# 12th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer

## June 8–9, 2012

## The Williamsburg Lodge
## Williamsburg, Virginia

St. Jude Children's Research Hospital
ALSAC • Danny Thomas, Founder

Jointly sponsored by St. Jude Children's Research Hospital and the National Cancer Institute

# Contents

# General Information

## Educational Objectives

At the conclusion of the 12th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer, participants should be able to:

- Describe the relationship between cognitive function, education and earning potential
- Discuss the structural and organizational development of the brain
- Explain the relationships between neurotransmitters and learning
- Identify the relationship between visual-spatial perception and mathematics
- Define the relationship between auditory-language perception and reading
- Describe the use of magnetic resonance imaging for evaluation of cognitive function
- Explain the use of activity interventions for cognitive problems
- List pharmacological interventions for cognitive problems
- Tell the use of exercise interventions and cognitive function

## Participants

Participants will include, but are not limited to, US and international practitioners involved in the interdisciplinary fields of medicine, surgery, pediatric hematology/oncology, radiation oncology, counseling, clinical research and other health care professionals.

## Messages and Notices

Messages may be left at the registration desk. A message board will be located near the registration desk. Please check this at regular intervals as no responsibility can be taken to deliver messages personally.

## Mobile Phones and Pagers

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

## Name Badges

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

## Registration Desk and Check In

The registration desk will be open at *Conference Registration II* (Virginia Foyer, lower level) from 6:00 PM to 8:00 PM on Thursday, June 7, 2012, for registration. In addition, the registration desk will be open at the following times:

| | |
|---|---|
| Friday, June 8, 2012 | 7:00 AM – 2:00 PM |
| Saturday, June 9, 2012 | 8:00 AM – 2:00 PM |

Registration fee includes the *Program/Proceedings*, Welcome Reception (June 7), admission to all scientific sessions, poster session, conference materials, breakfast, lunch, refreshment breaks, dinner (Friday, June 8).

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

## Speaker Preparation Room

For your convenience, the Williamsburg Lodge's Business Center (main level) is equipped with computers for presenters to preview his/her presentation. If you have your own laptop, you may also use the Williamsburg Lodge's Computer Lounge (main level).

## Accreditation Information

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through joint sponsorship of the National Cancer Institute and St. Jude Children's Research Hospital. St. Jude Children's Research Hospital is accredited by the ACCME to provide continuing medical education for physicians.

## CME Credit Hours

The St. Jude Children's Research Hospital designates this live activity (*12th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer, June 8–9, 2012*) for a maximum of **11.5** *AMA PRA Category 1 Credit(s)*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

## Disclosure of Conflicts of Interest

St. Jude Children's Research Hospital requires all Instructors, Planners, and other individuals in a position to control the content of this live activity to disclose any real or apparent conflict of interest they may have as related to the content of this CME activity. All relevant conflicts of interest will be shared with those in attendance to ensure fair balance of information presented.

## Ground Transportation

Information on Ground Transportation is available at the Registration Desk.

## Poster Exhibition (Friday, June 8)

A cash bar will be available at 6:30 PM with a buffet dinner served from 7:00–10:30 PM (Virginia ABCD). Poster viewing will be from 7:30–10:00 PM (presenters in attendance). Posters will be on display in the Virginia Room ABCD and Piedmont Room through Saturday, June 9, at noon

