory)^	87	13	0
CD27-CD10+-CD38+-IgD+ (Naive B)^	0	23	77
CD27+IgD+IgM+ (Marginal Zone B)^	77	17	6
CD27+IgD-IgM- (Switched Memory B)^	53	41	6
CD27-IgD- (Double negative B)^	0	59	41

Ranges according to ages and to literature *(Morbach H et al, Clin Exper immunol 2021, van Gent et al Clinical Immunology 2008)*
^ perfomed in 17/24

CV-1

Cardiometabolic Outcomes after Bariatric Surgery in Adult Survivors of Childhood Cancer in the St. Jude Lifetime Cohort Study

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Background/Purpose: Survivors of childhood cancer are at increased risk for obesity which can potentiate risk of treatment-related late-effects. Bariatric surgery for treatment of obesity is associated with improved outcomes in the general population but has not been studied in survivors.

Methods: Five-year survivors of childhood cancer enrolled in the St. Jude Lifetime Cohort with a history of bariatric surgery for treatment of obesity (n=33) and survivors with severe obesity (body mass index (BMI) ≥35 kg/m2) who did not have bariatric surgery (n=542) were included in this retrospective cohort study. Survivors had at least one follow-up after baseline (time of bariatric surgery or first recorded BMI ≥ 35 kg/m2 for those without surgery). BMI change from baseline was described. Multivariable logistic regression compared the prevalence of cardiometabolic outcomes (hypertension, dyslipidemia, diabetes, prediabetes, elevated alanine aminotransferase (ALT)) at follow-up reported as odds ratios (OR) with 95% confidence intervals (CI) adjusted for sociodemographic and treatment factors. Piecewise exponential models compared rates of major cardiovascular events, secondary malignant neoplasms (SMNs), and mortality.

Results: The majority of survivors that underwent bariatric surgery were female (69.7%), non-Hispanic White (87.9%), and had a history of a hematologic malignancy (57.6%). Mean age at follow-up was 41.4 years (standard deviation (SD): 9.2) among survivors that had bariatric surgery and 38.7 years (SD: 9.7) among those that did not. Among survivors who underwent bariatric surgery, BMI decreased by an average of 11.8 kg/m2 (standard deviation (SD): 8.7) from pre-surgery, while among survivors without a history of bariatric surgery, BMI increased by 0.7 kg/m2 (SD:4.2) after median follow-up of 6.1 years and 5.3 years, respectively. At follow-up, survivors with a history of bariatric surgery had significantly lower odds of dyslipidemia (OR: 0.3, 95%CI: 0.1-0.8), prediabetes (OR: 0.4, 95%CI: 0.2-0.8), and elevated ALT (OR: 0.4, 95%CI: 0.2-1.0) compared to survivors without bariatric surgery (Table 1). There were no statistically significant differences in rates of major cardiovascular events (rate ratio (RR): 0.7, 95%CI: 0.1-4.0), SMNs (RR: 0.9, 95%CI: 0.2-4.1) and all-cause mortality (RR: 0.5, 95%CI: 0.1-3.9) in this short follow-up period.

Table 1. Model-adjusted odds ratios of cardiometabolic conditions at follow-up in survivors with bariatric surgery compared to survivors without bariatric surgery

Cardiometabolic Condition	Prevalence in Survivors with Bariatric Surgery, n (%)	Prevalence in Survivors without Bariatric Surgery, n (%)	Odds Ratio (95% Confidence Interval)	P-value
Hypertension	18 (54.5)	249 (45.9)	1.6 (0.7-3.8)	0.25
Dyslipidemia	4 (12.1)	141 (26.0)	**0.3 (0.1-0.8)**	**0.019**
Diabetes	10 (30.3)	172 (31.7)	0.8 (0.3-1.8)	0.55
Prediabetes	11 (33.3)	309 (57.0)	**0.4 (0.2-0.8)**	**0.014**
Elevated ALT	18 (54.5)	386 (71.2)	**0.4 (0.2-1.0)**	**0.039**

All models adjusted for age at diagnosis, age at follow-up, sex, race, BMI at follow-up, and insurance status; Hypertension model was also adjusted for nephrectomy, abdominal radiation, total body radiation, smoking; Dyslipidemia, Diabetes, and Prediabetes models were also adjusted for abdominal radiation, total body radiation; Elevated ALT model was also adjusted for hepatic surgery, abdominal radiation, thioguanine, and stem cell transplant
Odds ratios that were statistically significant are in bold.

Conclusions: Bariatric surgery is associated with substantial, sustained BMI reduction in survivors of childhood cancer as well as reduced risk for cardiometabolic conditions. Bariatric surgery should be considered for treatment of obesity in eligible survivors as it is effective for long-term weight loss and may reduce obesity-related morbidity and mortality as survivors age.

Health Services Research-33

Financial Hardship and Non-Adherence to Lifestyle and Screening Recommendations in Adult Survivors of Childhood Cancer: a Report from the Childhood Cancer Survivor Study (CCSS)

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Background: The association between different aspects of medical financial hardship and non-adherence to healthy lifestyle recommendations and screening for subsequent neoplasms (SN) and cardiomyopathy in long-term survivors of childhood cancer is unknown.

Methods: A randomly selected subset of participants in the CCSS completed a financial hardship survey and a follow-up survey assessing lifestyle behaviors and adherence to recommended screening. Presence of financial hardship was determined by affirmative response to ≥1 item in material (e.g., high out-of-pocket costs), behavioral (e.g., delaying care due to cost), or psychological (e.g., worry about financial situation) hardship domains. Outcomes included "not meeting physical activity guidelines" (<9 metabolic-equivalent-of-task-hour/week moderate to vigorous activity), "problematic drinking" (>7 drinks/week or >3 drinks/day [women], >14 drinks/week or >4 drinks/day [men]), current smoker, unhealthy BMI (<18.5 or ≥30 kg/m2), and non-adherence to screening for breast, colorectal, and/or skin cancer, and cardiomyopathy screening according to the Children's Oncology Group guidelines. Logistic regression models, adjusted for age at the most recent survey, sex, race/ethnicity, education, and chronic health conditions, examined the association of material, behavioral, and psychological hardship with healthy lifestyle and screening outcomes.

Results: A total of 3,322 survivors, at a median of 34.4 (range:19.7-51.4) years from diagnosis and 41 (range: 20-69) years of age at the most recent survey were included. Presence of material hardship alone was associated with higher risk of not meeting physical activity guidelines (odds ratio [OR] 1.6, 95% confidence interval [CI] 1.2-2.1) and unhealthy BMI (OR 1.4, 95% CI 1.1-1.8). Presence of both material and behavioral (OR 1.8, 95% CI 1.2-2.6) or material and psychological (OR 1.8, 95% CI 1.4-2.4) hardships further increased the risk for unhealthy BMI. Presence of all 3 hardship domains was associated with higher risk of unhealthy BMI (OR 2.2, 95% CI 1.8-2.7). Behavioral hardship (OR 2.2, 95% CI 1.1-4.6) and psychological hardship (OR 3.9, 95% CI 2.4-6.4) alone were associated with higher risk of being a current smoker at time of follow-up, with presence of both further increasing the risk for smoking (OR 4.1, 95% CI 2.3-7.3) (Table 1a). Presence of psychological hardship was associated with higher non-adherence to cardiomyopathy screening (OR 1.3, 95% CI 1.0-1.8) among those at high risk. Associations between hardship and SN screening were not observed (Table 1b).

Conclusions: Financial hardship is associated with non-adherence to healthy lifestyle and recommended screening for cardiomyopathy among adult survivors of childhood cancer. Findings underscore the need for strategies to identify and mitigate financial hardship and improve adherence to recommended lifestyle and screening.

Table 1a: Associations between financial hardship (qualitative: Yes/No) and health behaviors in childhood cancer survivors

Hardship categories	Physical activity <9 MET-hours/ week vs. ≥9 MET-hours/ week		Problematic drinking behavior (Yes vs. No)		Current smoker vs. never/ former smoker		Unhealthy BMI vs. healthy BMI	
	OR	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**
Material hardship only	**1.6**	**(1.2-2.1)**	0.8	(0.6-1.0)	0.7	(0.4-1.4)	**1.4**	**(1.1-1.8)**
Behavioral hardship only	1.0	(0.7-1.6)	0.9	(0.6-1.4)	**2.2**	**(1.1-4.6)**	1.0	(0.6-1.5)
Psychological hardship only	1.0	(0.8-1.4)	1.2	(0.9-1.6)	**3.9**	**(2.4-6.4)**	1.1	(0.8-1.5)
Material and behavioral	0.8	(0.5-1.2)	1.1	(0.7-1.6)	**2.2**	**(1.1-4.4)**	**1.8**	**(1.2-2.6)**
Material and psychological	1.2	(0.9-1.7)	0.9	(0.7-1.3)	**3.0**	**(1.8-5.0)**	**1.8**	**(1.4-2.4)**
Behavioral and psychological	1.0	(0.7-1.6)	1.0	(0.7-1.5)	**4.1**	**(2.3-7.3)**	1.1	(0.7-1.6)
All three types of hardships	**1.3**	**(1.0-1.6)**	1.0	(0.8-1.3)	**3.7**	**(2.5-5.4)**	**2.2**	**(1.8-2.7)**

Table 1b: Associations between financial hardship (qualitative: Yes/No) and non-adherence to screening in high-risk childhood cancer survivors

Hardship categories	Non-adherence to breast cancer screening		Non-adherence to colorectal cancer screening		Non-adherence to skin cancer screening		Non-adherence to cardiac dysfunction screening	
	OR	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**
Material hardship	0.4	(0.2-1.0)	0.6	(0.4-1.1)	0.9	(0.7-1.3)	0.7	(0.5-1.0)
Behavioral hardship	0.9	(0.3-2.2)	0.8	(0.5-1.4)	1.1	(0.8-1.5)	0.7	(0.5-1.0)
Psychological hardship	2.2	(0.9-5.3)	1.1	(0.7-1.9)	1.2	(0.9-1.6)	**1.3**	**(1.0-1.8)**

Quality of life/Behaviors-7

Weekly Physical Activity Patterns in Short- and Long-Term Survivors of Childhood Cancer Compared to Controls. the PACCS and SURfit Studies

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BACKGROUND: To develop targeted interventions to increase physical activity (PA) in childhood cancer survivors (CCS), in-depth knowledge beyond weekly averages of time in PA is important. We aimed to identify and describe weekly PA patterns in CCS and compare them to age- and sex-matched controls.

METHODS: This study includes child/adolescent (9-18 yrs) CCS and controls from the Physical Activity in Childhood Cancer Survivors (PACCS) study, young adult (18-49 yrs) CCS from the survivor fitness (SURfit) study, and young adult controls from the Norwegian Physical Activity Surveillance Study 2. Moderate-to-vigorous PA (MVPA) was measured with accelerometry (ActiGraph GT3X+), and accelerometer data was harmonized according to suitable criteria for either children/adolescents or adults. Weekly PA patterns were identified by latent class mixed models. We ran separate models for child/adolescent and young adult CCS and controls. We used weekday as timescale and daily average minutes in MVPA as longitudinal outcome. We ran models with 1-8 classes and determined the optimal number of classes using fit indices (AIC, BIC, entropy). We calculated the posterior probability of class membership.

RESULTS: The child/adolescent CCS (n=434, mean age 12.1±2.2 years, 52% males) were, on average, five years old at diagnosis, and 47% were survivors of leukemia. The young adult CCS (n=156, mean age 30.6±8.6 years, 55% males) were, on average, seven years old at diagnosis, and 35% were survivors of leukemia. Compared to controls (n=107 child/adolescent; n=911 young adult), a higher percentage of child/adolescent CCS was overweight/obese (30 vs. 11%), while in the older group, the percentage of overweight/obese was lower among the CCS (33 vs. 43%). We identified the 4-class model as being the best model for MVPA across all samples (Figure). The highest posterior probabilities for the allocated classes ranged from 0.75-1.0. Three classes were comparable between both child/adolescent and young adult CCS and controls. In child/adolescents, slightly more CCS were allocated to a low regular class (~50 min/day; 86 vs 81% in controls), and fewer to a medium, drop weekend class (~90 min on weekdays; 8 vs 13% in controls), or a medium, peak Sunday class (~150 min on Sunday; 2 vs 5% in controls). In young adults, fewer CCS were allocated to a low regular class (~30 min/day; 69 vs 89% in controls), and more to a low, peak weekend class (>60 min on the weekend; 10 vs 5% in controls). Both young adult groups were allocated to a class with regular MVPA on weekdays, but with different levels of MVPA (~70 min for CCS (21%) and ~90 min for controls (5%)).

CONCLUSIONS: The majority of both child/adolescent and young adult CCS were allocated to a low MVPA class. However, while more child/adolescents CCS than controls were allocated to this class, fewer young adult CCS than controls were. Unfavorable PA patterns may exacerbate CCS' already elevated risk of late effects from cancer treatment.

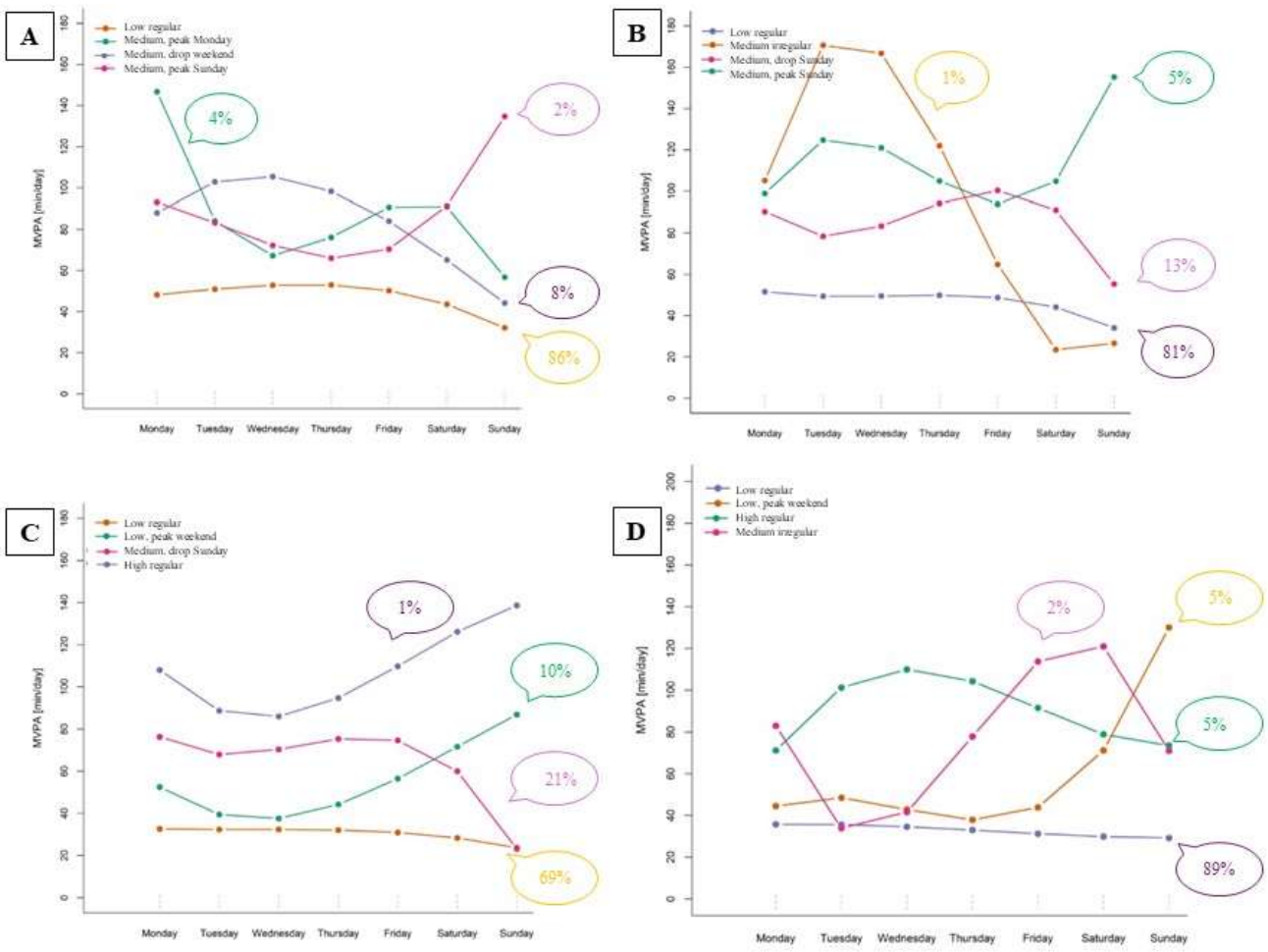


Figure: Identified average trajectories of MVPA in child/adolescent CCS (A) and controls (B), and in young adult CCS (C) and controls (D)

Quality of life/Behaviors-8

Quality of Life of Leiomyosarcoma Survivors: Continued Screening for Recurrence

Caroline Brown, Joseph Gallo

Previous research has found anxiety, stress, and issues with body image in the experiences of those who have survived reproductive cancer, especially women. There have also been reports of Scanxiety, in which survivors experience significant spikes in anxiety in the periods before and after screenings for cancer recurrences. The goal of this study is to assess the association between Scanxiety and surveillance.

Leiomyosarcoma is a rare sarcoma most commonly found in people assigned female at birth. It can occur in several locations in the body, but uterine leiomyosarcoma is the most common site (Byar & Fredericks, 2022). Over the last few decades, the prognosis of the disease during a first occurrence has improved significantly, but recurrences a few decades after treatment are common. Once leiomyosarcoma patients have reached the point of having no evidence of disease, they typically begin screening at fixed intervals based on an individual's disease. Anomalies may cause more frequent screenings, and long stretches without concerning results typically result in longer periods between additional screenings.

Some patients become extremely anxious around screenings due to concerns about recurrence, the financial burden of travel, and the pain sometimes involved in screenings. Some studies have explored the impacts of these feelings in more common cancers, finding high rates of anxiety especially among the newly diagnosed (Bui et al., 2022; Derry-Vick et al., 2023).

Participants will be recruited through the LMSDR support group on Facebook. This project will be conducted virtually with no direct contact with participants. Interested members of the LMSDR Facebook group will follow a link or QR code to be screened for eligibility in Qualtrics. Eligible participants will then receive access to the study questions.

The survey is a one-time virtual survey. First, we will collect demographic information to characterize the sample, including age, race or ethnicity, and gender. We will then collect more specific details to help us characterize the sample, including information on past leiomyosarcoma recurrences, travel to screenings for recurrence, and interactions with medical providers. Many of these questions are open-ended with boxes to allow participants to share details about their experiences. Next, we include the GAD-7 (General Anxiety Disorder) and PHQ-8 (Patient Health Questionnaire) instruments to assess symptoms of anxiety and depression. Finally, we invite participants to share any additional thoughts in open-ended questions.

We will begin analyzing the data by examining frequencies and distributions of all quantitative data and explore text data from open-ended questions. We will examine the demographic characteristics of the sample and do cross tabulations to compare data across relevant characteristics such as sex and age.

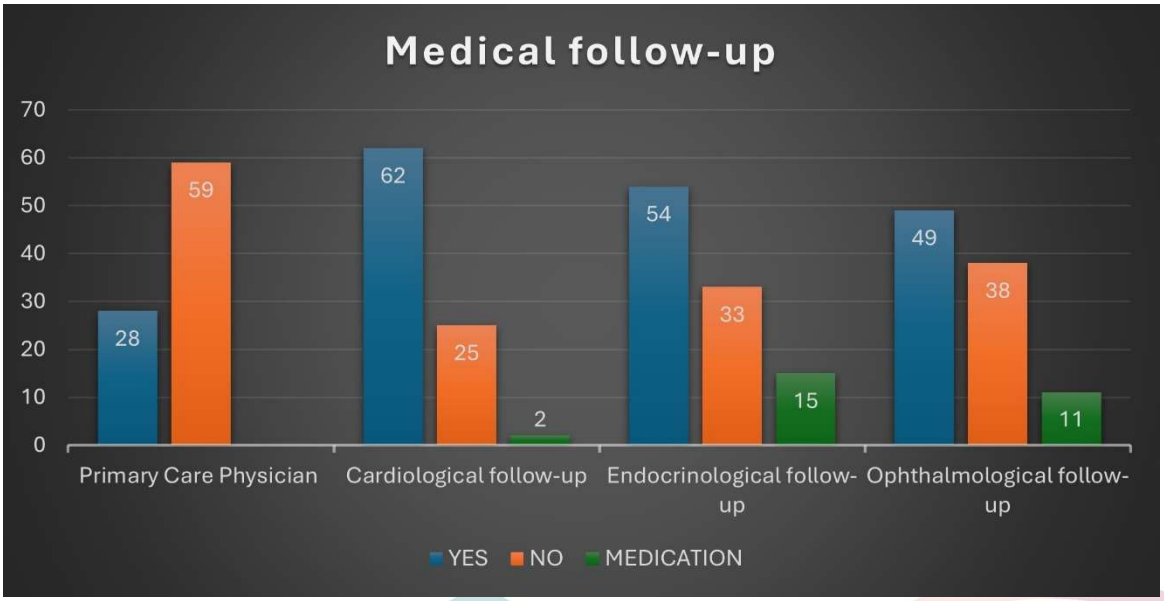
Continuity of Medical Follow-Up in Pediatric Cancer Survivors

Constanza Cafferata, Romina Corona, Paola Lidia Francisca Reichel

BACKGROUND: Follow-up of pediatric cancer survivors is necessary for the early detection of possible sequelae and complications. Unfortunately, a small percentage of patients may access post-treatment check-ups due to multiple reasons: distances, economic resources, age limits for pediatric care, and a lack of trained human resources. The objective of this study is to evaluate the continuity of medical follow-up in oncology patients once chemotherapy treatment has been completed.

METHODS: The medical records of patients treated in our Oncohematology Service over the past 8 years were analyzed. Patients who had completed intravenous chemotherapy treatment up to 5 years after diagnosis were included. Deceased patients and patients with neurofibromatosis were excluded. The following data were collected: availability of a primary care physician or pediatrician, follow-up by a specialist (cardiology, endocrinology, ophthalmology), and whether they had any treatment sequelae or a second illness.

RESULTS: A total of 87 patients were included. The main oncological diagnosis was Acute Lymphoblastic Leukemia. Twenty-nine patients (33.3%) had a primary care physician who was familiar with their medical history and whom they could contact in emergencies. 63.2% (55 patients) were followed by a specialist (cardiology, endocrinology, or ophthalmology), and 32% received some type of medication from them. The most frequently found sequelae were hypothyroidism and vitamin D deficiency. Eleven patients (10%) wear glasses. Two patients developed a second illness within 5 years of diagnosis.



CONCLUSIONS: The care of childhood cancer survivors is important and requires an organized healthcare system for such care. Although few patients have primary care physicians, more than half continue follow-up with a specialist. This may be due to patients continuing to attend check-ups in the Oncology Service, where the functions of the primary care physician are covered.

Implementing Disease-Based Long-Term Follow-Up Care Plans for Childhood Cancer Survivors: a Comprehensive Protocol

Jiaoyang Cai, Yin Ting Cheung, Melissa Hudson

Background: Long-term follow-up care is essential for childhood cancer survivors (CCSs) due to the risk of late effects and chronic health issues. Survivors often face fragmented care, leading to poor adherence and delayed detection of complications. Despite guidelines emphasizing survivorship care, there is a lack of disease-specific, structured care plans tailored to individual patient needs. A disease-based long-term follow-up (LTFU) care plan for managing late effects and promoting health maintenance could address these gaps by offering personalized, structured guidance for both patients and healthcare providers. The goal is to assess the effectiveness, feasibility, adoption, and impact of a structured LTFU model to enhance survivorship care.

Methods and Analysis: The study consists of three phases: the development phase, which involves creating and refining disease-based LTFU care plans through expert consensus and stakeholder input; the implementation phase, where the care plans are piloted at selected institutions and integrated into routine survivorship care; and the evaluation phase, which assesses effectiveness, adherence, patient and provider feedback, and scalability. Disease-based LTFU care plans will be developed based on existing guidelines (COG and International Guideline Harmonization Group [IGHG]). The implementation of disease-based LTFU care plans will follow a multi-faceted strategy, including provider training, patient education, clinical integration, and continuous quality improvement. This prospective, multi-center implementation study will utilize the RE-AIM (Reach, Effectiveness, Adoption, Implementation, and Maintenance) framework to guide the development and evaluation of disease-specific LTFU care plans. Key outcomes will include care plan utilization rates, adherence to follow-up care, patient-reported outcomes, health outcomes, patient satisfaction, and long-term integration of structured LTFU programs into clinical practice. Descriptive statistics will be used for LTFU adherence rates and health outcomes. Logistic regression models and thematic qualitative analysis will be used to identify predictors of adherence and provider/patient feedback, respectively. By implementing disease-specific LTFU care plans, we anticipate: higher adherence to follow-up visits and screenings; improved early detection of late effects; better coordination between oncologists, primary care physicians, subspecialty physicians, and survivorship teams; increased patient satisfaction and engagement; and scalability of disease-based LTFU models to other pediatric cancer centers.

Table 1. RE-AIM Matrix for Disease-Based LTFU Care Plan

RE-AIM Dimension	Definition	Key Measures
Reach	Proportion of childhood cancer survivors engaged in the LTFU care plan	Number of eligible survivors enrolled; demographic disparities in access
Effectiveness	Impact of LTFU on health outcomes, adherence, and patient satisfaction	Follow-up adherence rates, detection of late effects, patient QoL scores
Adoption	Integration of LTFU into oncology and primary care settings	Provider participation, institutional buy-in, interdepartmental collaboration
Implementation	Processes used to implement disease-specific LTFU care plans	Fidelity to care plan guidelines, provider training, workflow integration
Maintenance	Sustainability and long-term integration of LTFU care plans	Long-term follow-up adherence, EMR tracking, expansion to new sites

Discussion: The RE-AIM framework will ensure a comprehensive assessment of how well disease-based LTFU care plans function in real-world clinical settings. This study will provide critical insights into how survivorship programs can be systematically improved, and serve as a foundation for policy development in pediatric oncology survivorship programs.

Health Services Research-19

Mapping of Current Resources and Models of Care for Paediatric Cancer Survivors in Asia: a Multinational Survey

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Background: Pediatric cancer survivorship is an emerging priority in the current global child health agenda. The models of long-term follow-up (LTFU) care in Asia may vary widely based on differences in healthcare systems and resources. This study aims to characterize the models of care and current resources available for pediatric cancer survivors in Asian countries.

Methods: This multinational, cross-sectional survey study was conducted from February to May 2024. Study participants included clinicians who are practicing in an institution/center in the United Nations geoscheme. They were recruited using a combination of purposive and snowball sampling, and were identified through the 18th St Jude-Viva Forum in Singapore and through local professional societies. Each participating institution was invited to nominate a representative to complete a structured questionnaire, which focused on the institution's characteristics of LTFU care, the availability of risk-based screening tests according to the Children's Oncology Group Long-term Follow-up Guideline, and the availability of recommended services in an LTFU program.

Results: The survey recruited participants representing 87 pediatric oncology units/institutions from 28 Asian countries/regions (27% HICs, 30% UMICs and 43% LMICs). There were no significant differences between LMICs, UMICs, and HICs in providing the majority of the basic late-effects screening tests.

The majority of the institutions provided LTFU care through specialized LTFU clinics (44%) or oncologist-led clinics (45%). Significantly more institutions with specialized LTFU clinics offered assessments by multidisciplinary professionals, e.g. motor skills (74% versus 46%, p=0.01) and speech/language (66% versus 36%, p=0.008) assessments, than institutions adopting other models of LTFU care. Institutions with LTFU clinics are also more likely to provide health risk counselling (p=0.03), fertility preservation (p=0.018), pain clinics (p=0.008), and nutrition programs (p=0.018).

Half of the institutions (57%) reported adhering to an established international or local survivorship guideline to determine the type and frequency of screening practices. The remaining 43%, of which half were from LMICs, reported that their LTFU practices were determined solely at the clinician's discretion. Institutions that reported adhering to a LTFU guideline were more likely to provide more comprehensive visual assessment (p=0.012) and provide health risk counselling (p<0.001) than institutions that did not adhere to any specific guideline.

Conclusion: Our findings demonstrated that establishing a LTFU clinic according to evidence-based guidelines can facilitate more comprehensive late-effects screening and support for survivors. Regional collaborations should aim to develop resource-stratified recommendations and policies for coordinated and integrated LTFU care in Asian countries.

Neurocog-1

Trajectory of Cognitive Complaints and Its Association with Role Functioning in Chinese Adolescents and Young Adults with Cancer

Yin Ting Cheung, Panpan Xiao, Yihui Wei, Yan Kate Chow, Chun-Kit Ngan, Alex Wing-Kwan Leung, Herbert Ho Fung Loong, Chi Kong Li

Background/Purpose: Changes in the cognitive functioning of adolescent and young adult (AYA) patients throughout the cancer continuum may have implications on their functional limitations in everyday life. This study aims to identify clinical characteristics associated with cognitive functioning trajectory and its association with role functioning outcomes.

Methods: This multicenter prospective study comprised AYAs diagnosed with cancer (aged 15–39 years) who were followed every 4 to 6 months from baseline to one year after recruitment. At each time-point, AYAs reported their role functioning in performing work/school, home and leisure activities (Life Functioning Questionnaire). The predictive characteristics include symptom burden (Rotterdam Symptom Checklist), cognitive complaints (CCSS-Neurocognitive Function Questionnaire), and baseline clinical and sociodemographic characteristics. Generalized estimating equation was used to test for changes in role functioning and cognitive functioning scores, with interacting terms (time*factor) added to identify differences in the score trajectory, adjusting for age, sex, and cancer diagnosis.

Results: Overall, 421 AYAs (female: 59.6%, mean age: 31.51 ± 8.35) were recruited, of whom 71.3% were diagnosed in young adulthood. At baseline, AYAs reported significant cognitive complaints (T-score>65 points relative to community controls) in task efficiency (23.5%), emotional regulation (24.7%), organization (15.9%), and memory (18.1%). Survivors reported functional limitations in performing family duties (26.2%) and disruptions (29.7%) or limitations (14.9%) at work/school. In this preliminary analysis, a subgroup of 120 AYAs completed follow-up assessment at mean duration 23.9 [SD=16.7] weeks. In terms of treatment characteristics, AYAs who received radiation experienced greater functional decline in duties at home (P=0.011) than those who did not. AYAs who reported higher symptom burden at baseline reported significantly more memory decline (p=0.025) and disruption in work/school functioning (p=0.0117). AYAs with more severe problems in task efficiency at baseline demonstrated greater decline in quality interaction with family (p=0.025) and performing duties at work/school (p=0.013). Subsequently, an increase in self-reported task efficiency problems over time was associated with greater declines in work/school (p=0.0049) and family (p=0.0002) role functioning.

Conclusions: This preliminary data suggests that characterizing functional outcomes trajectories in AYA patients during the cancer care continuum may help identify high-risk groups and the appropriate window for implementing supportive interventions. For example, AYAs who presented with deficits in high-order thinking skills, such as task efficiency complaints, should undergo interventions early before symptoms negatively affect functional outcomes later in survivorship.

Other late effects-11

Vaccine-Mediated Humoral Immunity in Childhood Cancer Survivors: Are They Protected?

Smita Dandekar, Renee Rencher, Jamie Cashell, Scott Schmid, Myron Levin, Amy Brown, Melanie Comito

BACKGROUND: Cancer affects children of all ages, disrupting planned immunizations against vaccine preventable diseases. Additionally, cancer therapy significantly alters the immune system both during and after completion of therapy. No validated guidelines exist for surveillance testing or re-immunization in this population. This study aimed to determine the proportion of pediatric cancer patients who have lost humoral immunity to selected previously received vaccines by end of cancer directed therapy and the proportion of this group who regained vaccine-mediated immunity at 6 and 12 months off therapy respectively.

METHODS: Thirty-one patients between the ages of 15 months to 18 years who had received at least 1 dose of the vaccines of interest and were within 6 months from completion of all cancer directed therapy were recruited to the research study from Penn State Health Children's Hospital and Upstate Golisano Children's Hospital. Subjects were tested for antibody levels to hepatitis-b, tetanus, varicella, rubeola, and pneumococcus (strains 4, 6B, 9V, 18C, 19F, and 23F, those present in PCV7 and PCV13 vaccines) at three time points: end of therapy, 6 months and 12 months off therapy via commercial laboratory testing methods. Following the 12 months off therapy titer results, recommendations were given to each child's pediatrician so the appropriate vaccinations could be repeated. If a child did not demonstrate immunity following revaccination, referral was made to Pediatric Immunology for a comprehensive immunologic work-up.

RESULTS: This study demonstrated that of the 31 childhood cancer survivors who had recently finished cancer treatment, only 16% of the patients retained humoral immunity to >50% of pneumococcal strains tested at the end of therapy with no further change at the 12 months post chemotherapy timepoint. On the other hand, all patients retained immunity to tetanus at all 3 times points (end of therapy, 6 months off therapy and 12 months off therapy), which is consistent with the high immunogenicity of tetanus toxoid. 90% of the patients retained immunity to measles at end of therapy with sustained response at 12 months off therapy. Hepatitis B and Varicella titers were lower at the end of therapy for all participants and about 50% of the subjects regained immunity over the course of the 12 months. Of those who were non-immune to pneumococcus at the 12 months off therapy standpoint, 4 patients were unable to demonstrate adequate titers despite vaccination with the polyvalent pneumococcal vaccine Pneumovax 23 and were identified to have an immunodeficiency (inherent vs acquired post cancer) and are followed by immunology.

CONCLUSIONS: A significant percentage of children treated for cancer do not retain immunity to previously administered childhood vaccines. Standardized guidelines are needed to protect this population from vaccine-preventable illness in the post chemotherapy period.

Other late effects-1

Effect of Pelvic External Beam Radiation Therapy on Lower Urinary Tract Function

Michael Edwards, Andrew Nicklawski, Gemma Beltran, Elizabeth Stein, Jennifer Pyrzanowski, Nicholas Cost

Background: Children and young adults with pelvic solid tumors often receive multi-modal treatment including chemotherapy, external beam radiation therapy (EBRT), and organ-sparing surgery. This combination approach affords the best chance of cure while avoiding the morbidity of pelvic exenteration, but long-term effects on lower urinary tract (LUT) function are not well-describe. This study investigates the effect of EBRT on LUT function by comparing patient-reported outcome measures, non-invasive urodynamic studies, and post-void residuals (PVRs) amongst childhood cancer survivors (CCS).

Methods: All subjects were CCS >1 year off-therapy for a pediatric solid tumor. Subjects were divided into two cohorts: a study cohort of patients who received pelvic EBRT and a control cohort who received only chemotherapy. Research subjects completed the Dysfunctional Voiding Scoring system (DVSS) survey, uroflow testing, and PVR bladder scan.

Results: Thirty-two patients enrolled. Sixteen patients received pelvic EBRT. There were eight female and eight male patients in each cohort. There were an equal number of patients exposed to alkylators (69%) in each cohort. Patients were an average of 14.6 years old and 5.3 years off therapy in the study cohort and 12.0 years old and 4.0 years off therapy in the control cohort. The radiation-exposed group was more likely to have abnormal uroflow patterns (81% vs 56%, p=0.12), both exceeding the 10-15% expected in a healthy population. The flow pattern distribution differed between groups (p=0.03); the study cohort was more likely to have a “plateau” shaped curve (44% vs 6%), indicating possibility of bladder outlet obstructive physiology. Accordingly, the study cohort had significantly higher post-void residual (PVR) values (39ml vs 14ml, p=0.0008) and odds (OR 9.0, p=0.002) of an abnormal PVR compared to age-based norms. In conditional LR model, adjusting for time off therapy, those who received radiation had 5.78x the odds of having an abnormal uroflow pattern (p=0.077). There did appear to be a dose-based response, as those with high-dose radiation (>20Gy, n=8) had an OR of 13.2 (p=0.057) compared to those who did not receive radiation, and those with low-dose radiation had an OR of 2.23 (p=0.4). There was no difference in DVSS scores between cohorts, nor was it shown to be an accurate screener for abnormal niUDS, with a sensitivity and specificity of 54.5% and 50%, respectively.

Conclusion: EBRT appears to affect LUT function in CCS who received pelvic EBRT, resulting in an increased rate of high PVRs and abnormal uroflow patterns. DVSS does not appear useful as a screening tool in this population. Further study is needed to better appreciate the impact of EBRT on LUT function, to study the progression of patient-reported outcomes, and develop more accurate screening tools.

CV-2

Prevalence and Risk Factors of Diastolic Dysfunction among Adult Swiss Childhood Cancer Survivors – Results of the CardioOnco Study

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Background/Purpose: Diastolic dysfunction is associated with an increased risk of all-cause mortality in the general population. Evidence from the literature indicates that diastolic dysfunction precedes systolic dysfunction in adults after cardiotoxic cancer treatment and may therefore play an important role in the progression of heart failure. Identifying childhood cancer survivors with diastolic dysfunction and preserved left ventricular ejection fraction (EF) may be beneficial to early detect survivors at risk for cardiotoxicity.

Methods: As part of the CardioOnco study, a prospective multicenter cohort, we invited childhood cancer survivors ≥18 years of age, diagnosed between ages 0–20, treated in one of five pediatric oncology centers across Switzerland between 1976–2019, and who survived ≥5 years. Survivors received an echocardiographic assessment of diastolic function. We measured average E/e' (E velocity divided by mitral annular e' velocity), septal and lateral e' velocity (mitral annular e' velocity), tricuspid regurgitation velocity (TRvmax) and left atrial volume index (LAVI) and classified diastolic function according to the 2016 American Society of Echocardiography (ASE) / European association of Cardiovascular Imaging (EACVI) guidelines.

Results: We performed echocardiography in 570 survivors, with a median age at study of 32 years (interquartile range [IQR] 25 – 39) and a median time since cancer diagnosis of 25 years (IQR 17 – 32). 446 survivors had complete echocardiographic assessment to investigate diastolic function. The overall prevalence of diastolic dysfunction was 4.5% (20/446) with the highest proportion among survivors exposed to anthracycline and heart-relevant radiotherapy (6.2%, 5/81). In survivors with preserved ejection fraction (EF), the prevalence of diastolic dysfunction was 0.5% (2/428). In 90% (18/20) of survivors with diastolic dysfunction, reduced EF was present. Factors associated with higher odds of diastolic dysfunction were cumulative anthracycline dose (odds ratio (OR) = 2.1; 95%CI 1.3 – 3.8; per 100 mg/m² increase), hematopoietic stem cell transplantation (HSCT) (OR = 22.96; 95% CI 4.11 – 150) and smoking (OR = 1.2 per pack year; 95% CI 1.0 – 1.3). Cumulative heart-relevant radiotherapy was not associated with higher odds of diastolic dysfunction (OR 0.9; 95% CI 0.56 – 1.30; per 10 Gy increase).

Multivariable Logistic Regression - ASE/EACI

Variable	Odds Ratio (95% CI) OR[1]	95% CI[1]	p-value
Age at examination	1.085	1.00, 1.19	0.065
Sex			
Female	1.192	0.29, 5.36	0.8
Cumulative dose anthracyclines *per 100mg/m2 increase*	2.085	1.25, 3.77	0.008
Cumulative Dose CRT *per 10 Gy increase*	0.885	0.56, 1.30	0.6
Cumulative alkylating agents *per 100mg/m2 increase*	1.007	1.00, 1.01	0.054
Cumulative cisplatin *per 10mg/m2 increase*	1.012	0.98, 1.04	0.4
Cumulative steroids *per 100mg/m2 increase*	0.998	0.97, 1.02	0.9
HSCT, yes	22.96	4.11, 150	<0.001
Dyslipidemia	0.372	0.01, 3.14	0.4
Smoking *per pack year*	1.147	1.00, 1.30	0.026

Table 1: Multivariable logistic regression for diastolic dysfunction. OR = odds ratio; CI = confidence interval

Conclusion: Overall prevalence of diastolic dysfunction in adult childhood cancer survivors was low and mainly concurrent with systolic dysfunction. Survivors who were treated with anthracyclines, hematopoietic stem cell transplantation and who smoked had higher odds for cardiac dysfunction. Given the evidence that diastolic dysfunction may precede systolic dysfunction after cardiotoxic therapy, we weren't able to detect early diastolic dysfunction by using the ASE/EACVI guideline. Further research with different approaches is needed to detect survivors at risk for early cardiotoxicity.

Genetics/Genomics-2

Two Novel Loci Associated with the Risk of Vestibular Dysfunction among Childhood Cancer Survivors

Jennifer French, Matthew Wogksch, Johnnie K. Bass, Clinton Stewart, Melissa Hudson, Greg Armstrong, Yadav Sapkota, Kiri Ness

Background: Childhood cancer survivors have an increased risk of cancer treatment-related vestibular dysfunction (VD). The potential role of genetic susceptibility in risk of VD in survivors remains unclear.

Methods: We included 1,762 childhood cancer survivors of European (EUR) genetic ancestry (276 with VD) and 326 of African (AFR) genetic ancestry (98 with VD) from the St. Jude Lifetime Cohort, all of whom had whole-genome sequencing and VD testing. VD was assessed using the sensory organization test with computerized dynamic posturography and defined as the ratio of time spent in normal sway with eyes closed and a moving surface compared to with eyes open and a stable surface < 0.93. Logistic regression estimated the association between common genetic variants and VD risk in EUR, adjusting for age at assessment, age at primary childhood cancer diagnosis, sex, exposures to carboplatin, cisplatin, aminoglycosides (AGs), vincristine, and first three genetic principal components. The 3 most common AGs were gentamicin, amikacin, and tobramycin in both EUR and AFR. None of the survivors included in the analysis were exposed to radiation. Loci with P≤1x10-6 in EUR were examined in AFR and evaluated in stratified analyses by treatment exposures.

Results: The mean (standard deviation) age at diagnosis was 8.8 (6.0) years in EUR and 8.6 (5.8) years in AFR. Two loci (TTC7B and LRRC3B) were suggestively associated with VD risk among EUR. An intronic variant in TTC7B, rs2896142-T, was associated with an increased odds of VD in EUR (minor allele frequency [MAF]=0.01; odds ratio [OR]=5.25, 95% CI=2.76-9.99, P=4.5x10-7) and decreased odds in AFR (MAF=0.30; OR=0.62, 95% CI=0.41-0.93, P=0.022). An intronic variant in LRRC3B, rs140916738-A, was associated with VD in EUR (MAF=0.03; OR=2.88, 95% CI=1.89-4.39, P=9.3x10-7) but not in AFR (MAF=0.008, P=0.68). The association of rs2896142-T with VD was stronger in EUR exposed to AGs (OR=29.67, 95% CI=3.90-225.2, P=0.0010than unexposed (OR=4.32, 95% CI=2.14-8.74, P=4.5x10-5), while no association was observed (P=0.30) among AFR when stratified by AGs exposure. rs2896142-T was associated with VD risk among EUR (OR=6.03, 95% CI=3.11-11.71, P=1.1x10-7) and AFR (OR=0.57, 95% CI=0.36-0.89, P=0.013) survivors unexposed to cisplatin, but not exposed survivors (P=0.99 and 0.37, respectively). rs140916738-The prevalence of rs140916738-A was not sufficiently high among cisplatin-exposed EUR and AFR for stratified analysis. The TTC7B protein is a component of a complex required to localize phosphatidylinositol 4-kinase to the plasma membrane and for myelin formation. LRRC3B encodes membrane proteins in olfactory receptor neurons; expression is associated with impaired membrane transport of calcium.

Conclusions: While neither TTC7B nor LRRC3B have previously been associated with dizziness, hearing loss, or VD, these data suggest a potential combined role of genetics and chemotherapy treatment exposure for VD.

Endo-1

Bone Health and Physical Activity in Pediatric Cancer Survivors

Jordan Fritch-Hanson, Melissa Acquazzino, Reece Blay, Laura Bilek, Crystal Krause, Christopher Wichman, Melissa Cole

Background: While there is a growing population of pediatric cancer survivors (PCS) due to improved treatment efficacy, PCS are at high risk for treatment-related complications, including poor bone health and various metabolic conditions. Bone mineral density (BMD) illustrates the effect of lifetime exposures and habits on the skeleton and is used to assess fragility and predict fracture risk. Bone mass rapidly increases during childhood and adolescence, a time during which PCS experienced diseases and treatments that changed their bone metabolism and hormone production. When there is disruption of bone formation at an early age, children are at risk of having lower peak bone mass and higher risk of fractures throughout their life. In healthy children, bones are strengthened by the mechanical stress of physical activity (PA). Studies have shown people who perform at least 75 minutes of weekly vigorous-intensity PA (VPA) had higher BMD. PA may improve bone loss from cancer treatment. Data is limited on the effects of PA on bone health in PCS, and guidelines to prevent loss of and improve bone mineral density (BMD) are lacking.

Objectives: To evaluate the effect of PA on bone health.

Design/Method: Prospective cohort study enrolled acute lymphoblastic leukemia and lymphoma survivors (ages 5-18) that were 1-13 months post-treatment. At baseline and 6 months, metabolic health (labs/DXA body composition), bone density (DXA) and activity level (accelerometry/questionnaire) were evaluated. For primary outcome evaluation, bone density change between baseline and 6 months was compared between participants of low and high activity level using Wilcoxon's Rank Sum test.

Results: From January 2022 to December 2023, 37 survivors were enrolled. Baseline participant characteristics are shown in Table 1. Survivors that met moderate-to-vigorous PA (MVPA) recommendations were younger at study enrollment and cancer diagnosis and farther off treatment. There was no difference in BMD at baseline or change in BMD at 6 months between survivors that met recommended MVPA (n=31) or VPA (n=11) levels versus those that did not (n=6 and 26). There was no difference in BMD at baseline or change in BMD at 6 months between the survivors that had vertical impact counts greater than the median (n=11) versus those that were below the median (n=26). Majority of survivors did experience an improvement in BMD over the 6-month study period. Data analysis is ongoing.

Conclusion: Poor bone health is seen in ALL/lymphoma PCS after therapy completion. Final study results may help design an interventional PA study to improve bone health in PCS. Study conclusions limited due to small sample size.

Table 1 Baseline Characteristics Based on Physical Activity Status (N=37)

Characteristics	Met MVPA Recommendations (*n* =31)	Not Met MVPA Recommendations (*n* = 6)
Age, yrs		
Median (IQR)	8.0 (5.5-15.5)	15.0 (11.0-16.75)
Gender		
N% Female	14 (45.2%)	3 (50.0%)
Age at Cancer Diagnosis		
Median (IQR)	5.0 (3.0-12.8)	12 (8.0 – 14.5)
Months Since Treatment		
Median (IQR)	2.0 (1.0-6.0)	6.0 (2.8-7.8)
BMI		
Median (IQR)	18.9 (16.2-23.4)	20.5 (16.5-30.0)
BMI Z-score		
Median (IQR)	0.8 (-0.1-1.4)	0.5 (-0.5-1.6)
Race/Ethnicity		
Number (%)		
White/Not Hispanic	20 (64.5%)	3 (50.0%)
White/Hispanic	6 (19.4%)	2 (33.3%)
Black or African American	1 (3.2%)	1 (16.7%)
More than one race	2 (6.5%)	0 (0.0%)
Unknown / DNR	2 (6.5%)	0 (0.0%)
Diagnosis		
B-cell ALL	22 (70.9%)	4 (66.7%)
T-cell ALL	4 (12.9%)	0 (0.0%)
Hodgkin lymphoma	3 (9.7%)	0 (0.0%)
Non-Hodgkin lymphoma	2 (6.5%)	2 (33.3%)
Cancer Treatment		
Steroids (Dex + pred + prednisolone)	31 (100%)	6 (100%)
High dose methotrexate	11 (35.5%)	3 (50.0%)
Vincristine	30 (96.8%)	6 (100%)
Cranial radiation therapy	1 (3.2%)	0 (0.0%)
Activity Questionnaire		
PAQ Score, Median (IQR)	2.6 (2.0-3.3)	2.7 (2.7-2.7)

Quality of life/Behaviors-9

Incorporating Psychiatric Behavioral Health Screening in the Oncology Survivorship Clinic

Kahla Gagne-Loparo, Lisa Hackney, Amelia Baffa

Background/Purpose: It is well documented in the literature that survivors of childhood cancer experience psychological late effects. International Guidelines Recommend Screening for Anxiety and Depression at every survivorship encounter regardless of age. This can be difficult to obtain in a fast-paced clinical care setting where patients have increasingly complex behavioral health (BH) needs. This presentation will describe our experience of embedded Psychiatric Nurse Practitioner (PMHNP) and her students as a front line for screening in referral in a busy oncology survivorship clinic.

Methods: The start of each survivorship encounter begins with PMHNP, who screens patients for symptoms of depression and anxiety PROMIS after being roomed by the MA. She then triages mental health needs of the patient during her encounter. Length of visit varies from 10-20 minutes based on the severity of need. The focus of the visit is to screen for depression and anxiety during their annual survivorship visit. The goal is identifying any needs they may have and helping coordinate their mental health resources. If they do not have a provider, then work them up diagnostically and develop a treatment plan. She'll continue to care until she can help them transfer to a community mental health provider. Referral is made if necessary to outside Behavioral Health Organizations, to therapy with Oncology BH LISW and potential medication management as appropriate by PMHNP, her assessment gives the physician and Pediatric Nurse Practitioner with data on the overall psychological wellbeing prior to the survivorship visit. An additional benefit is that the patient and families are made aware of the psychosocial needs and normalizes the needs assessment as part of routine survivorship care.

Results: PROMIS screening identified BH needs with symptoms in 20 % (1/2) of patients. The majority of previously unidentified or untreated patients had mild to moderate symptoms and were candidates for interventions with PMHNP. Although less than half were referred to outside services, 10% related to mental health needs in the community.

Conclusions: In our experience incorporating PMHNP and PMH students into our survivorship visits has been well received by patients and has decreased the time that the medical team is spending discussing these areas. As an added benefit this helps to meet the patients where they are and connects them to much needed interventions in the community. In larger programs or areas with less robust pediatric mental health opportunities this model may not fit. This model is a worthy time investment that allows for interdisciplinary collaboration and makes room for survivorship medical team to complete a very thorough Review of Systems and educate on late effects as the patient's distress is addressed the start of the visit.

Health Services Research-34

Barriers to, Facilitator of, and Implementation Strategies for Global Pediatric Cancer Survivorship Care

Nicholas Geoorge, Amela Siječić, Grace Cross, Sara Malone, Lisa Force, Melissa Martos, Nickhill Bhakta, Matthew J. Ehrhardt, Maura Kepper

Background: As more patients with childhood cancer experience improved treatment outcomes, challenges arise with ongoing care needs due to a higher risk of mortality and chronic health conditions compared to the general population. Survivorship care is essential for managing both the physical and psychosocial effects of cancer treatment, as well as preventing secondary health problems. To improve follow-up care globally, it is important to understand how care is provided and identify the barriers and facilitators, especially in low and middle-income countries (LMICs). While existing research in high-income countries has highlighted issues such as insurance access, racial disparities, and program funding, challenges in LMICs have not been fully explored. This study used the Consolidated Framework for Implementation Research (CFIR) to systematically examine the multi-level barriers, facilitators, and strategies for implementing survivorship care in LMICs.

Methods: This systematic review was conducted from a larger systematic review (PROSPERO registration CRD42021242548). A total of 8,456 articles were reviewed. The search identified 10 eligible articles mentioning barriers and facilitators to survivorship care across LMICs. Data were extracted from these articles using the CFIR domains of innovation, outer setting, inner setting, and individuals. Assigned CFIR constructs were then paired with Expert Recommendations for Implementing Change (ERIC) strategies using the CFIR-ERIC matching tool.

Results: The 10 studies were published between 2003-2020, representing the following countries: India, Brazil, Turkey, China and Thailand. Inner setting barriers included lack of available resources—funding, space, materials and guidelines. Outer setting barriers were related to financing, policies, and laws. Individual patient barriers reported were low health literacy, distance to care centers, and low prioritization of follow-up. No common facilitators were noted; however, established survivorship clinics with care protocols were detailed in Brazil and China. The most feasible ERIC strategies for the barriers identified involved accessing new funding, developing educational materials, tools for quality monitoring, resource sharing agreements along with local survivorship care needs assessment.

Conclusions: Limited published data of childhood cancer survivorship care barriers in LMICs exist, with low resource availability being a primary barrier in the articles reviewed. As accessing funding can be difficult, resource sharing of contextually tailored clinical care guidelines and educational materials in these settings can serve as an implementation strategy to improve childhood cancer survivorship care globally.

Health Services Research-2

Entrance and Retention to Survivorship Program at Primary Children's Hospital by Rurality and Distance

Taumoha Ghosh, Jennifer Sweatman, Claire Miller, Kellee Parker, Caleb Hocutt, Ashley Kresser, Kasey Bozzer, Stephanie Neerings, Maddy Schneider, Martha Markovitz, Douglas Fair

Purpose: Our institution serves a vast geographic area including rural communities. Recognizing access to survivorship care in rural and small-town (RST) communities may be limited and distance to health care services may be a barrier, we describe rates of entrance and retention to our survivorship program based on distance and rurality.

Methods: Distance to Primary Children's Hospital (PCH) (less than vs greater than 100 miles), and Rural-Urban Commuting Area (RUCA) code status were compared between patients seen in our survivorship program from 2022-2024 (n=565) and pediatric oncology patients seen between 2020-2024 (n=6870) to assess entrance to survivorship. Within the survivorship cohort, distance and RUCA codes were compared among those seen for a single visit (n=89) or multiple (2+) visits (n=189) to assess retention. Entrance and retention rates by primary cancer type were also assessed. Statistical evaluation was completed using Chi-square analyses.

Results: Those who entered our survivorship program were less likely to live far compared to the oncology population (12.8 vs 18.5%, $p < 0.001$). However, far distance did not deter retention (68%), with 14.8% of returning patients travelling far (p=0.84). Those who entered survivorship were as likely to be from RST communities (8.9 vs 7.2%, p=0.16), and there was a similar likelihood of being from an RST community and returning to survivorship (7.4%, p=0.44). When evaluating by primary cancer type, absolute differences were noted in rates of patients travelling far distances for entrance and retention (entrance: 13.4% leukemia (n=284), 18% sarcoma (n=61), 6.1% brain tumor (n=49), p=0.18; retention: 15% leukemia (n=93), 29.2% sarcoma (n=24), 9.1% brain tumor (n=11), p=0.20). Rates of patients from RST communities entering survivorship by cancer type were similar (9.2% leukemia, 8.2% sarcoma, 8.2% brain tumor, p=0.95). Absolute differences in rate of RST communities among returning patients by cancer type were seen (7.5% leukemia, 16.7% sarcoma, and 0% brain tumors, p=0.13).

Conclusions: Patients are invested in continued survivorship care even when facing presumed barriers to access such as rurality. Though distance to care deters entrance into survivorship, retention is not affected, suggesting an ongoing need for outreach and consideration of possible solutions such as telehealth models. Absolute differences in entrance and retention by primary cancer type suggest additional barriers may impact brain tumor patients and further investigation is needed.

Endo-2

Prevalence of Endocrine Conditions among Swiss Childhood Cancer Survivors and Their Association with Health-Related Quality of Life

Tiara Greber, Christina Schindera, Fabien Belle, Claudia Kuehni, Grit Sommer

Background: Endocrine conditions, including thyroid disorders, growth hormone deficiency (GHD), early and late puberty onset, and diabetes mellitus, are common among childhood cancer survivors (CCS). Limited evidence exists on how endocrine conditions in CCS affect their health-related quality of life (HRQOL). We determined the prevalence of endocrine conditions in CCS and investigated associations with HRQOL.

Methods: This study included CCS from the Swiss Childhood Cancer Survivor Study (SCCSS), who were registered in the Swiss Childhood Cancer Registry, had been diagnosed at age <21 years, were resident in Switzerland, alive and aged >=16 years at time of study. We assessed HRQOL (SF-36), endocrine conditions (thyroid disorders, GHD, medication for early/late puberty, diabetes mellitus) and sociodemographic information using questionnaires. Data on cancer diagnoses and treatment originated from the Swiss Childhood Cancer Registry. We compared HRQOL between CCS with and without endocrine conditions using t-tests and multivariable linear regression to investigate associations with HRQOL adjusting for socio-demographic (age at study, sex, parental education, region) and clinical factors (age at cancer diagnosis, cancer type, chemotherapy, radiotherapy, surgery, haematopoietic stem cell transplantation).

Results: With an overall response rate of 59%, we included 2422 participants (48% women; median age 24 [IQR 20-31]) with data on HRQOL and endocrine conditions. Twenty percent (506/2422) reported at least one endocrine condition. Most common were thyroid disorders (15%, n=367), followed by GHD (8%, n=183), early/late onset puberty (4%, n=101), and diabetes mellitus (2%, n=43). CCS with endocrine conditions had reduced HRQOL in all SF-36 dimensions (difference in mean norm-based score for physical functioning -2.8; role physical -3.3; bodily pain -1.7; general health -4.4; vitality -3.3; role emotional -2.4; social functioning -3.0; mental health -1.6; all p<0.001). In multivariable linear regression analyses, thyroid disorders (coef. -1.5, 95%CI -2.5 to -0.50), GHD (-2.9, 95%CI -4.4 to -1.4) and diabetes mellitus (-3.4, 95%CI -6.2 to -1.1) were associated with poor physical HRQOL, and thyroid disorders (-1.6, 95%CI -2.8 to -0.45) and diabetes mellitus (-3.3, 95%CI -6.2 to -0.4) with poor mental HRQOL. Having received medication for early/late puberty onset was not associated with physical or mental HRQOL and GHD was not associated with mental HRQOL.

Conclusion: We observed reduced HRQOL among CCS with endocrine conditions, in particular among CCS with thyroid disorders, GHD and diabetes mellitus. Future studies should explore interventions to mitigate the impact of endocrine conditions on HRQOL, informing clinical care and survivorship support programs.

Intervention Research-1

Virtual Reality During Lumbar Punctures in Acute Lymphoblastic Leukemia

Alissa Groisser, Shelby Smith, Alexander Black, Raj Shekhar, Pamela Hinds, Reuven Schore, Jennifer Levine

Background/Purpose: Acute lymphoblastic leukemia (ALL), the most common childhood cancer, requires over 20 lumbar punctures (LPs) for administration of intrathecal (IT) chemotherapy over the course of treatment. Propofol sedation, a form of general anesthesia (GA), is the standard of care for managing pain and anxiety due to LPs in pediatric oncology. Recent studies have linked cumulative propofol exposure to long-term neurocognitive impairment in pediatric patients, so identifying alternative strategies is an imperative. Virtual reality (VR), a non-pharmacologic, distraction-based intervention, has shown promise in reducing pain and anxiety during minimally invasive pediatric procedures. However, its feasibility as an alternative to GA for LPs in pediatric oncology has not been established. This study aims to evaluate the feasibility of using VR combined with local anesthesia and optional anti-anxiety medication as an alternative to GA for LPs in pediatric patients with ALL.

Methods: We conducted a single-site, prospective, non-randomized feasibility study involving patients aged 7 years and older with ALL, acute lymphoblastic lymphoma, or mixed phenotype acute leukemia undergoing standard therapy. Participants chose between undergoing LP with VR or with GA. Participants who chose VR were scheduled to undergo their next routine LP without GA, using a VR headset during the procedure instead. Participants who chose GA had no changes to their scheduling or procedure. At time of enrollment, all participants were asked to elaborate on their reasons for choosing VR or GA in a structured interview. All participants also completed validated pain and anxiety scores at enrollment and on the day of the LP. For patients who chose VR, satisfaction was evaluated through structured interviews. Feasibility was determined by the successful delivery of IT chemotherapy during the LP.

Results: To date, 16 patients have been enrolled in the study. Of the 8 participants who chose the VR arm, 6 have had the opportunity to complete the first study LP. All have undergone successful LPs, and IT chemotherapy was successfully delivered in each instance. This exceeds the futility threshold of 3 successful LPs among the first 8 participants. All 6 also opted to attempt a second LP using the same method. Reasons for choosing VR have been variable, including wanting to avoid the side effects of anesthesia, wanting to avoid fasting, and being excited to use VR. The reason for choosing GA has primarily been reported as wanting to avoid feeling the needle or experience pain.

Conclusion: These preliminary findings suggest that VR may be a feasible and acceptable alternative to GA for LPs in pediatric oncology. Future studies should further investigate the potential for VR to help reduce neurocognitive deficits caused by propofol exposure.

CV-3

Systematic Review of Prognostic Models for Cardiomyopathy and Heart Failure Applicable to Survivors of Adolescent and Young Adult Cancer

Louise Guolla, J. Callum Mullen, A. Felipe Fajardo, Brynne Stewart, Kriti Kakar, Lehana Thabane, Sumit Gupta, Paul Nathan

Background: Survivors of adolescent and young adult (AYA) cancer who receive cardiotoxic chemotherapy and/or radiation are at risk of developing cancer therapy-related cardiac dysfunction (CTRCD), including asymptomatic reduction in left ventricular ejection fraction and symptomatic heart failure. Early detection and intervention using risk-adapted surveillance strategies can reduce morbidity and mortality. While numerous risk prediction models (RPM) have been developed and/or validated for CTRCD in pediatric or older adult cancer populations, it is unclear whether they can be applied to survivors of AYA cancer.

Methods: We undertook a systematic review of cardiovascular RPM (including CTRCD) development/ validation studies in survivors of cancer diagnosed at any age. We searched MEDLINE, EMBASE, and Web of Science with additional hand searching until November 2024. Two reviewers screened abstracts and full texts; we included studies that used real-life patient data to predict asymptomatic or symptomatic CTRCD (per European Society of Cardiology guidelines) ≥1 year from diagnosis and after completing therapy. We excluded abstracts, non-English studies, and RPM which used data not routinely accessible in outpatient clinics. We extracted study data and applied the Prediction model Risk of Bias ASsessment Tool for risk of bias (RoB) and applicability to AYA cancer survivors. When not reported, we estimated AYA (age 15-39) proportions using cancer incidence patterns. We used descriptive statistics to evaluate studies, models, included risk factors, and participants overall and by proportion of AYA. Meta-analysis was not possible given limited overlap in the identified models.

Results: We screened 12740 abstracts and 249 full text articles; of these, 100 studies underwent a second full text screen to identify CTRCD models. We identified 22 studies (7 enrolled >20% AYA) which developed and/or validated 64 models (32.8% machine learning) to predict CTRCD (54.7% symptomatic) in 129077 cancer survivors (10.7% AYA) using clinically available data. Nine (14.1%) models validated existing RPM (e.g. those developed in non-cancer populations); the remainder were newly developed models, with age at diagnosis, diabetes, hypertension, and anthracycline dose the most common predictors (>50% of models). Most models (n=54) were at high RoB, primarily due to concerns with analytical reporting. Only 2 studies/8 models were rated as both low RoB and high applicability to AYA cancer survivors.

Conclusions: Several RPM for subclinical and overt CHF are available for pediatric and adult cancer survivors, with varying applicability to AYA cancer survivors. Adherence to recommended statistical reporting methods is poor and RoB high, further limiting utility. Additional development and validation of high-quality RPM for heart failure in AYA cancer survivors is warranted.

Table 1: Characteristics of Studies and Prediction Models for Heart Failure of relevance to Adolescent and Young Adult (AYA) Cancer Survivors

	Number of Studies (%)	Number of Models (%)	Number of People (%)	Number of AYA (%)^
Total	22	64	129,077*	13,750 (10.7)
Age Group				
Adult	13 (59.1)	40 (62.5)	86,283 (66.8)	2096(15.2)
Pediatric	5 (22.7)	14 (21.9)	38,702 (30.0)	9561 (69.5)
Mixed	4 (18.2)	10 (15.6)	4092 (3.2)	2093 (15.2)
Percent AYA in study population				
0%	2 (9.1)	2 (3.1)	33,198 (25.7)	0
>0 to ≤5%	2 (9.1)	4 (6.3)	33,032 (25.6)	1220 (8.9)
>5% to ≤10%	6 (27.3)	28 (43.8)	19,030 (14.7)	666 (4.8)
>10% to ≤20%	5 (22.7)	14 (21.9)	16,135 (12.5)	2812 (20.5)
>20%	7 (31.8)	16 (25.0)	27,952 (21.7)	9052 (65.8)
Cancer Type				
Mixed	8 (36.4)	22 (34.4)	103,592 (80.3)	10226 (74.4)
Breast	9 (40.9)	30 (46.9)	21,263 (16.5)	1421 (10.3)
Post-HSCT	3 (13.6)	6 (9.4)	2659 (2.1)	961 (7.0)
Lymphoma	2 (9.1)	6 (9.4)	1563 (1.2)	1142 (8.3)
Outcome Predicted[#]				
≥Gr 2/Asymptomatic CTRCD	11 (50.0)	29 (45.3)	15,844 (12.3)	1565 (11.4)
≥Gr 3/Symptomatic CTRCD/ CHF	13 (59.1)	35 (54.7)	122,821 (95.2)	12,766 (92.8)
Type of Model				
Useable Machine Learning	3 (13.6)	21 (32.8)	10,805 (8.4)	1027 (7.5)
Model	1 (4.5)	1 (1.6)	130 (0.1)	10 (0.07)
Biomarker Model	5 (22.7)	12 (18.8)	3345 (2.6)	806 (5.9)
Echocardiogram/ECG Model				
Validation of Existing Risk Prediction Model	7 (31.8)	9 (14.1)	66246 (51.3)	883 (6.4)
Developed ≥1 Novel Model	18 (81.8)	55 (85.9)	63861 (49.5)	13,156 (95.7)
Validated ≥1 Novel Model		*Number of validations*		
Internal Only	9 (40.9)	31 (48.4)	44473 (34.5)	8328 (60.6)
External Only	2 (9.1)	4 (6.3)	798[$]	203[$]
Both Internal/External	2 (9.1)	11 (17.2)	25,018[$]	4366[$]

*Note, some overlap in individual patients is expected due to re-use of same survivor cohort for new model development. ^ Where not reported, AYA percentage is estimated from (1) descriptive statistics (mean+/-standard deviation, median /IQR) using closest age cutoff provided, (2) SEER cancer incidence statistics by age group, or (3) equal distribution by age if necessary. #: Grade (Gr) 2 and 3 is per CTCAE criteria for cardiomyopathy and is roughly aligned with asymptomatic/symptomatic CTRCD. $: Includes number of patients in external validation cohorts, thus percentage not reported. AYA: adolescent and young adult, CTRCD: Cancer-therapy related cardiotoxicity, CHF: congestive heart failure, ECG: electrocardiogram, HSCT: hematopoietic stem-cell transplant.

Making Moves: a Type 1 Hybrid Effectiveness-Implementation Trial of a Digital Education Program to Engage Childhood Cancer Survivors in Physical Activity

Lauren Ha, Callum Joyner, Christina Signorelli, David Mizrahi, Karen Johnston, Rachel Baldwin, Richard Cohn, Natalie Taylor, Claire Wakefield

Purpose: Engaging in physical activity can improve aerobic fitness and reduce the risk of cardiovascular disease, however, 86% of childhood cancer survivors do not meet physical activity guidelines. We developed "Making Moves", an online education program aimed to engage survivors in physical activity at home. We demonstrated that our program is feasible to deliver and accepted by survivors. Most evidence-based interventions are not adopted in "real-world" settings; therefore, the aim of our study was to evaluate the effectiveness of Making Moves on survivors' physical activity self-efficacy and simultaneously explore the context for implementation to inform future adaptations.

Methods: We conducted a type 1 hybrid effectiveness-implementation study. For the effectiveness pre-post trial, we recruited childhood cancer survivors aged 8-21 years to complete Making Moves, an 8-week online physical activity program with educational health modules, five telehealth sessions with an exercise professional, tailored goalsetting and a wearable activity tracker. For the implementation study, we used the Consolidated Framework for Implementation Research 2.0 to guide interviews with potential implementers.

Results: To date, 25 survivors have opted in (recruitment rate 36% plus four pending participants). Currently, 14 survivors (mean age 12.0 SD 3.1 years) have completed the study, with no adverse events reported. Two survivors dropped out of the study (n=1 not interested, n=1 too busy). Survivors' mean physical activity self-efficacy scores (+5.6 mean change, $p<.01$) and aerobic fitness levels (+131m mean change, $p<.05$) significantly increased after participating in Making Moves. We did not observe any significant changes in muscular endurance, symptoms of depression, exercise enjoyment or health-related quality of life. For the implementation study, 19 representatives across five potential implementers completed interviews from n=3 community organisations and n=2 hospital survivorship clinics. Key barriers to implementation included limited trained staff to deliver the intervention, limited capacity to maintain the online platform, and financial barriers to hiring an exercise professional into the team. Facilitators included organisational support for implementing a physical activity program for survivors, and compatibility with the organisation's missions and goals.

Conclusions: Making Moves has the potential to improve physical activity and self-efficacy among survivors. Further consideration of factors impacting its implementation in the community is needed. Future research will focus on adapting the intervention to preserve its core components while modifying elements to improve compatibility.

Genetics/Genomics-8

GenEFCCSS: a Resource for Investigating Genetic Predispositions to Late Events in Childhood Cancer Survivors

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Introduction: Late adverse events in childhood cancer survivors are expected to have an underlying genetic component, as they are not fully explained by treatment and baseline clinical characteristics. This study investigates genetic variants associated with these events in survivors from the Extended FCCSS cohort (GenEFCCSS).

Material and Methods: GenEFCCSS cohort includes 8471 patients, of whom 2673 with available blood or saliva samples underwent whole-genome sequencing (WGS) using the NovaSeq X+ Illumina platform. Sequencing achieved an average depth of 30X. Raw FASTQ files received from CNRGH were preprocessed for quality base filtering, adapter trimming, and polyG tail trimming using Fastp. Subsequent analyses were performed using the nf-core/sarek pipeline for germline variant detection. Alignment was conducted with BWA-MEM2, followed by duplicate marking using GATK MarkDuplicates. Variants were called using HaplotypeCaller, and joint calling was subsequently performed to generate a final VCF file for all samples. Finally, variant filtration was conducted using GATK VQSR.
Baseline clinical characteristics were obtained from hospital records. The sex ratio is approximately 1:1, with a median age at diagnosis of 6 years (IQR 2–12) and a median follow-up time of 28 years (IQR 19–36). Among the sequenced patients, 1518 received radiotherapy, while 2130 underwent chemotherapy for childhood cancer. Chemotherapy doses for both initial treatment and relapse were collected. Additionally, for patients who received radiotherapy, radiation dose distribution was estimated individually for each organ of the entire body using technical records of radiation therapy and in-house software. GenEFCCSS is followed through self-questionnaires and the French National Hospital and Medical Insurance database (SNDS). To date, late events identified from SNDS and self-questionnaires, and subsequently validated, include 337 cases of secondary cancer, 212 of cardiac disease, 135 of hearing impairment, 94 of diabetes, 63 of chronic kidney disease, 49 of cerebrovascular disease, and 26 of cataracts.

Results: This database serves as a valuable resource for advancing knowledge on the occurrence of adverse events, their association with genetic variations, and the in-depth study of interactions between known risk factors and genetic predisposition. We welcome collaborations to further explore these aspects and deepen understanding in this subject.

CV-4

Clonal Hematopoiesis and Heart Disease in Cancer Survivors

Robert Hayashi, Aecha Ybarra, Joshua Mitchell, Kara Felts, Emily Lafrentes, Debra Spoljaric, Jie Zheng, Manish Aggarwal, Randi Foraker, Pamela K Woodard, Kenneth Walsh

Purpose: To assess the presence of clonal hematopoiesis, (CH) in pediatric cancer survivors exposed to anthracycline chemotherapy with and without evidence of cardiac injury on cardiac MRI (cMRI).

Methods: Pediatric cancer survivors, with a history of anthracycline exposure who had completed cancer therapy and who were assessed for cardiac injury using cMRI were approached for blood sample submission to identify and quantify CH. Toward this end, genomic DNA was isolated from blood and analyzed by a targeted sequencing panel from ArcherDX/Invitae VariantPlexÒ. This custom panel comprised 16 of the most prevalent clonal hematopoiesis genes (e.g. DNMT3A, TET2, ASXL1, TP53, PPM1D, etc.). Using ultradeep, error-corrected sequencing, CH-mutations with variant allele frequency (VAF)s as low as 0.5% were able to be confidently identified. Only mutations with the potential to influence protein's structure were further considered. Patients were deemed CH positive if they had a functional mutation in a driver gene at or above 0.5% VAF threshold.

Results: Of the 30 subjects who underwent cMRI evaluation, (9 with signs of cardiac injury, 21 without) 27 consented to specimen submission for CH analysis, (9 with signs of cardiac injury, 18 without). CH was detected in 3/9 (33%) of those demonstrating signs of cardiac injury by cMRI verses 3/18 (17%) of those with a normal cMRI. Mean age of those with demonstrable CH regardless of cMRI findings = 21.1 s.d. + 8.6 years verses 18.2 s.d + 4.2 years without CH. Mean cumulative anthracycline exposure of those with demonstrable CH was 197 s.d + 111.5 mg/m2 verses 154.9 s.d + 112.1 mg/m2 without. Time from end of therapy of those with demonstrable CH was 12.3 s.d + 7.5 years verses 7.9 + s.d 5.1 years without.

Conclusion: CH can be detected in pediatric cancer survivors exposed to anthracycline chemotherapy and may be more prevalent in those demonstrating cardiac injury using cMRI. Additional investigations examining larger cohorts will hopefully clarify the relationship of CH to cardiac injury due to anthracycline chemotherapy.

Health Services Research-3

Neurosensory Screening in Survivors

Robert Hayashi, Ashley Housten, Thomas Kannampallil, Kara Felts, Emily Lafrentes, Belinda Sinks, Anna Perlmutter, Johnnie K. Bass

Purpose: We sought to assess whether screening patients under the care of their primary treating oncology team for neurosensory deficits would result in improved acceptance of recommendations for formal diagnostic testing and therapy follow-up.

Methods: Eligibility included patients, off therapy for at least six months but had not reached a time from completion of therapy (2 years) when they were transitioned to our survivorship program. Age was restricted (7-18 years) to accommodate the validity of the screening tools. Automated searches of the electronic health record identified patients exposed to therapies placing them at risk for neurosensory deficits (i.e., vision, hearing, peripheral nerve, vestibular function). Consented patients underwent screening utilizing standard procedures established in our survivorship program. Patients with abnormal screening results were referred by the primary treatment team to the appropriate services for formal diagnostic testing or therapy. The primary outcome was the successful referral to an appropriate specialist in patients demonstrating abnormal neurosensory screens.

Results: 477 patients were identified with eligible treatment exposure; 395 were ineligible due to age or their time off treatment migrated out of the window of eligibility once available for participation. Of the 81 patients approached for participation, 52 declined and 29 (36%) consented. Age range was 8-18 years, median (IQR)=11.0 (9.5, 15) years. Median time off therapy was 12 months (9.0, 16.5). Diagnoses included leukemia (18), lymphoma (4), solid tumor (6), CNS (1). Four of 29 (14%) patients were identified in need of additional diagnostic or treatment servicers (1/1 hearing, 1/2 vestibular, 1/15 peripheral neuropathy, 1/26 vision screens) with three of four (75%) receiving appropriate services. The screening abnormality rate was lower than what was observed in our survivorship program for patients more than two years off therapy (42%) where only 43% of patients successfully follow through with successful diagnostic testing or therapy.

Conclusions: Although patients who had neurosensory screening abnormalities were often successfully referred for therapy services, the frequency of abnormal screening was lower that what has been observed in patients with longer follow-up in our survivorship program. Furthermore, most patients under the care of their primary treating oncology team declined to participate. This suggests that patients further from therapy completion who had transitioned to survivorship programs may be more open to participating in neurosensory screening and may be more likely to demonstrate abnormal screening as more time has passed for sensory deficits to develop. Challenges remain in improving follow-through with diagnostic and therapeutic interventions.

Health Services Research-20

Childhood Cancer Survivors and Their Caregivers are Amenable to Survivorship Surveillance with Community-Based Primary Care Providers

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Background: Nearly 95% of childhood cancer survivors (CCS) develop chronic conditions associated wtih their cancer therapy. While 87% of pediatric oncology centers offer survivorship programs for guideline-concordant surveillance of chronic conditions, <30% of CCS access this care. More CCS might receive recommended surveillance if delivered by community-based primary care providers (PCP); however, little is known about whether CCS and their caregivers are amenable to this strategy, especially among populations vulnerable to health disparities.

Objectives: To describe preferences for site of survivorship surveillance and to determine associations between CCS characteristics and preference.

Design/Methods: We analyzed baseline data from the multi-site BRIDGES randomized, non-inferiority trial (NCT05448560). Randomization was to usual care at the enrolling site's survivorship program vs. surveillance with PCP following individualized telehealth education to the CCS and PCP. Participants were diagnosed with cancer at <21 years, 2-4 years off-therapy, English- or Spanish-speaking, and treated at one of four geographically diverse hospitals. After consent and before randomization, CCS or their caregivers (for CCS <18 years) reported their socio-demographics and preference for survivorship surveillance site (survivorship program vs. PCP vs. no preference). Associations with preference were examined with bivariate analysis. For continuous outcomes, Kruskal-Wallis test was used. For categorical outcomes, Fisher's exact test was used.

Results: 214 of 235 (92%) participants (48% female, 31% non-White, 36% Hispanic, 44% with public insurance, median age 12 years at enrollment) responded to the question regarding their preference for survivorship surveillance. Overall, 62% of CCS > or =18 years old and 64% of caregivers were "amenable to" (i.e. preferred PCP or no preference) PCP-based surveillance. Those preferring PCP-based surveillance lived farther from the survivorship program (median 53 miles; p=0.02) and required longer driving times (median 70 minutes; p=0.03) compared to those preferring the survivorship program (median 23 miles, 43 minutes) or those having no preference (median 26 miles, 45 minutes). Non-White respondents more frequently preferred the survivorship program (Asian 67%, Black 47%, Other 56%; p=0.01) compared to those who identified as White (29%). Ethnicity, insurance type, and household income relative to the federal poverty level, were not associated with preference in the study sample.

Conclusion: The majority of CCS and their caregivers from a geographically diverse sample were amenable to PCP-based survivorship surveillance. Delivery of this important care by PCPs may improve accessibility to guideline-concordant surveillance, especially for CCS living farther from their respective survivorship program.

Health Services Research-4

Patterns of Follow-Up after Initial Survivorship Clinic Visit among Childhood Cancer Survivors from a Regional Childhood Cancer Survivorship Clinic

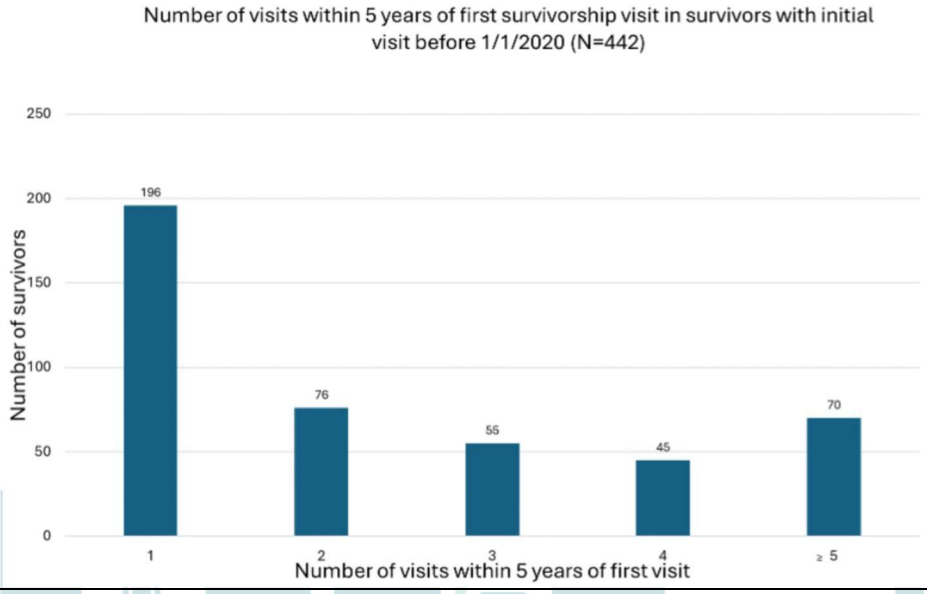
Carlos Hernandez Castillo, Rozalyn Rodwin, Jaime Rotatori, Sophia Kujawski, Justin Gardner, Claudia Auerbach, Lyn Balsamo, Nina Kadan-Lottick

Background/purpose: Childhood cancer survivors require lifelong surveillance of late effect. Little is known about ongoing follow-up of patients after their first childhood cancer survivorship clinic visit. In a regional childhood cancer survivorship clinic, we aimed to 1) determine the proportion of survivors who returned to survivorship clinic within two years of their initial visit and factors associated with follow-up, and 2) describe frequency of follow-up within five years of initial visit among patients with ≥5 years of follow-up.

Methods: Among childhood cancer survivors (<21 years at diagnosis) with an initial visit to the HEROS regional childhood cancer survivorship clinic between 1/1/2003-1/1/2023, the medical record was reviewed for date(s) of follow-up visit(s) and patient characteristics (current age, sex, race, ethnicity, primary cancer diagnosis, treatment exposures, number of Common Terminology Criteria for Adverse Events [CTCAE] Grade I-IV late effects at initial survivorship visit, insurance, and zip code). HEROS clinic monitors for late effects, as per the Children's Oncology Group Long-Term Follow-up Guidelines, beginning 2 years post-therapy with subsequent lifelong follow-up at least annually. The proportion of survivors who followed up within 2 years of the initial visit was calculated; characteristics associated with follow-up were examined using chi-squared and two sample t-tests. Follow-up frequency distribution of survivorship visits within 5 years of initial visit was calculated for survivors whose initial visit was before 1/1/2020.

Results: Among 544 survivors (52.2% female, 23.0% Hispanic, 20.8 % non-White, mean age at first visit 18.3 ± 8.4 years, mean 10.1 ± 6.6 years post-therapy, history of leukemia/lymphoma [61.6%], central nervous system [CNS] tumors [8.5%], and non-CNS solid tumors [29.9%]), 290 (53.3%) followed up within 2 years of initial visit. Survivors who followed up within 2 years (vs. did not) were more likely to be <15 years old at initial visit (45.5% vs. 29.5%, p<.001), and to have received chemotherapy (99.3% vs. 93.7%, p<.001). Other characteristics (sex, Hispanic ethnicity, non-White race, years since therapy, history of CNS tumor, radiation, surgery, or stem cell transplant, average number of CTCAE Grade I-IV late effects at first visit, public insurance, and distance residing from clinic) did not differ between groups. The 442 survivors with ≥5 years of follow-up had a median of 2 follow-up visits (range 1-6, Figure) over the next 5 years.

Conclusions: Nearly half of childhood cancer survivors initially evaluated at a regional survivorship clinic did not receive ongoing follow-up. Patients' perspectives regarding barriers to follow-up in survivorship clinic are needed to identify ways to sustain attendance, or develop alternative models for survivorship care delivery, especially among older survivors.



Health Services Research-5

Association Between State Opioid Limiting Laws and Opioid Prescription among Medicaid-Enrolled Survivors of Childhood Cancer

Xin Hu, James Klosky, Deo Kumar Srivastava, Zhanji Zhang, Tara Brinkman, Kevin Krull, Paul Nathan, Claire Snyder, Greg Armstrong, Vikki Nolan, Yutaka Yasui, Sharon Castellino, Xu Ji

Background: At least one third of childhood cancer survivors experience moderate to severe pain in adulthood. While opioid analgesics are recommended for acute cancer pain, they are generally not the class of drug choice for chronic pain. Further, by 2019, 39 states have enacted opioid-limiting laws that restrict opioid prescriptions, often capping the duration of opioid prescriptions at seven days without clear exemptions for cancer survivors. However, the impact of these laws on opioid prescription and potential misuse among childhood cancer survivors remains unknown.

Methods: We linked data from the Childhood Cancer Survivor Study (CCSS) Medicaid administrative claims from 2009-2019. Eligible survivors were aged ≥18 years by 2009, had a known zip code, did not relocate across states with differing opioid-limiting laws during the study period, and had continuous Medicaid coverage (≥11 months of enrollment) in one given year. Outcomes were dichotomous indicators for any filled opioid prescription, opioid prescriptions exceeding seven days of supply, and potential opioid misuse (any opioid prescription with daily dose ≥100 Morphine Milligram Equivalents, opioid overlap, opioid and benzodiazepine overlap, or opioid dose escalation) in each year. A difference-in-differences linear probability model assessed the association between opioid-limiting law implementation and these outcomes, adjusting for sociodemographic and clinical characteristics. Adjusted probability differences (marginal effects) were reported.

Results: Our analyses included 2,355 unique survivors followed for 15,347 person-years. Half (50.7%) were aged 21–29 years, 57.0% were female, 10.1% were non-Hispanic Black, and 9.7% were Hispanic. The percent of survivors who filled any opioid prescription ranged from 15.2% to 22.7%, with 6.0% to 12.2% of prescriptions exceeding seven days of supply and 4.0% to 8.7% with potential opioid misuse in 2009-2019. Multivariable difference-in-differences models showed that opioid-limiting laws were associated with a 1.8 percentage point (ppt) reduction (95% CI: -3.6 to -0.1) in prescriptions exceeding seven days, with larger declines among older survivors (40-64 years: -3.5 ppts, 95% CI: -6.5 to -0.4), survivors with grade 3-4 chronic health conditions (-2.6 ppts, 95% CI: -4.7 to -0.4), and those with second cancer (-8.1 ppts, 95% CI: -12.5 to -3.6). No significant changes were seen in any opioid prescription or potential opioid misuse following the implementation of state opioid-limiting laws.

Conclusions: Among Medicaid-enrolled childhood cancer survivors, state opioid-limiting laws were associated with a reduction in opioid prescriptions exceeding seven days of supply, with no significant impact on potential opioid misuse based on available measures. Future research will examine whether the observed restrictions have led to undertreated pain, particularly among older survivors and those with severe chronic conditions or second cancer.

Health Services Research-6

Childhood Cancer Survivors' Perceptions of a Low-Threshold Screening Program for Hearing Loss: a Qualitative Study

Philippa Jörger, Carina Nigg, Leonie Schreck, Christina Schindera, Katharina Fessler, Nicolas Waespe, Zuzana Tomášiková, Marc Ansari, Annika Frahsa, Claudia Kuehni

Purpose: Childhood cancer survivors (CCS) are at risk for chronic health problems, including hearing loss after ototoxic treatments. Follow-up care clinics screen for incident health problems such as hearing loss. However, many adult CCS do not attend long term follow-up care due to barriers such as accessibility and emotional concerns associated with revisiting medical facilities. To address those barriers, the HEAR-study piloted a new low-threshold hearing screening program leveraging the extensive network of hearing aid shops across Switzerland. As part of this program, childhood cancer survivors completed audiometric screening at a hearing aid shop. In case of marginal or pathological results, the hearing aid shop advised them to consult with a medical doctor. We explored CCS' perceptions of this novel screening program.

Methods: We conducted semi-structured interviews with 29 participants who completed a audiometric screening at a hearing aid shop as part of the HEAR-study. We used thematic analysis of interview transcripts, supported by MAXQDA for data analysis.

Results: Thematic analysis revealed two key themes: First, participants appreciated the program's practicability, highlighting the efficiency and ease of integrating it into daily life. At the same time, some noted concerns about the hearing test being an additional appointment. Some survivors would prefer centrally organized follow-up care, where different examinations to screen for chronic health conditions are done at the same location within the same day, ideally consulting with one person regarding all results. Second, many participants valued the personal and approachable environment at the hearing aid shop as a relaxed alternative to medical facilities, while others would prefer hearing tests as part of an appointment with physicians, valuing immediate advice and contextual knowledge, especially in case of pathological findings.

Conclusions: From CCS' perspectives, this screening program shows promise as a practicable and accessible way to evaluate hearing after childhood cancer.

Intervention Research-8

Impact of Multidisciplinary Intervention on Overweight and Obese Childhood Cancer Survivors and its Psychosocial Determinants

Gauri Kapoor, Payal Malhotra, Sandeep Jain, Navneet Singh, Sakshi Dudeja, Juhi Sharma, Aayushi Khaneja

Background: Obesity is becoming a global epidemic and is emerging as a significant long-term complication among childhood cancer survivors (CCS), including in India. Its importance lies in its association with metabolic syndrome, which increases the risk of hypertension, diabetes, and stroke.

Purpose: This study aimed to identify overweight and obese CCS and implement active multidisciplinary (MD) interventions to address and manage obesity.

Materials and Methods: This was a prospective, interventional study. Overweight (>85th–<95th percentile) and obese (>95th percentile) CCS were identified using the WHO BMI criteria. Participants were recruited from the survivorship clinic if they were 2 years off therapy and 5 years post-diagnosis, after informed consent and ethical approval. Survivors with physical disabilities were excluded. A team of dieticians, physiotherapists, and psychologists performed baseline MD assessments followed by appropriate interventions. Participants underwent a 24-hour dietary recall and received a personalized diet plan and counseling from the dietician. They completed the Global Physical Activity Questionnaire (GPAQ), a 6-minute walk test, and received tailored physical activity recommendations under guidance of a physiotherapist. The intensity of physical activity was calculated in mean metabolic equivalents (MET) minutes per week. The psychologist administered a baseline questionnaire and compared CCS with non-obese controls (N=30) , also assessed barriers to obesity management. Follow-up reinforcement sessions were conducted in-person and telephonically. Repeat assessments were scheduled at 8 weeks, 6 months, and 1 year.

Results: Out of 250 survivors screened, 91 (36%) were overweight or obese, and 62 consented to participate. Their median age was 12 years, 73% were male, acute leukemia (52%), lymphoma (28%) and bone sarcoma (9%) were the most common primary cancers. Dietary recall and questionnaire revealed 85%(53/62)survivors consumed high calorie and low protein diet as compared to their RDA. Initial assessments revealed that overweight/obese CCS were more likely to live in joint families, had easier access to junk food, and experienced more sleep, fatigue, and appetite issues compared to controls ($P<0.05$). Post-intervention, 0%, 8% (5/62), and 19% (12/62) lost weight at 8 weeks, 6 months, and 1 year, respectively. Post intervention (counselling and exercise plan) there was 22% and 31% improvement in overweight and obese patients GPAQ scores. The mean MET scores increased for overweight CCS but not for obese CCS. The 6-minute walk test showed a 20-30% improvement in compliant CCS, while dietary changes showed only a 3% improvement.

Conclusion: This study's findings will help refine future interventions in managing obesity among CCS.

Genetics/Genomics-3

Epigenetic Impact of Social Vulnerability in Adult Survivors of Childhood Cancer with African Ancestry: an Epigenome-Wide Association Study from the St. Jude Lifetime Cohort

Yoonji Kim, Xiaoxi Meng, Jaesung Choi, Tiffany Eulalio, Noel-Marie Plonski, Heather Mulder, John Easton, Emily Walker, Geoffrey Neale, Anthony Zannas, Kiri Ness, Melissa Hudson, Greg Armstrong, I-Chan Huang, Zhaoming Wang

Background/Purpose: Late-onset health conditions associated with cancer treatment exposures may be exacerbated by social vulnerability. This study aims to enhance understanding of the biological embedding of social determinants of health (SDOH) among survivors of African ancestry leveraging the social vulnerability index (SVI), which aligns with the objectives of Healthy People 2030.

Methods: Survivors of African ancestry from the St. Jude Lifetime Cohort study were included. Neighborhood-level SDOH factors were measured using the SVI (overall and four domains: socioeconomic status, household composition and disability, racial and ethnic minority status, and housing type and transportation), as well as personal-level educational attainment, and income. DNA methylation (DNAm) profiles were generated with EPIC BeadChip V1 using peripheral blood mononuclear cells (PBMCs)-derived DNA. An epigenome-wide association study (EWAS) approach was employed to agnostically evaluate the association between DNAm levels at each CpG site and each SDOH factor, adjusting for age at blood draw, sex, cancer treatment exposures, leukocyte subtype composition, as well as top genetic and epigenetic principal components. In addition, multiple linear regression evaluated associations with epigenetic age acceleration (EAA) with SDOH adjusting for sex and cancer treatment exposures.

Results: The study included 471 survivors of African ancestry (51.2% female; median age at blood draw for DNAm = 29.5, interquartile range = 25.3-37.0 years). EWAS identified three epigenome-wide significant ($p < 9.0\times10\text{-}8$) associations: DNAm levels of cg25793377 (FFAR4; RBP4) (beta = 0.17, SE = 0.03, p = $4.68\times10\text{-}8$) and cg17939805 (SKOR2) (beta = 0.08, SE = 0.01, p = $8.35\times10\text{-}8$) were positively associated with SVI overall, and the DNAm level of cg10652386 was negatively associated with the household component and disability domain of the SVI (beta = -0.07, SE = 0.01, p = $7.81\times10\text{-}8$). The expression quantitative trait methylation (eQTM) analysis showed statistically significant associations of DNAm levels of cg25793377 with log transformed mRNA expression levels of GZMK (beta = 3.27, SE = 1.53, p = 0.035) and TNFRSF17 (beta = 5.37, SE = 2.47, p = 0.032), genes implicated in immune functions. In addition, significantly greater EAA was associated with worse household composition and disability domain of SVI as well as educational attainment.