## Welcome Reception Oval Garden, lower level

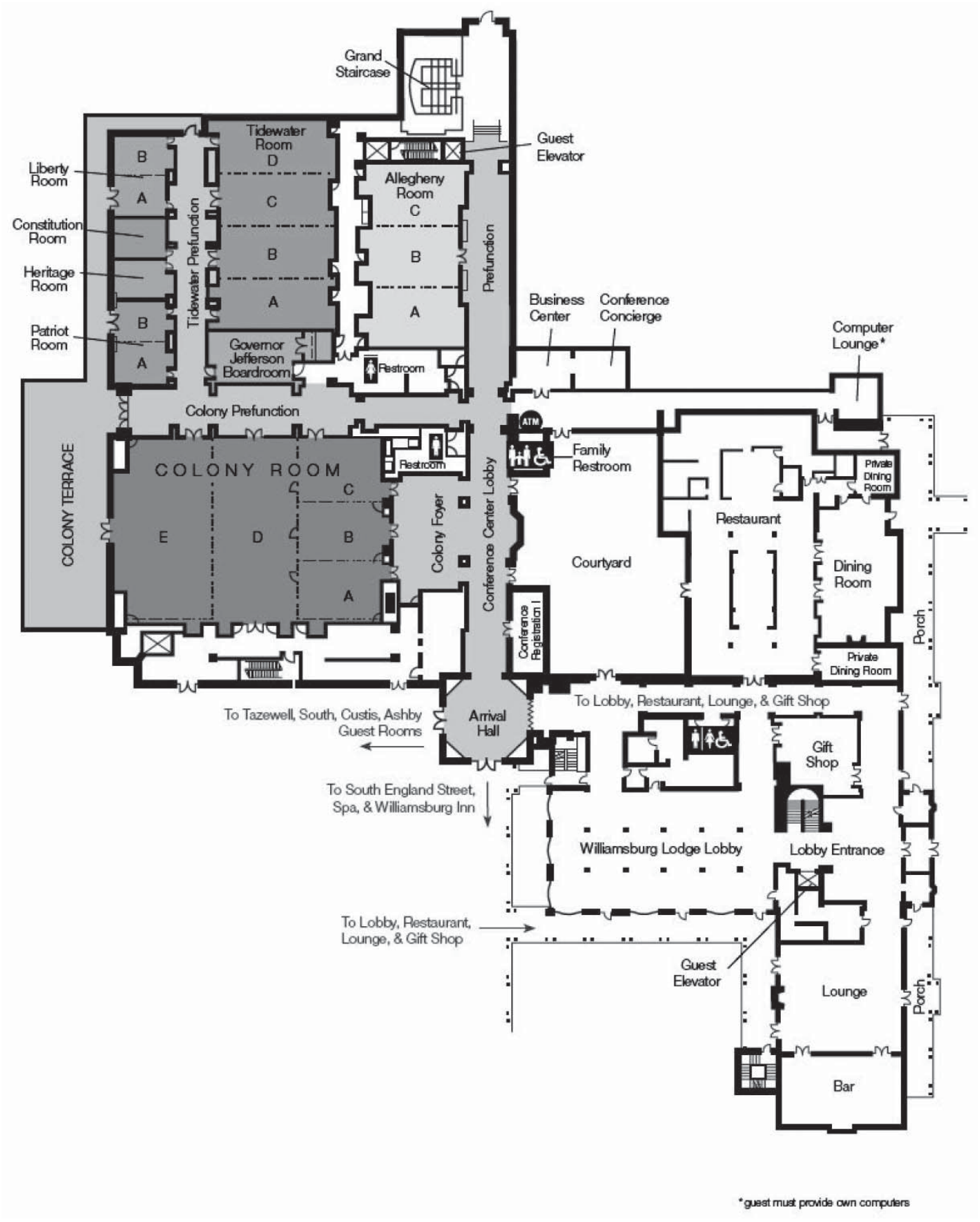
The Welcome Reception will be held on Thursday, June 7, in the Oval Garden (lower level). This will be held from 6:00 to 8:00 pm and will include wine and appetizers. The cost of this function is included in your registration fee.

## Sponsor Acknowledgement

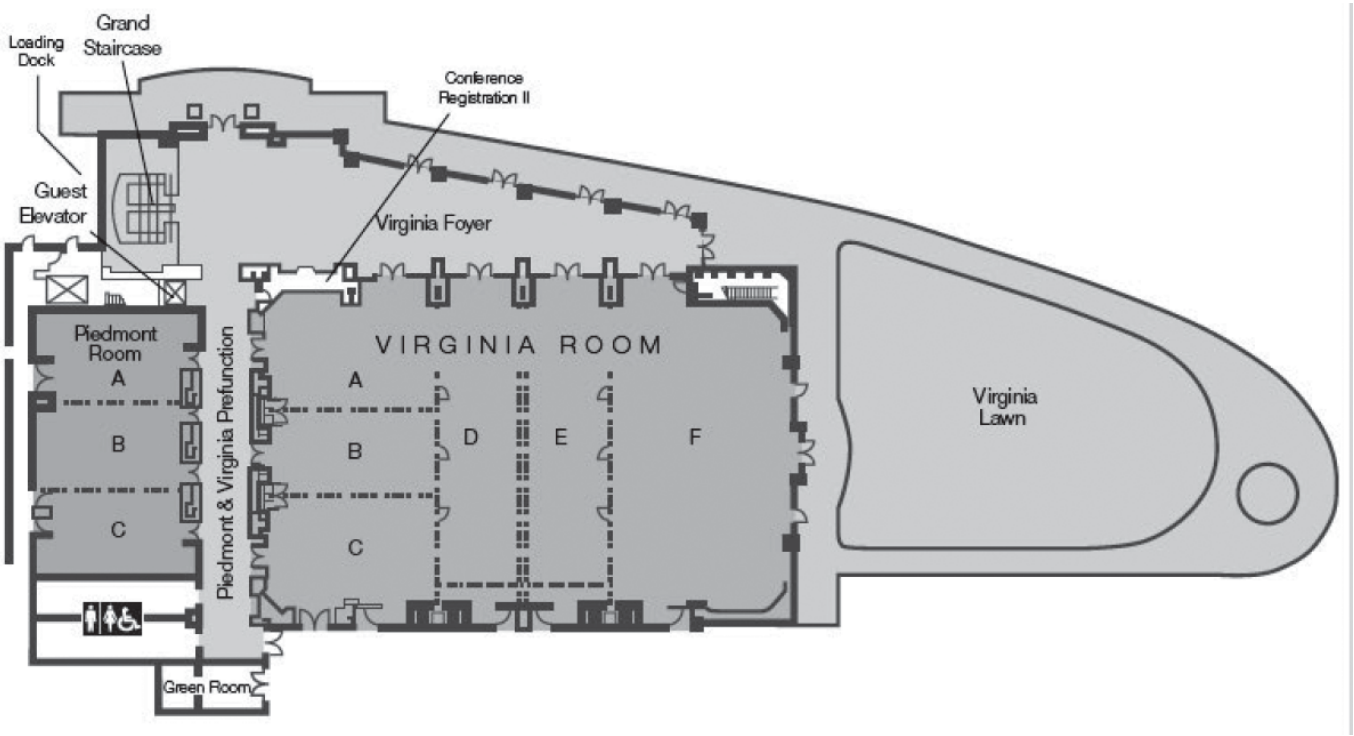
The 12th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer gratefully wishes to acknowledge support from St. Jude Children's Research Hospital and financial support of the National Cancer Institute.