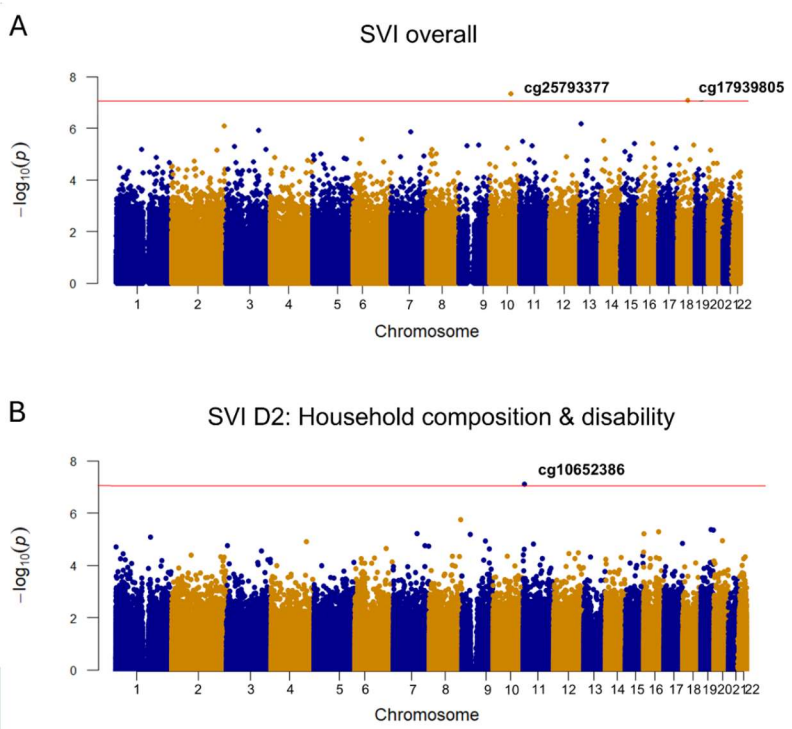


Figure 1. Manhattan plot for associations between DNAm level of CpGs and SVI overall index (A) and household component & disability domain of SVI (B). EWAS analyses included 471 individuals of African ancestry. The red horizontal line represents the epigenome-wide significance threshold of ($p = 9\text{x}10^{-8}$). Two CpG sites exceeded the EWAS significance threshold for SVI overall index and one CpG site for household component & disability domain of SVI.

Conclusions: This study highlights the potential impact of neighborhood-level SDOH on epigenome alterations among childhood cancer survivors of African ancestry, suggesting mechanisms by which socioeconomic vulnerability confers biological effects at the molecular level. These findings support the hypothesis that distal SDOH factors are biologically embedded through epigenetic modulation, potentially influencing adverse health outcomes in long-term survivors of childhood cancer.

Health Services Research-21

Enhancing Survivorship Care for Childhood Cancer Survivors: Highlights from Beta Testing of the Passport for Care mhealth App with Latinos

Jason King, Yu Ra Kim, Michael O'Connor, Justin Parker, Brian Arriaga Solis, Harold Tinoco-Giraldo, Anthony Adams, Maria Gramatges

BACKGROUND/PURPOSE: Survivors of childhood cancer face lifelong risks for the late effects of treatment. In response, we developed the Passport for Care (PFC), a web-based clinical decision support tool, which generates personalized survivorship care plans and provides education for late effects screening. The PFC is available in both English and Spanish, recognizing that medically underserved Latino populations often experience health disparities and face challenges in accessing care. Building on insights gathered from literature and earlier formative assessments with survivors and clinician that use PFC, we developed the PFC mHealth App with a more simplified sign-up process and inclusive of additional video-based educational resources (Q&A videos). This mobile app will allow users dual language access to their treatment history, care guidelines, educational resources, and includes capability to securely communicate with their survivorship clinic. In this report, we summarize the results of beta testing from semi-structured interviews of survivors and their parents/caregivers, with a focus on medically-underserved Latino survivors.

METHODS: We interviewed 23 individuals (7 parents / 16 survivors; 18 female / 5 male; 12 Latino; survivor mean age of 29.6 [range: 18–50]; diverse cancer diagnoses [e.g., Ewing's sarcoma, Hodgkin's lymphoma, neuroblastoma] and late effects, including two survivors reporting cognitive disabilities, and one hearing disabled). Interviewers presented a prototype of the app in English or in Spanish and inquired about features, educational content, intention to use, and other items.

RESULTS: We conducted a conceptual content analysis on the transcribed data using a mixed-methods approach on participant interview data, assigning codes, and mapping emergent themes. All participants expressed strong interest in using the app to access PFC tools and resources, assigning high value to the educational resources, Q&A videos, and capability to communicate via text with one's survivor clinic. Proposed suggestions, many of which have now been incorporated in the application, include the use of more vibrant visuals and welcoming content, an 'FAQ' feature, an opportunity for personal story-sharing to foster a "survivorship community" within the app, inclusion of a medication tracker, inclusion of a calendar to track upcoming appointments, an option to include self-reported health conditions, and an emergency notification feature.

CONCLUSIONS: Beta testing suggested high potential of the app to enhance the survivorship experience in the test population. The mHealth app includes many of the features offered in the PFC supplemented with added features informed by testing and a simplified enrollment process to reduce the enrollment burden on survivors and clinics. We will begin app rollout in select clinics in 2025.

CV-9

Recommendations for Anthracycline and Anthraquinone Equivalence Ratios for the Risk of Cancer Therapy-Related Cardiac Dysfunction after Childhood Cancer Treatment from the International Guideline Harmonization Group

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Background/Purpose: Anthracycline and anthraquinone agents are major causes of asymptomatic cardiac dysfunction and symptomatic heart failure, collectively termed cancer therapy-related cardiac dysfunction (CTRCD), after childhood cancer. Currently, equivalence ratios for these agents are often based on hematologic toxicity. Evidence-based equivalence ratios for estimating the risk of developing CTRCD have not yet been included in international surveillance guidelines. Therefore, the International Late Effects of Childhood Cancer Guideline Harmonization Group organized a guideline panel of international multidisciplinary experts to develop a clinical practice guideline for equivalence ratios for doxorubicin, daunorubicin, epirubicin, idarubicin and mitoxantrone in relation to CTRCD after treatment for childhood cancer (up to 21 years at primary cancer diagnosis) to inform and optimize follow-up strategies.

Methods: The guideline panel formulated clinical questions, performed a systematic literature review, developed evidence summaries, appraised the evidence and formulated recommendations on the basis of available evidence, clinical judgement, and consideration of benefits versus harms. The GRADE Evidence-to-Decision framework was used to translate evidence to recommendations.

Results: We identified 2 eligible studies with overlapping cohorts. Therefore, we focused on the largest study that included data from three large international childhood cancer survivor cohorts (the Childhood Cancer Survivor Study, the Dutch Children's Oncology Group's LATER study and the St Jude Lifetime study) and described 399 CTRCD events in 28423 childhood cancer survivors. The panel concluded that the risk of CTRCD is lower after daunorubicin and higher after mitoxantrone, compared to doxorubicin (moderate-quality evidence, strong recommendation). The panel agreed that it is reasonable to use a ratio of approximately 0.6 to calculate the daunorubicin-to-doxorubicin equivalent dose and a ratio of approximately 10.5 to calculate the mitoxantrone-to-doxorubicin equivalent dose (low-quality evidence, moderate recommendation). No recommendations could be formulated for epirubicin and idarubicin due to inconclusive evidence (see Table).

Conclusion: This guideline presents harmonized international recommendations for the use of CTRCD risk equivalence ratios for anthracycline and anthraquinone agents after childhood cancer treatment. Simplified ratios of 0.5 and 10 for daunorubicin and mitoxantrone, respectively, may facilitate implementation of risk-equivalent cardiac surveillance after treatment for childhood cancer in order to promote optimal care and preservation of cardiac health in childhood cancer survivors. Further research, including validation of analyses among contemporarily treated survivors and evaluation of the CTRCD risk of novel agents, is encouraged to strengthen our recommendations and allow for broader applicability of this guideline.

Table: Recommendations for cancer therapy-related cardiac dysfunction risk equivalence ratios for anthracycline and anthraquinone agents after childhood cancer treatment

Daunorubicin versus doxorubicin
It is justifiable to assume that the risk of CTRCD after childhood cancer treatment with daunorubicin is lower than after treatment with doxorubicin (moderate-quality evidence, strong recommendation).
It is reasonable to use a ratio of approximately 0.6 to calculate the daunorubicin to doxorubicin equivalent dose with respect to the risk of CTRCD after childhood cancer treatment (low-quality evidence, moderate recommendation). Estimates vary depending on cumulative dose*.
Mitoxantrone versus doxorubicin
It is justifiable to assume that the risk of CTRCD after childhood cancer treatment with mitoxantrone is higher than after treatment with doxorubicin (moderate-quality evidence, strong recommendation).
It is reasonable to use a ratio of approximately 10.5 to calculate the mitoxantrone to doxorubicin equivalent dose with respect to the risk of CTRCD after childhood cancer treatment (low-quality evidence, moderate recommendation). Estimates vary depending on cumulative dose†.
Epirubicin versus doxorubicin
No recommendation can be formulated to use a ratio other than 1‡ to calculate the risk of CTRCD after childhood cancer treatment with epirubicin compared with treatment with doxorubicin (low-quality evidence).
Idarubicin versus doxorubicin
No recommendation can be formulated to calculate the idarubicin to doxorubicin equivalent dose with respect to the risk of CTRCD after childhood cancer treatment (no studies identified).

**95% CI 0.4-1.0, range depending on dose category: <150mg/m² 0.8, 150-299mg/m² 0.6, ≥300mg/m² 0.5.*
†95% CI 6.2-19.1, range depending on dose category: <150mg/m² 11.2, 150-299mg/m² 4.0, ≥300mg/m² 16.8.
‡95% CI 0.5-2.8, range depending on dose category: <150mg/m² 1.3, 150-299mg/m² 0.6, ≥300mg/m² 0.5.

Research Methods-2

Deep Learning-Based Age Estimation for Premature Aging Assessment in Childhood Cancer Survivors: a Pilot Study on Treatment-Related Biomarkers

Jarmila Kruseova, *Vladimir Socha*, *Umer Asgher*, *Lenka Levicka*, *Sarah Blagodarna*, *Tomas Eckschlager*

Background: Premature aging is linked to oncological treatment, particularly in childhood cancer survivors (CCSs) undergoing chemo and/or radiotherapy. This condition contributes to cognitive decline, reduced regeneration, increased frequency and earlier onset of age-related diseases. To investigate underlying mechanisms, a dataset of CCSs diagnoses, treatment details, and biochemical markers was compiled. Convolutional neural networks (CNNs) were used for objective age estimation.

Methods: A CNN-based age detection model was trained on 40,000 facial images of healthy individuals (ages5–65) with preprocessing and augmentation to improve generalizability. The dataset was split (70/10/20) into training, validation, and test sets. A gender classification model enhanced accuracy. The CNN achieved over 80% accuracy, and regression-based age estimation resulted in a Mean Absolute Error (MAE) of ~5 years. After testing, the model was applied to CCSs data, where predicted age reflected biological rather than chronological age due to training on a healthy population. The difference between these two "agediff," was analyzed for clinical associations. Multiple machine learning approaches were tested, with K-nearest neighbors (KNN) outperforming others, where all features were standardized for comparability. SHAP (SHapley Additive exPlanations) quantified feature contributions on premature aging. The methodological approach and key results are depicted in Fig.1.

Results: Key predictors included AgeAtExam, time from treatment start to final control (TTC), blood count lymphocyte (BClymphocyte), insulin-like growth factor1 (IGF1), interleukin-2 (IL2), serum calprotectin (Scalprotectin), transepidermal water loss (TEWL), skin hydration (SCHBefore), BS score (BSBefore) before skin stripping and at 5 minutes after the procedure (BS 5min). Advanced age and prolonged TTC correlated with lower age difference, likely due to greater variability in aging patterns. Conversely, elevated IGF1, IL2, and BClymphocyte levels were associated with a higher biological age difference, indicating accelerated aging. Higher SCHBefore, BSBefore, and BS 5min values increased age difference, while TEWL 5min and lower Scalprotectin had a protective effect. Findings suggest premature aging is driven by systemic inflammatory and metabolic dysregulation.

Conclusion: This preliminary study explores the impact of child oncological treatment on premature aging, identifying potential biochemical, immunological, and treatment-related associations. While CNN offers initial insights, validation with larger datasets and longitudinal studies is needed. Future research will refine models, integrate multi-modal data, and develop targeted interventions for CCSs.

Supported by Ministry of Health of the Czech Republic grant AZV (NW24-08-0028) and co-funded by the EU and the state budget of Czechia OPJAC project SALVAGE No. CZ.02.01.01/00/22-008/0004644

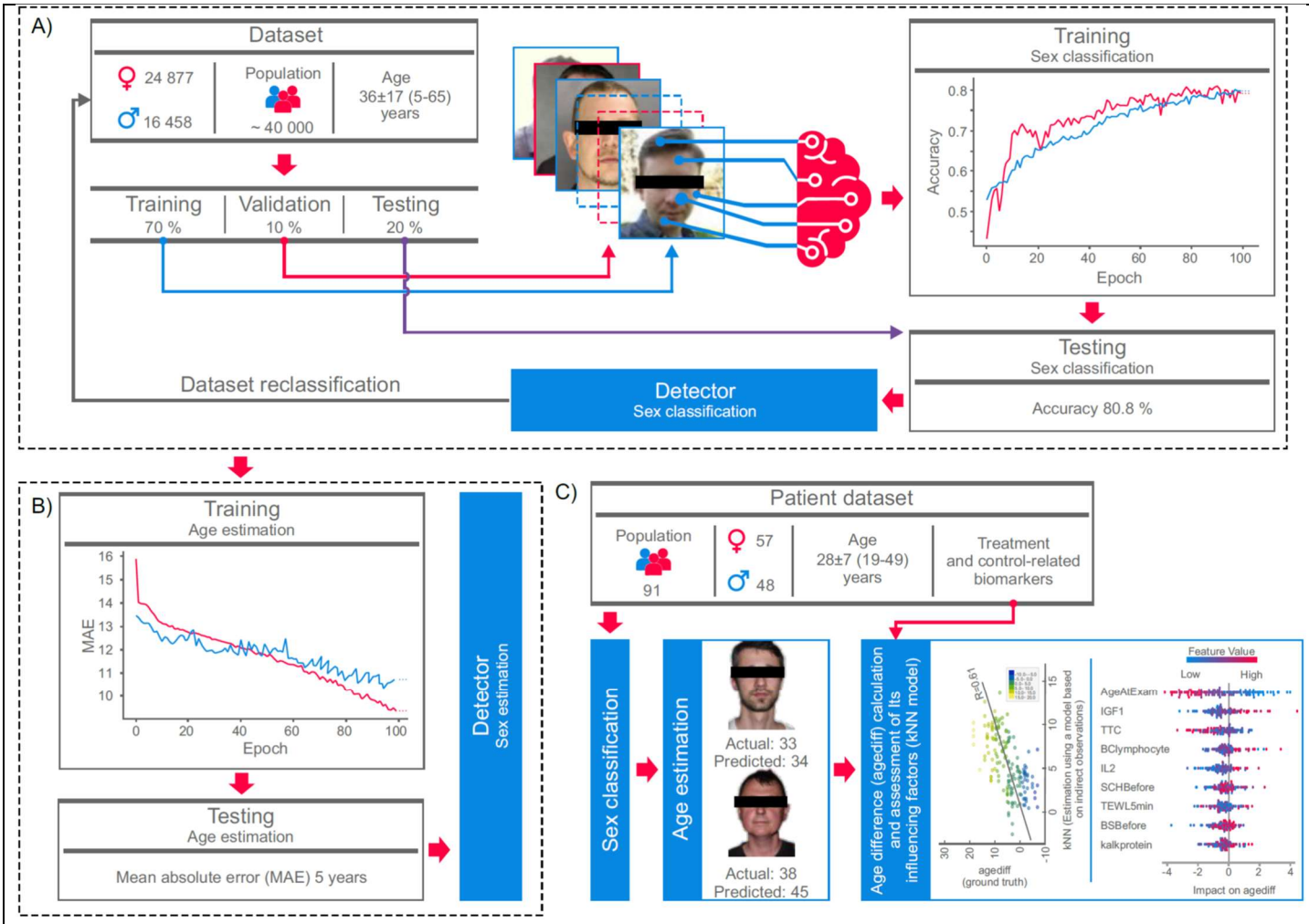


Fig. 1: CNN-based methodology for gender classification (A) and age estimation (B), with key results on premature aging influencing factors in CCSs (C).

Research Methods-3

Skin Barrier Lipidomics as a Noninvasive Method for Predicting Late Adverse Events in Childhood Cancer Survivors

Jarmila Kruseova, Sarah Blagodarna, Lenka Stolova, Marie Rychla, Tomas Eckschlager, Lukas Opalka, Katerina Vavrova

Background: Research in recent years has focused on finding new diagnostic tool to identify child cancer survivors (CCSs) at highest risk for late effects (LE). Many LE arise as a result of premature aging. Structural and functional skin changes are one of the most obvious features of human aging. The objective of the present study is to establish a skin barrier assessment to evaluate premature aging in CCSs.

Methods: We evaluated a cohort of 264 CCSs treated between 1980 and 2011 for solid tumors, median age at diagnosis was 11.77 yrs., (IQR 4.77-15.28), from these 119 were females. Median age at study evaluation was 25.68 yrs., (IQR 21.43-32.28). Individuals lacking a personal history of cancer were utilised as controls (n=51), median age at the time of examination was 27.27 yrs., (IQR 25.12-31.46). We measured eight uppermost stratum corneum layers for protein and lipid analysis (sphingolipids) and recorded transepidermal water loss (TEWL) before tape stripping and immediately after the procedure. Samples were obtained by tape-stripping method using D-squame stripping discs.

Results: Our pilot data – measured so far 26% of our study cohort show already significant changes in the sphingolipid profile and skin barrier function. Total ceramides (sum of all sub-classes) were significantly (p=0.0296) increased in cancer survivors compared to control samples. TEWL was also higher in survivors than in healthy individuals.

Conclusions: Our preliminary data showing alterations in epidermal sphingolipid metabolism warrant further investigation. We plan to continue the research in a larger group of CCSs. We will correlate those results with measurement of visceral fat, metabolic and longevity serum markers and with the occurrence of other LE.

Supported by Ministry of Health of the Czech Republic grant AZV (NW24-08-00289) and co-funded by the EU and the state budget of Czechia OPJAC project SALVAGE No. CZ.02.01.01/00/22-008/0004644

Neurocog-8

Building a Framework for School Support in Pediatric Oncology Patients

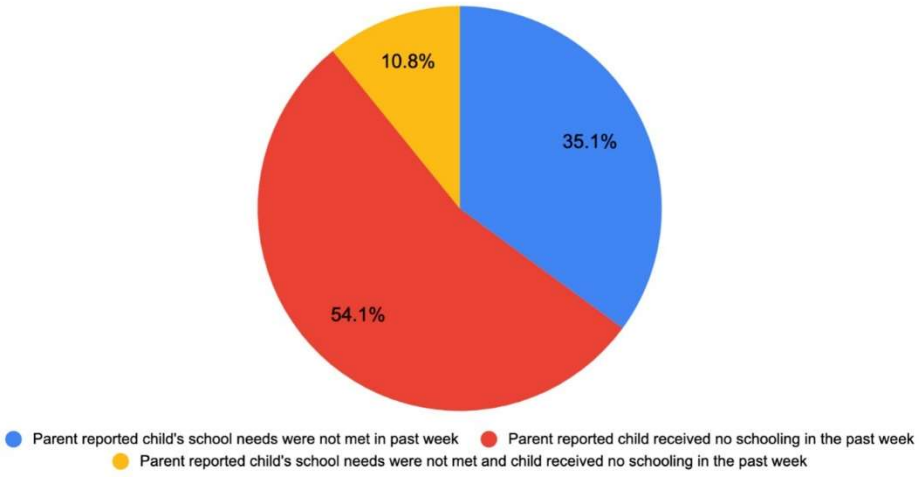
Sophia Kujawski, Jaime Rotatori, Justin Gardner, Lyn Balsamo, Claudia Auerbach, Nina Kadan-Lottick, Rozalyn Rodwin

Background/Purpose: School support for children with cancer is recommended from diagnosis through survivorship. Standardized school support programs are needed to ensure ongoing schooling and school re-entry support and address communication between the community school and the medical team. We aimed to develop and assess the feasibility of a standardized school support program with a school support specialist and weekly electronic monitoring to address childhood cancer patients' schooling needs.

Methods: School-aged (kindergarten-12th grade) patients within 1 month of starting treatment with chemotherapy and/or radiation for newly diagnosed cancer or relapsed disease at the Yale regional pediatric hematology/oncology clinic were eligible if they had a parent literate in English or Spanish and life expectancy >6 months. Enrolled patients met with a school support specialist (licensed teacher in the state with a master's in education) who educated families on schooling options, assisted with 504 paperwork if needed, and coordinated with the community school to develop an education plan for the patient. This might include in-person, remote, or hybrid instruction. The school support specialist acted as an ongoing liaison with the school through treatment and in some cases school re-entry. Parents completed 2-minute weekly surveys (via RedCap) reporting their child's school attendance (in-person and remote), if they had unmet schooling needs, and if they requested to meet with the school support specialist. Surveys were routed to the school support specialist electronically to provide additional assistance if no school was attended during the past week or if parents reported their child's needs were not being met.

Results: From October 2023 through December 2024, 14 of 28 (50%) eligible patients enrolled (mean age of 11.7 + 4.8 years, 50% female, and diagnosed with leukemia [28.6%], lymphoma [28.6%], central nervous system tumor [7.1%], and other solid tumors [35.7%]). One patient left the study prior to completion. A total of 179 surveys were sent to the 13 remaining participants, and 113 (63.1%) were completed. Among completed surveys, 37 (32.7%) were routed to the school support specialist for follow-up (Figure). Examples of concerns addressed in follow-up included scheduling homebound teachers, obtaining materials and assignments from community schools, and planning for re-entry.

Figure: Reason for school support specialist follow-up in 37 routed surveys



Conclusion: A standardized school support program offering individualized care and ongoing electronic follow-up beginning at the time of cancer-diagnosis can help identify and address unmet schooling needs and improve continuity of learning. Future research is needed to evaluate patient, parent, and educator perspectives of the program so it can be tailored to better engage all patients and community stakeholders, and to understand how the program impacts long-term school success and quality of life in childhood cancer survivors.

Intervention Research-4

Engaging Adult Primary Care Providers in Survivorship Care with Interactive Phone Calls

Sophia Kujawski, Jaime Rotatori, Wilhelmenia Ross, Lyn Balsamo, Justin Gardner, Claudia Auerbach, Nina Kadan-Lottick, Rozalyn Rodwin

Background/Purpose: Even with the availability of specialty survivorship clinics and the Children's Oncology Group Long-Term Follow-Up Guidelines (COG-LTFUG) <30% of childhood cancer survivors receive ongoing recommended follow-up in adulthood. Engaging primary care providers (PCPs) is a potential strategy to improve care for adult childhood cancer survivors. We aimed to assess the feasibility and acceptability of an interactive phone call between a survivorship nurse and PCPs of adult childhood cancer survivors regarding their individual post-therapy care needs.

Methods: A registered nurse from a regional childhood cancer survivorship clinic telephoned the PCPs (or covering advanced practice provider or nurse) of all patients ≥18 years who had an adult PCP and were seen January-August 2024 to review their individualized cancer treatment history, surveillance schedule to screen for potential chronic health complications as per the COG-LTFUG, and any recommendations from their recent survivorship visit. We calculated the proportion of PCP staff successfully contacted by the survivorship nurse, medians/ranges of attempts and durations of calls, and PCP rating of helpfulness (1-10 for least-most).

Results: Eighteen eligible survivors (63% female, median age 26.7 [range 21.5-35.6] years, median 13.2 [range 2.9-31.3] years post-therapy after Hodgkin Lymphoma [33%], leukemia/non-Hodgkin lymphoma [33%], central nervous system tumor [17%], and other solid tumors [17%]) with PCPs were identified. For these survivors, the survivorship nurse spoke with a PCP (or member of the clinical team) at 16 offices (89%): 2 (11%) were not reached after 6 attempts. Among PCPs contacted, the survivorship nurse spoke with 6 physicians (38%), 5 advanced practice providers (31%), and 5 nurses (31%) after a median of 2 attempts (range 1-6) for a median duration of 5 minutes (range 4-11). A PCP was reached on the first attempt in 7 instances (44%). The median helpfulness rating was 8 (range 6 – 10). PCP questions/feedback for the survivorship nurse included how to refer new patients for a survivorship clinic consultation, clarifying questions regarding COG-LTFUG surveillance schedule, and their enthusiasm regarding accepting more childhood cancer survivors into their practice.

Conclusion: A brief, interactive phone call from a survivorship nurse to the PCP of adult childhood cancer survivors is a feasible and acceptable way to engage PCPs in survivorship care of shared patients. Further research is needed to determine how PCPs can share responsibility in COG-LTFUG surveillance as a strategy to improve adherence to ongoing survivorship care.

Neurocog-9

Integration of a Computerized Neurocognitive Rehabilitation Program into Routine Childhood Cancer Survivorship Care

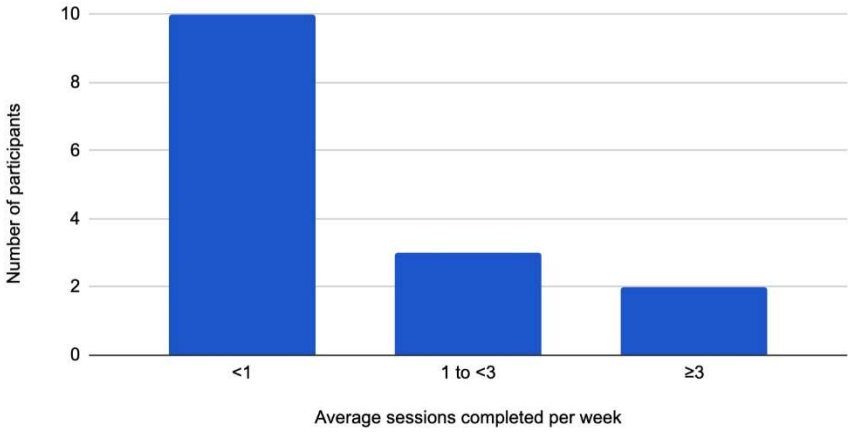
Sophia Kujawski, Jaime Rotatori, Claudia Auerbach, Nina Kadan-Lottick, Justin Gardner, Lyn Balsamo, Rozalyn Rodwin

Background/Purpose: Childhood cancer treatment can lead to neurocognitive impairment. CogMed is a computerized cognitive rehabilitation program that improves working memory in childhood cancer survivors in the research setting, yet implementation into survivorship care has not been evaluated. We aimed to assess participation rates and ongoing engagement in CogMed when offered as part of routine survivorship care.

Methods: Survivors from the Yale Childhood Cancer Survivorship Clinic, ages ≥4 years, at risk for neurocognitive impairment (history of brain tumor, or received methotrexate, high dose cytarabine, cranial radiation, or allogeneic stem cell transplant) and English-speaking, were offered CogMed participation 10/2/2023-11/18/2024. Participants were instructed to complete at least 3 training sessions/week until they completed all sessions and were assigned a coach per CogMed administration guidelines (oncologist, psychologist, or school support specialist). Participation rates among eligible survivors, and average sessions completed/week within 14 weeks (the timeframe needed to complete up to 40 scheduled sessions) were calculated. Patient characteristics and baseline impaired working memory and attention (measured by NIH Toolbox standardized scores <85) were compared in participants versus non-participants, and those with ongoing engagement in CogMed (completed an average of ≥1 session/week) versus non-engagers (completed an average of <1 session/week) using Fisher's exact tests and two sample t-tests.

Results: Among 134 eligible survivors (mean age 19.6+10.4 years, mean time since therapy completion 11.7+16.0 years, 44.8% female), 25 (18.7%) elected to participate in CogMed. Enrolled survivors were a mean age of 17.3+9.6 years, mean time since treatment completion of 11.4+10.5 years, 56% female, and had primary cancer diagnoses of leukemia/non-Hodgkin lymphoma (84%), central nervous system (CNS) tumors (12%), and non-CNS solid tumors (4%). Of 25 enrolled patients, 10 (40.0%), did not complete any CogMed sessions. The remaining 15 participants completed a mean of 1.0+1.1 sessions/week (compared to ≥3 recommended). Only 5 of 25 enrolled participants (20.0%) were engagers, and 2 (8.0%) completed an average of ≥3 sessions/week (Figure). When comparing enrolled versus non-enrolled, and engagers versus non-engagers, there were no significant differences in sex, age, time since therapy completion, history of CNS tumor, or history of radiation between groups. Baseline impaired working memory and attention did not differ between engagers and non-engagers.

Figure: Average sessions completed per week among 15 participants who started CogMed



Conclusions: Although prior studies show CogMed improves working memory in childhood cancer survivors, few survivors in our regional survivorship clinic agreed to start CogMed or engage in the program even after agreeing. Barriers to using CogMed must be evaluated, and modifications to CogMed or alternative interventions to improve neurocognitive function are needed.

Health Services Research-7

Financial Toxicity in Households of Pediatric Acute Lymphoblastic Leukemia Patients

Emily Lafrentes, Robert Hayashi, KC Donaldson, Kara Felts

Purpose: With more than three thousand children diagnosed with acute lymphoblastic leukemia (ALL) each year, the short-and long-term financial impact for childhood cancer can have a substantial impact on those living within the household. For these households, financial toxicity or the burden of cost due to cancer care, would be expected to be reported at higher rates in those households with children currently receiving therapy in comparison to their off-therapy peers. Assessing financial toxicity for ALL cancer survivors may be an important tool for providing subsequent support for them.

Methods: Families of patients diagnosed with ALL were recruited to assess their financial toxicity. Recruitment for this report took place from October 2024 to February 2025. Data was collected from households with children diagnosed with ALL who were currently receiving care at St. Louis Children's Hospital. Families of subjects undergoing active antineoplastic therapy or recent completion (within 3-36 months) were included. Inclusion criteria included a diagnosis of ALL, no known pre-existing medical conditions, and patient age between 5-17.99 years. Parents of the children completed study measures during routine scheduled clinic visits, utilizing the COST-FACIT measure to quantitate financial distress. A calculated score of 25 or less indicated financial toxicity, with a score range of 0 to 44.

Results: Forty-five patients were identified as eligible for participation; 9 declined when approached for recruitment. Of the eligible patients, 19 families signed consent (1 withdrawal) for participation but only 16 families (active therapy =10, completed therapy =6) completed all measures at time of this analysis. The mean time of patients who had completed therapy to the time of this assessment was 29.0 months. For those currently receiving therapy, the mean length of time from diagnosis was 10.4 months. Both active and completed therapy patients were found to have financial toxicity reported by their family members (Mean COST Score active therapy = 20.68, SD= 2.55; completed therapy 22.6, SD= 3.65).

Conclusions: Families of patients with ALL appear to experience financial toxicity both during and after therapy completion. Further investigations characterizing the durability of this financial toxicity and identification of strategies to reduce financial toxicity are needed.

Other late effects-9

Late Effects of Acute Leukemia Treatment in Polish Pediatric Patients

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Background: The improvement in the effectiveness of childhood cancer treatment has contributed to an increase in the number of survivors. Unfortunately, it appears that the treatment applied in childhood causes an increase in long-term complications. Leukemia is the most common childhood cancer, with a current cure rate of over 80%. In this multicenter study, we evaluated the frequency of complications in a group of Polish children and young adults many years after completing childhood cancer treatment.

Methods: The study group included 829 participants treated for acute leukemia (acute lymphoblastic leukemia ALL – 734, acute myeloblastic leukemia AML– 75, other leukemia – 20) in childhood, selected from The Polish National Childhood Cancer Survivors Registry (n = 1783). Children were diagnosed between 1988 and 2016. The mean age at diagnosis was 5.62 years (range 0.00-17.85), and the follow-up was 6.68 (range 0.42-23.22). Radiotherapy was used in 243 participants. All patients were treated according to international protocols approved by the Polish Pediatric Leukemia and Lymphoma Group.

Results: Normal function of all organs was presented by 136 (16.4%) participants. Abnormalities in one organ or system were developed by 121 (14.6%) children, in two organs or systems by 126 (15.2%), in three organs or systems by 119 (14.3%), and at least four by 327 (39.5%) participants of the study. In the entire study group, the most frequent (>20% of cases) dysfunctions concerned the following organs/systems: skin (42.3%), musculoskeletal (38.2%), circulatory (32.7%), immune (29.8%), male gonad (25.9%), oral and masticatory dysfunction (23%), urinary (22.9%), and gastrointestinal (20.7%). According to the age of diagnosis, children under six years old presented a higher incidence of smell and/or taste abnormalities ($p = 0.021$) than older patients. In the subjects with longer follow-up (>10 years), we observed more frequent liver ($p < 0.001$), hearing ($p = 0.019$), female (0.036), and male ($p = 0.006$) gonads dysfunctions. Moreover, there was a lower prevalence of immune system abnormalities in the same analysis ($p = 0.003$). Comparing types of leukemia, patients treated from AML had a higher incidence of female gonad ($p = 0.001$) dysfunction than ALL patients. In contrast, subjects with T cell ALL were more frequently reported to have deterioration of vision ($p = 0.034$) compared to type B ALL. Among participants who received radiotherapy, we noticed greater prevalence of thyroid gland ($p = 0.005$), male gonad ($p = 0.007$), and neurological system ($p = 0.002$) dysfunctions.

Conclusions: Most childhood cancer survivors (CCS) presented more than one complication. Radiotherapy appears to be a crucial factor in the occurrence of some late effects, especially those affecting the endocrine and nervous systems. This study confirmed the need for constant observation and long-term care of leukemia CCS.

Health Services Research-22

smartCARE Project: a Digital Solution for Enhancing Cancer Survivorship in Europe

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Background: The millions of Europeans living with and beyond cancer are a testament to decades of progress in treatment and care. However, diagnosis marks the beginning of a complex pathway, with ongoing challenges, including side effects, late effects and co-morbidities. smartCARE aims to develop a European-level mobile and web-based Cancer Survivor Smart Card, to enhance quality of life, health outcomes, and communication between individuals affected by cancer and their healthcare professionals (HCPs).

Methods: This project involved (1) a user needs assessment across diverse cancer patients, survivors, caregivers, and HCPs from multiple European countries, covering various tumour types, ages, and co-morbidities, and (2) the development and pilot testing of a mobile and web-based prototype. The assessment included a review of and interviews with existing digital tools, patient-led workshops, a pan-European survey (>1,000 responses) in 17 EU languages. A roundtable with HCPs was also held and regular meetings with project partners helped define app specifications, including treatment summary variables, symptom tracking, and language framework. The findings informed the development of a prototype, supervised by the European Cancer Organisation's Patient Advisory Committee and supported by a 41-organisation consortium, spanning patient organisations, HCPs, and civil society groups. The prototype was pilot tested in five cancer centres in Europe, and further evaluation was conducted through semi-structured interviews, gathering feedback on usability and perceived benefits.

Results: The developed prototype included early versions of four modules: MyHealth (medical data storage/portability and management, symptom tracking, Survivorship Passport integration), Telehealth (virtual consultations, chat, file sharing), Resources (educational materials), and Community (peer support). Although tested before fully functional, users rated it positively across all performance measures. The average satisfaction score was 3.1/5, with top-rated features including communication with HCPs (3.9/5), remote healthcare connectivity (4.2/5), and medical data management (3.9/5). AYA cancer survivors showed higher satisfaction trends (though the sample was small), yet only 30.6% were satisfied with their current follow-up care underscoring Smart Card's potential to bridge this gap.

Conclusions: A prototype mobile app was co-developed with cancer survivors, patients, caregivers, HCPs, and civil society groups. Extensive testing demonstrated that a digital tool for cancer survivorship could be highly beneficial in improving access to medical records, facilitating communication with HCPs, and providing peer support and educational resources. Future development should focus on refining usability, expanding functionality, and integrating the app into existing healthcare systems. Key recommendations were submitted to the European Commission to define the second phase.

Quality of life/Behaviors-11

Developing the Initial Items of Cancer-Related Emotional Distress Scale Through Qualitative Study for Adolescent with Cancer

Shu-Li Lee, Li-Min Wu

Background: Cancer-related emotional distress is an important issue that requires monitoring and caring in adolescents with cancer. However, a cancer-related emotional distress scale specifically designed for tailoring developmental characteristics of adolescents is rare.

Purpose: To develop the initial items of cancer-related emotional distress in adolescent with cancer.
Methods: Adopting a qualitative design, this study explored the perspectives and experiences of adolescents with cancer about cancer-related emotional distress for establishing a scale measuring cancer-related emotional distress in adolescents with cancer. In-depth interviews were conducted by adolescents with cancer enrolled through a convenience sampling. The interview content was collected by audio recording during the interview process and then transcribed into a text. The texts were analyzed by phenomenological method, with meaningful sentences categorized to emerge themes. The themes were transcribed into dimensions, and the meaningful sentences under each theme were transcribed into initial items.

Results: A total of 19 adolescents with cancer aged 10 to 19 years were included from a hospital in southern Taiwan. Cancer-related emotional distress in adolescents with cancer consisted of seven dimensions, including cancer itself, treatment process, symptoms, body image, ego identity, family, peer, and emotion. These seven dimensions comprised a total of 94 items.

Conclusions: The preliminary version of the 94-item Adolescent Cancer-Related Emotional Distress Scale, developed through prior qualitative research, will do further psychometric testing to refine the items and test its reliability and validity. The finalized scale can be used in clinical practices and research.

Key Words: adolescents, cancer, emotional distress, scale.

Childhood Cancer Survivor and Caregiver Perspectives on Participation in Pediatric Oncology Rehabilitation: a Qualitative Study of Barriers and Facilitators

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Background: As pediatric cancer survival rates continue to rise, it is important to address the long-term health needs of childhood cancer survivors (CCS). Many CCS experience changes in physical, cognitive, and/or psychosocial functioning because of cancer and its treatment. Rehabilitation (e.g., physical and occupational therapy) can ameliorate these impairments and enhance quality of life for CCS. Though rehabilitation is recommended in over ten pediatric oncology clinical guidelines, pediatric oncology rehabilitation programs are underutilized. The aim of this study was to characterize CCS and caregiver barriers and supports to rehabilitation access and participation throughout the cancer care continuum.

Methods: We recruited CCS ages 12-21 years and caregivers of children diagnosed with cancer before age 19 from two U.S. children's hospitals. Participants completed a semi-structured interview designed to capture factors that supported and/or impeded participation in rehabilitation following a cancer diagnosis. We conducted a qualitative content analysis of audio recorded and transcribed interviews to identify themes.

Results: Forty-six individuals (13 CCS, 33 caregivers) participated across two sites; 36% of children represented had blood cancers, 33% CNS tumors, and 31% non-CNS solid tumors. All participants were referred to physical therapy (100%), 95% to occupational therapy, and 52% to speech-language pathology. We organized findings into seven themes: (1) service transitions; (2) rehab in home communities; (3) costs and insurance coverage; (4) environmental factors; (5) consistency in care; (6) parental involvement; and (7) unique needs of CCS (Table 1). Overall, these findings highlight the importance of multi-level support for families navigating rehabilitation throughout and following their cancer care. Participants appreciated organizational and provider supports while transitioning between therapy settings and navigating financial burden, such as automatic referrals or clear communication on therapy options and potential costs. Environmental factors, including setting, influenced experiences with rehabilitation, with some reporting difficulty finding appropriate services in their home communities. In partnership with their parents, CCS benefited from consistent rehabilitation care from providers equipped to address their cancer-specific needs.

Table 1. Themes and sample quotes from childhood cancer survivor (CCS) and caregiver participants.

Theme	Quote	Participant
Service transitions	"I think what could help make [discharge from therapy] easier is knowing ahead of time that you can have these periodic check-ins: Let's see each other again in one month or even two months. Something coming up, instead of it just being a full stop."	Parent of a 7-year-old with gaglio-neuroblastoma; Site 2
Rehab in home communities	"[The providers at academic medical center] said he still needed [occupational therapy]. Then back home, they say since he's got strength in his hands, he don't need it. And so we were at war with the [home community] OT."	Parent of a 16-year-old with medulloblastoma; Site 1
Costs and insurance coverage	"Perhaps one of the reasons we haven't pursued having people come over for physical therapy at home is because we have to do all that resource finding...Like I don't know what they're supposed to be doing. I don't know what I'm looking for. Like, that I don't have the bandwidth for that."	Parent of a 7-year-old with high risk neuroblastoma; Site 2
Environmental factors	"I think the fact that we were, I was in my own town, not in the hospital, kind of made me a little more relaxed to do physical therapy."	15-year-old survivor with Ewing's sarcoma of femur; Site 1
Consistency in care	"That was part of the reason we switched our OT in particular, 'cause we kept on cycling through different therapists."	Parent of a 6-year-old with AML; Site 1
Parental involvement	"[My parents] always gave me, like, choices and were able to—they left me to choose what I needed."	13-year-old with pilocytic astrocytoma; Site 2
Unique needs of CCS	"And so, having therapists that know how to handle [laughs] a kid that, you know, is just over having to work and be in the medical setting a lot is helpful" (Washington University in St. Louis, Caregiver 005)	Parent of a 6-year-old with AML; Site 1

Conclusion: We characterized multi-level barriers and supports to rehabilitation, as identified by CCS and caregivers. Families benefited from automated and transparent referral processes and were challenged by a variety of environmental factors that limited access to rehabilitation services. These findings can inform the development and evaluation of pediatric oncology rehabilitation programs designed to increase access to quality rehabilitation care for CCS. Further research is needed to explore the views of CCS and caregivers who chose not to participate in rehabilitation services.

Other late effects-2

A Phase IV Surveillance Trial of Pencil Beam Scanning Proton Therapy in Children

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Purpose/Objectives: Intensity modulated pencil beam scanning proton radiotherapy (PBS-PT) was approved for the treatment of childhood cancer based on substantial equivalence to photon radiotherapy. We designed a phase IV clinical trial to study the safety and effectiveness of PBS-PT when early reports suggested an increase in adverse events.

Methods: We screened 1,000 children, enrolling 995 eligible for PBS-PT on SJPROTON1 (NCT03223766) between July 2017 and January 2022, covering 2,916 irradiated sites. The median follow-up was 4.1 years (IQR 2.8-5.7). A mixed photon/proton approach was used in 12.4% of cases. The modified SJLIFE NCI CTCAE v4.03 was applied to estimate the cumulative incidence of grade 3 or higher (G3+) non-hematologic complications attributable to PBS-PT at baseline and through five years after PBS-PT. Additional outcomes included hospitalization, toxicity-related procedures, and treatment-related mortality. Pre-specified toxicities including necrosis, vasculopathy, neurologic deficits, and fracture/osteoradionecrosis were further characterized (any grade) as a secondary objective. Total toxicity burden (TTB) at each timepoint was quantified as an exploratory objective. Event-free (EFS) and Overall Survival (OS) were estimated using the Kaplan Meier estimator. The cumulative incidence (CI) of events were calculated using the Aalen-Johansen estimator and Fine-Gray subdistribution hazard model was used to evaluate predictors of ≥grade 3 PBS-PT attributable toxicity.

Results: At four years, the EFS and OS were 66.7% (95%CI, 63.7-69.9%) and 78.4% (95%CI 75.9-81.3%) respectively. The CI of treatment- and non-treatment-related deaths at four years was 0.8% (95%CI 0.04-1.6%) and 27.7% (95%CI 24-31.4%) respectively. The CI of treatment-related malignancies and benign tumors was 1.2% (95%CI 0.6-2.4%), and 1.8% (95%CI 0.9-3.2%), respectively. Baseline and post-PBS-PT trial evaluations identified 6,348 toxicities. The CI of G3+ toxicity events at four years was 34.8%, including CNS necrosis (3.7% 95%CI 2.5-5.3%), hearing impairment (11.3% (95%CI 9.1-13.8%), neurologic deficit (11.6%), and osteoradionecrosis (0.1% 95%CI 0-0.8%). The four year CI of hospitalization and procedures due to PBS-PT-attributable toxicity was 4% (95% CI 2.9-5.4%) and 5.5% (95% CI 4.1-7.1%), respectively. Predictors of an increased event-specific hazard for any G3+ toxicity in the patients treated for CNS tumors and leukemia included baseline TTB (HR 1.02, 95% CI 1.01-1.04, p=0.02). Conversely, the use of proton therapy (relative to mixed photon/PBS-PT) (HR 0.38, 95% CI 0.27-0.53, p<0.001), focal brain RT (HR 0.63, 95% 0.46-0.86%, p<0.001) or focal spine RT (HR 0.46 95% CI 0.07-3.11, p=0.2) (relative to craniospinal) predicted a decreased event-specific hazard for any G3+ toxicity. No key predictors were identified in the non-CNS patients.

Conclusions: Children selected for treatment with PBS-PT have positive long-term outcomes and a low overall risk of severe events including hospitalization. The incidence of reported G3+ toxicity events suggest that while PBS-PT is generally effective, there is a notable risk of specific adverse events that require further evaluation. Baseline TTB, mixed-modality therapy, and treatment volume are predictors of G3+ toxicity in selected patients. This study provides valuable insights into the safety and effectiveness of PBS-PT in treating childhood cancer.

SMN-2

Subsequent Neoplasms in Survivors of Neuroblastoma

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Background: Data on subsequent neoplasms (SN) and subsequent malignant neoplasms (SMN) in patients with neuroblastoma (NB) treated with multimodal therapy are limited. We sought to characterize SN and SMN in a cohort of NB survivors.

Methods: Retrospective review of survivors of NB ≥5 years from diagnosis, diagnosed 1980—2018, and followed at a tertiary cancer center. SN were defined as subsequent benign tumors and basal cell carcinomas (due to their indolent nature); SMN were defined as new primary malignancies occurring 5 years or later from the date of NB diagnosis. Clinical factors and treatment exposures were abstracted from the medical record. Descriptive statistics were used to characterize SN/SMN.

Results: Of 372 survivors of NB (56% male; median age at diagnosis: 2.9 years), 36 (9.7%) were diagnosed with ≥1 SN or SMN. Among these patients, median age of first SN/SMN diagnosis was 14.9 years (range 5.3-32.0) and a median of 9.6 years from primary NB diagnosis (1.5-27.2 years). Median follow-up time from diagnosis was 18.6 years (8.2-38.2 years). Most of these patients (89%) had stage 4 neuroblastoma at diagnosis and 39% had MYC-N amplification. Most patients received multiagent chemotherapy and RT; 50% also had autologous stem cell transplantation (Table 1). Additionally, 89% received anti-GD2 directed antibody therapy and 11% received metaiodobenzylguanidine (MIBG) therapy. In total, these 36 patients had 50 SN and SMN diagnoses; 25 (50%) were benign and 25 (50%) were malignant. 18 SN and 5 SMN were in the radiation field or following MIBG. The most common SN diagnoses were non-melanomatous skin cancer, all occurring in the RT field, and meningioma (5 out of 6 in the RT field). The most common SMN diagnoses were hematologic malignancies (n=8, 16%), papillary thyroid carcinoma [n=4, 8%], and osteosarcoma (OS) [n=3, 6%]. Two thyroid cancers and two OS diagnoses occurred outside of RT fields in patients who also were not exposed to MIBG therapy. One patient had five total SN/SMNs; germline testing has been negative. One patient had three SN/SMN diagnoses, also with negative genetic testing. Eight patients had two SN/SMN diagnoses, and the remainder of the cohort had one SN/SMN each. At time of last follow-up, 8/36 patients with SN/SMN were deceased, two from relapsed/recurrent NB and six from complications related to their SN/SMN diagnosis, which included acute myeloid leukemia, recurrent atypical meningioma, glioblastoma multiforme, synovial sarcoma, malignant peripheral nerve sheath tumor, and OS. Median time from NB diagnosis to death for these patients was 17.9 years (range 9.8-38.8 years).

Conclusion: NB survivors treated with multimodal therapy are at risk for a variety of SN and SMN, including 2 thyroid cancers and 2 cases of OS outside the RT field. Longer follow-up of larger cohorts will allow for more detailed analysis of SN and SMN development by risk group and treatment exposures.

Table 1a: Characteristics of NB survivors who developed at least one SN/SMN

Patients with SN/SMN	N (%)
Total patients with SN/SMN	36 (100%)
Age at NB diagnosis (y), median (range)	3.3 (0.3-24.5)
Age at SN/SMN diagnosis (y), median (range)	14.9 (5.3-32.0)
Time from NB to SN/SMN diagnosis, median (range)	9.6 (1.5-27.2)
Alive at last contact	28 (77.7%)
Sex	
Male	20 (55.6%)
Female	16 (44.4%)
Stage at Diagnosis	
Stage 1	1 (2.8%)
Stage 2	1 (2.8%)
Stage 3	2 (5.6%)
Stage 4	32 (88.9%)
MYC-N Amplification	
Yes	14 (38.9%)
No	16 (44.4%)
Unknown	6 (16.7%)
Primary Site	
Abdominal	33 (91.7%)
Mediastinal	2 (5.6%)
Other	1 (2.8%)
Relapsed Disease	
Yes	13 (36.1%)
No	23 (63.9%)
Radiation Therapy	35 (97.2%)
Abdominal	34 (94.4%)
Brain/Skull	10 (27.8%)
Mediastinum/periaortic/ paraspinal	18 (50.0%)
Bone	17 (47.2%)
Other	7 (19.4%)
Chemotherapy	
Cyclophosphamide	34 (94.4%)
Ifosfamide	5 (13.9%)
Etoposide	34 (94.4%)
Doxorubicin	32 (88.9%)
Cisplatin	33 (91.7%)
Immunotherapy	
Anti-GD2 monoclonal antibody	32 (88.9%)
MIBG Therapy	4 (11.1%)
Autologous stem cell transplant	18 (50.0%)

Table 1b: Characteristics of diagnosed SN/SMN

Subsequent Neoplasms	N=50
Benign, n(number in RT field)	25 (18)
Meningioma	6 (5)
Non-melanomatous skin cancer	6 (5)
Other central or peripheral nervous system lesion$_1$	3 (2)
Soft tissue or bony lesion$_2$	6 (3)
Other$_3$	4 (3)
Malignant, n(number in RT field)	25 (5)
Hematologic	8 (n/a)
Thyroid	4 (2)*
Osteosarcoma	3 (1)
Central nervous system tumor	3 (0)
Renal cell carcinoma	2 (0)
Other$_4$	5 (2)

*In RT field or following MIBG therapy

$_1$ Diagnoses include: astrocytoma, schwannoma, neurofibroma

$_2$ Diagnoses include: fibrous histiocytoma, osteoma, pilomatrixoma, benign phyllodes, dermatofibroma, hidradenoma

$_3$ Other SN diagnoses include: lymphangioma, pancreatic ganglioneuroma, cystic nephroma, adrenal adenoma

$_4$ Other SMN diagnoses include: ovarian teratoma, synovial sarcoma, malignant peripheral nerve sheath tumor, PEComa, sebaceous carcinoma

Quality of life/Behaviors-10

Supporting Electronic Evaluation of Symptoms for Anxiety and Depression after Childhood Cancer Treatment (SEE-SAD-ACT)

Jordan Marchak, Karen Effinger, Yvette Reynolds, Naadira Upshaw, Megan Pruitt, Heather Emery, Ebonee Harris, Corine Ice, Rebecca Williamson Lewis

Background: The Children's Oncology Group Long Term Follow-Up Guidelines have recommended mental health (MH) screening for survivors of childhood cancer for more than twenty years, yet most pediatric institutions have not implemented evidence-based screening programs. Guided by the RE-AIM framework, this study evaluated the implementation of electronic health record (EHR) integrated electronic screening (e-screening) for anxiety and depression in survivorship care.

Methods: Participants (N=568) included survivors aged 8.0-17.9 years presenting for survivorship care from April 2024 to December 2024. At clinic visit check-in, patients (≥13 years) or caregiver proxies (patients <13 years) electronically completed respective PROMIS (Patient-Reported Outcomes Measurement Information System) Depressive Symptoms 8a/6a and Anxiety 8a short forms via a patient-facing EHR application (i.e., Epic Welcome). EHR data were abstracted to characterize the reach and implementation of MH e-screening. A subset of patients (N=150) completed surveys on the acceptability, appropriateness, and usability of MH e-screening as measured via the Acceptability of Intervention Measure (AIM), the Intervention Appropriateness Measure (IAM), and After Scenario Questionnaire (ASQ) immediately following the completion of e-screening.

Results: The MH e-screening program reached 77.4% of survivors at point-of-care during the study period (439/567). Nearly one-third of survivors (31.9%, 140/439) who were screened reported mild to severe depression or anxiety (Table 1). Providers adhered to workflows for critical alerts for moderate-to-severe depression or severe anxiety (49/439) with high fidelity by referring to psychology (38/49) or confirming active community MH supports (11/49). In response to referrals, psychology consults were provided at point-of-care (27/38), MH follow-up occurred post-survivor visit (4/38), or families declined MH support (4/38). Survey results from N=75 caregivers (60% non-Hispanic White, 81% female, M=41 years old) and N=75 survivors (43% non-Hispanic White, 44% female, M=15 years old) indicated high acceptability and appropriateness of e-screening (Caregivers: AIM M=4.27 [SD=0.72], IAM M=4.39 [SD=0.70]; Survivors: AIM M=4.02 [SD=0.67], IAM M=4.26 [SD=0.57]). ASQ results showed high usability (Caregivers: M=6.55 [SD=0.86]; Survivors: M=6.01 [SD=0.95]).

Table 1. Pediatric survivor clinic depression and anxiety screening results

	Anxiety		Depression	
	PROMIS Parent Proxy Anxiety – Short Form 8a	PROMIS Pediatric Anxiety – Short Form 8a	PROMIS Parent Proxy Depressive Symptoms – Short Form 6a	PROMIS Pediatric Depressive Symptoms – Short Form 6a/8a
Symptoms	**M (SD) [range]**		**M (SD) [range]**	
T-score	47.9 (8.67) [39-70]	48.9 (8.40) [39-80]	48.4 (7.97) [41-71]	47.6 (8.91) [40-76]
Prevalence	**N (%)**		**N (%)**	
Within normal limits	315 (55.5%)		320 (56.3%)	
Mild (t-score 55-59)	69 (12.1%)		51 (9.0%)	
Moderate (t-score 60-69)	37 (6.5%)		44 (7.7%)	
Severe (t-score >70)	2 (0.4%)		4 (0.7%)	
No screener completed	148 (25.5%)		149 (26.2%)	

PROMIS: Patient-Reported Outcomes Measurement Information System, M: Mean, SD: Standard deviation

Conclusions: This study demonstrates that EHR-integrated e-screening is a feasible and acceptable approach to implementing guideline-recommended mental health surveillance, ensuring survivors receive timely identification and intervention to support their long-term well-being. Findings highlight the urgent need for routine, EHR-integrated mental health screening in survivorship care, given the prevalence of anxiety and depression among young survivors and the strong acceptability, appropriateness, and usability of e-screening among survivors and their caregivers.

The Impact of Socioeconomic Status on Mortality in Hepatoblastoma

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Survival rates for hepatoblastoma (HB) continue to improve, yet limited data exist on the impact of social determinants of health on mortality. This analysis includes 674 HB cases (diagnosed 1989-2017) enrolled in the Children's Oncology Group ACCRN07 protocol or identified from the California Cancer Registry. We linked HB cases to the National Death Index to assess mortality. We geocoded address at the time of diagnosis and assigned census tract-level Yost Index, an area-based socioeconomic status (SES) composite score derived from the following aspects of a census tract: median household income, median house value, median rent, percent below 150% of poverty line, education index, percent working class, and percent unemployed. A subset (n=143) had limited diagnostic data (stage at diagnosis) available. We assessed overall survival within the entire cohort and, separately, among 2-year survivors by Yost index quartiles (Q1 to Q4, corresponding to the most disadvantaged versus least disadvantaged Yost Index scores). We estimated hazard ratios for the association between area-based SES quartile and all-cause mortality using multivariable Cox proportional hazards models, adjusting for sex, age at diagnosis (<1, 1 to <3, 3 to <6, ≥6), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Non-Hispanic Asian/Pacific Islander, Hispanic, other/unknown), and decade of diagnosis. Separate models additionally included stage at diagnosis. Among 674 cases who had a median follow up of 8.3 years (IQR: 5.7-10.5) there were 100 deaths during follow up. Among 602 2-year survivors, there were 28 deaths during follow up. All-cause mortality cumulative incidence among the entire cohort at 2 years did not reveal differences by area-based SES (Q1: 8.7%, 95% confidence interval [CI] 5.1-13.5%; Q2: 15.2%, 95% CI 9.9-21.5%; Q3: 10.2%, 95% CI 6.4-15.1%; Q4: 9.6% 5.8-14.5%; p-value: 0.38). Among 2-year survivors, all-cause mortality incidence at 10 years showed statistically significant differences by area-based SES quartile (Q1: 10.6%, 95% CI 6.3-16.1%; Q2: 1.6%, 95% CI 0.3-5.3%; Q3: 4.1%, 95% CI 1.6-8.3%; Q4: 1.9%, 95% CI 0.5-5.1%; p-value: 0.001). In multivariable models among the entire cohort, adjusted effect estimates suggest an increased hazard of mortality among more disadvantaged area-based SES groups compared to the highest quartile (Q1 v Q4: 1.6, 95% CI 0.9-2.9). Inclusion of stage at diagnosis in the model resulted in increased effect estimates and a similar dose-response trend but substantially reduced precision. This analysis suggests that social determinants of health impact mortality after HB diagnosis, and that differences are driven by mortality among those who survive the initial stages of treatment. Additional analyses in large, clinically annotated datasets are needed to further elucidate the association between individual- and neighborhood-level social factors and HB mortality and to identify opportunities for intervention to improve outcomes.

Table: Hazard ratios and 95% confidence intervals for the association between census tract-level Yost index at the time of diagnosis and mortality, overall and among 2-year survivors

	Overall		2y survivors	
Yost quartile	Model 1*	Model 2†	Model 1*	Model 2†‡
Q1	1.63 (0.90-2.94)	7.95 (1.64-38.5)	5.87 (1.81-19.0)	-
Q2	1.48 (0.80-2.72)	6.21 (1.19-32.3)	0.82 (0.14-4.66)	-
Q3	1.21 (0.67-2.18)	5.69 (1.16-28.0)	1.76 (0.48-6.44)	-

Yost Q4 (highest area-level SES quartile) is the referent

* Adjusted for sex, age at diagnosis, race/ethnicity, decade of diagnosis

† Additionally adjusted for stage at diagnosis

‡ Hazard ratios were not estimable due to small cell counts

Endo-3

Pregnancy Rates and Reproductive Outcomes in Female Adolescent and Young Adult Cancer Survivors: a Retrospective Analysis Using Epic SlicerDicer

John Mariano, Jessica Cohen, Alissa Huston, Wendy Vitek

Background/Purpose: Fertility preservation and reproductive outcomes are crucial concerns for adolescent and young adult (AYA) cancer survivors. This study aims to assess pregnancy rates and reproductive outcomes in female AYA cancer survivors using Epic SlicerDicer.

Methods: We conducted a retrospective analysis of female cancer patients at the University of Rochester Medical Center between January 1, 2015 to January 1, 2025 who were age15-39 at diagnosis. Using Epic SlicerDicer, we identified 1674 patients with acute myeloid leukemia (AML, 9.6%), acute lymphoblastic leukemia (ALL, 9.3%), breast cancer (53%), and lymphoma (31.1%). We extracted data on pregnancy rates, miscarriages, spontaneous abortions, recurrent pregnancy loss, infertility, and sexual dysfunction.

Results: The current age distribution of patients was: <20 years (2.8%), 20-30 years (13%), 30-40 years (35.1%), 40-50 years (36.1%), 50-60 years (9.5%), 60-70 years (2.2%), and >70 years (1.3%). Median current ages were: lymphoma (37 years), AML (36 years), breast cancer (42 years), and ALL (29 years). Overall pregnancy rate was 17.3%, with variations among cancer types: lymphoma (19.2%), AML (11.7%), breast cancer (17.9%), and ALL (12.3%). Other reproductive outcomes included miscarriages (3%), spontaneous abortions (2.6%), recurrent pregnancy loss (0.657%), female infertility (9.4%), sexual dysfunction (0.29%), and dyspareunia (4.7%).

Conclusion: This study provides valuable insights into the reproductive outcomes of female AYA cancer survivors in real time utilizing real-world data. The findings highlight variations in pregnancy rates among different cancer types and underscore the importance of fertility preservation and reproductive health monitoring in this population. Further research is needed to understand the factors influencing these outcomes and to develop targeted interventions for improving reproductive health in AYA cancer survivors.

Health Services Research-9

Exploring Late Effects Care for PTLD Survivors Using the Consolidated Framework for Implementation Research

Mary Claire McGlynn, Vikas R. Dharnidharka, Bryan A. Sisk, Robert Hayashi, Allison A. King

Background/Purpose: Pediatric cancer survivors experience late effects. Coordinated care mitigates late effects. Post transplant lymphoproliferative disease (PTLD) is a lymphoma-like cancer that occurs in solid organ transplant (SOT) recipients. PTLD survivors experience late effects from cancer, yet less than 10% of PTLD survivors at St. Louis Children's Hospital (SLCH) follow in late effects clinic. With qualitative interviews we aim to 1-Describe barriers and facilitators for PTLD survivors' access to late effects care. 2-Investigate clinicians' perceptions of current and ideal PTLD late effects care. Our long-term goal is to develop and pilot implementation strategies to standardize PTLD late effects care.

Methods: We will recruit 20-25 PTLD survivors or their caregivers and 10-15 health care workers (HCW) from oncology, late effects, and SOT teams at St. Louis Children's Hospital (SLCH). We will then conduct qualitative semi-structured interviews based on the Consolidated Framework for Implementation Research (CFIR). A preliminary codebook will be based on CFIR and refined through transcript review. We will perform team-based coding. Team-based coding includes double coding and checking for intercoder reliability. Finally, we will generate coding reports to understand themes and identify barriers and facilitators of late effects care.

Results: We hypothesize survivors, caregivers, and HCWs will identify actionable factors to inform future studies to optimize late effects care. We will examine the CFIR inner setting (resources, communication, structural characteristics), outer setting (local attitudes, external pressures), innovation domain (adaptability, evidence-base, relative advantage), individuals domain (need, opportunity, motivation), and implementation process domain. Our contribution will be novel. 1-This is the first assessment of barriers and facilitators for late effects care in pediatric PTLD survivors. 2-We will consider input from HCWs across various disciplines delivering care to PTLD survivors. 3-We anticipate identifying unique contextual factors in PTLD survivors that will influence implementation of evidence based late effects care.

Conclusions: No prior studies have evaluated ideal delivery of late effects care for PTLD survivors. Our findings will inform an implementation trial to improve delivery of late effects care for PTLD survivors.

Health Services Research-10

Implementing Paediatric Cancer Survivorship Care Plans in Primary Care: a Qualitative Study of Practitioners' Experiences

Jordana McLoone, Joseph Elias, Christina Signorelli, Shuang Liang, Skye McKay, Carolyn Mazariego, Claire Wakefield, Richard Cohn, Natalie Taylor

Background/Purpose: Primary Care Practitioners (PCPs) report lacking confidence in managing childhood cancer survivors' care. Personalised, specialist-developed survivorship care plans (SCPs) can potentially develop the PCP workforce to manage complex care locally, relieving pressure on the tertiary healthcare system and increasing convenience for survivors. Engage, a remote childhood cancer survivor (CCS) intervention, provided personalised SCPs (including cancer diagnosis, treatment summary, chronic health conditions and follow-up care needs), to support PCPs in caring for CCSs, especially low-risk survivors discharged from hospital-based care. Our qualitative study explored PCPs' preferences for the content and format of the Engage SCP and identified barriers and facilitators to implementing recommendations for care in primary practice.

Methods: Semi-structured interviews were conducted with 20 PCPs recruited from primary care networks and referrals obtained from PCPs for Engage participants to receive the intervention. Interviews were guided by implementation science and cognitive interviewing frameworks. Thematic analysis was conducted using NVivo 14, with deductive coding based on the Consolidated Framework for Implementation Research and the Theoretical Domains Framework to specify multi-level constructs influencing successful implementation. Inductive analysis, underpinned by principles of phenomenology, generated themes.

Results: Most PCPs were female (70%), trained in Australia (65%), and worked in a private (90%) metropolitan (75%) practice, and represented 7 of 8 Australian states. PCPs desired clearer identification of high priority requests within their scope of practice, visual aids such as tables to present dense information, accessible contact details for involved specialists, and explanations for why certain follow-up recommendations were made (e.g., frequency of surveillance tests). Implementation barriers included organising care for patients living regionally/remotely or those with financial constraints, navigating community and specialist resources, time pressures due to workload, and challenges in patient adherence to appointments or health recommendations.

Conclusion: PCPs found the Engage SCPs acceptable, appropriate, and mostly feasible to implement, considering them valuable educational resources for a rare disease they seldom encounter.
Our findings support refining the structure and content of SCPs to enhance sustainable CCS care within primary practice. Future work should focus on developing user-friendly SCPs, providing targeted PCP education and improved access to specialist expertise, to ensure PCPs optimise survivorship care delivery.

Research Methods-5

Feasibility of Measuring Heart Rate Variability Using a Wearable Device: a Report from the St. Jude Lifetime Cohort Study (SJLIFE)

Ashley McNickle, Aimee Santucci, Daniel A. Mulrooney, Stephanie B. Dixon, Bonnie Ky, Deo Kumar Srivastava, Robyn Partin, Sean O'Neil, Joshua Burns, Greg Armstrong, Melissa Hudson, Kiri Ness

BACKGROUND: Recent data indicate that childhood cancer survivors are at risk for cardiac autonomic dysfunction, contributing to risk for major adverse cardiac events (MACE). Advances in wearable technology provide an opportunity to detect this impairment in survivors without overt symptoms, identifying those at increased risk for MACE.

PURPOSE: The aims of this study were to evaluate the feasibility of using the WHOOP® wearable device to collect heart rate variability (HRV) data and compare cancer survivors to age-specific normative HRV data.

METHODS: The study recruited adult survivors of Hodgkin Lymphoma (age ≥18 years) exposed to ≥20 Gray (Gy) chest radiation who were participants in SJLIFE. Participants were consented remotely and mailed the device with instructions for setting up the application on their phone. A study team member assisted with setup and activation via teleconferencing if needed. Participants were asked to wear the device for a minimum of 48 hours during all regular activities except bathing and swimming. Additionally, participants were evaluated in-person to assess concordance between short term electrocardiogram (ECG) and the WHOOP measured HRV (10-minutes of simultaneous wear in a supine position). Descriptive statistics were used to describe outcomes and to classify risk for myocardial infarction. Bland Altman methodology was used to compare wearable device and ECG values.

RESULTS: Thirty-three (82.5%) of 40 approached survivors consented (median age 41 years; range 21-56 (66.3% female, 15.2% non-white). Twenty-nine of 33 (87.9%) participants had ≥3 hours of usable data (median 8.9 (4.6-13.1) hours) after removal of noise. The mean age specific z-score (standard deviation (SD)) for the standard deviation of N-to-N intervals (SDNN) was -1.90±1.83 with 52.9% of survivors having an age-specific SDNN z-score <-1.5 SD. Using the classification proposed by Kleiger for patients post myocardial infarction, 31.0% of survivors had SDNN values below 50 millisecond (ms) (unhealthy by HRV) and 34.5% had SDNN values 50–100ms (compromised health by HRV). Ten-minute natural log root mean square standard deviation values between the two measures differed by 1.00±0.86ms. Values from the wearable device were consistently higher than those from the ECG.

CONCLUSIONS: HRV captured with a wearable device is feasible, consistent with ECG measurement of HRV, and identifies HL survivors at potential risk for MACE.

Quality of life/Behaviors-1

Psychologic Distress Amongst Adolescent and Young Adult Cancer Survivors and Parents

Kaille Meguiar, Afsoon Gazor, Lili Sun, Tatsuki Koyama, Bruce Compas, Debra Friedman, Adam Esbenshade

Background/Purpose: Increasing survival in adolescent and young adult (AYA) cancer patients has led to a growing population at risk for poor psychological outcomes. We sought to identify risk factors for the development of psychologic distress and post-traumatic stress (PTS) in AYA survivors and their parents.

Methods: In a single-institution prospective cohort study, survivors ages 10-25 years old completed a self-report review of systems (ROS) and psychosocial surveys at initial and follow up visits, including the Youth (YSR) or Adult Self Report (ASR) assessing psychologic distress and the Impact of Events Scale (IES) assessing PTS. Parents of patients ages 10-18 years completed the Childhood Behavior Checklist (CBCL) assessing their child's psychologic distress. Parents completed the Beck Anxiety (BAI) and Depression (BDI) Index and IES assessing their personal anxiety, depression, and PTS. Psychologic distress and PTS were defined dichotomously with an internalizing problems T-score >/= 60 on YSR/ASR/CBCL and IES >/= 24, respectively. Psychologic distress and PTS were further analyzed as continuous variables in multivariable linear regression models with age, diagnosis, gender, time from end of therapy (EOT), substance use, sexual dysfunction, ROS, and therapy intensity. Spearman correlation coefficients were computed to assess relationships between patient and parent scores.

Results: The study enrolled 135 patients and 72 parents, of which 37 were parents of 10–18-year-olds. Median age of patients at diagnosis was 15 years and median time from EOT was 3.2 years. 50% were female, 65% had a hematologic malignancy, and 92% were white. 20% of patients reported psychologic distress. 17% of patients and 17% of parents reported PTS. 10% and 13% of parents reported at least moderate anxiety and depression, respectively. In multivariable regression, psychologic distress was associated with a higher number of patient-reported systems (Slope estimate = 2.98, $p < 0.01$) and shorter time since EOT (-0.45, $p = 0.03$). PTS was associated with a higher number of patient-reported systems (1.46-fold, $p < 0.01$). Multivariable regression analyses in parent data showed parent-reported psychologic distress of patient was associated with a higher number of patient-reported systems (6.01, $p = 0.03$). Positive correlations were seen between parent-reported psychologic distress of patient and patient self-reported psychologic distress ($R = 0.58$, $p <0.01$) and also with patient self-reported PTS ($R = 0.51$, $p < 0.01$). Parent reported psychologic distress of patient was positively correlated with parent self-reported anxiety ($R = 0.45$, $p = 0.01$) and also with parent self-reported PTS ($R = 0.42$, $p = 0.02$).

Conclusion: A meaningful minority of survivors and parents face psychologic distress and PTS. A larger study is ongoing to expand upon our preliminary findings and examine the trajectory of psychologic distress and PTS in survivorship.

Health Services Research-35

Adherence to the Children's Oncology Group Long-Term Follow Up Guidelines at a Mid-Size Pediatric Oncology Program to Guide Quality Care

Brinda Mehta, Dana Stephens, Angela Bennett, Amanda Marcanio

Background/Purpose: The Children's Oncology Group Long-Term Follow Up guidelines (COG LTFU) are risk-based, exposure-related clinical practice guidelines to provide recommendations for screening and management of late effects in survivors of pediatric cancers. These are utilized widely especially at the North American centers to standardize and guide evidence-based care for pediatric cancer survivors. We analyzed the compliance and adherence to these guidelines to ensure that quality care is being provided at our survivorship clinic.

Methods: Charts of patients seen at the After completion of therapy (ACT) clinic over a 1-year period (March 2023-March 2024) were reviewed and adherence to COG LTFU guidelines was assessed by looking at the frequency of recommended blood tests, urine analysis, ECHO, pulmonary function tests (PFT) and DEXA scans. These tests were ordered ahead of the patient visit after reviewing the cancer treatment summaries at the pre-visit planning meetings.

Results: There were 103 long-term pediatric cancer survivors seen at the ACT clinic during the 1-year review period. Of these patients, 46.6% (48/103) had leukemia/lymphoma, 7.8% (8/103) with CNS tumors, 33% (34/103) with solid tumors, 11% (11/103) with sarcomas, and 1.9% (2/103) with Langerhans cell histiocytosis (LCH) (Table I.). There was 100% (81/81) compliance in adhering to ECHO guidelines, 96% (22/23) for PFT's, 73% (33/45) for DEXA scan guidelines, 75% (18/24) for audiograms, 86% (89/103) for blood tests and (100%) 75/75 for urine analysis (Table I). Labs that were missed during the ordering process were serum magnesium (4), serum phosphorous (4), BMP (2), HbA1c (3) and lipid panel (2).

Table I.

Diagnoses	**Patients seen at ACT clinic between March 2023-2024 N=103**
Leukemia/lymphoma	48
CNS tumors	8
Solid tumors	34
Sarcomas	11
LCH	2
Total	103
COG LTFU screening test	**Compliance rate (%)**
ECHO	81/81 (100%)
PFT	22/23 (96%)
DEXA scan	33/45 (73%)
Audiology	18/24 (75%)
Blood tests	89/103 (86%)
Urine analysis	75/75 (100%)

Conclusions: Our ACT clinic adhered appropriately to the COG LTFU guidelines based on review of the cancer treatment summaries at the pre-visit planning meetings. Risk screening tests that had best adherence were ECHO's, urine analysis and pulmonary function tests. Screening tests that required scheduling with ancillary departments such as DEXA scan and audiograms had lower adherence both from the provider ordering perspective and patient completion rate. Our goal is to utilize this information to improve our screening and scheduling processes as well as continue to prevent over utilization of tests if not clinically indicated.

Development and Validation of a Principal Component Analysis Statistical Shape Pediatric/Adolescent Breast Model for Dose Reconstruction of Pre-Ct Era Radiotherapy Pediatric Patients in Long-Term Outcome Studies

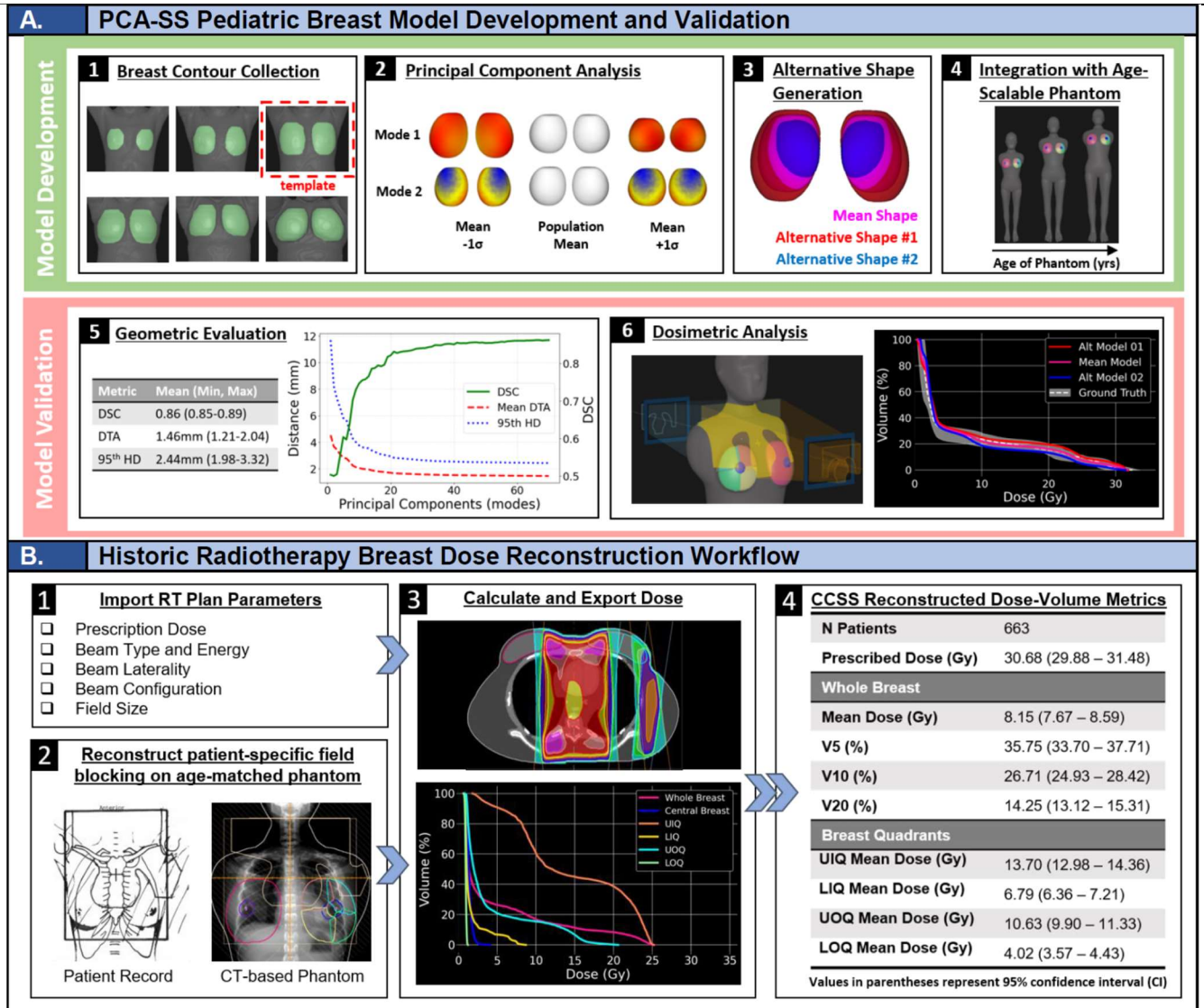
Taylor Meyers, Constance Owens, Caleb O'Connor, Tera Jones, Susan Smith, Aashish Gupta, Donald Hancock, Kristy Brock, Laurence Court, Arnold Paulino, Chelsea Pinnix, Chaya Moskowitz, Matthew J. Ehrhardt, Danielle Friedman, Cindy Im, Choonsik Lee, Wendy M Leisenring, Lindsay Morton, Joseph P. Neglia, Vikki Nolan, Kevin Oeffinger, Sander Roberti, Cecile Ronckers, Deo Kumar Srivastava, Lucie Turcotte, Greg Armstrong, James Bates, Rebecca Howell

Purpose: Prior Childhood Cancer Survivor Study (CCSS) subsequent breast cancer (SBC) dose-response models relied on chest dose as a surrogate for breast dose, lacking dose-volume metrics needed to optimize radiation therapy (RT). Breast doses were not reconstructed for females ≥12 years due to the absence of a model for developing/developed breasts. We aimed to (1) develop and validate an anatomically realistic pediatric/adolescent population-based breast model, (2) integrate it into an age-scalable phantom, and (3) assess breast dose reconstruction feasibility for CCSS females aged ≥12 years at RT.

Methods: Breast contours were collected from CTs (one reference, 70 training, eight testing) of 79 females (12–21 years) with Hodgkin lymphoma. Principal component analysis statistical shape modeling (PCA-SSM) was performed on training contours to capture population deformations. A population-mean breast model and two alternative shapes were generated and integrated into an age-scalable phantom. Geometric accuracy was assessed using Dice similarity coefficient (DSC), distance-to-agreement (DTA), and Hausdorff distance (HD). Dosimetric accuracy was evaluated by comparing reconstructed whole breast and breast quadrant dose-volume metrics from the PCA models against "ground truth" breast anatomy from the eight test patients CTs. RT was then reconstructed for 663 CCSS females diagnosed 1970-1999 at 31 institutions, aged ≥12 years.

Results: DSC (min-max) was 0.86 (0.85–0.88), DTA was 1.46mm (1.21-2.04mm), and 95th HD was 2.44mm (1.98-3.32mm), demonstrating the model's ability to capture anatomical variations. Absolute percent differences for mean breast doses (normalized to prescription dose) between ground truth and mean model (alternative #1, alternative #2) were 2.63% (3.57%, 2.22%). Differences in lower quadrants were within 10% for each model, while upper-inner and upper-outer quadrants showed larger deviations at 16.12% (20.49%, 10.70%) and 10.06%(9.65%, 10.53%), respectively. Dose-volume metric differences (V5–V30) were typically within 5%. Our population-mean model breast doses closely aligned with ground truth doses, validating it as a representative model for pediatric populations. Among 663 CCSS survivors, reconstructed mean (95% CI) breast doses, V5, and V20 were 8.15Gy (7.67-8.59Gy), 35.75% (33.70-37.71%), and 14.25% (13.12-15.31%), respectively. On average, total chest dose overestimated breast dose by a factor of 11.46 (9.42-13.51).

Conclusion: A pediatric/adolescent population-based breast model was developed, validated, and used to reconstruct breast doses for a subset of females in CCSS aged ≥12 years at RT. This PCA-based breast model enables dosimetry for females ≥12 years at RT, which when paired with existing methods for younger girls, will be used to develop novel breast dose-volume-based SBC dose-response models to refine dose-volume constraints for RT planning in newly diagnosed girls/adolescents and guide their survivorship care.



(A) PCA-SS Pediatric Breast Model Development and Validation: (A1) Breast contours from 71 chest CTs (females aged 12–21 years) were collected and pre-processed. One contour was selected as the anatomical template, while the remaining 70 were spatially normalized and deformably registered to it using a symmetric thin-plate spline robust point matching (sTPS-RPM) method. **(A2)** Principal component analysis captured the dominant modes of shape variation, generating **(A3)** a population-mean breast model and two alternative statistical shape models, which were integrated into a pediatric reference computational phantom that can be **(A4)** scaled to any age using an in-house algorithm. All three models were **(A5)** geometrically evaluated, achieving DSC, DTA, and HD values of 0.86, 1.46mm, and 2.44mm, demonstrating their ability to reconstruct global and local shape variations. **(A6)** Dosimetric analysis showed that the mean model accurately captured both anatomical and dose distribution tendencies, with its dose-volume histogram (DVH) closely aligning with the mean DVH of the ground truth, validating it as a robust baseline for dose reconstruction. The alternative models represented realistic anatomical extremes, producing DVHs corresponding to the upper and lower bounds of the ground truth, reflecting variations in breast size and shape.

(B) Historic Radiotherapy Breast Dose Reconstruction Workflow: The process involves **(B1)** importing RT plan parameters from historical records into RayStation using an in-house auto-planning script. **(B2)** Patient photos and diagrams aid in reconstructing patient-specific blocking, after which **(B3)** breast region dose-volume metrics are calculated and exported. **(B4)** To date, we have reconstructed breast dose-volume metrics (population average and 95% CI) for 663 female survivors in the Childhood Cancer Survivor Study diagnosed with eight primary cancers between 1970 and 1999, aged 12–20 years.

SMN-5

Thyroid Carcinoma in Childhood Cancer Survivors Who Received Total Body Irradiation: a Single Institution's Experience

Sommer Mims, Palmer Dempsey, Angelica Gonzalez, Jonathan Forkey

Background/Purpose: The Life After Cancer Program (LACP) team at a free-standing pediatric hospital performs long-term screenings according to the Children's Oncology Group (COG) follow-up guidelines. Childhood cancer patients treated with radiation are at risk of developing secondary malignancies, with thyroid cancer being most prevalent (Ho & Zacharin, 2016). Our program has observed an increase in the detection of thyroid carcinoma and abnormal thyroid ultrasound in patients who underwent preparative total body irradiation (TBI) for Hematopoietic Stem Cell Transplant (HSCT). Currently, thyroid palpation remains the surveillance standard of care per COG international guidelines. This retrospective cohort study aims to investigate the incidence of thyroid carcinoma and other thyroid abnormalities in childhood cancer survivors who received TBI as part of their treatment for HSCT at our institution.

Methods: Institutional Review Board (IRB) approval has been obtained, data collected through retrospective chart review. Data analysis is ongoing, but a preliminary review of 27 patients found 16 patients with abnormal findings on ultrasound, with median age of 18.74 and median years post TBI of 9.4 years. Descriptive analysis of the data was performed using IBM SPSS Statistics 25 with multiple variables (age, gender, physical exam findings, lab abnormalities, primary oncologic diagnosis, TBI dose, years post TBI) to assess their correlation with the development of thyroid carcinoma and other related pathologies. For patients formally diagnosed with thyroid carcinoma, germline mutation results were reviewed if available.

Results: Our analysis identified 27 patients who underwent TBI as part of their HSCT treatment. Among these patients, 16 exhibited an abnormal thyroid ultrasound finding with five diagnosed with papillary thyroid carcinoma (one relapsed post thyroidectomy), two with nodular hyperplasia (one with additional follicular adenoma), one with potential risk for follicular neoplasm, and eight nodules requiring close surveillance. Six have undergone a thyroidectomy, one had a right lobe resection, and one refused recommended thyroidectomy. Of the 16 ultrasound detected abnormalities, only 3 were detectable by palpation. Full analysis is ongoing.

Conclusion: Palpation is currently recommended as the standard assessment, with ultrasound specifically advised to evaluate palpable nodules (COG, 2023). Our preliminary findings show that 59.3% of patients who underwent ultrasound surveillance exhibited abnormal thyroid findings with 19% with pathology confirmed malignancy. Physical examination by palpation missed 80% of the thyroid abnormalities which supports Atlas et al.'s (2022) recommendation to revise COG standard assessment methods to include ultrasound examinations. This study seeks to advocate for improved surveillance practices while additionally considering cost vs. benefit of ultrasound for patients and families.

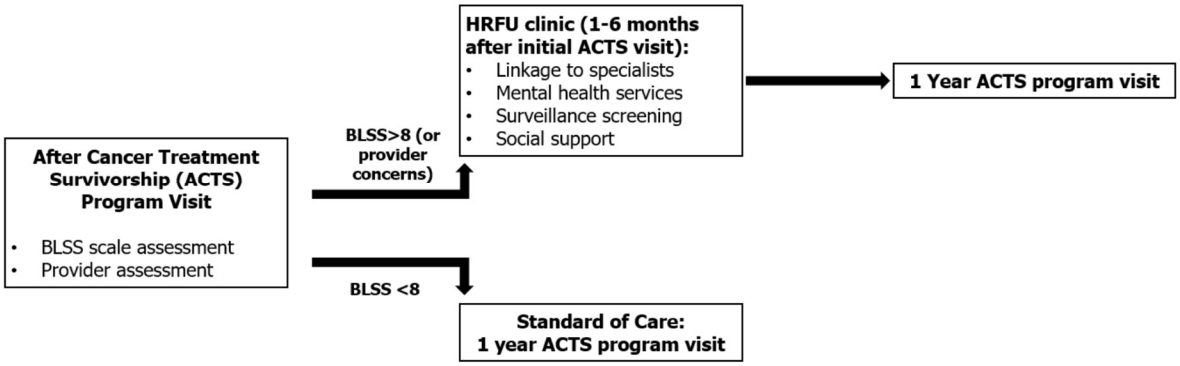
Intervention Research-5

Evaluating the Effectiveness of High-Risk Follow-Up Visits in Adolescent/Young Adult (AYA) Childhood Cancer Survivors (CCS) for Improved Long-Term Survivorship Transition Readiness

Sonia Morales, Christine Yun, Joel Green, Carol Lin, Lilibeth Torno, Abby Mecham, Karen Llave

Background: Adolescent/young adult childhood cancer survivors (AYA CCS) often face challenges during the transition to long-term survivorship care, including limited health literacy, suboptimal referral linkage, and poor adherence to surveillance recommendations. This pilot study aimed to identify patients at high risk of not meeting long-term follow-up (LTFU) transition requirements using the Bob's Levels of Social Support (BLSS) scale and to assess whether an enhanced high-risk follow-up (HRFU) intervention improves LTFU attendance, adherence to surveillance guidelines, and linkage to care.

Methods: Between March 2023 and February 2025, AYA CCS patients ≥16 years completed a risk assessment at their survivorship clinic visit. High risk patients (BLSS score ≥8 or per health provider concerns) received HRFU intervention within 1-6 months, which included individualized case management, psychosocial support, and tailored education provided via telehealth by a nurse practitioner and social worker (Figure 1). TRxANSITION Index™ scores were collected at yearly survivorship visits.



Results: Sixty-five patients have been deemed eligible for the HRFU clinic to date. Of these, 35 patients (Mage = 20 ± 3.14 years), have now completed their subsequent annual survivorship visit and are part of the evaluable cohort. This cohort was predominantly Hispanic (69%), on government insurance and diagnosed with leukemia/lymphoma. Some patients indicated moderate to severe depression (44%; PHQ-9) and moderate to severe anxiety (29%; GAD-7). Most patients (63%) demonstrated middle risk level based on their BLSS scores. Ninety-one percent attended their following subsequent annual LTFU visit, 91% of those who needed surveillance testing completed it, and 71% of patients referred to specialists were successfully linked. On average, TRxANSITION Index™ scores increased between survivorship visits. A paired-samples t-test comparing pre- and post-HRFU clinic transition readiness scores showed a significant mean difference of 1.20 ($p < .01$). There was no significant correlation between BLSS score and follow-up outcomes.

Conclusions: High risk follow-up visits improved care linkage, completion of LTFU surveillance tasks and enhanced transition readiness for AYA CCS. Correlation between risk and follow-up outcomes were not observed but could be due to most of the cohort completing linkage and LTFU surveillance tasks. Visits highlighted communication barriers with specialists, indicating the need for both self-management education and care coordination. Despite overall improvements, some patients required multiple follow-up communication due to ongoing psychosocial challenges. Tailoring HRFU interventions to individual risk factors may help bridge gaps for those with greater difficulties in care coordination and task completion. Future studies will look at randomization of standard of care to a HRFU intervention in a greater number of patients.

Intervention Research-3

Improving Pediatric Cancer and HSCT Survivor Physical Activity Through a Novel Triathlon Training Program

Jocelyn Morin, Jennifer Hoag, Deb Schmidt, Katrina O'Malley

Background/Purpose: Differences in physical activity between children with cancer and healthy peers begin during treatment and are maintained for decades. The side effects of treatment paired with a sedentary lifestyle can exacerbate late side effects of treatment and lead to further chronic disease in survivorship. Our center developed a triathlon training program for pediatric survivors of childhood cancer and hematopoietic stem cell transplant (HSCT) to improve physical activity and patient outcomes.

Methods: Team Survivors is a collaboration between the cancer survivorship and sports medicine programs. Eligibility includes age 9-17 years, history of cancer or HSCT, and receiving maintenance therapy or off treatment. Participation is free and open to children of all abilities. The team trains together twice a week for 12 weeks and concludes their season competing in a youth triathlon in the community. Practices are led by an athletic trainer with volunteer support and focus on building community, increasing strength and flexibility, and integrating games with skills practice. The program is philanthropically funded. Qualitative and quantitative data is gathered for quality improvement purposes.

Results: Forty-one survivors from four cohorts have participated. Mean age is 11.7 years, 51% male, with Leukemia/Lymphoma (56%), Solid Tumor (24%), and Brain Tumor (7%) diagnoses; 12% have been HSCT survivors. Programmatic challenges have included recruitment/marketing, patient transportation, legal liability, and limited facilities for practice. Facilitators include a dedicated program coordinator, the partnership with sports medicine, community support, and consistent funding.

Conclusions: Development of a triathlon training program is a feasible way to improve the physical activity of pediatric cancer and HSCT survivors. Future directions include broadening participation to siblings and other disease groups, incorporating other aspects of healthy living (e.g., nutrition), and engaging triathlon alumni. Comprehensive metrics of the physical and mental health impacts of the program will be gathered.

Health Services Research-23

Implementation of the Survivorship Passport Digital Tool: Experience of Its Use Within the PanCare Projects

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Background:
Over the past fifty years, childhood cancer survival rates have improved dramatically, with more than 80% of children now surviving in most European countries. As the population of childhood cancer survivors (CCS) continues to grow, personalized long-term follow-up care has become essential. To address this need, the Survivorship Passport (SurPass), a digital tool designed to generate treatment summaries (TS) and personalized follow-up recommendations, was developed. Recent updates to SurPass, from version 1.1 to version 2.0, were made possible through two complementary European projects: PanCareFollowUp (PCFU) and PanCareSurPass (PCSP).

Methods: SurPass was developed through collaboration among several European clinical centers, incorporating updates from PCFU and PCSP. The PCFU project focused on creating consistent European guidelines for long-term screening, improving person-centered care for CCS, and implementing SurPass v1.2 at the Gaslini Institute. New variables and algorithms were incorporated in the SurPass platform to support this. The PCSP project tested SurPass v2.0 across six clinical sites in Europe and sought to integrate the SurPass with local electronic health systems (EHS) using the HL7 FHIR standard, improving survivorship care through interoperability.