# Conference Center Map

## Williamsburg Lodge Conference Center Main Level



## Williamsburg Lodge Conference Center Lower Level



# Invited Speakers

**Scott M. Lynch, PhD**

Professor, Department of Sociology, Princeton University, Princeton, NJ

**Dr. Rima Obeid**

Department of Clinical Chemistry and Laboratory Medicine, Saarland University, Saarbrucken, Germany

**Marcia A. Barnes, PhD**

Professor of Pediatrics and Chair in Childhood Reading and Learning, Children's Learning Institute, University of Texas Health Science Center, Houston, TX

**Jack M. Fletcher, PhD**

Distinguished Professor of Psychology, University of Houston, Houston, TX

**Bryan Kolb, PhD**

Department of Neuroscience, University of Lethbridge, Lethbridge, Alberta, Canada

**Erin Bigler, PhD**

Department of Psychology, University of Utah, Provo, UT

**Richard J. Caselli, MD**

Neurology, Mayo Clinic, Phoenix, AZ

**Elizabeth Skidmore, PhD, OTR/L**

Rehabilitation Science, University of Pittsburgh, Pittsburgh, PA

**Arthur Kramer, PhD**

Department of Psychology, University of Illinois, Urbana, IL

# Conference Program

## Thursday, June 7

| | |
|---|---|
| 6:00 – 8:00 PM | **Advance registration** (Conference Registration II, Virginia Foyer, lower level) |
| 6:00 – 8:00 PM | **Welcome reception** (Oval Garden, lower level) |

## Friday, June 8

| | |
|---|---|
| 7:00 AM – 8:00 AM | **Continental breakfast** (Virginia Foyer, lower level) |
| 7:00 AM | **Registration** (Conference Registration II, Virginia Foyer, lower level) |
| 8:15 AM | **Welcome/Introductions/Faculty Disclosure Review**—Daniel M. Green, MD, Conference Chairman (Virginia Room E, F) |

## Session I

| | |
|---|---|
| 8:30 AM – 12:00 PM | **Invited Speakers**—Moderator: Kevin Krull, PhD, St. Jude Children's Research Hospital, Memphis, TN |
| 8:30 AM | *Childhood Cognitive Function, Educational Attainment, and Adult Earnings Potential*<br>Scott M. Lynch, PhD, Department of Sociology, Princeton University |
| 9:00 AM | *Methylation and Neurodegeneration*<br>Rima Obeid, Department of Clinical Chemistry and Laboratory Medicine, Saarland University |
| 9:30 AM | **Refreshment break** |
| 10:00 AM | *Mathematics Development and Difficulties: The Role of Visual-Spatial Perception and Other Cognitive Skills*<br>Marcia A. Barnes, PhD, University of Texas Health Science Center |
| 10:30 AM | *Alternative Approaches to Outcomes Assessment: Beyond Psychometric Tests*<br>Jack M. Fletcher, PhD, University of Houston |
| 11:00 AM | **Discussion** |
| 12:00 PM | **Lunch** (Colony Room DE, main level) |

## Session II

| | |
|---|---|
| 1:30 PM – 5:00 PM | Platform Presentations—Moderator: Kevin Oeffinger, MD, Memorial Sloan-Kettering Cancer Center, New York, NY |
| 1:30 PM | *Late Occurring Stroke after Cranial Radiation and Association with Atherosclerotic Risk Factors in Adult Survivors of Pediatric Cancer: Results from the Childhood Cancer Survivor Study*<br>Sabine Mueller, MD, PhD |
| 1:45 PM | *Neurocognitive Function and Brain Imaging in Adult Survivors of Childhood Hodgkin Lymphoma*<br>Kevin Krull, PhD |
| 2:00 PM | *Dexamethasone and Memory Function in Adult Survivors of Childhood Acute Lymphoblastic Leukemia*<br>Michelle N. Edelmann, PhD |
| 2:15 PM | *Longitudinal Patterns of Psychological Distress in Adult Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study*<br>Tara Brinkman, PhD |
| 2:30 PM | *Scarring, Disfigurement and Quality of Life in Long-term Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study*<br>Karen E. Kinahan, MS, PCNS-BC |