Results: The current SurPass platform includes 242 variables for TS and 47 algorithms that facilitate the automatic generation of recommendations for potential late complications based on the PCFU guidelines. After preliminary algorithm validation, 207 CCS were enrolled in the PCFU project and SurPass v1.2 automatically generated 1,647 algorithms recommending surveillance tests (average recommendations for CCS: 8, range: 1-18). Out of these, 233 recommendations were deselected due to pre-existing late effects (n=139, 8.4%) or normal values already tested (n=94, 5.7%). The integration of automated algorithms reduced the time needed to generate personalized recommendations to under one minute, while the median time for collecting TS was 65 minutes (range 23-140, IQR 55-85) for cases involving a single tumor diagnosis. Time may vary depending on treatment complexity. The PCSP project improved SurPass using HL7 FHIR to allow seamless integration with local EHS. Preliminary analysis showed that HL7 FHIR interoperability reduced TS manual data entry by 30% to 69%. Furthermore, SurPass 2.0 received certification as a Class I medical device.

Conclusions: SurPass offers a valuable solution for improving long-term care for CCS by automating the generation of personalized follow-up recommendations and streamlining the TS data collection process. With its Class I medical device certification, SurPass is well-positioned to enhance survivorship care across Europe, ensuring that CCS receive person-centered care based on the latest clinical evidence. Future updates will expand the platform's capabilities, including a standardized follow-up form.

Research Methods-4

Assessment of Artificial Intelligence-Generated Long-Term Follow-Up Care Plans for Childhood Cancer Survivors

Trish Murphy, Bao Truong, Natalie Wu, Kenneth Lester, Robert Goldsby

Background: Recent advances in childhood cancer treatments have led to a growing population of childhood cancer survivors. It is crucial for these survivors to understand the long-term risks associated with cancer and its therapies.

Objective: We aimed to evaluate the capabilities of artificial intelligence (AI) to generate long-term follow-up (LTFU) plans, which contain specific recommendations based on an individual's treatment exposures.

Methods: Childhood cancer survivors who were at least two years post-treatment and were seen in our Survivorship Program at UCSF Benioff Children's Hospitals between January 2021 and October 2023 were eligible. Their medical histories were reviewed and summarized, and a LTFU plan was created by healthcare professionals (HCP) in our program. Each summary included the patient's diagnosis as well as exposures to chemotherapy, surgical interventions, radiation therapies, and hematopoietic transplantation. Based on these summaries and guidelines from the Children's Oncology Group (Version 5), supplemented by our program's additional standards of practice, an LTFU plan for each patient was generated by OpenAI GPT-4o. These AI-generated plans were then compared with the LTFU plans created by HCPs. The prompts were modified and enhanced using two groups of 20 patients each. Subsequently, a separate validation cohort (N=40) was used to test the optimized prompts. The sensitivity and positive predictive value (PPV) of the AI-generated plans were assessed.

Results: The LTFU plans of 40 survivors in the validation cohort, generated by both AI and HCP methods, were compared. The LTFU plans matched on 385 follow up items. There were 61 LTFU items included in the HCP generated LTFU plans that were not included in the AI generated plan (false negatives) and there were 82 LTFU items included in the AI generated plan that were not in the HCP plan (false positives). Overall, the sensitivity was 86% and the PPV was 82%.

Conclusion: To our knowledge, this is the first test of an AI-directed LTFU plan strategy. Although the AI-generated plans did not completely align with the human-derived plans, the overall accuracy, which can be further enhanced, was impressive. Most discrepancies were due to co-morbidities not recognized by the AI algorithm or items that could be easily identified with additional AI prompts. Given that creation of manual LTFU plans can be time-consuming, the near-instantaneous generation of plans by AI could significantly enhance efficiency, especially in resource-restricted environments.

Acknowledgement: Supported by funding from Swim Across America

Health Services Research-24

Bridging to the Next Steps after Cancer Treatment Nursing Facilitated Transition Care

Julie Nichols, Jocelyn Morin

Background: Pediatric cancer survivors experience physical, emotional, and social health challenges related to their care both during and after active treatment which require attention1. Transitioning off active treatment is one of the most stressful time periods in cancer care2 3.

Methods: Children's Wisconsin (CW) conducted a pilot study in 2017 to understand the feasibility and acceptability of a structured transition program in a pediatric, adolescent, and young adult cancer center4. Bridge to Next Steps is a novel two-visit program to support patients and families during the transition from active to off treatment (Figure 1). This program was developed based upon patient and caregiver feedback.

Results: Since 2017, the program has completed 972 Bridge visits for 464 patients, with mean age of 12.5 (<1-24). To date, 41% patients that have completed the Bridge visits have transitioned to the multidisciplinary Next Steps Clinic. Reasons patients have not transitioned are timing of disease surveillance (42%), relapse (6%), declined further care (1%), transferred care (4%), lost to follow-up (3%), and deceased (3%). Over half of patients (63%) completed treatment for hematologic malignancies and 26% for non-CNS solid tumor malignancies. The remaining 11% of patients completed treatment for CNS malignancies, a group with historically unique complex care regimens, requiring increased attention to individualized visits.

"Bridge" visits are coordinated by the Survivorship Nurse Clinician in conjunction with already scheduled Oncology clinic visits. The in person or virtual visits create dedicated time for anticipatory guidance, survivorship education, and psychosocial screening during a stressful transitional period. This program has been found to decrease caregiver distress and anxiety and leads to better preparedness for patients and families transitioning off treatment2.

Conclusions: A multidisciplinary team leveraging nursing expertise is critical to the success of patient education programs, such as Bridge to Next Steps which supports seamless transition of care and improves both caregiver distress in an otherwise challenging phase of treatment.

Other late effects-3

Say Cheese! Dental Screening in a Pediatric Multidisciplinary Survivorship Clinic

Julie Nichols, Katy Tomlinson, Jocelyn Morin, Deb Schmidt, Rachel Phelan

Background: Childhood cancer treatment increases the risk for dental health problems. Survivors are at risk for disconnecting from their dental providers due to the complexities of diagnosis. Studies show dental visits can be delayed or absent after treatment ends. Survivorship Clinics are positioned to provide quality education around dental health and the importance of follow-up screening. A dental screening was implemented in a multidisciplinary survivorship clinic setting (NS Clinic) as a strategy to increase education, access to dental health and follow-up care for survivors.

Methods: At Children's Wisconsin (CW), The Next Steps (NS) Survivorship Program has a bi-monthly NS Clinic for pediatric cancer and bone marrow transplant survivors. This includes a dental resident with a three-month rotation who attends one clinic a month. The RN Coordinator performs a pre-clinic phone call to patients and families one week before the scheduled clinic date. This documented phone call includes screening questions created in collaboration with the dental team (Figure 1). Patients are provided the Children's Oncology Group Health Link, "Dental Health after Cancer Treatment," as standard written dental education4. They get additional information and recommendations if seen by a dental resident. An excel database is maintained to track these patients.

Results: The NS Clinic has 12 slots shared by two days per month. From July 2024- January 22ndth, 2025, there were 12 total NS Clinic dates and 37 scheduled patients. A dental resident was present at 42% of those clinic visits resulting in 54% of scheduled patients having dental access. A dental resident examined and provided education to 25% of those scheduled patients and 8% were found to have cavities. Reasons patients did not see a dental resident include resident availability, cost, existing established dentist, and no pre-clinic questionnaire screening.

Figure 1. Dental Screening Question

1.Do you have dental insurance?
2.What is your dentist's name?
3.Where is your dentist located?
4.When was your last dentist visit?
5.Do you have any dental concerns (pain)?
6.Would you be interested in having a Children's Wisconsin dental screen at your future visits?

Conclusions: Providing pediatric survivors of childhood cancer an opportunity to have dental screening and increased education in the NS Clinic may impact and enhance quality of life after cancer treatment. Incorporating a dental resident showed an increase in screening, attention, and education on this topic. Future considerations to increase dental health education and awareness include 1) consistently screen all patients scheduled in the NS Clinic via pre-clinic phone call, 2) create and disseminate a post clinic survey to evaluate effectiveness of a dental resident in the multidisciplinary setting, 3) determine an age threshold for these screenings, and 4) increase referrals to dental care at CW or in the community.

CV-5

Lifestyle and Metabolic Late Effects in Long-Term Survivors of Pediatric Hematopoietic Stem Cell Transplantation

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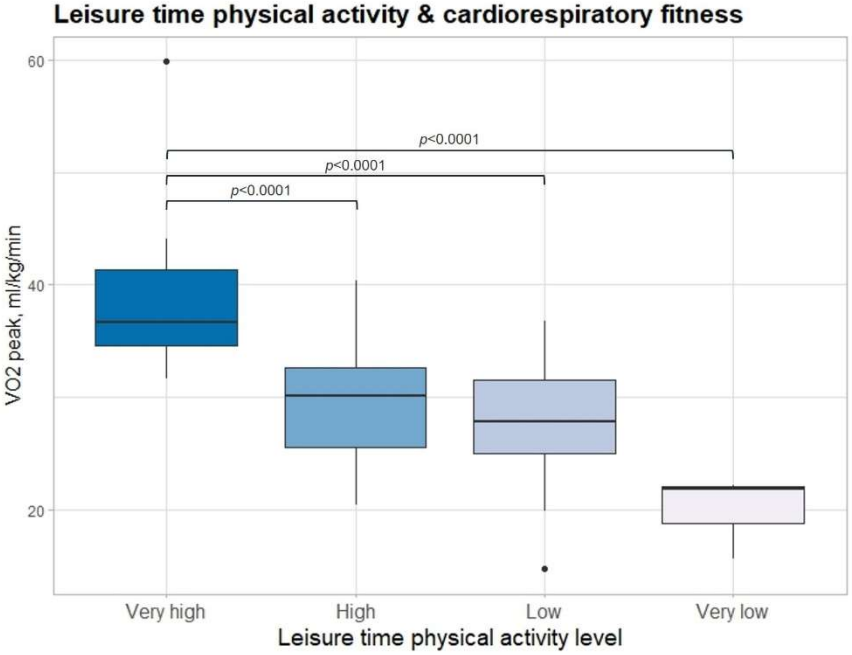
Background: The population of long-term survivors of pediatric, allogeneic hematopoietic stem cell transplantation (HSCT) is growing, and late effects such as low physical capacity and cardiometabolic disease, including metabolic syndrome (MetS), are common. However, the cause for these late effects is unclear, and the role of the survivors' lifestyle remains unknown.

Methods: We examined 95 long-term survivors of pediatric HSCT (median age 30.2 years (range 19.6;53.0), 49 men), and compared them with a group of 288 age- and sex-matched controls from the Copenhagen General Population Study. The examined lifestyle factors (diet, leisure time and occupational physical activity level, smoking status, alcohol consumption) were assessed through a questionnaire, and a composite lifestyle score, a Healthy Lifestyle Index, was calculated. To examine the prevalence of MetS, blood pressure and waist circumference were measured, and plasma samples were analyzed for glucose, HDL cholesterol, and triglycerides. Cardiorespiratory fitness was assessed through a cardiopulmonary exercise test, and physical performance was assessed through handgrip strength, walking pace, and 6-minute walk, sit-to-stand, and timed-up-and-go tests. For group comparisons of the risk of categorical outcomes, a multiple logistic regression analysis adjusted for age and sex was applied. For group comparisons of levels of continuous outcomes, a multiple linear regression analysis adjusted for age and sex was applied. In the figure p-values are based on an analysis of variance.

Results: Long-term survivors of pediatric HSCT had an unhealthier diet than controls (OR 2.2, 95% CI [1.3;3.6], p=0.002), and a lower leisure time physical activity level (OR 2.7, 95% CI [1.7;4.3], p<0.001). A low leisure time physical activity level was associated with lower cardiorespiratory fitness (estimated difference -4.07 mL/kg/min, 95% CI [-7.1;-1.0], p=0.01) (see Figure), walking distance in the 6-minute walk test (-56.0 m, 95% CI [-93.9;-18.0], p=0.004), handgrip strength (right side: -6.3 kg, 95% CI [-9.9;-2.7], p=0.0007), and slower walking pace (-0.2 m/s, 95% CI [-0.4;-0.06], p=0.01). MetS was present in 29% of survivors and having an unhealthier diet associated with an increased risk of MetS (OR 5.3, 95% CI [1.6;17.9], p=0.007). Further, presence of MetS associated with a more unhealthy lifestyle in general as reflected by a lower Healthy Lifestyle Index (-2.15, 95% CI [-3.9;-0,4], p=0.02).



Conclusions: We here present a cohort of long-term survivors of pediatric HSCT with a lifestyle that appears to differ from that of the general population with regards to diet and leisure time physical activity level. The association between an unhealthier lifestyle and reduced physical capacity as well as MetS, highlights the potentially beneficial effects of lifestyle modifications in this population, which should be investigated further through lifestyle intervention studies.

Quality of life/Behaviors-3

Treatment and Lifestyle Profiles of Healthy Aging Survivors: a Report from the Childhood Cancer Survivor Study

Tim Ohlsen, Kerry Ye, Cindy Im, Rusha Bhandari, Yan Chen, Stephanie B. Dixon, Kiri Ness, Lucie Turcotte, Brent Weil, Yutaka Yasui, Jennifer Yeh, Greg Armstrong, Paul Nathan, Claire Snyder, Kevin Oeffinger, Eric Chow

Background: Survivors of childhood cancer are at elevated risk for adverse health outcomes, but many maintain excellent health throughout adulthood. We sought to characterize the trajectories of, and examine factors associated with, healthy aging across the lifespan.

Methods: We longitudinally surveyed ≥5 y cancer survivors (18-64 y) and sibling controls enrolled in the Childhood Cancer Survivor Study. "Healthy aging" was defined by 1) having a cumulative number of severe or life-threatening (i.e., grade 3+) chronic health conditions (CHCs) less than or equal to the mean of same age, same sex sibling controls; and 2) having no functional impairment or activity limitations. We then examined prevalences of healthy aging and its 2 component domains across survivor age groups (<30, 30-39, 40-49, ≥50 y). Multivariable logistic regression models adjusted for demographic, treatment, and lifestyle factors at cohort entry were used to estimate risk factors for healthy aging among survivors.

Results: We analyzed 17,263 survivors (median age 39 y, IQR 32-46) and 3,378 siblings. Among all sibling age/sex groups, mean grade 3+ CHC counts were <1. Of survivors, 53.4% (95% CI 52.7-54.2) had no Grade 3+ CHC, and 71.4% (95% CI 70.7-72.1) reported no functional impairment. Overall, 45.0% (95% CI 44.2-45.7) of survivors met criteria for healthy aging, but this prevalence decreased with age (Table). In multivariable analysis, treatment factors associated with lower odds of healthy aging included anthracycline dose (≥250 mg/m2 vs none: OR 0.60, 95% CI 0.52-0.69), alkylator dose (4-7.9 g/m2 vs none: OR 0.78, 95% CI 0.66-0.91; ≥8 g/m2 vs none: OR 0.76, 95% CI 0.67-0.86), and stem cell transplant (OR 0.60, 95% CI 0.41-0.89). High doses of radiation to any site were also associated with less healthy aging (e.g., ≥30 Gy to brain vs none: OR 0.22, 95% CI 0.19-0.26; ≥35 Gy to chest vs none: OR 0.62, 95% CI 0.47-0.83; ≥20 Gy to abdomen vs none: OR 0.56, 95% CI 0.43-0.71). Baseline physical activity >180 min/week was associated with healthy aging (vs <180 min: OR 1.23, 95% CI 1.11-1.37). Underweight, overweight, and obese baseline BMIs had lower odds of healthy aging compared with normal BMI (ORs 0.54 to 0.82, each p<0.05). Survivors treated in more recent decades were more likely to experience healthy aging (1990s vs 1970s: OR 1.26, 95% CI 1.06-1.50) even after adjusting for attained age.

Table: Prevalence (%) of outcomes across survivor age groups (95% CI)

	<30 y	30-39 y	40-49 y	≥50 y
CHC count ≤ sibling mean for age/sex	67.4 (65.8, 69.0)	59.3 (58.1, 60.5)	47.5 (46.2-48.9)	34.4 (32.6-36.2)
No functional impairment or activity limitations	76.0 (74.6, 77.5)	73.9 (72.8, 74.9)	69.4 (68.2-70.7)	64.1 (62.3-65.9)
Healthy aging*	58.0 (56.3, 59.7)	50.8 (49.5, 52.0)	39.2 (37.8-40.5)	27.2 (25.5-28.9)

*Defined as having both a low CHC count for age/sex as well as no functional impairment/activity limitations.

Conclusions: Among childhood cancer survivors, the prevalence of healthy aging declines with age but has improved in more recent treatment eras. Higher levels of exercise and normal BMI at baseline were associated with subsequent healthy aging, suggesting that the trajectory of aging could be improved through targeted interventions.

CV-6

Fitness and Cardiometabolic Risk Factors in Young Childhood Cancer Survivors: a Report from the St. Jude Lifetime Cohort Study (SJLIFE)

Sean O'Neil, Aimee Santucci, Daniel Mulrooney, Stephanie Dixon, Bonnie Ky, Deo Kumar Srivastava, Robyn Partin, Joshua Burns, Gregory Armstrong, Melissa Hudson, Kiri Ness

Introduction: Cardiopulmonary fitness is associated with markers of cardiometabolic risk in adolescents without a cancer history. Less is known about this association in young survivors of childhood cancer who are vulnerable to adverse cardiac outcomes because of their treatment exposures. The aim of this analysis was to determine the prevalence of impaired cardiopulmonary fitness and its association with cardiometabolic risk factors in young survivors of childhood cancer.

Methods: Participants were enrolled in the St. Jude Lifetime cohort study, had survived five or more years from their primary diagnosis and were younger than age 18 at assessment. Resting vital signs were taken after five minutes of quiet sitting. Weight was captured on an electronic scale and height with a stadiometer. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared. A fasting blood sample was obtained to evaluate lipids, insulin, hemoglobin A1c and glucose values. Participants completed maximal cardiopulmonary fitness testing, where breath by breath analysis was utilized to capture peak oxygen uptake (VO2 peak), which were converted into age and sex specific z-scores. Those with z-scores <-1.5 were classified with impaired fitness. Markers of cardiometabolic risk were compared between those with and without impaired fitness with two sample t-tests.

Results: Survivors (N=448, 50% female, 27.3% non-white) were a mean (±standard deviation [SD]) age of 13.5±2.8 years at assessment and 2.9±2.3 years at diagnosis with leukemia or lymphoma (37.1%), CNS tumor (15.0%), retinoblastoma (19.6%), neuroblastoma (7.5%), or other malignancy (20.8%). Mean ± SD values were 32.7 ±10.91 ml/kg/min for VO2 peak (z-score -1.02±1.16), with 34.8% of survivors having a VO2 peak z-score <-1.5. Survivors with VO2 peak z-score <-1.5, compared to those with VO2 peak ≥-1.5 had significantly higher mean systolic and diastolic blood pressure, resting heart rate, triglycerides, glucose, insulin and BMI, and lower mean high-density lipoprotein (Table).

Outcome	VO2 peak z-score <-1.5	VO2 peak z-score ≥-1.5	p-value
	Mean±SD	Mean±SD	
Systolic blood pressure (mmHg)	116±12	113±9	<0.01
Diastolic blood pressure (mmHg)	71±8	68±7	<0.01
Resting heart rate (bpm)	84±12	79±12	<0.001
Respiratory rate (breaths/min)	18±2	18±2	0.58
High density lipoprotein (mg/dL)	48.6±13.5	56.5±13.9	<0.001
Low density lipoprotein (mg/dL)	86.9±24.9	82.4±23.8	0.07
Total Cholesterol (mg/dL)	153.8±29.5	154.9±26.5	0.71
Triglycerides (mg/dL)	95.3±64.0	79.8±41.4	<0.01
Glucose (mg/dL)	95.6±9.1	93.8±6.5	0.03
Hemoglobin A1c (%)	5.4±0.31	5.4±0.26	0.24
Insulin (uIU/ml)	23.9±15.9	16.0±11.8	<0.001
BMI	25.5±6.8	20.6±4.1	<0.001

Conclusion: Over a third of childhood cancer survivors younger than 18 years of age have impaired cardiopulmonary fitness. Impaired cardiopulmonary fitness is associated with cardiometabolic risk factors.

Neurocog-2

End of Therapy Associations Between Neurocognitive and Social Adaptive Skills in Survivors of Childhood Acute Lymphoblastic Leukemia

Tanya Paes, Tara Brinkman, Kevin Krull, Heather Conklin, Cheng Cheng, Kendra Parris, Ching-Hon Pui, Sima Jeha, Lisa Jacola

Purpose: Survivors of childhood acute lymphoblastic leukemia (ALL) are at risk for neurocognitive deficits that emerge during therapy, continue through long-term survivorship, and negatively impact social attainment in adulthood. Few studies examine social function in early survivorship, a time when interventions may be more effective. The present study aims to characterize social adaptive functioning at the end of protocol-directed therapy for newly diagnosed ALL, and to examine associations with neurocognitive vulnerabilities.

Methods: Between 2007 and 2017, 598 patients were treated for newly diagnosed childhood ALL on the St. Jude Total Therapy Study 16. Of the 479 patients eligible for protocol-based neurocognitive monitoring, 400 (83.5%) completed assessments at the end of therapy (48.5% Low Risk, 58.8% male, 52.5% private insurance; mean age at diagnosis = 7.07 years). Assessments included performance measures of attention (Connors CPT3/Kiddie CPT2), working memory (Wechsler Digit Span Total), executive function (WJ3 Retrieval Fluency), and processing speed (WJ3 Decision Speed and Visual Matching), and caregiver ratings of executive function in daily life (BRIEF Global Executive) and social adaptive skills (ABAS2 Social Composite). Results are presented as age-adjusted Z scores (normative mean=0, standard deviation=1). Impairment was defined as Z scores >1.5 SD below the mean.

Results: On average, social adaptive skills were age appropriate (Z = -0.07). However, compared to the expected frequency of impairment in the general population (7%), a greater proportion of survivors had impaired social adaptive skills at the end of therapy (22.5% $p < 0.001$). The frequency of impaired social adaptive skills did not differ by sex, age at diagnosis, treatment risk arm, or insurance status. Results of bivariate correlations demonstrated that better performance on measures of executive function (Retrieval Fluency, $r = .17$, $p = 0.002$), working memory (Digit Span Total, $r = .14$, $p = 0.030$) and processing speed (Visual Matching, $r = .12$, $p = 0.033$) were associated with higher ratings of social adaptive skills. Elevated ratings of attention problems ($r = -.43$, $p < 0.001$) and executive dysfunction (Global Executive $r = -.48$, $p < 0.001$) were associated with lower ratings of social adaptive skills.

Conclusion: Survivors of childhood ALL are at elevated risk for problems with social adaptive skills at completion of therapy. An intervention targeted at ameliorating neurocognitive problems may also support social outcomes.

Genetics/Genomics-4

Epigenetic Age Acceleration in Survivors of Childhood Neuroblastoma: a Report from the St. Jude Lifetime Cohort

Robyn Partin, Zhaoming Wang, Joshua Burns, Ellen Grishman, Melissa Hudson, Sara Federico, Johnnie K. Bass, Greg Armstrong, Kiri Ness

Background: Children treated for neuroblastoma (NBL) are at risk for short stature and exposure-related adverse health outcomes usually prevalent in older adults, including low lean muscle mass, hearing loss, and restrictive lung disease. This study aimed to describe the prevalence of these outcomes and evaluate the association between epigenetic age acceleration (EAA) and adverse health outcomes in adult survivors of childhood neuroblastoma enrolled in the St. Jude Lifetime Cohort (SJLIFE).

Methods: Neuroblastoma survivors diagnosed from 1962-2012 and enrolled on SJLIFE completed an in-person assessment. Height z-score < -1.5 from a stadiometer, classified short stature and lean muscle mass z-score < -1.5, from dual x-ray absorptiometry classified low lean muscle mass. Audiometry and pulmonary function testing consistent with Common Terminology for Adverse Events grades ≥2 classified hearing loss and restrictive lung disease. Genome-wide DNA methylation data, generated with Infinium EPIC BeadChip, was used to estimate EAA (Levine's Clock). EAA residuals were calculated by regressing epigenetic age on chronological age. Residual EAA z-scores ≥1 were considered fast agers. Linear regression estimated associations between EAA and height and lean mass z-scores. Logistic regression estimated associations between EAA and hearing loss and restrictive lung disease.

Results: Participants included 148 (50% female, 82% Non-Hispanic White, mean ± standard deviation (SD) age at assessment 32.7±8.9, age at diagnosis 1.7±8.9 years) NBL survivors. Disease stage numbers were I (18), IIA (12), IIB (24), 3 (64) and 4 (20). Ten were missing stage information. All were treated with chemotherapy, 38 had radiation and 18 had transplant (1 allogeneic, 17 autologous). Mean ± SD z-scores were -0.33±1.28 for height and -0.57±1.64 for lean mass. Outcome prevalences were short stature 8.8%, low lean mass 31.8%, hearing loss 30.4%, restrictive lung disease 8.1% and fast ager 14.9%. Epigenetic age acceleration z-scores of ≥1 (i.e., fast ager) were associated with a lower lean mass z-score (mean difference -0.98±0.56, p=0.05) and increased odds of hearing loss (OR 1.37, 95% CI 1.01-2.67), but only among females. Epigenetic age acceleration was not associated with short stature or restrictive lung disease.

Conclusions: Low lean mass and hearing loss are prevalent in long-term survivors of NBL and are associated with EAA in females. Survivors should be screened for these outcomes early so that appropriate interventions, such as exercise for low lean mass and hearing aids/cochlear implants for hearing loss, can be provided.

Research Methods-6

Correlation Between the 2-Minute Step Test and Clinically Measured VO2 Peak: a Report from the St. Jude Lifetime Cohort Study (SJLIFE)

Kayla Payne, Matthew Wogksch, Robyn Partin, Daniel A. Mulrooney, Sarah Terrell, Katherine Zelinka, Jennifer Burgess, Maura Kepper, Stephanie B. Dixon, Bonnie Ky, Matthew J. Ehrhardt, Tara Brinkman, Elizabeth Salerno, Melissa Hudson, Greg Armstrong, Joshua Burns, Kiri Ness

Background: Peak oxygen uptake (VO2 Peak) during exercise is an important marker of health and longevity in the general population that has been associated with morbidity and mortality in childhood cancer survivors. Despite its utility as a biomarker of the success of both exercise and physical activity interventions, clinical testing is burdensome as it requires an in-person assessment, highly trained personnel, and medical supervision. We therefore aimed to evaluate concordance between clinically ascertained VO2 peak and a field test that can be delivered virtually, the 2-minute step test (2MST), in childhood cancer survivors.

Methods: Continuous gas exchange during treadmill based maximal cardiopulmonary exercise testing (CPET) was used to capture VO2 Peak. The 2MST was administered virtually using a telehealth video platform. Briefly, participants measured a point midway between their right patella and top of their iliac crest and placed a piece of colored tape on the wall at that point. The assessor counted the number of times the right knee reached that point while marching in place as quickly as possible for two minutes. Participants were allowed to touch the wall, a table or a chair for stability as needed. VO2 peak was estimated from the step test with the formula:

VO2 Peak=28.16+(0.99*Total Steps)-0.413*Body Mass Index

Descriptive statistics, Pearson r, interclass (ICC) and concordance correlation (CCC) coefficients were calculated to compare the measures. Bland Altman methodology was used to visually examine the data.

Results: Participants included 72 adult survivors of childhood cancer (median age 28 years (range 19-39), 56% female, 17% non-white, 31% with leukemia or lymphoma, 24% with CNS tumors and 46% with other solid tumors). Mean ±standard deviation VO2 peak values were 26.37±6.90 ml/kg/min from CPET and 26.51±3.58 ml/kg/min from 2MST. Correlation coefficients were 0.56 (Pearson r), 0.44 (ICC) and 0.43 (CCC). Bland Altman methodology identified one participant below and three above the 95% limits of agreement.

Conclusion: Underestimation of VO2 Peak with the 2MST was identified among survivors with higher CPET ascertained VO2 Peak values.

Neurocog-3

Failures to Address Pediatric "Chemobrain": a Narrative Review

Benjamin Pearson

Background: Chemotherapy-related cognitive impairment (CRCI), or "chemobrain," has been extensively documented across oncology, but research efforts have been divided into two explanatory models: emotional dysfunction and direct physiological alterations induced by treatment. Both frameworks have yielded significant insights into CRCI's etiology, yet their synthesis has not been effectively translated into clinical practice. In pediatric populations, developmental factors uniquely influence cognitive outcomes and assessment methodologies, but current studies have yet to fully integrate these dual perspectives. CRCI remains inadequately defined in both adult and pediatric contexts and lacks standardized tools for identification and intervention, particularly for children.

Methods: A comprehensive review of studies on chemotherapy-related cognitive impairment in both adult and pediatric populations was conducted using Eppi-Reviewer 6. We searched eight databases—PubMed/MEDLINE, Embase, CINAHL, Cochrane Library, PsycINFO, Scopus, Web of Science, and Google Scholar—focusing on underlying mechanisms, neurocognitive assessment, and psychosocial dysfunction.

Results: The literature provides evidence for both emotional and physiological mechanisms of CRCI, but adult and pediatric research has yet to systematically explore the interaction of these dual pathways. Existing pediatric studies report mixed findings on long-term cognitive deficits but are hindered by poor measurement tools, potential compensatory mechanisms, and a failure to distinguish between psychological and biological contributors. These limitations underscore the urgent need for integrated approaches to clarify CRCI's impact on children.

Conclusion: A dual-framework approach, integrating emotional and physiological mechanisms, is essential for understanding CRCI in pediatric populations. Future research should focus on disentangling these contributions in childhood cancer survivors to inform targeted identification and intervention strategies. Advancing our grasp of pediatric CRCI will require a bolstered definition, refined assessment tools, and heightened clinical attention to the interplay of psychological and biological factors, tailored to the diverse manifestations of CRCI across the cancer continuum.

Other late effects-4

Focal Nodular Hyperplasia in Childhood Cancer Survivors

Benjamin Pearson, Natalie Wu, Robert Raphael, Christine Dehlendorf, Thomas Hoffman

Background/Purpose: Focal Nodular Hyperplasia (FNH) is the second most common benign liver lesion which can be detected during follow-up imaging in childhood cancer survivors (CCS). Despite its typically benign course, the natural history and long-term complications of FNH in CCS remain poorly understood due to a paucity of dedicated studies. This gap in knowledge poses challenges, as distinguishing FNH from malignant tumors such as hepatocellular carcinoma is essential for guiding clinical decision-making. Our study seeks to characterize the CCS population affected by FNH and investigate rare cases of potential malignant transformation observed within this group.

Methods: We conducted a retrospective cohort study evaluating the distribution of demographic variables, age at diagnosis, and primary malignancy types among CCS suspected of having FNH. Data were collected from electronic health records of CCS treated at UCSF Benioff Children's Hospitals from 2012 to 2023. Subjects were £ 21 years of age at cancer diagnosis, with FNH identified at any point after diagnosis. Latency was defined as the time from primary cancer diagnosis to the respective date of FNH. The suspected FNH date was defined as the first instance where FNH was suspected on imaging and the confirmed FNH date was diagnosis utilizing MRI with hepatobiliary contrast (Eovist) or histopathological confirmation via biopsy. Statistical analyses were performed using Stata 18.

Results: A total of 81 patients were presumed or confirmed to have FNH. Among CCS who developed FNH, neuroblastoma was the most common primary cancer diagnosis (50.6%), followed by hematologic malignancies (17.3%) and CNS tumors (8.6%). Renal tumors and sarcomas were less common. Among the presumed or confirmed FNH patients, the average suspected latency was 62.9 months, and the confirmed latency was 78.4 months. Neuroblastoma patients had mean suspected and confirmed latencies of 49.2 months and 61.3 months, respectively. Two patients were identified as having likely malignant transformations of their FNH. One was initially diagnosed with choroid plexus carcinoma and a second with Ewing sarcoma. Both were treated with standard chemotherapy, high-dose chemotherapy with autologous stem cell rescue (HDC/ASCR), and surgery. Presumed diagnosis of FNH and transformation to hepatocellular carcinoma occurred at 67 and 113 months post-cancer diagnosis in the choroid plexus carcinoma patient and at 104 and 136 months in the Ewing sarcoma patient.

TABLE 1 FNH Frequency and Latency by Malignancy Category

Malignancy Category	Neuroblastoma	Hematologic	CNS	Other	Liver	Renal	Sarcoma	Total
N (%)	41 (50.6%)	14 (17.3%)	7 (8.6%)	8 (9.9%)	4 (4.9%)	4 (4.9%)	3 (3.7%)	81 (100%)
Suspected Latency (months)								
Mean	49.22	81.17	81.29	84.14	81.75	53.33	46.33	62.92
SD	45.48	58.97	32.13	74.79	56.41	51.60	50.00	52.60
Range	11–231	1–182	32–117	0–213	18–135	0–103	15–104	0–231
Confirmed Latency (months)								
Mean	61.30	97.73	80.67	136.80	124.00	86.00	56.33	78.39
SD	53.69	55.71	33.83	59.86	N/A	24.04	64.69	55.81
Range	11–234	25–194	36–117	47–213	124–124	69–103	17–131	11–234

Conclusion: FNH is an uncommon finding in CCS but has demonstrated potential for malignant transformation in exceptional cases. Among patients with FNH, most had a prior diagnosis of neuroblastoma, with predominantly high-risk disease treated with HDC/ASCR and abdominal radiation. We observed two instances of likely malignant transformation in our cohort of patients with FNH, but larger studies will be needed to understand the risk factors and natural history of FNH.

Genetics/Genomics-5

Genome-Wide Association Study for Lipid Traits in Childhood Cancer Survivors of Diverse Ancestries: a Report from the St. Jude Lifetime Cohort (SJLIFE)

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Background: While cardiovascular complications associated with dyslipidemia and other risk factors are well documented in childhood cancer survivors, the genetic factors contributing to lipid traits in this population have been underexplored. To our knowledge, no such study has been performed in survivors of African ancestry (AA).

Methods: The study included 3,555 five-year survivors of childhood cancer (3,014 European ancestry [EA] and 541 AA) from the SJLIFE cohort with comprehensive lipid traits measurements (total cholesterol, LDL-cholesterol, HDL-cholesterol, non-HDL-cholesterol, and triglycerides) and whole-genome sequencing data. Ancestry-specific genome-wide association studies (GWASs) were conducted to examine the association of common variants (MAF^{3}1%) with each of the five lipid traits, using multivariable linear regression adjusted for demographic factors, relevant cancer treatment exposures previously associated with dyslipidemia, lipid-lowering medications and the top ten genotype-based principal components based. Trans-ancestry meta-analyses were performed using a fixed-effect model that combined ancestry-specific results. Genome-wide significant loci (P<5x10-8) were further evaluated in stratified analyses by treatment exposures.

Results: A total of eight loci (APOE, NECTIN2, LDLR, CELSR2, CETP, LPL, LINC01250, and GCKR) showed genome-wide significant associations with one or more lipid traits in survivors. With the exception of LINC01250, all of the loci have been reported in the general population. Among lipid loci previously associated in the general population, six were identified in EA survivors (P<5x10-8), with two (APOE, NECTIN2) also showing nominally significant (P<0.05) associations in AA survivors. Another locus (GCKR: rs1260326-T) was associated in trans-ancestry meta-analysis. In AA survivors, a novel locus (LINC01250: rs140169025-G) was associated with lower triglyceride levels (β=-0.77; P=2.6x10-8), but this variant was monomorphic in EA survivors. Notably, rs1065853-T at the APOE locus was consistently associated with lower levels of total cholesterol (EA: β=-0.35; P=6.0x10-15 and AA: β=-0.45; P=2.8x10-7), non-HDL (EA: β=-0.42; P=2.5x10-21 and AA: β=-0.44; P=5.6x10-7) and LDL-cholesterol (EA: β=-0.51; P=1.7x10-29 and AA: β=-0.51; P=1.2x10-8) in both ancestral groups. In EA survivors unexposed to cranial irradiation, rs1065853-T was associated with nearly 2-times lower levels of total cholesterol, non-HDL and LDL compared to those who were exposed. In contrast, in AA survivors unexposed to cranial irradiation, rs1065853-T was associated with nearly 1.5-times higher levels than in those who were exposed.

Conclusions: These findings indicate potential shared genetic factors influencing lipid traits in both the general population and childhood cancer survivors from diverse ancestries, with potential effect modifications by treatments at certain genetic loci.

Endo-4

Risk Prediction of Dyslipidemia in Long-Term Survivors of Childhood Cancer: a Report from the St. Jude Lifetime Cohort (SJLIFE) and the Childhood Cancer Survivor Study (CCSS)

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Background: Dyslipidemia, a major cardiovascular risk factor, is often underdiagnosed and undertreated among childhood cancer survivors. At present, there are no available calculators to predict dyslipidemia risk in these individuals.

Methods: Childhood cancer survivors participating in the St. Jude Lifetime Cohort (SJLIFE; discovery, n=4,038) and the Childhood Cancer Survivor Study (CCSS; validation, n=7,510) with genotype data were assessed for dyslipidemia (CTCAE grade ≥2 hypercholesterolemia and/or hypertriglyceridemia). Demographic, cancer treatments previously associated with dyslipidemia, comorbidities, and five externally-validated general-population polygenic risk scores (PRSs) for total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides were evaluated at cohort entry (5 years post-primary cancer diagnosis) as potential predictors for dyslipidemia risk. Cox proportional hazards regression was used to predict the risk of dyslipidemia, with predictors selected by elastic net with a hyperparameter selected by 10-fold cross-validation. Model performance was evaluated using the time-dependent area under the receiver operating characteristic curve (AUC) at 25 years beginning cohort entry. Based on the predicted hazard ratio (HR) from the final model, survivors were classified into low (predicted HR <1.5), moderate (HR ≥1.5 and <3), and high (HR ≥3) risk groups. The cumulative incidence of dyslipidemia over the next 25 years following cohort entry was then estimated by group.

Results: Dyslipidemia was clinically-identified in 533 (13.2%) SJLIFE and self-reported in 925 (12.3%) CCSS participants. The AUC of a clinical model including demographics (sex, race, age at cancer diagnosis), cancer treatments (cisplatin, carboplatin, brain and abdominal irradiation), and comorbidities at cohort entry (growth hormone deficiency, hypothyroidism) was 0.69 (95% CI: 0.65-0.72) in SJLIFE and 0.65 (95% CI: 0.62-0.67) in CCSS. Adding the five lipid-trait PRSs significantly increased AUC to 0.76 (95% CI: 0.73-0.79, P=3.2×10-6) in SJLIFE and 0.71 (95% CI: 0.69-0.73, P=5.1×10-8) in CCSS. In high-risk group, the cumulative incidence of dyslipidemia with the inclusion of PRSs increased from 22.8% (95% CI: 20.2%-25.3%) to 28.28% (95% CI: 24.9%-31.3%) in SJLIFE, and from 13.9% (95% CI: 12.7%-15.0%) to 17.0% (95% CI: 15.5%-18.5%) in CCSS. The cumulative incidences in the low- and moderate-risk groups were similar regardless of the inclusion of the PRSs.

Conclusions: To our knowledge, this is the first independently validated prediction model estimating dyslipidemia risk among adult survivors of childhood cancer. In addition to clinical and treatment characteristics, the model incorporated genetic predictors, enhancing the accuracy of risk classification and facilitating personalized preventive cardiovascular counselling and screening.

Health Services Research-25

Re-Engaging Childhood, Adolescent, and Young Adult Cancer Survivors for Transition to Adult Survivorship Care

Allyson Pfluger, Katherine Cermin, Shafqat Shah, Gregory Aune, Debra Eshelman-Kent

Background: Our institution's pediatric survivorship program has been providing survivorship care to childhood, adolescent, and young adult cancer survivors (CAYA) for the past 11 years. The population served by our survivorship program includes 28 counties in Public Health Region 8, a large geographic area in South Texas, serving a predominately Hispanic population. A total of 344 survivors in our program are over the age of 18. As the median age of survivors within our program has increased, we recognized the need for adult clinical expertise to address the chronic health conditions of the CAYA population. An adult cancer survivorship service line within our academic institution was developed in 2022. Our goal was to implement a standardized process for transitioning survivors to the adult program, re-engage survivors not seen within the past year, and identify barriers to a successful transition.

Methods: A comprehensive approach, including implementation of the Transition Readiness Assessment Questionnaire (TRAQ), nurse-led navigation, and Epic™ tools, was initiated to facilitate transition to the adult program. Patients 25 years and older were referred to the adult survivorship program. Survivors ages 18-25 were screened for transition readiness with the TRAQ and educated about the transition process by the nurse coordinator. Inactive survivors (patients not seen within the past year) were contacted with an electronic health record (EHR) generated letter notifying them of the newly established adult survivorship program. Survivors without MyChart access were mailed the letter to the most recent address on file with instructions to call the survivorship phone number for personalized triage.

Results: Over two years, 79 (23%) of the 344 survivors were successfully transitioned to the adult program. The remaining 265 (77%) were identified as inactive survivors eligible for transition. In an attempt to re-engage these inactive survivors, 194 letters were delivered via mail and 71 via electronic MyChart Epic™ message. Five of the 265 inactive survivors responded requesting referral to the adult survivorship program.

Conclusion: Approximately one-quarter of our CAYA population has been successfully transitioned to the adult survivorship program. Even within an established survivorship program dedicated to transition, adherence to follow up care is suboptimal, indicating a need for further engagement strategies. Additional analysis of barriers affecting transition may improve engagement with the inactive survivor population.

Intervention Research-9

Preparing Primary Care for the Transition: a Novel Elective for Residents to Train in Cancer Survivorship

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Background/Purpose: As treatments for complex oncologic and hematologic diseases continue to advance, the number of cancer, gene/cell therapy, and hematopoietic cell transplant (HCT) survivors will continue to expand. Medical and psychosocial needs of survivors are unique and include comprehensive counseling and monitoring for ongoing and potential complications related to their prior therapy. It is vital that internal medicine and pediatric providers gain understanding of these needs, as they are often at the forefront of care as patients are further from active treatment or transition from the treating center and team.

Methods: The Childhood/Adult Cancer Survivorship Rotation is designed for any resident in the internal medicine/pediatrics or pediatric training programs at our academic center that are interested in learning more about the unique needs of survivors. Clinical experience is outpatient, with time at specialized and multi-disciplinary clinics located at the affiliated pediatric and adult-based institutions. Clinics include diverse experiences in both the pediatric and adult oncology, HCT, and survivorship clinics as well as the psycho-oncology and cardio-oncology clinics. Rotation objectives specific to survivorship are provided in the following areas: patient care, medical knowledge, practice-based learning/improvement, interpersonal/communication skills, professionalism, and system-based practice. Virtual didactics on various topics by content experts have been recorded and are available for viewing throughout the course of the elective (with topics including, but not limited to, endocrinology, primary care, screening/immunizations, oncofertility, radiation oncology, and genetic predisposition). As a culmination of knowledge, residents develop a Survivor Care Plan including a treatment summary and surveillance plan for a survivorship patient.

Results: Feasibility and acceptability assessments will be provided to residents at the conclusion of the rotation to tailor experiences for future learners. Knowledge assessments are being developed, with a plan to administer pre- and post-rotation. Based on interest and support from residency leadership, we will plan to expand to internal medicine residents.

Conclusions: As the number of cancer, gene/cell therapy and HCT survivors continues to grow, the need for continued care by our network of primary care physicians will remain essential. To facilitate transition and collaboration, education during training is critical. Although fellowship rotations focused on survivorship are offered at many training programs, targeting future primary care providers during their residency experience allows for a novel educational opportunity.

Endo-5

Reduced Beta Cell Function in Childhood Cancer Survivors: Impact of Total Body Irradiation and Abdominal Radiation

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Background/Purpose: Childhood cancer survivors (CCS), particularly those treated with total body irradiation (TBI) or abdominal radiation (AR), are at increased risk for developing diabetes mellitus (DM). The extent to which compromised insulin secretion and reduced insulin sensitivity increase this risk remains poorly understood. This study aimed to compare pancreatic beta-cell function and insulin sensitivity in CCS by treatment modality.

Methods: Long-term (≥3 years from diagnosis) CCS (ages 15–30y) treated with TBI (n=10), AR (n=10), or chemotherapy-only for acute lymphoblastic leukemia (n=10) underwent 1) 4-hour oral glucose tolerance test (OGTT) to assess glucose excursion and insulin sensitivity and 2) dual energy X-ray absorptiometry (DXA) scan to quantify body composition. 2-hour OGTT glucose (mg/dL) was used to define 1) impaired glucose tolerance (IGT): >=140 but <200 mg/dL and 2) diabetes: >=200 mg/dL. Beta-cell function was assessed using the disposition index (DI), calculated as the product of OGTT-related insulin secretion and insulin sensitivity, where lower values suggest impaired beta-cell function. ANOVA with Bonferroni correction or Kruskal-Wallis test was used to compare group differences in continuous variables with normal and non-normal distribution, respectively. Group differences in DI were analyzed using robust regression followed by pairwise comparisons. Statistical analyses were performed using Stata 18.0, with a two-sided p-value of <0.05 considered statistically significant.

Results: Participants were 56.7% (n=17) female. Mean age was slightly higher in TBI (22.2 ± 4.1y) vs. AR (20.4 ± 3.0y) and chemotherapy-only (18.04 ± 3.4y) groups. Median BMI Z-scores were similar across treatment groups: TBI: -0.1 (range -1.05 to 1.69), AR: 0.03 (range -2.26 to 2.69), and chemotherapy-only: 0.19 (range -0.51 to 1.21). However, DXA derived visceral adiposity was significantly greater in TBI vs. chemotherapy-only (P=0.02) and AR (P<0.01). IGT was present in 2 TBI (20%) and 4 AR participants (40%), while DM was identified in 1 TBI participant. Total DI was significantly lower in the TBI group compared to chemotherapy-only group (P=0.04). Although DI tended to lower in TBI vs. AR and in AR vs chemotherapy-only, these differences did not reach significance (P=0.4 and P=0.3 respectively).

Conclusions: CCS exposed to TBI demonstrated the lowest DI, suggesting impaired beta-cell compensation for insulin resistance, conferring the highest DM risk in this group. Although BMI Z-scores were similar across treatment groups, BMI does not fully capture differences in adiposity, particularly in radiation-treated cancer survivors. Visceral adiposity was highest in the TBI group which may contribute to the reduced DI and increased DM risk. These findings underscore the need for early metabolic screening and targeted interventions in high-risk CCS.