2:45 PM — *Psychiatric Disease in Childhood Cancer Survivors and Their Siblings: A Danish Cohort-Cohort Population Based Registry Study*
Lasse Wegener Lund, MD

3:00 PM — **Refreshment break**

3:30 PM — *Male Infertility in Childhood and Adolescent Cancer Survivors Diagnosed From 1970-1986: A Report from the Childhood Cancer Survivor Study (CCSS)*
Karen Wasilewski-Masker, MD

3:45 PM — *Childhood Cancer Survivors Exposed to Total Body Irradiation are at Significant Risk for Slipped Capital Femoral Epiphysis During Recombinant Growth Hormone Therapy*
Sogol Mostoufi-Moab, MD, MSCE

4:00 PM — *Genito-Urinary (GUI) Second Malignant Neoplasms (SMN) in Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)*
Margarett Shnorhavorian, MD, MPH

4:15 PM — *Renal Carcinoma Following Therapy for Cancer in Childhood: A report from the Childhood Cancer Survivor Study*
Carmen Wilson, PhD

4:30 PM — Second Cancer Risk Forty Years After Cure for Hodgkin Lymphoma
Michael Schaapveld, PhD

4:45 PM — *New Insights into the Risk of Breast Cancer in Childhood Cancer Survivors Treated with Chest Radiation: A Report from the Childhood Cancer Survivor Study (CCSS) and the Women's Environmental Cancer and Radiation Epidemiology (WECARE) Study*
Chaya S. Moskowitz, PhD

5:00 PM — **Adjourn**

6:30 PM — **Cash bar** (Virginia Foyer)

7:00 PM – 10:30 PM — **Buffet dinner** (Virginia Room E, F)

7:30 PM – 10:00 PM — **Poster viewing** (Piedmont Room, Virginia Room ABCD)

## Saturday, June 9

7:30 AM – 8:30 AM — Continental breakfast (Virginia Foyer, lower level)

8:00 AM – 2:00 PM — Registration (Virginia Registration II, lower level)

## Session III

8:45 AM – 12:00 PM — **Platform Presentations**—Moderator: Flora van Leeuwen, PhD, Netherlands Cancer Institute, Amsterdam, The Netherlands

8:45 AM — *Increasing Risk of Chronic Health Conditions in Aging Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor*
Gregory T. Armstrong, MD, MSCE

9:00 AM — *Longitudinal Changes in Health Care Utilization by Adult Survivors of Childhood Cancer in the Childhood Cancer Survivor Study (CCSS)*
Jacqueline Casillas, MD, MSHS

9:15 AM — *Iron overload in Childhood Cancer Survivors*
Kiran Reddy, MD

9:30 AM — *Symptom Profiles Associated with Health-Related Quality of Life in Adult Survivors of Childhood Cancer: A Report from the St. Jude Lifetime Cohort*
I-Chan Huang, PhD

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|---|---|
| 9:45 AM | *Risks Associated with Levels of Care Proposed by the National Cancer Survivorship Initiative (NCSI) for Childhood Cancer Survivors*<br>Clare Frobisher, PhD |
| 10:00 AM | *Cost-Effectiveness of the Children's Oncology Group (COG) Long-Term Follow-Up (LTFU) Guidelines in Reducing the Risk of Congestive Heart Failure (CHF) in Long-Term Childhood Cancer Survivors (CCS)*<br>F. Lennie Wong, PhD |
| 10:15 AM | **Refreshment break** |
| 10:30 AM | *Longitudinal Changes in Body Mass Index and Body Composition Among 417 Adult Survivors of Childhood Cancer*<br>Karin Blijdorp, MD |
| 10:45 AM | *Atherogenic Low Density Liprotein (LDL) Phenotype in Long-Term Survivors of Childhood Acute Lymphoblastic Leukemia*<br>Jyoti Malhotra, MD, MPH |
| 11:00 AM | *Dietary Intake and Metabolic Syndrome in Adult Survivors of Childhood Cancer*<br>Webb Smith, MS |
| 11:15 AM | *Valvular Disease Detected by Echocardiography in 5-Year Survivors of Childhood Cancer: A Long-Term Follow-Up Study*<br>Helena J. van der Pal, MD |
| 11:30 AM | *Predicting Cardiovascular Disease After Cancer: A Childhood Cancer Survivor Study Report*<br>Eric Chow, MD, MPH |
| 11:45 AM | *Cardiovascular Disease in Adult Life After Childhood Cancer in Scandinavia (ALICCS)*<br>Thorgerdur Gudmundsdottir, MD |
| 12:00 PM | **Lunch** (Colony Room DE, main level) |