Endo-7

Gonadotoxic Exposures on Contemporary Protocols: the Need for Fertility Preservation and Gonadotoxicity Surveillance

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Background: Certain treatment exposures in children and adolescents with cancer may lead to gonadal insufficiency, suboptimal fertility outcomes and sexual dysfunction. We analyzed the proportion of childhood cancer survivors at high risk of toxicity by decade of treatment.

Methods: Adult survivors of childhood cancer at the After Completion of Treatment Clinic were analyzed for the proportion who had received highly gonadotoxic treatment ; which was defined as either Cyclophosphamide equivalent dose (CED) > 8g/m2, allogeneic haematopoetic stem cell transplant (HSCT), hypothalamic-pituitary radiation > 30Gy, any testicular, ovarian radiation, or surgery involving bilateral gonad removal or within the HP region. The proportion receiving each modality of gonadotoxic treatment were analyzed by decade of treatment (from 1970s to 2010s).

Results: Of the 2631 adult survivors, 1868 (71 %) are male and 763 (29 %) female. Overall, 917 (34.9%), 660 (35.3%) males and 257 (33.9%) females have received highly gonadotoxic treatment – reasons being high CED in 805 (30.5%) survivors, radiation to pelvis/gonads in 121 (19.7 %), radiation to HP axis >30 Gy in 81 (19.4%) and surgery involving HP axis/gonads/spine in 37 (1.4%). Analysis of children treated after 2000 (n=1961) on contemporary protocols found that 27.8% are at high risk of gonadotoxicity. While the proportion who received high CED decreased from 45% pre-2000 to 26.5% post -2000 ($p<0.001$), there was no statistical difference in the other exposures across decades.

Conclusions: Despite reduction of gonadotoxic exposures in the past 2 decades, a substantial proportion of survivors treated on contemporary protocols remains at high risk of gonadotoxicity. There is an urgent need to recognize patients and survivors who would benefit from fertility preservation and gonadotoxicity surveillance. Improving awareness at all levels and access to oncofertility services, especially in resource-limited settings, remain a priority.

Other late effects-6

Long-Term Outcomes of Survivors of Ewing Sarcoma Diagnosed Between 1970 and 1999: a Report from the Childhood Cancer Survivor Study

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Purpose: Survivors of Ewing sarcoma (EWS) are at long-term risk of treatment- and disease-related complications, though it is not known whether these complications are affected by advances in treatment such as the addition of ifosfamide and etoposide (IE) to the previous chemotherapy regimen of vincristine, doxorubicin, and cyclophosphamide (VDC). The purpose of this study is to characterize long-term outcomes in EWS survivors after the addition of IE.

Methods: 5-year survivors of EWS diagnosed 1970-1999 from the Childhood Cancer Survivor Study were included. To examine mortality, subsequent malignant neoplasms (SMNs), and chronic health conditions (CHCs), cumulative incidence function and a proportional hazards model accounting for competing risk were applied to evaluate the impact of chemotherapy regimen (VDC, VDC+IE) and in comparison to siblings. Standardized mortality ratios (SMRs) compared late mortality (>5 years from diagnosis) between EWS survivors and the general population.

Results: Among 683 survivors with chemotherapy data available, there were 408 and 275 survivors in the VDC and VDC+IE groups, respectively. Evaluating SMRs adjusted for sex, death year, and age, EWS survivors had significantly more than expected all-cause (SMR: 8.36, 95% CI: 7.27 to 9.56), SMN-related (SMR: 13.1, 95% CI: 9.81 to 17.13), cardiac-related (SMR: 6.64, 95% CI: 4.11 to 10.16), and other health-related (SMR: 2.97, 95% CI: 1.82 to 4.59) mortality compared to general population. However, no significant differences were observed in the risk of all-cause late mortality, SMN-cause, EWS-relapse, cardiac/pulmonary, and other causes of late mortality between the VDC and VDC+IE groups (Gray's test p-values: 0.6, 0.18, 0.65, 0.72, 0.21, respectively). Compared to their siblings, EWS survivors had a significantly increased hazard of developing Grade 3-5 CHC (any: HR: 5.78, 95% CI: 4.79 to 6.96; cardiovascular: HR: 4.98, 95% CI: 3.96 to 6.26; neurological: HR: 2.83, 95% CI: 1.71 to 4.66; respiratory: HR: 5.62, 95% CI: 2.88 to 11; renal: HR: 5.27, 95% CI: 2.6 to 10.7; musculoskeletal: HR: 11.9, 95% CI: 7.85 to 18.1).
However, there was no significant difference in the hazard of developing SMNs or Grade 3-5 CHC (any, cardiovascular, neurological, or respiratory) between the VDC and VDC+IE groups. However, the VDC+IE group had a significantly higher hazard of Grade 3-5 renal complications (HR:3.55, 95% CI: 1.07 to 11.7).

Conclusion: There are no significant differences in late mortality, SMNs, and most CHCs between survivors who received VDC vs. VDC+IE. The VDC+IE group faces a slightly higher risk of renal CHCs, though the absolute risk remains low. As they age, EWS survivors demonstrate higher risk of late mortality and health risks relative to the general population underscoring the need for continued progress towards improving survivor outcomes.

Other late effects-5

Outcomes of Local Control Procedures in Peri-Articular Bone Sarcomas of the Knee – a Report from the Childhood Cancer Survivor Study

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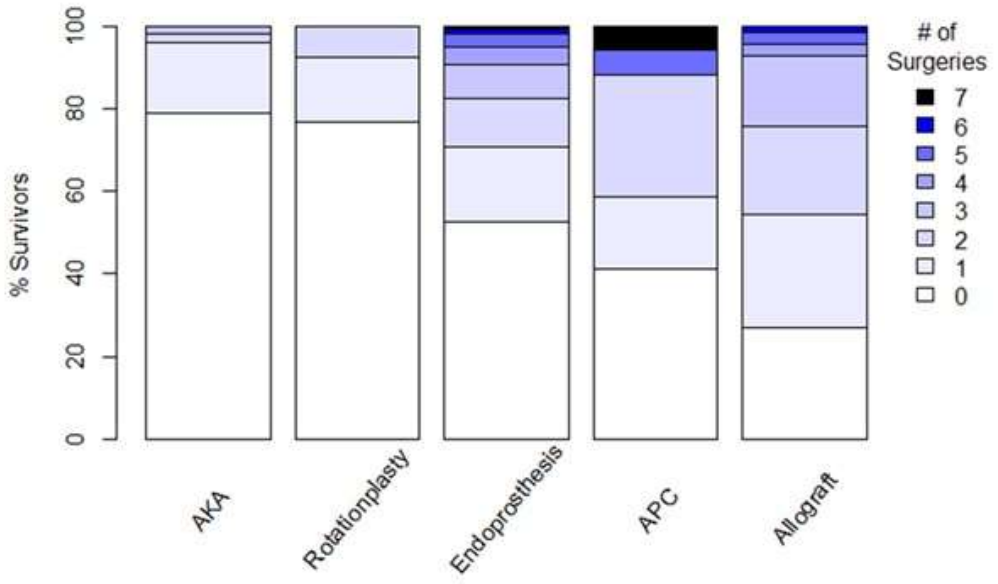
Background: Short- and long-term outcomes after local control of pediatric lower extremity sarcomas are difficult to ascertain with large sample sizes. Utilizing the Childhood Cancer Survivor Study (CCSS) data we sought to ascertain, for pediatric patients with peri-articular bone sarcomas about the knee, 1) the long-term functional and psychological outcomes of surgical management and 2) the frequency of and indications for unplanned reoperations after local control, including subsequent amputation.

Methods: Data regarding tumor location, local control procedure (LCP), and unplanned secondary surgeries were collected. Follow-up surveys collected survivors' SF-36 mental and physical component scores (MCS and PCS) as measures of quality of life and the Brief Symptom Inventory (BSI) for psychological well-being. Physical activity information was similarly self-reported, and unplanned surgical procedures within five years of diagnosis were abstracted from operative reports. Multivariable linear and proportional hazards regression models were used to compare outcomes among procedure groups while adjusting for confounding variables.

Results: 272 patients (189 distal femur, 92 proximal tibia tumors) underwent above-knee amputation (AKA) (19%), rotationplasty (5%), or limb salvage with endoprosthetic (44%), allograft (26%), or allograft-prosthesis composite (APC) (6%) reconstruction. At 35.5 years mean follow-up, PCS for AKA and endoprosthesis were >5 points (the minimal clinically important difference, [MCID]) below the population mean, with rotationplasty 5 points above (p=0.045). All LCPs had MCSs similar to the population mean(p>0.05). The GSI differed among groups (p=0.044); rotationplasty had the best score. Unplanned reoperations varied significantly (Figure); AKA and rotationplasty underwent the fewest. The proportion of unplanned amputations within five years of diagnosis were 0% (rotationplasty), 4.3% (allograft), 9.2% (endoprosthesis), and 17.6% (APC). Undergoing more reoperations was associated with lower odds of being physically active at most recent follow up. Patients with secondary (versus initial) amputations did not differ by PCS, MCS, GSI, or physical activity.

Conclusions: In this long-term study of pediatric sarcoma LCP outcomes, MCS was similar among groups and the population mean, though PCS varied significantly. Variations in unplanned reoperations, including amputation, impacted activity levels. It strongly validates the option of rotationplasty when possible and decided upon through shared decision-making.

Figure: The proportion of patients from each local control procedure who underwent specific numbers of subsequent unplanned surgeries.



Health Services Research-36

The Canary in the Coal Mine – a Survivor and a Mother Challenge the Future of Childhood Cancer Survivorship

Linda Rivard, Julia Stepenske

BACKGROUND: Childhood cancer survivors are living longer but are at risk for developing cardiovascular disease, metabolic dysfunction, neurocognitive impairment, and other age-related conditions decades earlier than the general population. Despite these well-documented risks, they are often lost within the healthcare system, aging prematurely without appropriate medical recognition. The survivorship guidelines remain focused on the child and young adult, leaving an entire population of survivors without a roadmap for aging related care. As a childhood cancer survivor (twice) and mother of an adult survivor, we have experienced firsthand the failures of the current survivorship model – not just as professionals but as individuals navigating a healthcare system that is not equipped to support long-term survivor health. Our combined professional and personal experiences highlight the critical gaps in long-term care and challenge survivorship leadership to rethink their approach to aging survivors.

METHODS: The poster applies a comparative framework to examine the trajectory of early-onset chronic diseases in survivors compared to the general population. Other key focus areas include barriers survivors face when transitioning out of pediatric oncology-based care and systemic failures in risk-based screening, preventive care, and financial coverage when survivors start entering their 30's and beyond. Our analysis is informed by both professional survivorship coordination experience and personal lived experience as a survivor and a mother of a survivor.

RESULTS: Survivors face an identity crisis in the healthcare system- no longer fitting into pediatric oncology but not yet recognized as part of aging populations. Current survivorship guidelines focus on late effects in the child and young adult but fail to prepare for long-term aging-related care. Survivors who enter mainstream healthcare (e.g., primary care or Medicare) are absorbed into an overburdened system unequipped to manage their complex histories. Existing research frameworks in oncology fail to bridge survivorship with broader aging and chronic disease initiatives.

CONCLUSION: Childhood cancer survivors are the canary in the coal mine, signaling a broader failure of reactive, short-term survivorship care models. The COG Late Effects Task Force has the opportunity to lead a paradigm shift by formally integrating survivorship care into chronic disease research for early-onset chronic disease. Their trajectory should serve as a model for rethinking chronic disease prevention and aging-related care across all populations. The survivorship community must extend its vision beyond childhood and young adult follow-up and into lifelong risk-based care models.

Health Services Research-26

Addressing Loss of Follow Up in a Childhood Cancer Survivorship Program in a Low-Middle Income Country: Implementation of a "Survivorship Care Navigator"

Rebeca Rivera-Gomez, Monica Medina, Adriana Vazquez, Martha Garcia, Angelica Martinez, Maribel Ramirez, Paula Aristizabal

BACKGROUND/PURPOSE: Loss of follow-up (LFU) remains challenging when delivering childhood cancer survivorship care (CCSC), with reports of up to 50% of LFU in high-income and low-middle income countries (LMIC). In Mexico, a LMIC, most off-therapy care is provided for 3-5 years after end of treatment, when patients are then discharged from their cancer center. At Hospital General-Tijuana, we established a CCSC program in 2019 and examined LFU.

METHODS: Between 2019 and 2022, a multidisciplinary CCSC team was assembled comprised of pediatric oncologists, social workers, psychologists, and general practitioners, with access to subspecialties (neuropsychology, endocrinology, cardiology, genetics, nutrition, psychiatry). In 2023 we created the role of the "Survivorship Care Navigator" with the goal of establishing contact with all childhood cancer survivors and their families registered in our database.

RESULTS: A psychologist was appointed as the "Survivorship Care Navigator". Activities in this role included contacting LFU survivors, and providing support, healthcare education, and navigation. Since the inception of the CCSC program, all patients undergoing treatment were educated on the importance of life-long CCSC beyond 5-years off-therapy. Between 2019 and 2024, 230 survivors (>5-years off-therapy) were identified from our cancer registry. Patients who were unreachable for ≥2-years were considered LFU. LFU decreased from 44% in 2022 to 18% in 2024 ($p<0.001$).

CONCLUSIONS: LFU decreased significatively in our cohort. Implementation of the "Survivorship Care Navigator" was key in establishing contact with a significant number of survivors LFU, building trust with families, providing psychosocial support, and facilitating complex healthcare navigation. Providing care to childhood cancer survivors at a general hospital allowed continuity of care in a familiar environment, streamlining transition to adult care. Future directions include expanding the activities of the "Survivorship Care Navigator" to include clinical care coordination and subspeciality appointment scheduling. Further, we will assess the impact of early education during cancer treatment regarding CCSC among patients and families on adherence to CCSC.

Health Services Research-27

Implementation of a Childhood Cancer Survivorship Program in Northwestern Mexico: Lessons Learned in the First Five-Years at Hospital General-Tijuana

Rebeca Rivera-Gomez, Adriana Vazquez, Monica Medina, Magdalena Perez, Paula Aristizabal

BACKGROUND/PURPOSE: While the burden of childhood cancer increases worldwide, survivorship care is very limited in low-and middle-income countries (LMIC). Historically in many LMIC, patients who finish cancer treatment are followed at cancer centers for approximately 3-5 years, mainly to monitor for recurrence without consideration of chronic disease prevention or early detection and management of late effects. Misinformation regarding the purpose of Childhood Cancer Survivorship Programs (CCSP), low adherence to follow-up care, and limited staffing contribute to the scarcity of CCSP in LMIC. We describe a newly established CCSP at Hospital General-Tijuana, the largest public hospital in northwestern México, aimed at providing multidisciplinary and comprehensive care to childhood cancer survivors.

METHODS: In 2019, the CCSP team was assembled: pediatric oncologists (1), social workers (2), and psychologists (1). In 2023, care navigators (1), and general practitioners (1) joined. Furthermore, international care guidelines were adapted to local practices. In 2024, access to specialty care was achieved (neuropsychology, endocrinology, cardiology, genetics, nutrition, psychiatry).

RESULTS: Between 2019 and 2024, the CCSP identified 230 survivors, with 159 (69%) currently (as of December 2024) receiving comprehensive care. Long-term complications have been detected in 111 (70%), including neurocognitive deficits (n=40, 21%), obesity (n=38, 34%), mental health disorders (n=31, 28%), ototoxicity (n=13, 12%), endocrine disorders (n=9, 8%), cardiotoxicity (n=8, 7%) and second neoplasms (n=3, 3%). The percentage of patients seen annually has increased steadily, approximately ~7% per year.

CONCLUSIONS: Despite several barriers faced, we successfully established a CCSP. A cohesive, multidisciplinary team provides holistic care to childhood cancer survivors. Ensuring access to specialists was challenging; however, a shared purpose, continued education to staff and families, evidence-based guideline implementation, and dissemination of progress to key stakeholders facilitated engagement and successful CCSP implementation. Hiring a care navigator and providing services at a general hospital enabled patient follow-up, healthcare navigation, and transition to adult-focused care. Next steps include raising awareness among local health authorities and community members to garner additional support for program expansion. Our model is a paradigm shift in our context and replicable in other LMIC.

Other late effects-10

Evaluating Phenotypic Age Acceleration among Adolescent and Young Adult Patients with Ewing Sarcoma and Osteosarcoma

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Background/Purpose: Ewing sarcoma (ES) and osteosarcoma (OS) are two common bone malignancies affecting adolescent and young adult (AYA) patients, often requiring intensive and multi-modal therapy. Cancer and its associated treatments may accelerate the aging process, as reflected in phenotypic age acceleration (PAA), leading to increased risk for developing chronic health conditions typically ascribed in older individuals. We conducted a pilot study to evaluate the impact of treatment completion for ES and OS on age acceleration among an AYA cohort using the validated phenotypic age (PheAge) instrument.

Methods: This pilot study included participants who completed treatment at Vanderbilt University Medical Center from 2012-present for either ES or OS between age 20 and 39 years. Phenotypic age at diagnosis and end of treatment was derived using a modified PheAge equation, which was validated for patients age ³20 years and based on chronological age and eight clinical biochemistry measurements, including albumin, creatinine, glucose, lymphocyte percent, mean cell volume, red cell distribution width, alkaline phosphatase, and white blood cell count. PAA was then calculated as the difference between PheAge and chronologic age. A positive PAA indicates an individual's phenotypic age is older than their chronological age, signifying accelerated aging. A descriptive analysis of PAA across patient demographics and disease strata was then conducted.

Results: Among 30 AYA participants included in our study, 15 participants were diagnosed with ES and 15 with OS. The mean age at diagnosis was 23.8 (Q1 21.8, Q3 27.5). There was an overall male predominance of 19 participants (63.3%). Among participants with ES, the median PAA was 16.1 years (13.8, 18.1) at diagnosis and 18.4 years (13.6, 25.8) at end of therapy. Among participants with OS, the median PAA was 16.0 years (12.9, 20.7) at diagnosis and 15.9 years (13.9, 19.7) at end of therapy.

Conclusions: This pilot study suggests that AYA patients with ES and OS had accelerated aging at diagnosis and ES patients may endure further age acceleration following treatment, while patients with OS had shown a nearly unchanged PAA. These results highlight the need for a larger and more comprehensive investigation into the contributing factors of PAA, including an evaluation of genetics, environmental exposures, cancer characteristics, treatment modalities, as well as acute and chronic toxicities of therapy. Such knowledge will contribute to understanding the etiology and cumulative and long-term impact of these common bone malignancies among AYAs.

CV-7

Paediatric Hematopoietic Stem Cell Transplantation and Cardiac Dysfunction- is Mitoxantrone More Cardiotoxic?

Beryl Rodrigues, H. Curry, E. Shirvington, H. Woodman, A. Chikermane, H. Jenkinson

Background & Aims: Hematopoietic stem cell transplantation (HSCT) is a potentially curative treatment for many refractory malignancies, bone marrow failure syndromes, and primary immune deficiencies. However, pre HSCT regimens containing chemotherapy and/or radiation present risks of enhancing cardiac toxicity in the survivors. This study aims to identify the impact of age, sex and exposure to anthracyclines/anthraquinone and radiotherapy on this risk.

Method: A retrospective analysis of sequential echocardiograms of paediatric HSCT in a single institution performed between 2009 to 2013 for haematological and oncological conditions were included. Ejection fraction of less than 55% or any evidence of ventricular dysfunction was considered abnormal. Anthracycline and Anthraquinone Mitoxantrone doses were converted to Doxorubicin equivalent.

Results: 97 patients treated with HSCT between 2009 and 2013 were entered in the study. There were 54 males and 43 females. 33 deaths in this cohort were all unrelated to cardiac disease. Among the 64 survivors, 24 received cardiotoxic treatment whereas 40 did not receive any anthracyclines or radiotherapy. Of the 24 patients who received cardiotoxic treatment, 1 was excluded as no serial echocardiograms were available and 3 were excluded for preexisting cardiotoxicity. Of the final cohort (n=20), the diagnoses included ALL (11), AML (8) and NHL (1). Sequential echocardiograms of this group were analysed and 14 (70%) had an abnormal echocardiogram.
In the group which had an abnormal echocardiogram (n=14), 71% were males with a median age of 9.6 years (range 2.5-18.65) at HSCT. They had serial echocardiograms for a median of 11.42 years post HSCT. 43% received high dose (≥250mgs/m2), 50% received moderate doses (100 <250mgs/m2) and 7% received low (<100mgs/m2) Doxorubicin equivalent doses. 64% received Mitoxantrone alone or in combination with another anthracycline. 86% received TBI with concurrent anthracyclines, of which over 50% received Mitoxantrone. 71% developed cardiac abnormalities within first 5 years post HSCT and one survivor presented as late as 11 years post HSCT. 7 survivors are under cardiology review and 2 have been commenced on treatment. These 2 survivors had received Mitoxantrone pre HSCT.

Conclusion: Our study shows that 64% survivors who developed cardiac abnormalities received Mitoxantrone warranting further investigation into other confounding factors and the accuracy of doxorubicin equivalent conversion.

Quality of life/Behaviors-12

Knowledge and Self-Efficacy for Survivorship Care Early Post-Therapy among Childhood Cancer Survivors and Their Parents

Wilhelmenia Ross, Brenna Mossman, Megan Roy, Stacy Bryant, Burton Appel, Jacqueline Casillas, Jenna Demedis, Andrew Smitherman, Leora Horwitz, Alejandra Hurtado-De-Mendoza, Jason Mendoza, Sheila Santacroce, Nina Kadan-Lottick

Background/Purpose: Less than 30% of childhood cancer survivors (CCS) receive recommended survivorship care. Lack of knowledge and self-efficacy (i.e., belief in one's ability to manage their own healthcare) are known barriers to care in long-term survivors. We aim to assess knowledge and self-efficacy for survivorship care in CCS and parents early post-therapy.

Methods: We analyzed baseline data from the BRIDGES randomized controlled trial (NCT05448560). Eligible patients from four geographically diverse cancer centers were 2-4 years post-therapy for cancer at <21 years with no prior survivorship clinic care. Parents/guardians (CCS aged <18 years) and adult CCS (≥18 years) completed a pre-randomization survey of demographics, knowledge (diagnosis, treatment exposures, risk of serious future health problems, and receipt of a written summary of diagnosis and treatment), and self-efficacy. Reported diagnosis and treatment were compared to medical records for accuracy. The Self-Efficacy for Managing Chronic Disease Scale assessed self-efficacy (0-low to 10-high) for survivorship care. Responses were characterized with descriptive statistics. Associations between CCS' age, sex, race/ethnicity, insurance type, and perceived risk of future health problems were analyzed with Fisher exact tests.

Results: 217 of 235 (92%) participants enrolled in BRIDGES (median age 12.1 years at enrollment, 52% male, 48% non-Hispanic White, 46% public/no insurance) completed the baseline parent (n=164) or adult CCS (n=53) survey. Most parents and CCS accurately reported the CCS' cancer diagnosis (84% & 77%) and if any chemotherapy exposure (99% & 100%) or radiation therapy exposure (94% & 91%). Only 34% of parents and 38% of CCS believed that the CCS' cancer treatment could cause serious future health problems (Table). Respondents with private insurance (vs. public/none) were more likely (41 vs. 27%) to indicate they knew about future health problems and less likely (32 vs. 53%) to answer "don't know" ($p<0.01$); there was no association with CCS' age at diagnosis, sex, or race/ethnicity. Most (75% of parents, 62% of CCS) recalled receiving a written summary of the diagnosis and treatment. Median self-efficacy scores were high for parents (8.3, range: 1.0-10.0) and CCS (8.0, range: 3.7-10.0).

Table: Belief that previous treatment could cause serious future health problems among baseline survey respondents

	Parents of CCS (n=164)* N (%)	Adult CCS (n=53) N (%)
Yes	55 (34%)	20 (38%)
No	39 (24%)	12 (22%)
Don't Know	69 (42%)	21 (40%)
*1 missing		

Conclusions: Early post-therapy, only a minority of parents or adult CCS respondents believed that the CCS were at increased risk of serious future health problems despite demonstrated knowledge of diagnosis and treatment exposures, high self-efficacy for managing their health, and receipt of a diagnosis/treatment summary in most CCS. Patients require additional education on late effects to understand their health needs post-therapy.

Research Methods-7

Development of Auto-Contouring Tools for Pediatric Organ Segmentation for Computed Tomography Images Used in Radiotherapy Treatment Planning - Results from the Childhood Cancer Survivor Study Expansion Pilot Study

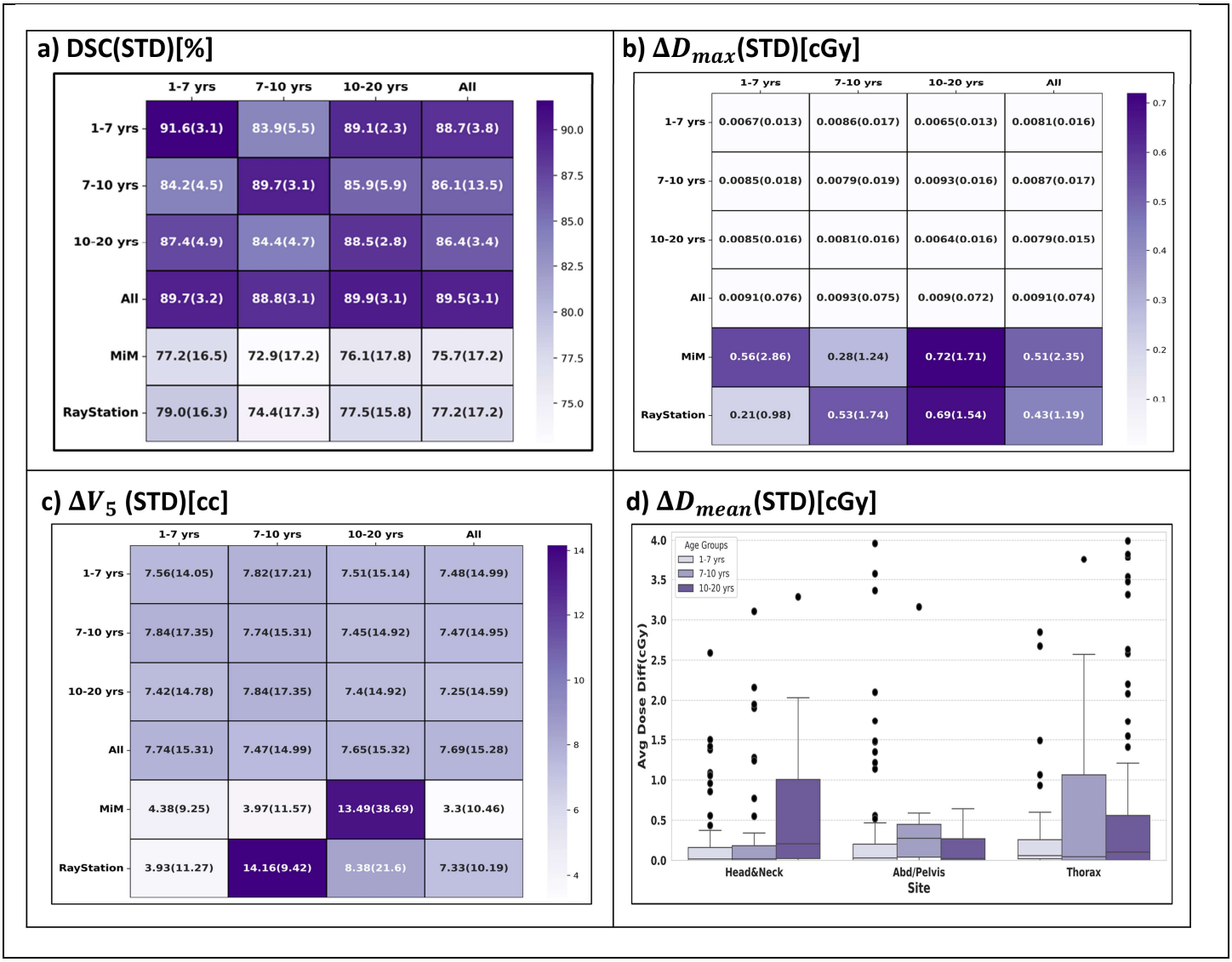
Sogand Sadeghi, Tucker J. Netherton, Arnold Paulino, Christine Chung, Meena Khan, Constance Owens, James Bates, Christine Hill-Kayser, Lei Dong, Ralph Ermoian, Sharareh Koufigar, Jie Fu, John Lucas, Thomas E. Merchant, Greg Armstrong, Rebecca Howell

Background/Purpose: A future expansion of the Childhood Cancer Survivor Study to include survivors treated with contemporary radiation therapy (RT) would require collection of CT-based treatment planning records as DICOM files rather than paper records. Once collected, dose-volume histograms will need to be generated for all organs within the computed tomography (CT) images that were not segmented. Auto-segmentation could overcome the time and resource limitations of manual segmentation at the time of treatment planning. However, existing commercial auto-segmentation solutions are trained on adult populations, potentially leading to suboptimal performance for pediatric patients. This study investigates whether pediatric age-specific models (for ages 1–7, 7–10, 10–20 years) and a combined model (1–20 years) can outperform adult-trained platforms (MiM, RayStation) for auto-segmentation in pediatric CT scans.

Methods: A total of 276 non-contrast pediatric CT scans (ages 1–20, 151 male, 125 female) treated with RT 2000-2022 were collected from four institutions for an ongoing CCSS pilot study assessing cohort expansion feasibility. Three age-specific cohorts (1–7, 7–10, 10–20) and one combined cohort (1–20) were defined for model development. Each dataset was used to train an nnUNet model using 5-fold cross-validation to report average performance. Metrics included Dice similarity coefficient (DSC) and dose–volume differences (Dmax, V5). Models were tested on their respective and other age groups for generalizability. Adult-trained models served as baselines.

Results: All pediatric models demonstrated high DSC values within their respective age groups (1-7 yrs DSC: 91.6±3.1; 7-10 yrs DSC: 89.7±3.1; 10-20 yrs DSC: 88.5±2.8). Notably, the 1–7 and 10–20 models performed consistently across each other's age groups (1-7 yrs DSC: 89.1±2.3 [10-20 yrs cohort]; 10-20 yrs DSC: 87.4±4.9 [1-7 yrs cohort]), suggesting anatomical similarities that support a unified model approach. In contrast, the 7–10 yrs model, yielded lower performance for the other two cohorts (1-7 yrs DSC: 84.2±4.5; 10-20 yrs DSC: 85.9±5.9) indicating that a dedicated, age-specific model may be warranted for the 7–10 years group to ensure optimal segmentation accuracy. The combined (1–20) model achieved consistently DSC (≥88.8%) across all age subsets. In contrast, adult-trained platforms showed lower DSC (as low as 72.9%) and larger deviations in Dmax (up to 0.72 cGy) and V5 (up to 38.69 cc). Pediatric-trained models exhibited minimal differences in dose–volume metrics (Dmax <0.01cGy, V5 ~7–8 cc) across the 1–20 years age cohort.

Conclusion: Pediatric-trained models, both age-specific and combined, significantly outperformed adult-trained commercial platforms across the 1–20 age range. A single combined model offers robust performance comparable to age-specific models, suggesting that routine pediatric radiotherapy workflows can benefit from a unified pediatric-trained approach.


a) DSC(STD)[%]
1-7 yrs
7-10 yrs
10-20 yrs
All
1-7 yrs
91.6(3.1)
83.9(5.5)
89.1(2.3)
88.7(3.8)
7-10 yrs
84.2(4.5)
89.7(3.1)
85.9(5.9)
86.1(13.5)
10-20 yrs
87.4(4.9)
84.4(4.7)
88.5(2.8)
86.4(3.4)
All
89.7(3.2)
88.8(3.1)
89.9(3.1)
89.5(3.1)
MiM
77.2(16.5)
72.9(17.2)
76.1(17.8)
75.7(17.2)
RayStation
79.0(16.3)
74.4(17.3)
77.5(15.8)
77.2(17.2)
90.0
87.5
85.0
82.5
80.0
77.5
75.0
b) ΔD_{max}(STD)[cGy]
1-7 yrs
7-10 yrs
10-20 yrs
All
1-7 yrs
0.0067(0.013)
0.0086(0.017)
0.0065(0.013)
0.0081(0.016)
7-10 yrs
0.0085(0.018)
0.0079(0.019)
0.0093(0.016)
0.0087(0.017)
10-20 yrs
0.0085(0.016)
0.0081(0.016)
0.0064(0.016)
0.0079(0.015)
All
0.0091(0.076)
0.0093(0.075)
0.009(0.072)
0.0091(0.074)
MiM
0.56(2.86)
0.28(1.24)
0.72(1.71)
0.51(2.35)
RayStation
0.21(0.98)
0.53(1.74)
0.69(1.54)
0.43(1.19)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
c) ΔV_5 (STD)[cc]
1-7 yrs
7-10 yrs
10-20 yrs
All
1-7 yrs
7.56(14.05)
7.82(17.21)
7.51(15.14)
7.48(14.99)
7-10 yrs
7.84(17.35)
7.74(15.31)
7.45(14.92)
7.47(14.95)
10-20 yrs
7.42(14.78)
7.84(17.35)
7.4(14.92)
7.25(14.59)
All
7.74(15.31)
7.47(14.99)
7.65(15.32)
7.69(15.28)
MiM
4.38(9.25)
3.97(11.57)
13.49(38.69)
3.3(10.46)
RayStation
3.93(11.27)
14.16(9.42)
8.38(21.6)
7.33(10.19)
14
12
10
8
6
4
d) ΔD_{mean}(STD)[cGy]
Age Groups
1-7 yrs
7-10 yrs
10-20 yrs
Avg Dose Diff(cGy)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Head&Neck
Abd/Pelvis
Thorax
Site

Health Services Research-14

An Evaluation of Health Disparities and Health Equity among Children and Adolescents with Cancer and Access to Fertility Care

Taryn Sandheinrich, Emily Lafrentes, Kara Felts, Robert Hayashi

Background/Purpose: Infertility is a source of stress in survivors of childhood and adolescent and young adult (C&AYA) cancer. Ability of patients to navigate care, costs, and in the context of their socioeconomic status have been identified as factors in pursuing fertility interventions in adults. The purpose of this study was to evaluate relationships between social determinants of health (SDOH), access to care, and patient and family attitudes toward fertility preservation in C&AYAs diagnosed with cancer.

Methods: A cross-sectional survey was administered to parents of C&AYA diagnosed with cancer who, at the time of survey, were post-pubertal and could pursue fertility preservation. Information obtained included: zip code, parent educational level, race/ethnicity, age at diagnosis, age at time of survey, household income, and questions pertaining to previous discussions around fertility and access to specialized fertility care.

Results: Fifty-eight parents of females of C&AYAs and 64 parents of males of C&AYAs consented to participation and completed the survey (N=122). Of parents of female C&AYAs, 53.4% and 63.5% of parents of male C&AYAs recall a discussion surrounding fertility at diagnosis. Of the parents of female C&AYAs, 77.6% and 73% of male's parents report their child desires to have biological children. Nineteen percent of males and 35.1% of females were referred to a fertility specialist. However, only 12.1% females banked oocytes and 24.2% males sperm-banked prior to therapy. The most reported barriers were perceived time constraints, acute illness, and lack of information. SDOH including income, race/ethnicity, and parent education were not significant factors in discussions regarding fertility, preservation options, or fertility specialist referral.

Conclusion: Most parents of C&AYA report their child's desire for future children. While SDOH did not appear to affect access to care, discussions of fertility preservation and specialist referral were lacking both before and after treatment. Continued efforts to educate pediatric oncology providers and an increase in fertility specialist referrals could increase rates of fertility preservation in C&AYA patients diagnosed with cancer.

CV-8

Left Ventricular Function and Its Longitudinal Changes in Childhood Cancer Survivors – Results of the CardioOnco Study

Christina Schindera, Yara Shoman, Fabien Belle, Severin Fankhauser, Eva Hägler-Laube, Reto Kurmann, Gabriela Kuster, Nana Poku, Eva Scheler, Tomas Slama, Thomas Suter, Nicolas Waespe, Nicolas Von Der Weid, Claudia Kuehni

Background/Purpose: Childhood cancer survivors (CCS) are at risk for cardiac late effects. Assessment of cardiac function by left ventricular ejection fraction (LVEF) is recommended for survivors treated with established cardiotoxic treatments (anthracyclines [AC], chest radiotherapy [RT]). The evidence on cardiotoxicity of other chemotherapeutic agents–including alkylating agents and cisplatin–is conflicting and the longitudinal changes in heart function are understudied. We assessed cardiac function in CCS exposed to known and potentially cardiotoxic treatments, factors associated with LVEF and studied LVEF over time.

Methods: We included CCS aged ≥18 years, diagnosed between ages 0–20, treated in 1 of 5 pediatric oncology centers across Switzerland between 1976–2019, who survived ≥5 years, and received any systemic anticancer therapy or chest RT. We invited them for an echocardiographic assessment including 2-dimensional LVEF (abnormal <54% for female, <52% for male). We stratified CCS in AC only, chest RT only, both, and potentially cardiotoxic treatments including any other chemotherapy and compared groups using ANOVA- and t-tests. We performed multivariable linear regression to investigate sociodemographic, treatment-, and lifestyle-related factors, and modelled linear, quadratic, and cubic models to assess time trends.

Results: We assessed 491 CCS with a median age at study of 32 years (interquartile range [IQR] 24–39) and a median time since diagnosis of 24 years (IQR 17–31). Overall prevalence of abnormal LVEF was 7.3% (36/491), 7.5% (20/266) for AC only, 3.6% (1/28) for chest RT only, 3.8% (3/83) for both, and 6.1% (7/114) for potentially cardiotoxic treatments. Overall mean LVEF was within normal range (59.4±5.8%). When comparing groups, LVEF was slightly lower in survivors exposed to AC only (58.7±5.6%, p<0.001), chest RT only (59.8±7.6%, p=0.24), and both (59.0±6.0%, p<0.01), compared to survivors exposed to potentially cardiotoxic treatments (61.2±5.1%; p=0.001). Female CCS had a lower risk for reduced LVEF [β coefficient = -1.3; 95%CI -2.24, -0.26], and higher cumulative anthracycline dose (per 100 mg/m²) was associated with decreased LVEF (−0.95; −1.32, −0.58). Chest RT, potentially cardiotoxic agents, and lifestyle were not associated with LVEF. Amongst 139 followed-up CCS (median 4.3 years of follow-up), mean LVEF decreased from 63% to 55%. Time trends analysis suggests a non-linear (curvilinear) relationship between time and LVEF changes (p<0.0001). Random effect of time showed substantial variability in LVEF changes across survivors [3.58, 95% CI: 2.83, 4.53].

Conclusion: Adult CCS are at risk for impaired LVEF when treated with higher cumulative anthracycline doses. We found no association between potentially cardiotoxic treatments and cardiac dysfunction when assessed by LVEF. The longitudinal LVEF decrease in our cohort highlights the need for continuous monitoring of cardiac function in long-term survivors.

Quality of life/Behaviors-4

Physical Fitness and Clinically Assessed Disease Burden in Long-Term Childhood Cancer Survivors – the SURfit Study

Christina Schindera, Anna Mayr, Iris Baenteli, Helge Hebestreit, Rahel Kasteler, Simeon Zuercher, Nicolas Von Der Weid, Susi Kriemler, Corina Rueegg

Background/Purpose: Childhood cancer survivors are at risk of adverse health outcomes that can accumulate over time. Physical fitness is a strong predictor of health and mortality. As physical fitness is reduced in childhood cancer survivors compared to the general population this could exacerbate their disease burden.
Objectives: This study aimed to 1) describe the burden of clinically ascertained adverse health outcomes in long-term survivors of childhood cancer, and 2) investigate the association between physical fitness and incidence of adverse health outcomes, before and after controlling for cancer related variables.

Methods: This study used baseline data of the SURfit study, a randomized controlled physical activity trial. We included 163 survivors, diagnosed <16 years, ≥16 years at enrolment, and ≥5 years since last cancer diagnosis. Clinically assessed adverse health outcomes were categorized using the Common Terminology Criteria for Adverse Events (CTCAE) and graded from 1-4 (grade 1, mild to grade 4, life-threatening). Physical fitness was assessed by cardiopulmonary-exercise-testing (CPET), hand-grip strength, and the 1-minute sit-to-stand test (STS), and we calculated a composite fitness score averaging the z-scores of the three fitness measures. We used multivariable Poisson regression models to investigate the association between physical fitness and adverse health outcomes incidence.

Results: We assessed participants with a mean age at study of 31 years (standard deviation [SD] 9) and a mean time since diagnosis of 23 years (SD 9). Overall, survivors had 1170 adverse health outcomes, with 99% of survivors having at least one. On average, participants had 7.2 (SD 4.5) adverse health outcomes (any grade) and 1.4 (SD 1.6) severe health outcomes (grades 3+). Survivors of childhood lymphoma had the least average events of any grade per person (5.8, SD 3.2), whilst central nervous system tumor and bone sarcoma survivors had the most adverse health outcomes (8.2, SD 3.6; and 8.2, SD 4.2) (Fig. 1). Higher levels of physical fitness were associated with fewer adverse health outcomes of any grade (CPET: Incidence rate ratio (IRR) 0.71 per watt/kg bodyweight, 95% Confidence Interval (CI) 0.63-0.81, p<0.001; hand-grip strength: IRR 0.60 kg/kg bodyweight, 95%CI 0.35-1.03, p=0.063; STS: IRR 0.90 per 10 repetitions, 95%CI 0.86–0.95, p<0.001; composite fitness score: IRR 0.81 per z-score, 95%CI 0.75–0.88, p<0.001).

Conclusion: Childhood cancer survivors experienced a high burden of adverse health outcomes, and nearly all survivors reported at least one adverse health outcome. Better physical fitness was associated with reduced disease burden irrespective of the survivor's cancer history; associations were found for CPET, STS, and the composite fitness score. Our study emphasizes the importance to counsel survivors on improving their fitness levels.

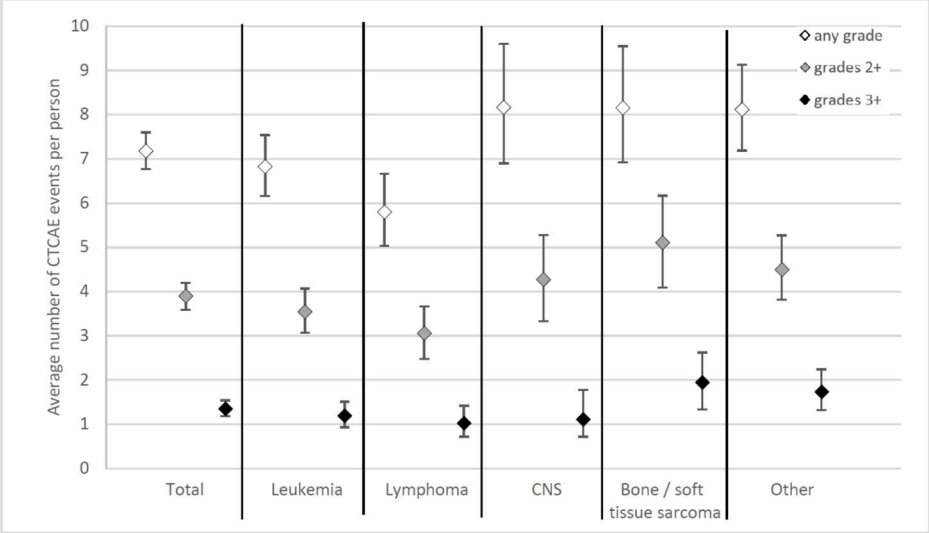


Fig. 1. Average number of adverse events per person for any grade (1-4), grades 2+ (2-4) and grades 3+ (3-4) overall (total) and stratified by primary cancer diagnosis. Error bars represent 95% Poisson distributed exact confidence intervals.
Abbr.: CNS, central nervous system tumor

Research Methods-8

The Development of a Pediatric Cancer Environmental Service

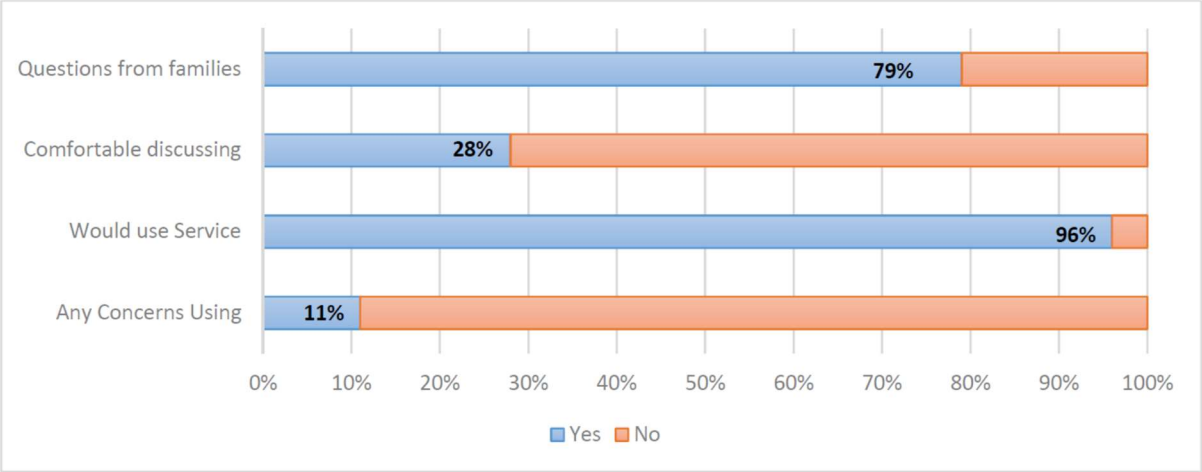
Omar Shakeel, Michael Scheurer

Background/Purpose: There has been growing evidence that several environmental exposures (i.e., toxicants) have adverse health impacts on survivors of childhood cancers. However, there is limited knowledge and awareness about how these environmental factors can affect the health of childhood cancer patients and survivors. We propose the development of a novel referral service to address these environmental exposures and provide counseling on protective measures.

Methods: In April 2024, we surveyed oncology providers at Texas Children's Cancer Center on their knowledge of environmental risk factors for pediatric cancer and their intention to use a pediatric cancer environmental service.