## Session IV

| | |
|---|---|
| 1:30 PM – 4:30 PM | **Invited Speakers**—Moderator: David Poplack, MD, Texas Children's Cancer Center at Baylor College of Medicine, Houston, TX |
| 1:30 PM | *Brain Development, Experience, and Behavior*<br>Bryan Kolb, PhD, University of Lethbridge, Lethbridge, Alberta, Canada |
| 2:00 PM | *Magnetic Resonance Imaging Evaluation of Cognitive Function*<br>Erin Bigler, PhD, University of Utah, Provo, UT |
| 2:30 PM | *Age-Related Memory Decline and the APOE Effect*<br>Richard J. Caselli, MD, Mayo Clinic, Phoenix, AZ |
| 3:00 PM | **Break** |
| 3:30 PM | *Activity-Based Interventions for Cognitive Problems*<br>Elizabeth Skidmore, PhD, University of Pittsburgh, Pittsburgh, PA |
| 4:00 PM | *Physical Activity, Exercise and Cognition*<br>Arthur Kramer, PhD, University of Illinois, Urbana, IL |
| 4:15 PM | **Discussion** |
| 4:30 PM | **Adjourn** |

# Invited Speakers Abstracts

**CHILDHOOD COGNITIVE FUNCTION, EDUCATIONAL ATTAINMENT, AND ADULT EARNINGS POTENTIAL** Scott M. Lynch and Jayanti Owens. *Department of Sociology, Princeton University, Princeton, NJ, USA*

A half century of research in sociology has examined the relationship between parents' socioeconomic attainment and that of their children. The relationship is a very strong one and appears to be becoming stronger. At the same time, over the last two decades, research expanding on the Barker hypothesis has shown that early health is strongly related to a variety of measures of later life health. Although these two lines of research have definitively established the link between early life conditions and adult outcomes, research has done little in terms of fleshing out the mechanisms via which status is transmitted and child health impacts adult health. In contrast, research in developmental psychology and family sociology and demography has expended considerable effort investigating family dynamics and cognitive and behavioral development of young, pre-school-age children. The key shortcoming of this line of research, however, is that it has to date not examined how these detailed early life interrelationships impact adult outcomes like completed educational attainment and early adult earnings. In this paper, we develop and discuss a conceptual model outlining the process of development from health at birth through cognitive and behavioral development and health at toddlerhood through grade school and high school performance, to completed educational attainment and earnings in adulthood. We then provide a detailed review of the state of the literature with respect to the model. Most importantly, we show that the literature has largely produced a piecemeal picture of the relationship between cognitive development and adult earnings. Finally, we use data on children of respondents from the National Longitudinal Study of Youth to produce a more detailed picture of the life course from birth to early adulthood.

**METHYLATION AND NEURODEGENERATION** Rima Obeid. *Department of Clinical Chemistry and Laboratory Medicine, University of Saarland, Saarbrucken, Germany*

Disorders in C1-metabolism have been related to several neurological and neurodegenerative disorders such as dementia, Alzheimer disease and polyneuropathy. Plaques rich in amyloid beta are one hallmark of Alzheimer disease. Amyloid precursor protein (APP) is an intra-membrane protein that is processed via the amyloidogenic or the non-amyloidogenic pathway. Another brain protein, tau, can accumulate when hyperphosphorylated. Methylation and phosphorylation play important roles for the formation and the removal of modified proteins. We studied the link between neurodegenerative processes and the methyl group metabolism.

In an earlier report, we observed a direct association between concentrations of P-tau and SAH in cerebrospinal fluid. We further tested the effect of homocysteine (Hcy), S-adenosylmethionine (SAM), and S-adenosylhomocysteine (SAH) on protein level of APP and its degradation product, C99 in Down syndrome fibroblasts (APP gene is located on Chromosome 21). In a culture medium that was free of the B-vitamins, SAM (100-300 μM) reduced the protein expression of APP and SAH (50-150μM) increased APP protein expression. SAH lowered C99 in cells incubated in a vitamin-free medium. Further experiments on hyperhomocysteinemic rats have shown that the expression of P-tau was increased in the brain, but a better folate status was associated with less accumulation of P-tau.

Metabolic hypomethylation (low SAM/SAH ratio) was also associated with lower intracellular vitamin B12 status and alterations in phospholipids in one study that included 90 patients with type 2 diabetes. The severity of polyneuropathy symptoms were related to higher Hcy or lower methylation potential.

Collectively, our results suggest that disorders in the methylation pathway can cause accumulation of P-tau, changes in APP processing or removal from the cells. The relationship to polyneuropathy seems to be at least partly related to alterations in the phospholipids. Modifying the methyl group metabolism has a potential to be tested in the context of prevention from neurodegenerative disorders.

**MATHEMATICS DEVELOPMENT AND DIFFICULTIES: THE ROLE OF VISUAL-SPATIAL PERCEPTION AND OTHER COGNITIVE SKILLS** Marcia A. Barnes, Kimberly P. Raghubar. *Children's Learning Institute, Department of Pediatrics, University of Texas Health Science Center at Houston and Department of Psychology, University of Houston, Houston, TX, USA*

Visual-spatial skills are thought to play an important role in mathematical development and performance. The role of visual-spatial skills, including visual-spatial working memory, in the development of mathematical knowledge in both the preschool years and at school-age will be discussed. The talk will focus on evidence for relations of specific neurocognitive abilities (including visual-spatial perception) and mathematical development and disability that is based on longitudinal studies of typically developing children and children at risk for difficulties in math. We will discuss "why" visual-spatial perception and visual-spatial memory might be important for mathematical learning and performance at different ages.

Neuroimaging studies and adult brain lesion studies provide evidence for the role of some aspects of visual-spatial perception for particular types of mathematical function. As well, many studies of preschool and school-age children with and without math disabilities provide correlational evidence for the relation of math outcomes to visual-spatial working memory, and other neurocognitive abilities such as verbal working memory, attention, and finger skills. One approach to better understand whether visual-spatial perception and

other neurocognitive abilities are implicated in the development of mathematical abilities and disabilities it to investigate whether competence in these proposed neurocognitive precursors in early childhood prior to formal schooling predict later mathematical achievement and performance at school-age. Data from two of our longitudinal studies on the link between mathematics and neurocognitive skills including visual-spatial perception and memory will be presented. One of these studies investigated whether visual-spatial perception and visual-spatial working memory, language-based abilities including verbal memory, and the child's early number sense at age 4 predicted his/her risk status in mathematics in kindergarten and first grade. The other study is a longitudinal investigation of children with the neurodevelopmental disorder spina bifida that is associated with a very high risk for mathematical disabilities. Findings on the importance of visual-spatial working memory and other neurocognitive abilities at 36 and 60 months of age for the later development of mathematical skills at 8-9 years of age will be presented. The findings for mathematics will be contrasted with those for reading to show that the early developmental precursors of later school achievement are somewhat different for reading and mathematics. In particular, while some verbal skills are related to both reading and math development, visual-spatial skills appear to be specifically related to mathematical development.

The presentation will end with a brief summary of what is known about interventions for mathematical difficulties, whether evidence-based interventions designed for children with math disabilities might be effective for children whose mathematical difficulties arise from neurological disorders, and whether there is any evidence for interventions that combine mathematical instruction with neurocognitive training in domains such as visual-spatial perception and memory. Potential applications of this research for children with cognitive effects of treatment for cancer will be discussed.

**ALTERNATIVE APPROACHES TO OUTCOMES ASSESSMENT: BEYOND PSYCHOMETRIC TESTS** Jack M. Fletcher, PhD. *Department of Psychology, University of Houston, Houston, Texas, USA*

Outcomes assessments in clinical trials involving cognition and behavior have traditionally relied upon IQ and neuropsychological assessments of children. Such assessments are viewed as key outcomes because they either broadly predict general levels of performance (e.g., IQ) or assess domains that are often affected by a treatment or other agent of interest, such as executive functions and attention. These psychometric procedures, while reliable and valid, may provide limited evaluations of key outcome domains that involve everyday functions because of limited generalizability. In addition, some participants may not be able to perform the tasks because they are low functioning or may represent missing data because the parent cannot come to the assessment site for follow-up. In contrast, interview-based assessments of a child's capacity to perform habitual daily living, communication, and socialization activities, commonly referred to as adaptive behavior scales, may yield results that more clearly reflect everyday functions. Adaptive behavior assessments like the Vineland Adaptive Behavior Scales-II and the ABAS-II are typically completed through interview procedures (desirable if blinding and social desirability are issues), or can be completed by caregivers and teachers as rating scales. These measures can also capture broad ranges of function and be done by telephone, thus resulting in loss of fewer participants because of an inability to perform a specific psychometric task. Similarly, it is well known that psychometric assessments of executive functions and attention are weakly related to parent and teacher ratings and behavioral observations at home and school. These rating and observational scales may provide a more accurate depiction of the child's functional level in these key domains. Coupling these kinds of assessments with procedures adapted from experimental approaches to assessing attention and executive functions, especially using tasks where the neural underpinnings are well-understood from functional neuroimaging studies, may provide a better understanding of the mechanisms underlying response to the intervention. Assessments of academic achievement, especially higher level reading comprehension and math tasks may also yield important insights into the child's everyday capacities in school. Using academic tasks in which the child has to perform quickly (i.e., fluency) for short periods of time may be especially sensitive to academic difficulties. This presentation discusses these alternative approaches to assessments, provides examples, and addresses the strengths and weakness of these alternative approaches to assessing cognitive and behavioral outcomes. The design on the neurobehavioral outcomes component of the follow-up study for the Management of Myelomeningocele fetal surgery trial will be discussed as an example of a clinical trial that incorporates some of these alternatives.

**BRAIN DEVELOPMENT, EXPERIENCE, AND BEHAVIOR** Bryan Kolb, PhD. *Department of Neuroscience, University of Lethbridge, Lethbridge, Alberta, Canada*

Cerebral development represents more than a simple unfolding of a genetic blueprint but rather represents a complex dance of genetic and environmental events that interact to adapt the brain to fit a particular environmental context. Brain development is prolonged and thus is influenced by prenatal, postnatal, juvenile, and adolescent experiences. This presentation will first review the general principles of brain development and then consider how various experiences alter brain development and behavior. Examples include the effects of sensory and motor stimulation, psychoactive drugs, including both illicit drugs and prescription drugs, stress, gonadal hormones, peer and parental relationships, and diet.