Results: Forty-eight oncology providers responded to our survey. Thirty percent were physicians, 15% were advanced practice providers, 32% were nurses, and 23% were social workers. Approximately 80% of respondents indicated that they receive questions from families on the impact of the environment on their child's cancer. While most reported receiving questions, nearly 75% were not comfortable discussing the topic with families. As such, 96% of providers would use the referral service, with 71% indicating that they would use the service in addition to addressing concerns themselves and 25% indicating that they would use the service in lieu of addressing concerns themselves. Approximately 90% of respondents indicated that they would not have any concerns using the referral service.

Figure 1: Experiences with Receiving Questions from Families on Environmental Risk Factors for Pediatric Cancers (N=48)



Conclusions: Environmental toxicants are important and potentially modifiable risk factors that need to be more fully explored childhood cancer survivors. We propose developing a novel pediatric cancer environmental service can help childhood cancer patients and survivors adopt a healthier lifestyle and potentially decrease morbidity and mortality in this vulnerable population.

Health Services Research-28

Primary Care Engagement and Perceptions among Adult Survivors of Childhood Cancer in a Specialized Long-Term Follow-Up Program

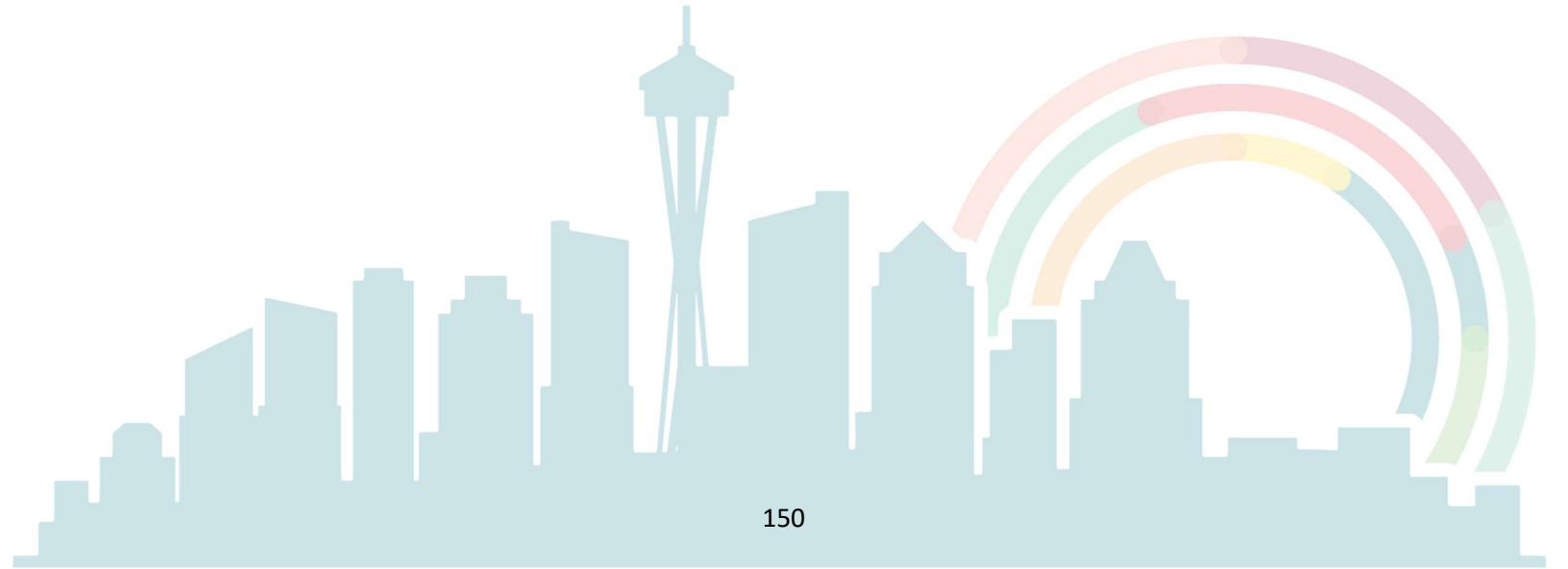
Archana Sharma, Dawn Carey, Angela Senger, Anusha Ramji, Meredith Reffner Collins, Karen Long Traynor, Katie Devine

Background/Purpose: There are different models of survivorship care (specialist-led, primary care-led, shared care). For patients who are followed in a specialist-led long-term follow-up program, it is recommended that they also engage in primary care. The purpose of this study was to describe engagement in primary care among a sample of adult survivors of childhood cancer followed in a long-term follow-up program and describe their perceived experiences with their primary care providers (PCPs).

Methods: Eligible participants (current age >18 years, at least one-year post-treatment) completed an online survey regarding healthcare utilization, perception of the extent to which PCPs have discussed aspects of survivorship care, and sociodemographic characteristics (i.e., race, ethnicity, gender, education, socioeconomic status). Descriptive statistics were used to characterize current engagement in primary care and experience with PCPs. Chi-square analyses examined associations with sociodemographic characteristics.

Results: A total of 125 survivors completed the survey (Mage = 26.3 years, SD = 6.1; 52% female, 48% male). Of the 125 participants, 95 (66.4%) reported having a PCP. Engagement in primary care was not significantly associated with any sociodemographic characteristic. Among those with PCPs, only 21 (22.1%) reported that their PCP is in contact with their oncology team regarding follow-up care, with 40 (42.1%) reporting no contact and 34 (35.8%) reporting I don't know. On a scale of 1 to 5, participants rated the extent to which PCPs discussed side effects of treatment received (M = 2.41, SD = 1.15), follow-up tests and future care (M = 2.39, SD = 1.26), monitoring for early detection of new or returning cancer (M = 2.10, SD = 1.16), and needs as a cancer survivor (M = 2.29, SD = 1.33).

Conclusions: While the majority of this sample was engaged in primary care, they reported little to moderate discussion of their cancer survivorship needs with their PCP. Multi-level interventions are needed to enhance care coordination and improve patient-provider communication and shared care.



Health Services Research-29

Coordinating and Tracking Transitions of Care from Pediatric to Adult Survivorship Programs Across Three Health Systems

Ksenya Shliakhtsitsava, Stephanie Lawrence, Andrea Betts, Laura Aubree Shay, Amy Hughes, Daniel Bowers, Cynthia Cochran, Rebecca Eary

Background/Purpose: An urgent need exists for better care transition processes for childhood cancer survivors (CSS) as they age into adult medical survivorship care. We aimed to assess the effectiveness of simultaneously using Epic's Care Everywhere Referrals Management, a tracking dashboard, and a program coordinator, to facilitate referrals for adult survivorship care. We sought a more seamless transition and continued quality care through enhanced patient tracking and follow-up.

Methods: Patients seen at the Children's Health/UT Southwestern Pediatric Survivorship (long term follow up) clinic were referred to the adult program during their last pediatric visit via CareEverywhere electronic referral. The Epic Tableau dashboard tracked all relevant referral metrics, including CareEverywhere referrals, within the receiving institution's database. The survivorship coordinator used referrals to schedule initial survivorship appointments via phone calls and portal messages. The number of scheduled visits and reasons for refusal were reported in the dashboard. We used summary statistics to describe the transition rate of our 3-pronged approach.

Results: Between December 1, 2022, and February 2025, a total of 164 referrals were placed for CCS aged 18-24 to the adult program using the electronic referral system. Of these, 105 (64%) were contacted via phone. Among those contacted, 81 (77%) were scheduled and attended an adult survivorship visit, while the remaining 24 (23%) were unable to schedule due to insurance status. These patients were referred to our county hospital survivorship program. The remaining 59 individuals (36%) did not respond after three phone call attempts.

Conclusions: Our referral model facilitated seamless transitions into adult survivorship for a majority of CCS patients. Future research should explore referral refusal patterns and care continuity between pediatric and adult programs, as well as between oncology and survivorship services.

Health Services Research-30

Communication in AYA Survivorship Clinical Settings: Best Practices and Challenges

Stephanie Smith, Briana C. Martin-Villa, Mary Anne Kochenderfer, Lidia Schapira

Background: Pediatric and adolescent/young adult (AYA) cancer survivors face long-term physical and psychosocial effects of their cancer treatment and are recommended to receive lifelong specialized survivorship care. While much research has focused on what information survivors need to know about their past cancer and future health, very little is known about how clinicians communicate with AYAs and their families about these topics. This study aimed to evaluate best practices and challenges with survivorship-related communication from the perspective of experienced clinicians.

Methods: We conducted semi-structured individual interviews with 12 survivorship clinicians from diverse practice settings across the United States between 11/2024-2/2025. Interviews queried communication best practices, perceived barriers, and recommendations for improving communication in AYA survivorship settings. All interviews were recorded, transcribed verbatim, and qualitatively analyzed using Dedoose software to identify key themes and patterns.

Results: Clinicians (9 female, 3 male) had been in practice for median 16.5 years (4-37 years) and were physicians specializing in pediatric oncology (N=7, including 2 also with med-peds training) or primary care with a focus on survivorship (N=3), or were nurse practitioners (N=2). Clinicians cared for pediatric (N=3), adult (N=3), or all (N=6) ages. Common barriers to effective communication included the complexity and volume of information (especially when feeling pressured to fit it all into one visit due to worry that survivors would not return to care), lack of time (exacerbated by extra time needed for language interpretation), and anxiety among AYA survivors and caregivers that affected communication dynamics among the triad (survivor, caregiver, clinician). Best practices for communication included building rapport (active listening, connecting on an individual level), a mindset to “meet the patient where they’re at” (prioritization of topics to discuss, not trying to address everything in one visit), use of clear, accessible language with visual aids, and contextualizing information such as health risks and associated uncertainty (adapting for past medical experiences that affect risk perception).

Conclusion: Effective communication between clinicians and AYA cancer survivors has the potential to improve health outcomes by promoting AYA engagement with care. Clinician communication strategies may help survivors understand health risks and manage associated uncertainty and anxiety. Addressing barriers to communication will be a focus of future interventions.

Intervention Research-6

Evaluating Survivorship-Related Communication Gaps to Develop a Community Health Worker-Led Intervention for Hispanic/Latino Young Adult Childhood Cancer Survivors and Their Families

Stephanie Smith, Briana C. Martin-Villa, Kevin Pu, Rebecca Lewinsohn, Mary Smith, Heidi Boynton, Lidia Schapira

Background: Open communication among young adult childhood cancer survivors (YA-CCS), parents, and clinicians helps YA-CCS understand their cancer history, health risks, and survivorship care needs. However, Hispanic/Latino (H/L) YA-CCS families who prefer a language other than English face significant communication barriers during clinical encounters with English speaking clinicians. As part of an ongoing study aimed at developing an intervention to facilitate family-centered communication, we report here on interviews conducted with H/L YA-CCS and their parents.

Methods: We held small group and individual interviews in English and Spanish with H/L YA-CCS (ages 18-25, ≥5 years post-diagnosis) and separately with parents of H/L YA-CCS. Transcripts were analyzed qualitatively using thematic analysis in Dedoose software. Participants were recruited through our collaboration with a community-based organization (CBO) and in a pediatric oncology clinic. Using a structured human-centered design process, we assembled a design team of community partners to ideate and prototype an intervention.

Results: Twelve YA-CCS (7 female, 5 male; all bilingual) and 11 parents (all female; Spanish-language preferred) participated, representing 15 families. YA-CCS were median age (min-max) 20.5 (18-25) years and 12 (6-15) years post-diagnosis. YA-CCS described knowledge gaps due to being excluded from parent-clinician conversations during treatment and ongoing avoidance of cancer discussions within families due to emotional burden. Many YA-CCS and parents shared that yearly survivorship clinic visits evoke stress, nervousness, and a sense of being unprepared, often leaving them overwhelmed. Some linked hesitancy to discuss cancer or ask questions during visits to their cultural norms. Guided by these insights, we leveraged our community-clinic partnership to co-develop an intervention to facilitate family-centered communication. In 3 design workshop sessions, CBO staff designed an early prototype for a "pre-visit preparation and post-visit debrief" communication intervention, in which a community health worker meets with each YA-CCS-parent dyad before and after a survivorship clinic visit to help elicit questions, clarify topics, and debrief action items.

Conclusions: Effective triadic communication is essential to bridge gaps in cancer survivorship care among H/L YA-CCS. Listening directly to H/L YA-CCS and parents identified communication barriers that are being addressed in the development of a culturally and linguistically tailored intervention to support families affected by cancer. Interviews and the intervention design process are ongoing and updated data will be presented at the meeting.

Adult Childhood Cancer Survivors Sharing Survivorship Through Photos

Debra Spoljaric, Rochelle Hobson, Bridgette Bobo, Janelle Donjon, Sarah Colby, Tiffany Zhu, Jessica Vanderlan, Amaris Tippey, Allison King

Background/Purpose: Nearly 15,000 children and adolescents are diagnosed with cancer each year in the United States (U.S. Cancer Statistics Working Group, 2022). Childhood cancer mortality rates have decreased, thus, the number of individuals surviving childhood cancer is increasing. Childhood cancer survivorship does not come without risks and burden. Many survivors experience late effects of their cancer treatments resulting in the need for more nuanced clinical care. Survivors also experience emotional distress and feelings of loneliness with limited opportunities for connecting to other childhood cancer survivors and sharing their experiences. Unique needs and experiences of childhood cancer survivors deserve greater attention from the healthcare community. The aim of the current project was to engage adult childhood cancer survivors in groups to reflect and identify relevant messages and images about their cancer experience.

Methods: Informed consent was obtained, and adult childhood cancer survivors recruited from an adult survivorship clinic attended a 6-week Photovoice (PV) group hosted in person or via Zoom. PV is a participatory visual method that involves asking participants to answer questions by taking photographs, discussing them in groups, writing captions for selected photos, and selecting photos for sharing with the community. Prompts focusing on various time points were used in sessions (i.e. Life before diagnosis, Life During Treatment, Life in Survivorship). Participants met weekly sharing photos, stories, and creating captions. To conclude each PV session, the participants identified recurrent concepts with guidance of facilitators.

"Grounded But Soaring" This balloon mirrors my post-cancer life - vibrant but slightly off-center and definitely not perfect. The tethers represent the clinic's crucial support, allowing me to reach new heights while staying connected to care.

Since my diagnosis, I think the longest time I've gone without a doctors appointment was about 3 months, but between all of my specialists and complications that arise, my average is more around every 3 weeks, even after 25 years from when I was diagnosed. Because of doctors appointments and hospitalizations, I feel like cancer has robbed me of so many memories I should have had. I have missed countless hours of school and work, holidays, events I spent months planning, milestones in my friends and family's lives, loved ones funerals, and so many other things that I can never get back. Childhood cancer does not stop when childhood does.

"You're so brave" Their sickly smiles are suffocating as they place an idea of me on a pedestal that only ever made them feel better. "You're my Hero" I must perform the role they want me to be, so I say thank you with a smile so big that no one ever doubts that I am anything but okay. That having cancer did not fuck me up and that they may good about it all and leave me alone. "You're an inspiration to us all." What the fuck did I do? Can I put, did not die on my resume? "Wow! You don't look sick at all" Looking healthy is one thing when you feel like your dying every day. And when I go to my Dr's appointments I must not look too healthy so they believe my symptoms but not so sick they want to admit me. Survivorship is not something I want to glamorize. I am also grateful to it, it gave me empathy, it gave me compassion, it gave me understanding, and emotional intelligence. Survivorship is having death as a close companion. Survivorship is making other people comfortable

Results: A total of 31 survivors consented, and 26 completed the project. The mean age = 27.3 years, range 22-43. Half of the participants were male and 82% identified as White. Childhood diagnosis of brain (43%) or hematological (36%) cancers were most common with an average age at diagnosis of 11 years old, mean 0-19 years. Participants were likely to have undergone chemotherapy (93%), radiation (57%), and/or surgery (57%). Participants discussed photos and captions weekly in a group setting. In the final week they chose one photo with a caption to share with a broader audience. The participants identified common messages such as a sense of loss, survivor's guilt, advocacy, family, and what now?! Photos and captions will be displayed in a presentation. Graphic shows three examples of final photos.

Conclusions: The unique voices of adult childhood cancer survivors serve as an opportunity to increase awareness of late and long-term effects of childhood cancer. PV is a viable method for building connections, sharing lived experiences, and communicating needs of adult childhood cancer survivors. As needs for survivorship care increase, patient voices, as shared in PV, can be used to better inform survivorship care.

SMN-3

Clinical Utility of 99 Breast Cancer Polygenic Risk Scores (PRSs) in Female Survivors of Childhood Cancer: a Report from the Childhood Cancer Survivor Study (CCSS) and St. Jude Lifetime Cohort (SJLIFE)

Aparna Srinivasan, Jian Wang, Gavriel Matt, Yadav Sapkota, Zhaoming Wang, Tianzhong Yang, Joseph P. Neglia, Lucie Turcotte, Melissa Hudson, Kiri Ness, Greg Armstrong, Jinghui Zhang, Leslie Robison, Xin Zhou, Yutaka Yasui, Cindy Im

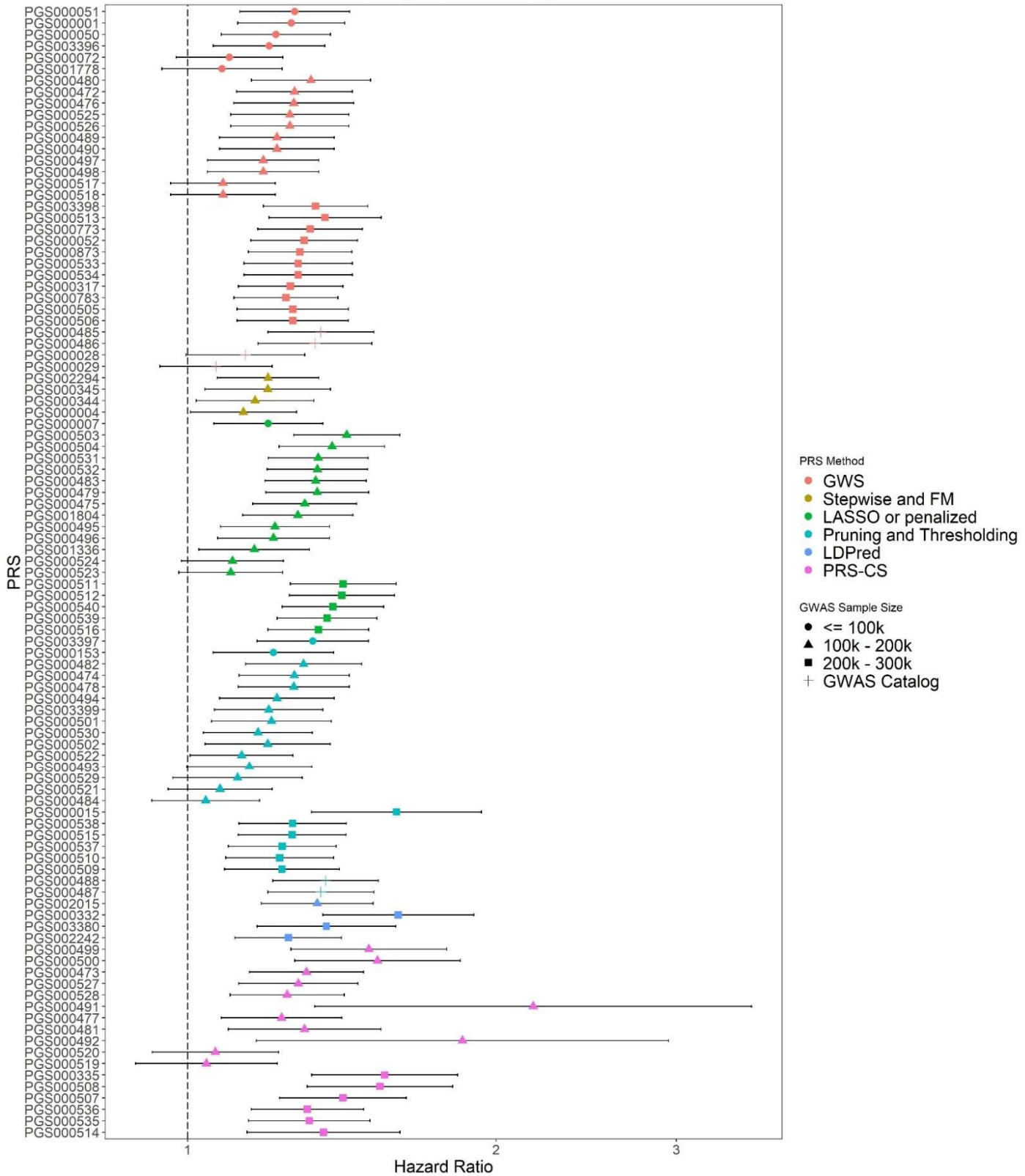
Background: Female childhood cancer survivors are at high risk for developing subsequent breast cancer (BC). The St. Jude Survivorship Portal, an open-access online survivorship data resource (https://survivorship.stjude.cloud), now includes 3271 PRSs for 541 traits from the PGS Catalog. For a single phenotype, there may be many PRSs, each reflecting different genome-wide association study (GWAS) sample sizes and PRS construction methods. In this study, we systematically evaluated 99 PRSs developed for primary BC for their ability to inform clinical risk stratification for subsequent BC.

Methods: Analyses were limited to the 99 general population PRSs developed for invasive or overall BC. Data for 5-year female survivors of European ancestry (EA) and African ancestry (AA) from CCSS and SJLIFE were analyzed, with PRSs computed under a uniform protocol using whole-genome sequencing or imputed array-based genotype data and pathology-ascertained breast subsequent neoplasms. Ancestry-specific hazard ratios (HRs) for PRSs (per one standard-deviation increase) were estimated with Cox regression using age as the time scale and adjusted for ancestry principal components, batch, chest radiotherapy (RT) and anthracycline doses. To validate a PRS association with HR=1.3, statistical power was 99% in EA survivors and 11% in AA survivors. PRS-RT interactions assessed whether PRSs modified risks conferred by chest RT dose.

Results: Analyses included 4689 EA (292 BCs) and 445 AA (9 BCs) survivors. Median attained age was 39 (IQR 31-47) and 31 (IQR 25-41) years for EA and AA survivors, respectively. Overall, 21% of EA and 13% of AA survivors were treated with chest RT. We observed wide variability in BC PRS effect sizes (Figure): in EA survivors, 86% of PRSs (HR median 1.27, range 1.04-2.17) were associated with BC ($P<0.05$); in AA survivors, 29% were associated (HR median 1.74, range 0.53-13.78). In AA survivors, 43% of the 7 PRSs from multi-ancestry/non-EA GWAS were validated (vs. EA GWAS: 28%). Both GWAS sample size and PRS development methods were associated with HR magnitudes in EA survivors ($P<0.05$). While no PRS-RT interactions were statistically significant in EA survivors, all 16 BC PRSs with differences ≥20% in HR estimates by chest RT dose had a higher HR estimate for those treated with ≤10 Gy, suggesting higher chest RT dose can mask BC polygenic risk. The BC PRS with the largest effect size and $P<5x10-8$ in EA survivors (HR 1.61, 95% CI 1.35-1.90) was from a GWAS with N~229K (~123K cases) and developed with a Bayesian method (LDPred, ~6.4 million variants). For comparison, a widely-studied BC PRS with 313 variants showed a weaker association (HR 1.13, 95% CI 1.00-1.28).

Conclusions: Among the 99 BC PRSs in the Portal, there is wide variation in their methodologic characteristics and effect sizes among childhood cancer survivors. Careful consideration of available BC PRSs is required when utilizing them for subsequent BC risk stratification.

Figure: HR and 95% CI for each breast cancer PRS (per SD increase) among female EA survivors in CCSS and SJLIFE annotated by methodology and GWAS sample size.



Endo-6

FSTL1 and its Paralogs in Assessing Body Composition: Correlation with Body Fat and Skeletal Muscle Mass in Childhood Cancer Survivors

Lucie Štrublová, Filip Zlámal, Jan Kučera, Jana Fialová-Kučerová, Tomáš Kepák, Jaroslav Štěrba, Julie Bienertová-Vašků

Background/Purpose: Our cross-sectional study investigated the relationship between body composition and circulating plasma levels of follistatin-like proteins (FSTLs; FSTL1, FSTL4, and FSTL5) in childhood cancer survivors (CCS).

Methods: The cohort consisted of 61 CCS (26 females and 35 males) aged 18-36 years (mean age 24.6±4.4 years), who were followed up at the Late Effects Clinic of St. Anne's Hospital in Brno. The mean age at diagnosis was 10.9±4.9 years, and the mean time after treatment was 12.0±5.1 years. Body composition was assessed by bioelectrical impedance analysis, with body fat percentage categorized according to Obesity Medicine Association (OMA) guidelines. Plasma FSTL levels were quantified using commercially available ELISA kits, and correlations were examined by linear regression analysis.

Results: Significant negative correlations were found between plasma levels of FSTL1 and FSTL4 and both body fat percentage and skeletal muscle mass.

Conclusions: Our results suggest that FSTL1 and FSTL4 may be potential biomarkers of obesity and muscle dysfunction in CCS. Further research is warranted to elucidate the mechanisms of muscle dysfunction after treatment and the role of FSTLs in this context.

Neurocog-4

Olfactory Function and Associated Neurocognitive Impairment among Adult Survivors of Childhood Cancer

Adrienne Studaway, Zachary Wooten, Ketaki Saokar, Emily Mott, Yoshiko Jackson, Belinda Mandrell, Kiri Ness, Melissa Hudson, Kevin Krull, Brian Potter, Nicholas Phillips

Background: The olfactory nerve is a key component of the limbic system with loss of smell linked to neurocognitive decline and neurodegenerative disorders in the general population. Olfactory dysfunction (OD) has been noted in cancer patients during treatment with chemotherapy and radiation. However, systematic evaluation of the prevalence of OD in pediatric cancer survivors and its associations between OD and neurocognitive impairment has not been undertaken.

Methods: 672 survivors of childhood cancer (52% female; median [IQR] age at evaluation = 28 [19-39] years) completed the Brief Smell Identification Test (B-SIT), a nationally normed test of olfactory function, as well as standardized neurocognitive testing. OD was defined as ≤8 items correct on the B-SIT. Non-English speakers and those with IQ < 70 were excluded. Neurocognitive performance was referenced to national normative samples to generate age-specific z-scores (m = 0, s = 1.0), with impaired defined as z < -1.33. The overall prevalence (95% CI) of OD was examined using a t-test. Multivariable regression was used for continuous neurocognitive variables to evaluate the associations between demographic, clinical, and behavioral factors, and OD. For binary neurocognitive outcomes, the risk of impairment in OD was examined using multivariable logistic regression, with radiation, chemotherapy, sex, and age at diagnosis as covariates.

Results: Among participants, 74% were non-Hispanic white, 19% received cranial radiation, 83% received chemotherapy, and 11% reported a history of smoking. The overall prevalence (95% CI) of OD was 20% (17-22%), which was higher than the reported prevalence in the general population (10-15%). Survivors with OD were more likely to be male (25%, p=0.006). No demographic, behavioral, or clinical variables were associated with OD. Survivors demonstrated impairment on all neurocognitive measures. When adjusting for age, sex, race, and treatment, survivors with OD demonstrated higher Odds Ratio (OR) for impairment with sustained attention (OR [95%CI] 2.8 [1.5-5]), attention variability (OR 2.1 [1.2-3.6]), focused attention (OR 2.9 [1.7-4.9]), short-term memory (OR 1.9 [1.2-2.9]) long-term memory (1.8 [1.2-2.8]), and word reading (OR 3.2 [1.8-5.9]) compared to those without OD, all significant ($p<0.05$) while controlling for multiple comparisons. OD was generally not associated with executive functions.

Conclusions: Survivors of childhood cancer demonstrate a higher frequency of OD compared to the general population. The presence of OD was associated with an increased risk of multiple neurocognitive impairments associated with the limbic system, as well as basic academic skills, which are often dependent upon intact cognitive functions during childhood. This pattern may suggest early impact on limbic system function in cancer survivors.

Other late effects-7

Immune Resilience after Pediatric Cancer Treatment

Smrithi Sugumaran Menon, E. Kaitlynn Allen, Kasi Vegasana, Velmurugan Balaraman, Kyla Shelton, Kubra Bahcivanci Kubra Bahcivanci, Siyao Bleynat, Matthew Wogksch, Emily Finch, Kiri Ness, Greg Armstrong, Paul Thomas

Advances in pediatric cancer treatment have increased the survival rate to 85%, yet survivors remain at higher risk for developing severe chronic diseases and infection-related mortality, likely due to immune dysfunction - a largely understudied area. An emerging hypothesis is that immune health is a dynamic manifestation of the basal immune state and adaptive immune memory. Cancer and its toxic treatment disrupt an individual's immune state, and it is unclear in survivors whether the immune system returns to its basal state or reconstitutes to a new immune state post treatment. To address this, slow off-rate modified aptamer (SOMA) scan serum sample measurement was done for cancer survivors who were diagnosed with Acute Lymphoblastic Leukemia (ALL) (n=75) or Hodgkin's Lymphoma (HL) (n=102) from the St. Jude lifetime cohort (SJLIFE) selected based on the progression of clinical outcomes such as frailty (age-associated physiological decline). The samples are profiled for immune as well as clinical markers compared to age matched healthy control (n=78). Preliminary data suggests that, compared to healthy non-frail controls, non-frail HL individuals show elevated inflammation-related markers (IL-3, IL-21R, IL-1RA, CRP) and reduced immune factors (G-CSF, serotransferrin, IL-9, IL-23, PDGF-A/B), along with changes in DNAJB9 and NELL-1. Non-frail ALL survivors show unique markers (TGF-beta-1, PD-L1, GM-CSF) compared to age matched healthy controls, along with shared markers with HL survivors (NELL-1, PDGF-A, IL-9, IL-3, IL-21R, IL-1RA), suggesting a unified biological response across cancer types. Additional analysis is underway to examine differences between non-frail and frail cancer survivors, factoring in cancer treatment history and chronic conditions. Longitudinal T cell repertoire profiling and assessment of T cell populations using single-cell sequencing, are also ongoing to deepen understanding of immune resilience post-treatment.

Genetics/Genomics-6

Assessment of Risk Factors for Platinum Induced Ototoxicity: a Single Institute Cohort Study

Shruthishree Sukumar, Joanna Gell, Ching Lau, Robin Arens, Mark Ferreira

Background: Platinum-based chemotherapy, such as Cisplatin and Carboplatin, are frequently used to treat pediatric cancers. Platinum-induced ototoxicity results in permanent bilateral sensorineural hearing loss at high frequencies (4-8 kHz). Risk factors include age, cumulative dose, frequency of administration, renal function, concurrent ototoxic medication, and cranial irradiation. With advancements in treatment, there are increasing cancer survivors with long-term side effects. Among patients receiving Platinum therapy, there is variability in the prevalence and severity of ototoxicity, likely due to genetic susceptibility. Traditional genome-wide association studies have identified single nucleotide polymorphisms in genes such as ACYP2, TPMT, and COMT.

Objective: To identify non-genetic and genetic risk factors for Platinum-induced ototoxicity.

Design/Method: A single center retrospective chart review with prospective administration of survey and biospecimen collection. SlicerDicer in EPIC was utilized to identify participants who received Platinum chemotherapy from October 1, 2018, to the current date. Clinical data collected include demographics, cancer diagnosis, treatments received (i.e. cumulative dose, frequency, duration of administration), cranial irradiation, cranial surgery, exposure to ototoxic medication, and usage of sodium thiosulfate (STS). Audiology tests were reviewed for ototoxicity based on SIOP Boston Ototoxicity Grading Scale. DNA was extracted with the Promega Wizard® Genomic DNA purification kit. The Illumina Infinium Global Diversity Array with Enhanced PGx was used to identify genetic variants.

Results: Of the 110 patients analyzed, a majority were male (n = 63, 57.27%) and children under 5 years of age (n = 48, 43.64%). The ethnic composition of the cohort included predominantly Caucasian, Other, and African American. The most common diagnoses were neuroblastoma (n = 29, 26.36%), osteosarcoma (n = 19, 17.43%), germ cell tumors (n = 18, 16.67%), and medulloblastoma (n = 12, 11.01%). Treatment exposure varied, with 52 patients (47.71%) received only Cisplatin, 25 patients (22.73%) only Carboplatin, and 31 patients (28.44%) received both agents. Additionally, two patients received oxaliplatin for refractory CNS germ cell tumors. STS was administered to only 12 individuals (10.91%). Hearing loss Grade 2 and higher was observed in 33 patients (30%). To date, 46 patients completed surveys and provided samples for genomic analysis.

Conclusion: The severity of irreversible platinum-induced ototoxicity varies likely due to individual genetic susceptibility. Identifying potential genetic variants could lead to the development of targeted otoprotective medications and help stratify the risk of hearing loss in future oncology patients. High-risk individuals may benefit from otoprotective treatments. Through the identification of specific genetic variants, we can better tailor interventions to mitigate this adverse effect.

Research Methods-9

Concordance of Six Minute Walk Test and Cardiopulmonary Exercise Testing: a Report from the St. Jude Lifetime Cohort Study (SJLIFE)

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Background: Childhood cancer survivors are at risk for exercise intolerance, defined as peak oxygen uptake (VO2 peak) <85% of predicted from cardiopulmonary exercise testing (CPET). Reduced VO2 peak is associated with a four-fold increased risk of mortality over four years in young adult survivors of childhood cancer, identifying a vulnerable population in need of intervention. However, CPET is costly and requires specialized equipment and personnel. The aim of this analysis was to evaluate concordance between CPET measured VO2 peak and performance on the six-minute walk test (6MWT), a more cost-efficient measure validated with CPET measured VO2 peak in other chronic disease populations.

Methods: Participants were enrolled in SJLIFE and completed CPET and the 6MWT in random order over 2-5 days. Maximal CPET used a Bruce or modified Bruce protocol on the treadmill and a ramping protocol on a cycle or arm ergometer for children and adults. Breath by breath gas analysis was used to capture VO2 peak. The 6MWT was completed on a 30-meter path in a level corridor. Distance walked in six minutes (distance) was captured in meters. Height was measured on a stadiometer and weight on an electronic scale. VO2 peak was estimated from the 6MWT with the formula VO2 Peak = - 18.34 + (0.036*distance) + (0.274*height in meters) -(0.155*weight in kilograms) - (0.245*age). Descriptive statistics, Pearson r, interclass (ICC) and concordance correlation (CCC) coefficients were calculated to compare the measures. Bland Altman methodology was used to visually examine the data.

Results: Data included 3112 observations from 2702 survivors median age 29 (range 7-70 years), 48.7% female, 22% non-white, 1336 with leukemia or lymphoma, 417 with CNS tumors, 309 with bone or soft tissue sarcoma, 178 with retinoblastoma, 166 with Wilms tumor, and 296 with other malignancies). Mean±standard deviation VO2 peak values were 27.66±9.22 ml/kg/min from CPET and 27.67±6.31 ml/kg/min from 6MWT. Correlation coefficients were 0.68 (Pearson r), 0.65 (ICC) and 0.66 (CCC). Bland Altman methodology identified some bias. Underestimation of VO2 Peak with 6MWT was identified among survivors with higher CPET VO2 Peak values.

Conclusions: Concordance between the 6MWT and clinically ascertained VO2 peak among childhood cancer survivors is good with systematic bias suggesting a ceiling effect of the 6MWT in this population.

Genetics/Genomics-7

Cancer Predisposition/Congenital Syndromes with Increased Cancer Risk in Childhood Cancer Survivors Cohort: a Monocentric Case Series

Ramona Tallone, Andrea Beccaria, Brigitte Nicholas, Valeria Capra, Patrizia De Marco, Patrizia Ronchetto, Silvia Merlo, Marina Francesca Strati, Roberta Canicatti', Sara Oberti, Monica Muraca, Riccardo Haupt, Carlo Dufour, Lisa Pelanconi

Background: Around 10% of pediatric cancers are due to congenital defects. The list of Cancer Predisposition Syndromes (CPS) continues to expand with advancements in diagnostics and increased awareness, especially for childhood cancer survivors (CCS) who face tumor recurrence and subsequent neoplasms (SN).

Aim: Identify CPS/Congenital Syndrome (CS) in CCS actively followed at AfterCare clinic at Gaslini Hospital (Genoa, Italy).

Materials and Methods: Between June 2021 and January 2025, we evaluated CCS (excluding CNS tumors) and recommended genetic testing for those who met the Jongmans' criteria, including karyotype, CGH-array (180 kb), NGS-oncological-panel/WES, and WGS. We used multiple analyses after multistep and multidisciplinary case discussion.

Results: Among 841 CCS in active follow-up, 109 (13%, male 48 %) were eligible for genetic investigation. The patient cohort predominantly had a history of solid tumors (60.5%,n=66), with 27.7% (n=30) of cases involving neuroblastoma. Regarding the haematologic aspect, 24% (n=26) had lymphoma, 14.8% (n=16) leukaemia,1.2 % others. In 4.6% (n=5) of cases, patients developed both a solid tumor and a haematologic malignancy; in 6.4% (n=7) a second tumour (SN) and in 5.5% (n=6) multiple SN (range 2-8). We analysed 109 CCS, with 71.5% (n=78) of cases using a single method, while 29% (n=32; range 2-5). The most commonly used method was WES in 66.6% (72) of cases, while genome sequencing was used in 3 cases (2.7%); 9% (n=10) are currently in progress. Currently, we identified 17 CPS (17.2%, ALK, APC, ATM, BRCA1,CBL-2, CEBP2-A, CHEK-2, ERCC2, ERCC4, FANCA, ITK, MAGT-1, PHOX2B, PALB-2, P53, RB,WRN), 5 CS (4%, 22q11.2 dupl./deletion syndrome, Beckwith Wiedemann and Klinefelter Syndrome) and 18 pathological VUS (18%); one incidental carrier of FANCA. In 4 patients, the mutation was also found in other family members with initiation of screening for CPS.

Table 1 Genetic characteristics of the AfterClinic_IGG cohort

Patient	Sex	Disease	Gene	SN	Transplant
1	F	HB	APC		No
2	F	AML	PALB-2	BC	Yes
3	F	HL	MAGT1	NHL	Yes
4	F	NB	PHOX-2B		No
5	M	AML	ATM+ITK	S+other,	Yes
6	M	ALL	BRCA1	ST	No
7	M	GCT	CBL2		No
8	F	AA	FANC-A		Yes
9	M	NHL	CEPB2-A		No
10	M	RB	RB+VUS ADARB-1	GNB	Yes
11	F	AT	P53		No
12	F	NB	ALK		No
14	F	NB	CHEK2		No
15	F	S	ERCC2		No
16	F	HL	WRN	BC,PC	No
17	F	ALL	ERCC4	ST	Yes
18	M	NB	ERCC4		No
19	M	NEP	BWS		No
20	M	NB	22q11.2 dupl.+MUTYH	MNG	Yes
21	F	HLH	22q112 del.	GNB	Yes
22	M	GCT	Klinefelter S.		No
23*	F	*	FANC-A carrier		No

Abbreviations; AA; Aplastic anemia, AT; adrenal tumor; ALL, Acute lymphoblastic leukemia; AML, Acute Myeloid leukemia; BC, Breast cancer; BWS,Beckwith-Wiedemann Syndrome; ES, Ewing Sarcoma; F, Female; GCT,germ cell tumor; GNB, ganglioneuroblastoma; HB; Hepatoblastoma; HLH, Hemophagocytic Lymphohistiocytosis; HL, Hodgkin Lymphoma; NHL, Non-Hodgkin Lymphoma;; MA, medullary aplasia; MNG,meningioma; NB, Neuroblastoma; M, male, NEP, nephroblastomatosis; PC, pulmonary cancer; RB,retinoblastoma; S,Sarcoma; SN, subsequent neoplasm; SC,Skin cancer; WT, Wilms Tumor *incidental FANCA carrier

Conclusions: CPS prevalence in our cohort is surprising higher than literature (17.2%). The multidisciplinary approach and the combined use of multiple methods enhance diagnostic capability. In addition, the recognition of intra-family mutations has made it possible to initiate ad hoc screening resulting in early cancer/comorbidity recognition. This study highlights the potential underestimation of CPS/CS in CCS.

Health Services Research-31

Improved Early Referral in Long-Term Survivor Care with Institutional Standardized Practice among Childhood Leukemia Survivors

Ji Yun Tark, Kayla Foster, Mary Shapiro, Shawki Qasim, Karen Rabin, Austin Brown, Maria Gramatges

Background: Curative treatment for childhood acute leukemia confers significant risk for late effects and follow-up care remains suboptimal. In 2018, the Texas Children's Hospital Leukemia Program established a practice standard (PS) for transition from treatment to survivorship care, which includes a reminder for referral to the Long-term Survivor (LTS) Clinic at two years from end of treatment (EOT). We evaluated the impact of implementing this PS on LTS attendance and engagement among leukemia survivors.

Methods: We identified 476 survivorship-eligible leukemia survivors diagnosed from 2011-2019 via cancer registry data, excluding those who died, were not in remission, or were treated with stem cell transplant. Sociodemographic, clinical, and area-based factors were extracted from electronic medical records. Attendance was defined as ever-attending LTS clinic by December of 2024, and engagement as continued follow-up after the initial LTS visit. Multivariable logistic regression was performed to estimate adjusted odds ratios (aOR) and 95% confidence intervals (CIs) for associated factors, with comparisons made before and after EOT in 2017 to capture PS effects.

Results: The mean age at EOT was 9.5 ± 4.9 years; 56% were male; and 57% were Latino. At 2-6 years from EOT, 52% were publicly insured and 4% were uninsured. Overall, 89% attended LTS clinic at least once, with no difference by EOT before or after 2017 (OR 0.99, 95% CI 0.56-1.79). In multivariable analysis, younger age at EOT (aOR 1.11, 95% CI 1.04-1.17) and Latino ethnicity (aOR 3.45, 95% CI: 1.56–7.69) were associated with a higher likelihood of attending LTS clinic. Survivors who were publicly insured or uninsured were less likely to attend LTS clinic (aOR 0.32, 95% CI: 0.15–0.65; aOR 0.20, 95% CI: 0.05–0.85). Of those attending an initial LTS visit, 95% were seen within five years of EOT and 86% remained engaged. Survivors with an EOT date in 2017 or later were more likely to be seen within 5-years of EOT (aOR=8.33, 95% CI: 2.38-50.0). Moreover, early follow-up was associated with a higher likelihood of ongoing engagement after the initial visit (aOR 8.51, 95% CI 2.97-24.70). Older age at EOT (aOR 0.91, 95% CI 0.85-0.96) and public insurance (aOR 0.42, 95% CI 0.21-0.83) were associated with lower engagement. Area-based factors, such as total travel time, total distance to LTS care, and the area deprivation index were not associated with either outcome.

Discussion: Our findings suggest the implementation of an institutional PS improved timely referral and initiation of LTS care, resulting in increased survivor engagement. However, factors such as age, race/ethnicity, and payer status remain significant predictors of LTS non-attendance and disengagement, suggesting certain populations may benefit from targeted interventions. These findings highlight the value of a standardized approach to off therapy monitoring and referral to overcome structural barriers to survivorship care.

Health Services Research-32

Predictors of Non-Attendance and Disengagement in Long-Term Survivorship Care among Childhood Cancer Survivors

Ji Yun Tark, Kayla Foster, Abiodun Oluyomi, Shawki Qasim, Omar Shakeel, Alicia Howell, Zoann Dreyer, Maria Gramatges, Austin Brown

Background: Timely and regular survivorship care is critical to prevent, detect and manage late effects of childhood cancer treatment. However, adherence to follow-up care remains suboptimal and varies across survivor populations. We examined factors associated with non-attendance and disengagement in long-term survivor (LTS) care.

Methods: We identified 1,136 survivorship-eligible childhood cancer survivors diagnosed at Texas Children's Hospital from 2011-2019 via cancer registry data, excluding those who died, were not in remission, or were treated with allogeneic stem cell transplant. Sociodemographic, clinical, and area-based factors were extracted from electronic medical records. Nonattendance was defined as never attending LTS clinic by December 2024 and disengagement as attending an initial visit without follow-up. Multivariable logistic regression estimated adjusted odds ratios (aOR) and 95% confidence intervals (CIs) for associated factors.

Results: The mean age at the end of therapy (EOT) was 9.3 ± 5.6 years; 56% were male, 50% were Latino, 42% were leukemia survivors, 71% had received chemotherapy, and 24% both chemotherapy and radiation. At 2-6 years from EOT, 50% had public insurance, 4% were uninsured. Overall, 21% never attended LTS clinic. Non-attendance was more frequent among older survivors (aOR=1.15, 95% CI: 1.11-1.18) and those with public (aOR=2.37, 95% CI: 1.65-3.44) or no insurance (aOR=2.58, 95% CI: 1.20-5.42). Nonattendance was more frequent among survivors of CNS tumors (aOR=2.73, 95% CI 1.33-5.43), lymphoma (aOR=2.49, 95% CI: 1.57-3.95), and solid tumors (aOR=5.23, 95% CI: 3.44-8.06) compared to leukemia survivors. Nonattendance at an older age at EOT was most pronounced in Non-Latino Black survivors (Figure 1a; P for interaction = 0.049). The impact of uninsurance increased with age at EOT but was not significant (Figure 1b; P for interaction = 0.13). Among survivors who attended an initial LTS visit (n=875), 25% did not return, with a higher likelihood for disengagement among survivors with older age at EOT (aOR=1.09, 95% CI: 1.05-1.12), public insurance (aOR=2.29, 95% CI: 1.55-3.42), CNS tumors (aOR=3.26, 95% CI 1.84-5.76), lymphoma (aOR=2.90, 95% CI: 1.81-4.65), and solid tumors (aOR=3.27, 95% CI: 2.06-5.22) compared to survivors of leukemia. Sex, language, and area-based factors (i.e., total travel time, total distance to LTS care, and area deprivation index) were not associated with non-attendance or disengagement.

Conclusions: Older age at EOT and public/uninsured status were associated with 1) never attending LTS clinic and 2) disengagement after initial LTS clinic visit in childhood cancer survivors. In addition, higher rates of non-attendance in non-leukemia survivors suggest potential gaps in referral practices and the need for a standardized approach to LTS care. Targeted interventions to address these individual and structural barriers are warranted for survivors most vulnerable to loss of follow-up.