**MAGNETIC RESONANCE IMAGING EVALUATION OF COGNITIVE FUNCTION** Erin D. Bigler, PhD. *Department of Psychology and Neuroscience Center, Brigham Young University, Provo, Utah, and Department of Psychiatry and The Brain Institute of Utah, University of Utah, Provo, UT, USA*

The role of magnetic resonance imaging in assessing cognitive function in the neurological and/or neuropsychiatric patient has a relatively short history because the ability for in vivo non-invasive imaging of the brain has only been available since the 1970's (see Oldendorf 1978). Although by 1980's computed tomography (CT) had become established along with the beginnings of what was then called nuclear magnetic resonance imaging, the forerunner to contemporary magnetic resonance (MR) imaging or MRI, the image quality of the brain was limited. Advancement in image clarity and presentation dominated neuroimaging through the end of the 20th century (see Bigler 1996a,b) with ever improving image display. While in the early days of brain imaging, studying brain-cognitive-behavior correlates were problematic because of the coarseness of the images and the limits of how pathology could be identified (Bigler 2009), by the beginning of the 21st century, thin-slice 3 Tesla MRI approximated what could be viewed at post-mortem. With issues of image quality now achieved, the next advancements occurred in image quantification. Once more refined image quantification was achieved, an explosion in the study of MRI findings and cognition occurred (Sullivan 2010).

**Tissue Segmentation:** At a gross morphological level, three main characteristics of the brain can be identified – white matter, gray matter and cerebrospinal fluid (CSF) filled spaces and cavities. There are also neuroimaging methods that permit viewing the cerebrovasculature, but in normal brain parenchyma, the small vessels and all capillaries embedded within tissue often cannot be differentiated from the white or gray matter wherein they are embedded. The above biological facts provide the basis for a simple classification in neuroimaging where white matter, gray matter and CSF are delineated in what is referred to as a segmented image. By setting aside a specific color for each tissue type, a color-coded white, gray and CSF brain is created as a 'classified' image that is identified by either region of interest (ROI) or a specific structure. This in turn provides a method for image quantification since each MRI slice used to generate an image of the brain has a slice thickness and a known distance from the next slice. Knowing these metrics provides the basis for volumetric measurements.

**Tissue Classification:** The next step in image quantification came with classifying anatomical regions. A variety of automated image analysis methods capitalized on key classification landmarks which provided a roadmap for anatomical identification. Using one type of image classification, from the program called FreeSurfer, many of the major anatomical divisions and ROIs of the brain may be quantified. The beauty of this technique is that it is reliable and automated, making the process ideal for analyzing large numbers of scans within a clinical population compared to a control sample (Bigler, Abildskov et al. 2010). With these types of quantitative measures, relationships between certain brain regions and cognition, like temporal lobe pathology and specifically hippocampal volume and memory could now be examined (Bigler, McCauley et al. 2010).

Another approach that capitalizes on the segmented image is to 'normalize' each brain within the same three-dimensional space. By using small voxels, based on the segmented image, that are either white, gray or CSF, a concentration count for each of these tissue types can be assessed and volumes inferred. This method is referred to as voxel-based morphometry (VBM) and can be used to compare and contrast two groups. VBM techniques can be used to examine the relationship of gray or white matter concentration and cognition.

**Neuroimaging of white matter tracts:** Diffusion Tensor Imaging (DTI) is a MRI method that specifically examines the directionality of water diffusion in the brain from which inferences can be made about tissue health and pathway connection. In traumatic brain injury, a pathway analysis may be extracted from the DTI using a technique referred to as DTI tractography.

**Functional MRI:** Neuroimaging of the functioning brain can also be achieved with MRI where the MR signal is sensitive to the blood-oxygen level dependent (BOLD) reflected in blood flow. Functional MRI (fMRI) infers regional changes in brain activity as reflecting whether a particular brain region is engaged or not in a time-linked neurobehavioral or neurocognitive task. For example, Inferences can even be made about functional connectivity in the brain by measuring in-phase features of BOLD signal while the brain is at rest—the so-called resting state (rs) fMRI.

**Three Dimensional (3-D) imaging:** By changing the magnetic field and frequency of radiowave pulses, contemporary MRI offers a variety of methods for structural imaging of the brain that comprehensively detect gross brain pathology if present. The traditional image sequences and the normal appearance of the brain for what is referred to as the T1 image identifies overall anatomy but is not necessarily that sensitive to certain types of pathologies; the T2 image that is more sensitive in detecting abnormal parenchymal tissue and CSF, but not necessarily in differentiating white and gray matter; the fluid attenuated inversion recovery sequence (FLAIR) is especially sensitive to white matter pathology and various versions of the gradient recalled echo (GRE) sequence are sensitive in detecting the hemorrhagic by-product hemosiderin, and therefore an excellent technique for detecting prior hemorrhagic lesions.