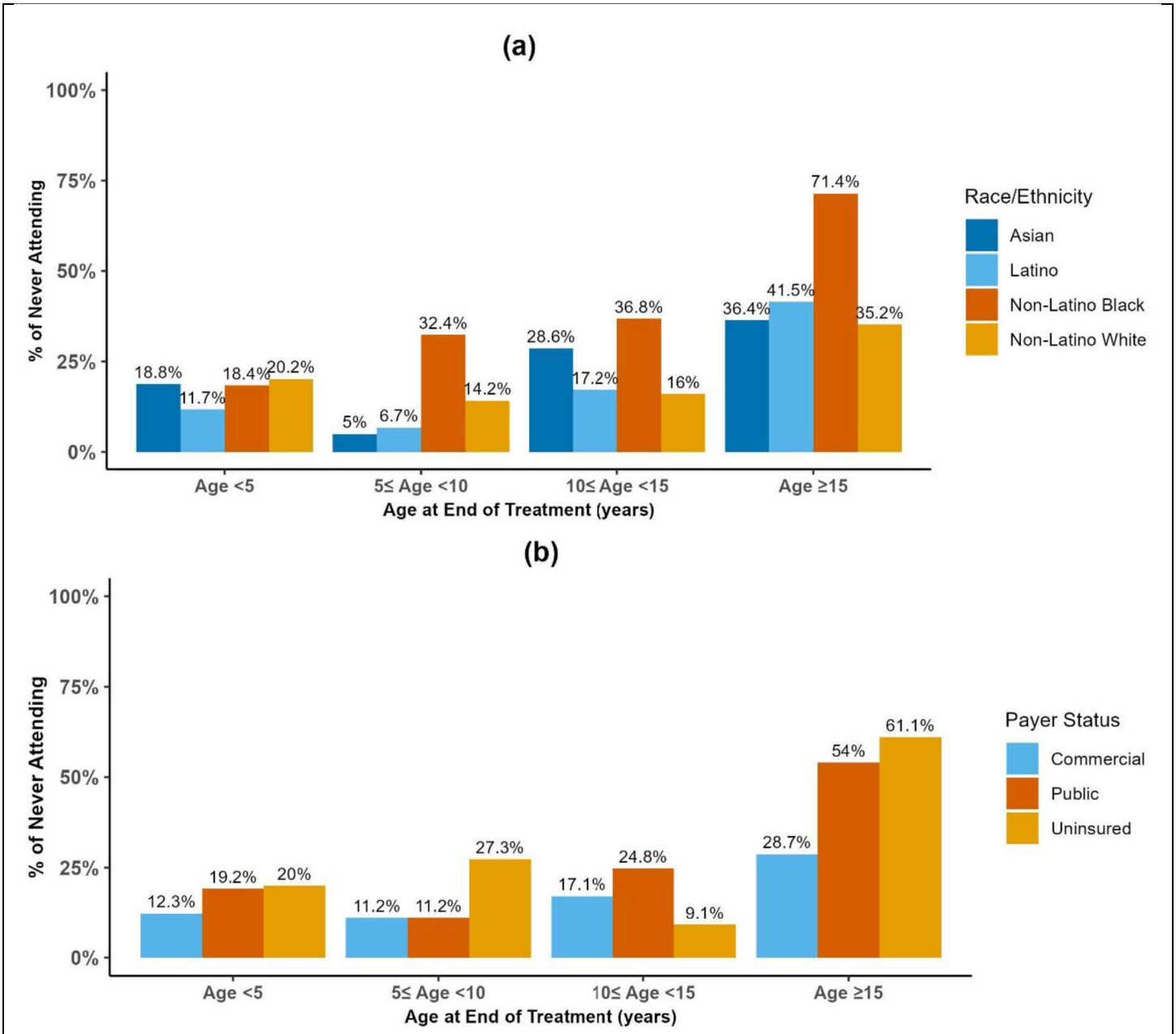


Figure 1. Prevalence of nonattendance in the long-term survivorship care by race/ethnicity (a) and payer status during 2-6 years of end of treatment (b) across age groups.

Intervention Research-7

Remotely Delivered Exercise Intervention Modestly Improves Peak Oxygen Uptake

Sarah Terrell, Robyn Partin, Sean O'Neil, Matthew J. Ehrhardt, Tara Brinkman, Elizabeth Salerno, Maura Kepper, Zhaoming Wang, Deo Kumar Srivastava, Melissa Hudson, Greg Armstrong, Daniel A. Mulrooney, Kiri Ness

Background: Over 60% of childhood cancer survivors have exercise intolerance (estimated peak oxygen uptake [VO2peak] <85% of predicted) at a mean age of 36 years. We randomized exercise intolerant cancer survivors to a remotely delivered supervised exercise intervention to assess impact on cardiopulmonary fitness.

Methods: Exercise intolerant cancer adult survivors participating in the clinically assessed St. Jude Lifetime Cohort Study (n=156) were randomized to either a 20-week virtually delivered, individually prescribed exercise intervention, including aerobic and strengthening components, or an attention control condition receiving general physical activity guidelines. The intervention included exercising 60 minutes, 3 days per week with 6 supervised exercise sessions over the first two weeks, tapering to biweekly weeks 3-4, once/weekly weeks 5-8, every other week weeks 9-16, and one session midway between weeks 17-20. The schedule was modified to accommodate participant needs, adherence, and response to exercise to gradually progress to 150-300 minutes of moderate aerobic activity and twice weekly strength training. The primary outcome was change in VO2peak, estimated from the remotely assessed two-minute step in place test, compared between groups with two sample t-tests.

Results: Evaluable participants included 131 childhood cancer survivors (64 intervention, 67 control; 83% of those randomized) who completed >50% of exercise sessions and the 20-week follow-up assessment. Baseline values listed in the table did not differ by randomization status (p's>.05). Compared to controls, estimated VO2peak significantly increased in the intervention group from pre- to post-intervention (10±15 vs. 4±9 steps, 1.00±1.76 vs. 0.29±2.01 ml/kg/min, p=0.04).

Conclusion: A 20-week personalized, virtually delivered exercise regimen increased exercise tolerance among survivors of childhood cancer. Even modest improvements in VO2peak have been associated with reduced all-cause mortality or all-cause hospitalization in patients with systolic heart failure. Sustainability will be evaluated in future analyses as well as associations with biomarkers of aging.

Baseline Values	
Sex, n (%)	
Female	56.5
Male	43.5
Age (mean ± SD)	
At cancer diagnosis	7.7 (5.7)
At baseline	29.2 (5.7)
Diagnoses, n (%)	
Leukemia/lymphoma	28.2
CNS	29.8
Bone/soft tissue sarcomas	16
Other solid tumors	26
Baseline outcomes (mean ± SD)	
Steps in 2 minutes	96 (18)
VO2peak (ml/kg/min)	25.9 (3.8)
Blood pressure (mmHg)	113/75 (13/10)
Resting heart rate (bpm)	83 (13)
Forced expiratory volume in 1 second (liters)	3.2 (0.8)
Peak expiratory flow (liters/minute)	456 (33)
Body mass index (kg/m^2)	28.5 (7.1)

Health Services Research-11

Development of an Oncology Primary Care Clinic: a Model to Address the Needs of Childhood, Adolescent, and Young Adult Cancer Survivors

Alique Topalian, Melinda Butsch Kovacic, Elizabeth Shaughnessy, Melissa Erickson

Background: Childhood, adolescent, and young adult (AYA) cancer survivors live decades after treatment and are at increased risk of early-onset health conditions such as hypertension, cardiomyopathy, obesity, and second primary malignancies. Cincinnati Children's (CCHMC) Survivorship Clinic provides lifelong survivorship care based on the Children's Oncology Group guidelines. These guidelines recommend survivors establish care with a primary care physician (PCP). However, PCPs report inadequate training in the care of cancer survivors; 20% of survivors do not even have a PCP. Many patient charts within primary care do not have accurate notation of the prior cancer diagnosis or treatment. To address these needs, an oncology primary care clinic was established and embedded within the University of Cincinnati Cancer Center.

Methods: The oncology primary care clinic was established in 2019 by a family medicine physician with extensive survivorship knowledge and includes two family medicine physicians trained in hospice and palliative care and a nurse practitioner. The clinic is open to survivors of childhood, AYA, and adult-onset cancers and individuals with hereditary cancer syndromes. CCHMC Clinic patients who do not have a PCP are referred to this clinic. To longitudinally track outcomes, a clinical registry was developed. Electronic medical records of all patients seen between 1/2021 and 1/2025 (n=901) were extracted and entered in REDCap. For this analysis, records of adult survivors of childhood cancer (diagnosed <18 years) or AYA cancers (diagnosed between the ages of 18-39) were queried and analyzed (n=120).

Results: Childhood and AYA survivors account for 13% of patients seen in the clinic. Patients were 20-74 years old (mean=34; SD=11.13), 30% were diagnosed in childhood, and 70% were diagnosed as AYAs. The most common cancers were hematologic (39%), brain (13%), and breast (9%). All patients had documented cancer therapies in their charts, with 79% having a history of chemotherapy, 48% having radiation and 9% having a stem cell transplant. Most patients (58%) were diagnosed with at least one cardiovascular condition (e.g., hypertension or hyperlipidemia), and 24% of the patients were on medications for this. Psychological conditions (e.g., depression or anxiety) were also quite common (66%), in addition to neurologic (48%) issues such as cognitive difficulties, neuropathy and headaches. Endocrinopathies were frequent, with 47% having conditions such as hypothyroidism and diabetes.

Conclusions: These patients need complex care management across their lifespan, and this clinic is well suited to provide this care. Its close connections with CCHMC allow for coordinated care between pediatric oncologists and PCPs and aids in transitioning survivors to adult sub-specialty care, such as cardio-oncology. Next steps include incorporation of patient-reported and longitudinal outcomes and creation of an oncology primary care fellowship.

Quality of life/Behaviors-5

Prevalences and Risk Factors for Poor Lifestyle Behaviours in Survivors of Childhood Cancer: a PanCareFollowUp Study

Selina R. van den Oever, Leontien C.M. Kremer, Helena J. H. van der Pal, Mieke Rijken, Gisela Michel, Eline Bouwman, Jeroen te Dorsthorst, Samira Essiaf, Lieke Feijen, Cecilia Follin, Line Elmerdahl Frederiksen, Hannah Gsell, Riccardo Haupt, Maria van Helvoirt, Rosella Hermens, Lars Hjorth, Tomas Kepak, Katerina Kepakova, Anita Kienesberger, Marietta Kokla, Monica Muraca, Kylie O'Brien, Marleen Renard, Katharina Roser, Carina Schneider, Roderick Skinner, Anne Uyttebroeck, Deveny Vanrusselt, Sabine Verschueren, Jeanette Falck Winther, Jacqueline Loonen, Saskia M. F. Pluijm, on behalf of the PanCareFollowUp Consortium

Background: Poor lifestyle behaviours may contribute to the development or worsening of late effects after childhood cancer. The aims of this study were to determine prevalences and risk factors for low physical activity, smoking, alcohol use, and drug use among childhood cancer survivors of the European PanCareFollowUp Care study cohort.

Methods: In four European countries, 812 survivors were recruited. Outcomes were self-reported and included low physical activity (<75 minutes of vigorous or <150 minutes of moderate to vigorous physical activity per week), current smoking (yes/no), alcohol consumption (≥3 units of alcohol per week), and drug use in the past year (yes/no). Prevalences of poor lifestyle behaviours were calculated and its associations with sociodemographics, cancer history, physical health, pain, fatigue, and survivors' level of empowerment were assessed using multivariable logistic regression analyses.

Results: For this analysis, 777 participants could be included of which 27% of survivors reported low physical activity, 15% smoked, 19% consumed ≥3 units of alcohol per week, and 6% used drugs in the past year. Survivors from the Czech Republic and Italy more often smoked than participants from Belgium (23% and 22% vs. 10%, respectively). Only 8 survivors from Sweden smoked (5%), precluding the comparison with participants from Belgium in the multivariable analysis. Newly identified risk factors included reduced physical health (for low physical activity), pain (for smoking), and fatigue (for alcohol use). Risk factors that were previously reported and confirmed by this analysis included male sex (for smoking and drug use), lower educational attainment (for smoking), and fatigue (for low physical activity).

Conclusions: Our findings show that the development and implementation of lifestyle interventions for survivors should be prioritised, in particular for survivors with reduced physical health, pain, and fatigue. In addition, public health strategies are needed to reduce the smoking prevalence in survivors from the Czech Republic and Italy. The findings of this paper can be used to improve and tailor lifestyle support for childhood cancer survivors, an essential tool in optimising their health and quality of life.

Neurocog-6

Early Executive Dysfunction in Newly Diagnosed Pediatric Acute Lymphoblastic Leukemia Patients

Ellen Van Der Plas, Mary-Kaylin Linch, Madison Sanders, Amy Conrad, Mara Whiteside

Background/Purpose: Neurocognitive deficits are common among survivors of acute lymphoblastic leukemia (ALL). Identification of early markers of abnormal neurocognitive development may inform targeted prevention and mitigation strategies. The goal of the present study was to contrast and compare neurocognitive performance in newly diagnosed ALL patients and cancer-free peers.

Methods: ALL patients, ages 3-10 years old, were enrolled in an ongoing, prospective longitudinal study that includes three assessments over a one-year period. The first assessment was conducted within approximately two months post-diagnosis, once patients were medically stable. Neurocognitive function was measured with the NIH Toolbox, the Beery-Buktenica Developmental Test of Visual-Motor Integration (Beery-VMI), and selected tasks from the Tablet-based Cognitive Assessment Tool (TabCAT). NIH Toolbox and Beery-VMI were reported as age-adjusted standard scores (mean=100; SD=15), whereas TabCAT measures used raw scores. Community controls completed the same assessments on a similar timeline as patients. Linear regression analyses were conducted to determine if group status (controls vs. patients) was associated with neurocognitive scores at baseline assessment. Models were adjusted for age where applicable.

Results: The sample included 23 controls (48% female; mean age=7.0 years; SD=1.6) and 11 ALL patients (64% female; mean age=6.7 years; SD=2.2). Relative to controls, ALL patients showed significantly poorer performance on measures of inhibitory control (flanker task; Estimate=-14.4, 95% confidence limits [CI]=-25.85, -3.6), flexibility/attention (dimensional card sort test; Estimate=-11.1, 95%CI=-20.3, -1.9), and receptive vocabulary (picture vocabulary task; Estimate=-9.5, 95%CI=-16.9, -2.2). By contrast, the groups did not differ on measures of processing speed, speeded matching, working memory, motor dexterity or visual=spatial integration.

Conclusions: Preliminary results suggest evidence of executive dysfunction in patients relative to controls. Some of the observed neurocognitive challenges are likely due to the acute effects of illness, although it is notable that patients exhibited similar performance to controls on some measures of cognitive function that are typically affected in survivors (e.g., dexterity). Certain tasks may be more sensitive indicators of early neurocognitive changes than others. Longitudinal, prospective assessments will provide insight into trajectories of change that could be useful in predicting long-term neurocognitive outcomes in survivors.

Neurocog-5

Neurocognitive and Psychosocial Outcomes in Survivors of Childhood Cancer Treated in Infancy Compared with those Treated as Older Children or Adolescents: a Report from the Childhood Cancer Survivor Study (CCSS)

Emily Walling, Jennifer Harman, Nivya George, Mingjuan Wang, Deo Kumar Srivastava, Kevin Oeffinger, Greg Armstrong, Kevin Krull, Robert Hayashi

Background: Infancy is a critical stage of development, attachment formation and milestone attainment. We hypothesized that survivors of childhood cancer diagnosed in infancy would be more vulnerable to impairment in neurocognitive and psychosocial outcomes compared to those diagnosed later in childhood.

Methods: The CCSS was used to compare survivors diagnosed in infancy (<1 year old) to survivors diagnosed as toddlers (1-3 years), pre-school age (3-6), school age (6-11), early adolescence (11-15) and late adolescence (>15). Outcomes included neurocognitive function (CCSS Neurocognitive Questionnaire [task efficiency, emotional regulation, organization, memory]), emotional function (Brief Symptom Inventory-18 [depression, anxiety, somatization]), and health-related quality of life (HRQOL; Medical Outcomes SF-36 [4 mental and 4 physical scales]). Survivor reported chronic health conditions (CHC) using the Common Terminology Criteria for Adverse Events (v4.03) were grouped into none/low (grade 1 condition or less), medium (>1 grade 2 and or 1 grade 3 condition)/high (>2 grade 3 or 1 grade 4 and 1 grade 3 conditions) /severe (>2 grade 4 or >2 grade 3 and 1 grade 4 conditions) accounting for frequency and grade of conditions. Unadjusted chi-square/exact chi-square tests evaluated comparison between age groups. Modified Poisson regression, adjusted for sex and current age, was used to assess outcome trends across diagnosis age groups and to conduct a subset analysis of the association between outcomes and CHC status.

Results: Significant differences (p's<0.001) were observed between diagnosis age group for all outcomes except emotional regulation (P=0.75). Survivors of infant cancer demonstrated the lowest frequency of impairment of all age groups in memory (15.3%), somatization (9.4%), general health (20.9%), physical functioning (10.1%), physical role functioning (14.1%), social role functioning (15.1%), vitality (18.8%) and pain (10.7%). There was an increasing deficit prevalence (P for trend <0.05) with increasing age at diagnosis for somatization (Relative risk[95%CI 1.11[1.07-1.51]), bodily pain (RR 1.10[1.07-1.13]) and similar results for all outcome measures except for task efficiency, emotional regulation, organization and anxiety. Medium/high/severe CHCs were prevalent across all age groups: infants 52.2%; toddler 57.7%; pre-school 56.4%; school age 63.2%; early adolescence 66.9%; late adolescence 72.4%. Survivors with medium/high/severe CHCs reported a greater degree of impairment for all outcome measures compared to survivors with none/low CHCs across all age groups except infants in emotional regulation, depression, and anxiety outcomes.

Conclusions: Infant cancer survivors have less neurocognitive impairment, emotional distress and superior HRQOL compared to older childhood cancer survivors. The presence of medium/high/severe chronic health conditions increased the prevalence of deficit in these domains across all age groups.

Health Services Research-13

European Transition Guideline

Jikke Wams, Elvira Van Dalen, Jaap Den Hartogh, Maria Otth, Tiago Costa, Jan Willem Gorter, Alied Van Der Aa, Anna Panasiuk, Bernhard Wörmann, Claire Berger, Edit Bardi, Elna Hamilton Larsen, Emma Potter, Esther Lasheras Soria, Gill Levitt, Gisela Michel, Helena Van Der Pal, Jelena Roganovic, Judith De Bont, Lieselotte Wauters, Lisa Pelanconi, Lorna Zadravec Zaletel, Magdalena Balcerek, Monica Muraca, Morven Brown, Oriana De Sousa, Rianne Koopman, Susan Mehta, Vassilios Papadakis, Leontine Kremer, Roderick Skinner, Katrin Scheinemann, Renee Mulder

Background/Purpose: Childhood and adolescent cancer survivors (age at diagnosis 0-21 years) are at increased risk for long-term health complications and less favorable outcomes in terms of functioning and societal participation. Moreover, they often experience inadequate healthcare transitions to appropriate services after leaving pediatric or adolescent services while the prevalence and severity of late effects increase as they become adults. To address transition challenges, we developed evidence-based recommendations as part of the EU-CAYAS-NET project with the goal to improve healthcare transitions to both long-term survivorship and adult care, ensuring continuity and addressing survivors' unique needs (Figure 1).

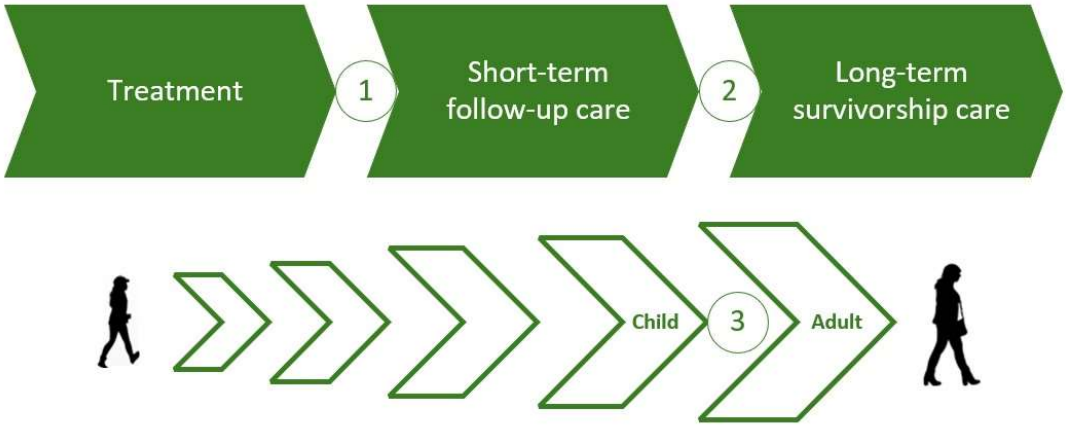


Figure 1. The transition process of childhood and adolescent cancer survivors, that includes three major transfer moments: 1) from active treatment to short-term follow-up care for recurrences and adverse effects of cancer treatment, 2) from short-term follow-up care to long-term survivorship care, typically starting 5 years after diagnosis or 2 years after end of treatment, and 3) from child to adult LTFU care.

Methods: Using evidence-based methods, an international and multidisciplinary panel developed a clinical practice guideline for healthcare transitions. Patient representatives were included at all steps of the development process. The panel systematically reviewed data from PubMed/MEDLINE (1990–2023) and graded the evidence using the GRADE methodology. In addition, existing guidelines and perspectives from patients, parents, and healthcare providers were taken into account when formulating recommendations.

Results: Of 1,982 citations identified, 75 articles met the inclusion criteria, focusing on healthcare transitions for cancer survivors up to age 21 years at diagnosis or for patients with chronic conditions (e.g., type 1 diabetes, asthma, inflammatory bowel disease) to extrapolate insights from these populations. Quality of evidence varied from very-low to moderate. Unique needs and preferences were captured, ensuring a comprehensive and patient-centered approach to the recommendations. In total, 44 strong recommendations were formulated for healthcare transitions of childhood and adolescent cancer survivors.

Conclusions: We integrated existing evidence and multistakeholder expertise and developed actionable recommendations to support smooth transitions for childhood and adolescent cancer survivors and improve their lives as an adult. Implementing this guideline will enhance care quality and improve quality of life by addressing the specific healthcare transition needs of this vulnerable population.

SMN-4

Identification of Childhood Cancer Survivors at Highest Risk of Developing Subsequent Thyroid Cancer: a Report from the Childhood Cancer Survivor Study

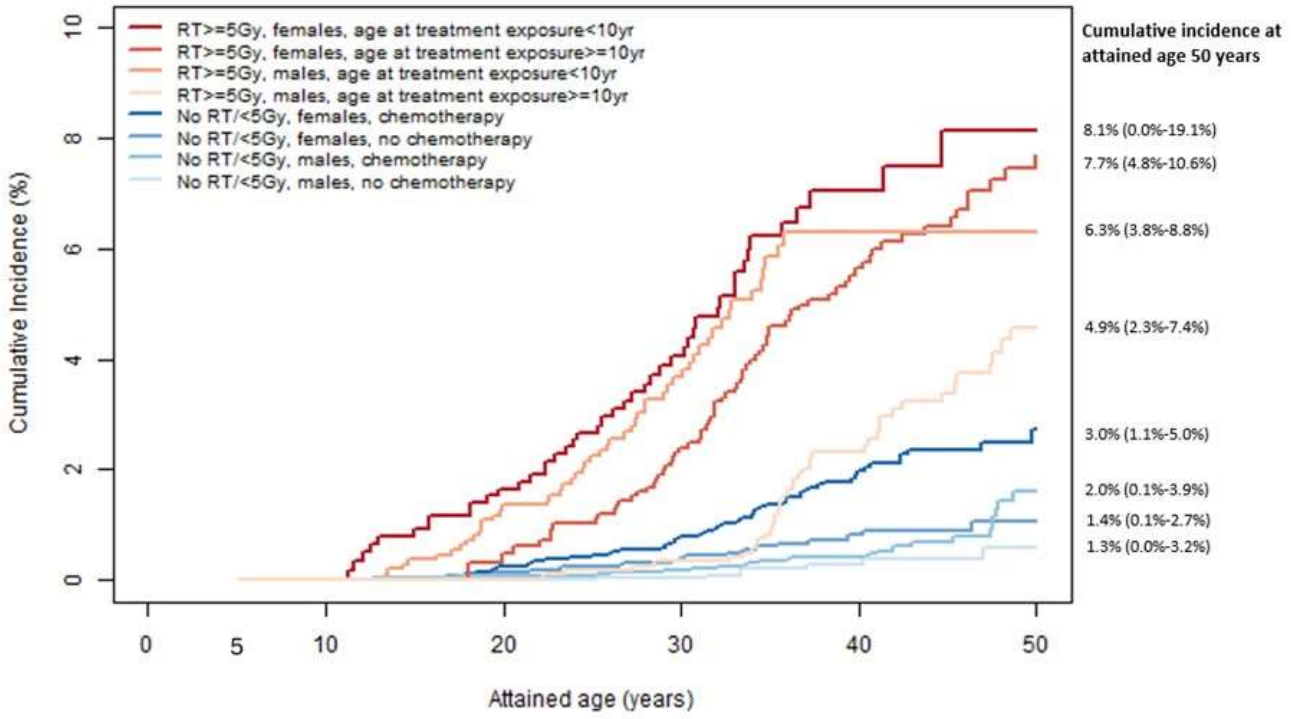
Yuehan Wang, Sara Schonfeld, Todd Gibson, Michael Arnold, Rebecca Howell, Susan Smith, Sogol Mostoufi-Moab, Siddharth Roy, Paul Albert, Cari Kitahara, Lene Veiga, Wendy M Leisenring, Yutaka Yasui, Joseph P. Neglia, Lucie Turcotte, Greg Armstrong, Lindsay Morton

Background/Purpose: Prior treatment with radiotherapy is a well-established risk factor for the increased risk of subsequent thyroid cancer (STC) observed among childhood cancer survivors. Current thyroid cancer screening guidelines for survivors are primarily based on radiotherapy exposure, while the role of other factors and their potential joint effects with radiotherapy on STC risk remain poorly understood. Using data from the Childhood Cancer Survivor Study (CCSS), we aimed to elucidate the interplay among potential STC risk factors and identify survivors at the highest risk of developing STC to inform potential further risk-stratification of the current thyroid cancer screening guidelines for childhood cancer survivors.

Methods: The study included 20,590 five-year survivors diagnosed with a first primary cancer between 1970-1999 at ages <21 years and with complete information about chemotherapy and thyroid radiation dose. Mean dose to the left and right lobes of the thyroid was estimated based on radiotherapy records. We estimated relative risks (RRs) and 95% confidence intervals (CIs) using Poisson regression models adjusting for sex, attained age, thyroid radiation dose, and age at exposure, overall and stratified by thyroid radiation dose (no or <5 Gy versus ≥5 Gy). We then calculated cumulative STC risks stratified by risk factor, accounting for competing risk of death.

Results: During a median follow-up of 26.7 years (interquartile range (IQR) 21.1-34.7) since primary cancer diagnosis, 334 survivors developed an STC. Survivors who received ≥5 Gy of radiation to the thyroid (versus none) had a five-fold or greater increase in STC risk with the highest risks at 10-<20 Gy (RR 11.4, 95% CI 8.0-16.3), particularly among those exposed before age 10 (RR 15.6, 95% CI 9.6-25.3). In analyses stratified by thyroid radiation dose, female sex was consistently associated with increased STC risk compared to males (RRno/<5Gy 2.6, 95% CI 1.7-3.8; RR≥5Gy 1.5, 95% CI 1.1-1.9). Receipt of chemotherapy was associated with STC only among survivors with no thyroid radiation or <5 Gy (RR 2.3, 95% CI 1.5-3.5). No clear dose-response associations emerged for any of the chemotherapeutic classes. At age 50, the highest cumulative incidence of STC was observed for female survivors exposed to ≥5 Gy thyroid radiation at age <10 years (8.1%, 95% CI 0.0%-19.1%; Figure) and ≥10 years (7.7%, 95% CI 4.8%-10.6%), followed by males exposed to ≥5 Gy thyroid radiation at age <10 years (6.3%, 95% CI 3.8%-8.8%) and ≥10 years (4.9%, 95% CI 2.3%-7.4%). Among survivors with no thyroid radiation or <5 Gy, cumulative incidence of STC was <5.0% at age 50 years for females and males, regardless of chemotherapy exposure.

Conclusions: Beyond thyroid radiation exposure, sex and age at treatment exposure could be valuable factors for consideration in risk-stratified screening guidelines to optimize the long-term clinical care of childhood cancer survivors.



No. at risk at attained age	20 years	30 years	40 years	50 years
RT>=5Gy, females, age at treatment exposure<10yr	673	454	197	53
RT>=5Gy, females, age at treatment exposure≥10yr	581	1,083	716	321
RT>=5Gy, males, age at treatment exposure<10yr	945	588	222	72
RT>=5Gy, males, age at treatment exposure≥10yr	653	1,121	692	296
No RT/<5Gy, females, chemotherapy	3,608	3,053	1,466	405
No RT/<5Gy, females, no chemotherapy	2,649	2,122	1,094	334
No RT/<5Gy, males, chemotherapy	4,019	3,385	1,632	471
No RT/<5Gy, males, no chemotherapy	2,513	1,952	973	292

Research Methods-10

Why Did the Childhood Cancer Survivor Die? Comparison of Death Certificate vs. Medical Record Review Cause of Death in a Contemporary Cohort of Childhood Cancer Survivors

*Rebecca Williamson Lewis, Xu Ji, Ann Mertens (*in Memoriam), Sharon Castellino*

Background: Identifying the cause of death in cancer survivors is challenging. We compared the death certificate cause of death versus medical chart review in a population of childhood cancer survivors ≥2 years post-therapy completion.

Methods: This is a post hoc analysis of deaths in a cohort of childhood cancer survivors (n=3,366) diagnosed 2002-2016 and treated at a free-standing pediatric hospital. We received death certificate cause of death (combination of state vital records and National Death Index (NDI) data) from the Georgia Cancer Registry for deaths occurring before 12/31/2020. Cause of death was categorized as primary cancer relapse, subsequent malignancy (SMN), treatment late effects, or external causes by one reviewer (ACM) using solely death certificates and a second reviewer (SMC) using death certificates alongside the electronic medical records (EMR). Agreement was assessed using Cohen's kappa (κ).

Results: There were 97 deaths: 62.9% male, 37.1% non-Hispanic Black, and 6.2% Hispanic—with even distribution by initial cancer diagnoses. Deaths occurred at a median age of 18.9 years (IQR: 11.8, 22.8), with a median of 7.2 years (5.4, 9.4) from diagnosis. Using death certificates, 57.7% were attributed to primary cancer relapse, 11.3% SMN, 13.4% treatment late effects, 11.3% external causes, and 6.2% unknown.
Compared to those without EMR documentation near the time of death, the 73 patients (75.3%) reviewed were younger at both diagnosis [median age (IQR): 7.8 (3.2, 12.1) vs 17.0 (15.1, 17.7); p<0.001] and death [16.3 (10.3, 20.9) vs 23.7 (21.6, 26.9); p<0.001]; there were no demographic, diagnosis, or time from diagnosis differences. Death certificate and EMR review for the cause of death agreed for 65.8% [κ= 0.45 (95% CI: 0.20, 0.70)]. Among 47 deaths attributed to primary cancer relapse by death certificate, EMR review classified 31.9% (n=15) differently: 4 as SMN, 4 as late effects, and 7 as external (Table 1). In 3/8 (37.5%) classified as SMN by death certificate, EMR review classified as primary cancer relapse. For deaths attributed to late effects by death certificate (n=9), EMR review classified 3 (33.3%) differently. EMR review agreed with all deaths classified as external and classified 80% (4/5) of the unknown with a more specific cause. Finally, 40.0% (4/10) of deaths attributed as late effects by EMR review were classified as primary cancer relapse by death certificate. Notably, 30.1% (22/73) of patients with EMR review were not marked as deceased in our EMR system with no age, demographic, or diagnosis differences with those who were listed as deceased.

Table 1. Comparison of Death Certificate to EMR Review Cause of Death in Pediatric Cancer Survivors with Data Available in the Medical Record (n=73)

	Cause of death by Medical Record (EMR) Review					
Death Certificate Cause of Death	Primary Cancer Relapse	Second Malignancy	Treatment Late Effects	External Cause	Unknown	Total
Primary Cancer Relapse	**32**	4	4	7	0	47
Second Malignancy	3	**5**	0	0	0	8
Treatment Late Effects	2	0	**6**	1	0	9
External Cause	0	0	0	**4**	0	4
Unknown	1	2	0	1	**1**	5
Total	38	11	10	13	1	73

Conclusions: While death certificates are important for identifying death and cause of death in survivors who age out of pediatric care, there is moderate agreement on attribution of death when compared to EMR review in a contemporary cohort. Deaths due to late effects may be incorrectly classified as primary cancer relapse based solely on death certificates.

Other late effects-8

Intravitreal Chemotherapy in Pediatric Retinoblastoma: a Multicenter RIVERBOAT Consortium Analysis

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Background: Retinoblastoma (RB) is the most common intraocular cancer in children, comprising around 2% of all pediatric malignancies. Historically, enucleation was the primary treatment, but the use of systemic chemotherapy has significantly improved eye salvage rates to nearly 100% of International Classification of Retinoblastoma (ICRB) Groups A, B, C eyes when combined with laser and cryotherapy. However, advanced RB (ICRB Groups D&E), characterized by diffuse vitreous or subretinal seeds, are often more resistant to therapy. In particular, vitreous seeds often require more intensive treatments like intravitreal chemotherapy (IvitC), which delivers high intraocular drug concentrations while minimizing systemic toxicity. Studies on IvitC agents and dosages are still limited. We evaluated IvitC agents in the Research Into Visual Endpoints and RB Health Outcomes After Treatment (RIVERBOAT) consortium, the first and largest international multicenter, multi-racial and multi-ethnic consortium of retinoblastoma survivors, designed to study health outcomes. We aim to describe the treatment courses and secular trends in the use of IvitC for retinoblastoma, with a focus on variations in medication dosages and combinations.

Methods: A secondary analysis of data from the RIVERBOAT consortium was conducted to include pediatric RB patients (0–17.99 years) who received at least one cycle of IvitC between 2008 and 2023. Both retrospective and prospective records were collected. Key variables included demographics, tumor classification, drugs used for IvitC, total treatment sessions, combination with IvitC or systemic chemotherapy, documented ocular toxicities, and visual acuity outcomes. Dosing decisions were assessed relative to tumor response, and dose adjustments were tracked over successive treatments. Descriptive and trend analyses were performed in R version 4.3.3.

Results: Among 103 RIVERBOAT consortium patients receiving IvitC (median 4.0 cycles, IQR 2.0–6.0), 52.5% had unilateral and 47.5% bilateral retinoblastoma. Eye-level data from 159 eyes revealed that melphalan was the most frequently used agent: 80 eyes had a median dose of 20.4 mcg (IQR 20.0–26.8) across a median of 4.0 cycles (IQR 3.0–6.0). Topotecan therapy was documented in 38 eyes, with a median dose of 20.0 mcg (IQR 20.0–22.0) and a median of 1.0 cycle (IQR 0.0–4.0). Overall, 30% patients received melphalan alone, 3% topotecan alone, and 21% with both agents. The number of injections for both agents increased from 2012 to 2017, peaking at around 6 injections per patient, followed by a decline and stabilization at around 2-3 injections from 2017 to 2023.

Conclusions: Melphalan-based IvitC remains central to the treatment of advanced retinoblastoma, with topotecan increasingly used alongside in recent years. The observed rise in both agents' combined use from 2012 to 2017 followed by stabilization, thereafter, highlights the evolving and increasingly tailored treatment approach.

Quality of life/Behaviors-6

Lower Extremity Neuromuscular Impairments and Everyday Functional Task Performance in Childhood Acute Lymphoblastic Leukemia Survivors: a Report from the St. Jude Lifetime Cohort

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Background: Children treated for acute lymphoblastic leukemia (ALL) are at risk for lower extremity neuromuscular impairment which interferes with function for everyday tasks during treatment, and into survivorship. Impairments in strength and flexibility (range of motion) are amenable to intervention; thus, it is important that we address these impairments early in survivorship. This analysis aims to describe lower extremity neuromuscular impairments and their associations with functional activities of daily living.

Methods: Participants less than 18 years of age were enrolled in the St. Jude Lifetime Cohort, survived at least five years after their ALL diagnosis and completed functional performance testing as part of a comprehensive clinical assessment. Active dorsiflexion range of motion was measured with goniometry; knee extension, ankle dorsiflexion and ankle plantarflexion strength with isokinetic dynamometry; and peripheral neuropathy with the pediatric modified total neuropathy score (ped-mTNS). Measured values were converted to age- and sex-specific z-scores for analysis. Functional outcomes related to activities of daily living included the six-minute walk test (6MWT), timed up and go test (TUG) and Bruininks-Oseretsky Test of Motor Proficiency Short Form version 2.0 (BOT2). Associations between ankle range of motion and ankle/knee strength z-scores and each functional outcome were evaluated with general linear regression.

Results: Participants (N=116) were 55% female, 23% non-white race, and a mean ± standard deviation (SD) age at diagnosis 3.6±2.0 years, and age at assessment of 13.9±2.4 years. Mean±SD z-scores were -4.11±1.58 for active dorsiflexion range of motion, and -0.88±1.76 for knee extension strength, -0.50±1.04 for dorsiflexion strength, and -4.11±0.86 for plantarflexion strength. Mean±SD values were 2.86±3.08 for the ped-mTNS, 540.25±92.7 meters for the 6MWT, 5.34±2.14 seconds for the TUG and 38.31±29.64 percentile score for the BOT2. In linear models adjusted for age, sex and all other lower extremity measures, shorter 6MWT distance was associated with decreased active dorsiflexion range of motion (-14.75±5.32 meters per SD, $p < 0.01$), lower knee extension strength (-11.64±4.96 meters per SD, $p < 0.01$) and a higher score on the ped-mTNS (-7.71±3.02 meters per SD, $p<0.01$). A slower time on the TUG was associated with decreased dorsiflexion range of motion (-0.44±0.13 seconds per SD, $p < 0.01$) and lower knee extension strength (-0.28±0.12 seconds per SD, $p<0.01$). Performance on the BOT2 was associated with decreased dorsiflexion range of motion (-4.64±1.79 percentile per SD, $p<0.01$).

Conclusions: Survivors of childhood ALL, on average have impaired lower extremity range of motion and strength which are associated with reduced performance on everyday tasks. Interventions to remediate these impairments early in survivorship are needed.

Other late effects-12

Lung Function in Children after Cancer Treatment

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Background: Childhood cancer survivors (CCS) are at risk for pulmonary late effects, but little is known about early lung function deficits in children with and without exposure to pulmotoxic treatments. Also, benefits of novel potentially more sensitive lung function tests, such as nitrogen multiple breath washout (N_2MBW), are not well studied. This study aims to assess lung function in pediatric CCS and evaluate whether N_2MBW provides additional value in detecting early pulmonary deficits.

Methods: In this multicenter prospective cohort study, we enrolled CCS aged 6–20 years who completed cancer treatment and were in regular pediatric oncology follow-up. Participants were classified as high-risk if they had received pulmotoxic treatments (thoracic radiotherapy, thoracic surgery, chemotherapy with busulfan/bleomycin/nitrosoureas, or allogeneic hematopoietic stem cell transplantation) and standard-risk if they had received any other chemotherapy, immunotherapy, or targeted agents. Primary outcomes were forced expiratory volume in first second (FEV1) and functional vital capacity (FVC) from spirometry, transfer factor for carbon monoxide (TLCO) from diffusion capacity of the lung for carbon monoxide (DLCO), and global lung clearance index (LCI) from nitrogen multiple breath washout (N2MBW). We calculated z-scores using the Global Lung Function Initiative references, defined pathological z-scores as <-1.64 for FEV1, FVC, TLCO and >1.64 for LCI, and compared them between risk groups using one sample t-test and a two-sample z-test for proportions.

Results: By February 2025, we recruited 225 children (90% response rate), 53 (24%) in the high-risk and 172 (76%) in the standard-risk group. Median age at study was 14 years [IQR 10–17] and median time since diagnosis 7 years [IQR 4–10]. Mean z-scores for FEV_1 were -0.75 in high-risk vs. -0.10 in standard-risk participants ($p<0.001$), -0.94 vs. -0.23 for FVC ($p<0.001$), and -0.28 vs. 0.33 for TLCO ($p=0.002$). We found no difference for LCI between exposure groups (0.03 vs. 0.01, $p=0.913$). The proportion of participants with pathological z-scores was significantly higher in high-risk compared to standard risk survivors for FEV_1 (23% vs. 6%, $p<0.001$) and FVC (28% vs. 9%, $p<0.001$), but not for TLCO (11% vs. 5%, $p=0.139$) or LCI (3% vs. 7%, $p=0.342$).

Conclusion: We found that high-risk CCS exhibited poorer lung function than standard-risk survivors, with more frequent abnormalities in FEV_1 and FVC, despite mean values remaining within normal range. N_2MBW did not seem to be more sensitive in detecting lung function deficits, indicating limited value in early post-treatment surveillance. These findings support risk-stratified pulmonary follow-up in CCS exposed to pulmotoxic treatments to enable early detection and optimized long-term care.

Neurocog-7

Association of Neurocognitive Impairment and Financial Hardship in Adult Survivors of Childhood Cancer: a Report from the Childhood Cancer Survivor Study (CCSS)

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Background/Purpose: Adult survivors of childhood cancer are at high risk for financial hardship due to the cumulative lifetime costs of cancer-directed therapy and chronic health conditions. Whether neurocognitive impairment increases the risk for financial hardship is unknown.

Methods: Childhood cancer survivors (≥5-year survivors, diagnosed <21 years of age between 1970-1999) enrolled in CCSS completed a validated self-report Neurocognitive Questionnaire (NCQ) in 2014 and a subsequent financial hardship survey (age ≥26 at survey completion) 3 years later. The NCQ measured neurocognitive impairment in four domains: (1) memory; (2) task efficiency; (3) organization; (4) emotional regulation. NCQ was the exposure and operationalized as the number of impaired domains (0-4); in each domain, impairment was defined as a Z-score >90th percentile. Financial hardship outcomes were measured in behavioral (e.g., delaying care due to cost), material (e.g., high out-of-pocket costs), and psychological (e.g., worry about financial situation) domains, as well as two discrete outcomes of debt collection and bankruptcy. Multivariable linear and logistic regressions were used to analyze associations adjusting for age, sex, and race/ethnicity.

Results: 3023 survivors completed the NCQ (mean age 38.8, SD=8.6 years) and a subsequent financial hardship survey (mean age 41.5, SD=8.7 years). 13.9%, 8.1%, 6.0%, and 2.6% of survivors had neurocognitive impairments in 1-4 domains, respectively. Individuals with NCQ impairment had significantly higher mean standardized scores across all three financial hardship domains than those without NCQ impairments (Table). Each ordinal increase in the number of impaired NCQ domains was associated with a higher mean standardized score for both behavioral and material financial hardship. Individuals with impairments in all four NCQ domains were more likely to be sent to debt collection (54% vs. 25%, OR=3.82, 95% CI: 2.27-6.43) and file for bankruptcy protection (21% vs. 8%, OR=2.81, 95% CI: 1.53-5.17) compared to those without impairments.

Table. Standardized mean differences (SMD) of each financial hardship domain by number of NCQ impairments compared to no NCQ impairments

Number of NCQ domains impaired	Behavioral Domain SMD (95% CI)	Material Domain SMD (95% CI)	Psychological Domain SMD (95% CI)
1	0.21 (0.11-0.31)	0.20 (0.10-0.29)	0.41 (0.31-0.50)
2	0.39 (0.27-0.51)	0.32 (0.20-0.44)	0.38 (0.25-0.50)
3	0.48 (0.34-0.63)	0.35 (0.20-0.49)	0.44 (0.30-0.58)
4	0.72 (0.51-0.93)	0.72 (0.52-0.94)	0.74 (0.53-0.94)

Conclusions: Cancer survivors with neurocognitive impairment are particularly vulnerable to financial hardship. This survivor population should be specifically assessed for these outcomes and offered support to prevent and mitigate financial challenges.

Research Methods-1

Machine Learning-Based Prediction of Overall Survival in U.S. Adults with Cancer Incorporating Comprehensive Social Risk Factors

Yiwang Zhou, Samira Deshpande, Ahmed Motiwala, Jaesung Choi, Greg Armstrong, Madeline Horan, I-Chan Huang

Background: Cancer survivors in the U.S. have a higher mortality risk compared to the general population, with social risk factors playing a critical role, especially among those with comorbidities. However, traditional mortality risk prediction models often emphasize treatment exposures and basic demographic factors while neglecting social risk factors. This study aims to develop a machine learning (ML) model that integrates comprehensive social risk factors with traditional predictors to improve overall survival prediction for adults with cancer, including young adults, in the U.S.

Methods: We analyzed data from 6,181 nationally representative adults diagnosed with cancer from the National Health Interview Survey (NHIS; 2013-2014). A total of 74 risk factors were included in the model, encompassing basic demographics (e.g., age at the survey, sex, marital status, body mass index [BMI]), personal and household socioeconomic status (SES; e.g., education, food insecurity), lifestyle, social support, and health status (e.g., chronic health conditions [CHCs], disability). The primary endpoint was 5-year overall survival from the survey completion date, with 1- and 2-year survival as secondary endpoints. Death from any cause after the survey was defined as an event and subjects were censored 5 years post-survey. The sample was randomly split into 70% training and 30% testing sets. We developed a random survival forest (RSF) model to predict survival. Model performance was evaluated using the time-dependent area under the receiver operating characteristic (AUROC) curve and the Brier score (BS). Both AUROC and BS range from 0 to 1, with higher AUROC for higher accuracy (discrimination) and lower BS for better alignment between predicted and observed risk (calibration). The Shapley additive explanations (SHAP) values were used to interpret variable importance in the established RSF model.

Results: The mean age of subjects during the survey was 65.6 years, and 40.2% were male. For the established RSF model, the AUROC (mean ± standard deviation) for predicting 1-, 2-, and 5-year survival was 0.795 ± 0.026, 0.810 ± 0.018, and 0.831 ± 0.011, respectively, demonstrating high and improved predictive accuracy over time. The BS for 1-, 2-, and 5-year survival was 0.039 ± 0.004, 0.065 ± 0.005, and 0.119 ± 0.005, indicating excellent calibration. The top five variables, ranked by SHAP values, were age at the survey (0.048), use of special equipment due to health problems (0.029), employment status (0.020), number of CHCs (0.016), and BMI (0.015).

Conclusions: By incorporating social risk factors alongside traditional risk predictors, we developed an ML model that predicts overall survival with high accuracy and excellent calibration for adults with cancer in the U.S. Identifying key risk social factors enables targeted interventions, potentially improving health outcomes and management for the adult cancer population.

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