Table I: MRI Appearance of Commonly Scanned Tissues

| Tissue | T1 - Weighted | T2 - Weighted | Proton Density-Weighted |
|---|---|---|---|
| Gray matter | Gray | Light gray | Light gray |
| White matter | White | Dark gray | Gray |
| CSF or water | Black | White | Dark gray |
| Fat | White | Black | Black |
| Air | Black | Black | Black |
| Bone or calcification | Black | Black | Black |
| Edema | Gray | White | White |
| Demyelination or gliosis | Gray | White | White |
| Ferritin deposits (e.g., in basal ganglia) | Dark gray | Black | Black |
| Calcium bound to protein | White | Dark gray | Dark gray |
| Proteinaceous fluid | White | Variable | Variable |
| Note: On fast spin echo (FSE) sequences (a faster variant of the SE sequence), fat appears bright in T2- and proton density- weighted images. | | | |

## References


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## AGE-RELATED MEMORY DECLINE AND THE APOE EFFECT


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Studies of asymptomatic carriers of genes that are known to predispose to Alzheimer's disease (AD) have facilitated the characterization of preclinical AD. The most prevalent genetic risk factor is the e4 allele of apolipoprotein E (APOE) (1,2). Neuropathological studies of young deceased e4 carriers have shown modest but abnormal amounts of neocortical amyloid and medial temporal neurofibrillary tangles (3) that are also reflected in cerebrospinal fluid (CSF) biomarkers, abeta-amyloid and phosphotau in particular (4). MRI studies have shown progressive hippocampal and gray matter atrophy with the advent of mild cognitive impairment (MCI) (5), and fluorodeoxyglucose PET scans show reduced cerebral metabolism in posterior cingulate and related AD regions evident even in 30 year olds (6,7). Cerebral amyloidosis disclosed by more recent amyloid ligand PET studies in asymptomatic 60 year olds increases in parallel with e4 gene dose (8). Longitudinal neuropsychological studies have revealed accelerated memory decline in e4 carriers beginning around age 55-60 years whose severity again parallels e4 gene dose (9). The clinico-pathological correlation of declining memory and AD-like neuropathological change defines preclinical AD and has set the stage for the accelerated evaluation of presymptomatic AD treatments (10).

APOE e4 carriers have been found to be more susceptible to a wide variety of neurological insults including head trauma, cardiac arrest, carotid endarterectomy, subarachnoid hemorrhage, and multiple sclerosis as well as milder stressors including fatigue (11) and anxiety (12,13). We have found that, even in the absence of symptomatic cerebrovascular disease that APOE e4 homozygotes with cerebrovascular risk factors (any combination of hypertension, diabetes mellitus, hyperlipidemia, and history of cigarette smoking) exhibit earlier and more severely accelerated memory decline than e4 homozygotes without such risk factors (14). The interaction of APOE genotype with cancer therapies such as whole brain radiation for pediatric brain tumors is less clear and the limited studies to date have produced conflicting results.

Cognitive outcomes positively correlate with aerobic fitness more strongly in e4 homozygotes than e4 noncarriers (15) suggesting that a healthy lifestyle is of particular importance to e4 homozygotes. Other healthy lifestyle choices such as the Mediterranean diet and moderate amounts of red wine correlate with a reduced incidence of Alzheimer's disease in epidemiological studies but it is not yet known whether these effects are further moderated by APOE genotype (nor have they been formally tested in randomized clinical trials).

Among patients with mild cognitive impairment and frank dementia, there are six pharmacotherapeutic categories of concern to be addressed although not each category will require intervention in every patient. These are:

1. Prevention (primary and secondary)
2. Intellectual decline: cholinesterase inhibitors
3. Behavioral Disorders
4. Sleep Disorders
5. Comorbid Conditions
6. Abrupt Decline

This list is further elaborated in the table to provide a basic clinical guide to the types of management issues clinicians should address with each patient because these issues influence the quality of life for both patient and caregiver (16).

**Pharmacotherapy of Alzheimer's Disease**

| | FDA Approved | Other |
|---|---|---|
| Prevention | None | Physical fitness, manage comorbidities, |
| | | Mediterranean diet, etc. |
| Intellectual Decline | | |
| Mild-Moderate Stage | Donepezil | Generic available |
| | Rivastigmine | Patch available |
| | Galantamine | Generic available |
| Moderate-Severe Stage | Memantine | |
| Behavioral Problems | | |
| Depression | SSRI's prefererred | |
| Anxiety | SSRI's, Buspirone | Antipsychotics |
| Agitation, Agression, and Psychosis | None | Antipsychotics |
| Sleep Disorders | | |
| Insomnia | Zolpidem, etc. | Trazadone |
| REM Behavior Disorder | None | Clonazepam |
| Obstructive Sleep Apnea | CPAP | |
| Nocturia | Oxybutinin, tolteridine | Intermittent catheterization |
| Common Comorbidities | | |
| Parkinsonism | Levodopa/carbidopa, etc. | Rx only if necessary |
| Incontinence | Oxybutinin, tolteridine | Intermittent catheterization |
| Dysphagia | None | Advance directives |
| Abrupt Decline | | |
| Community | Evaluate | Infections, med errors, etc |
| Hospital/Post-operative | Evaluate | Antipsychotics, etc. |

With regard to the cognitive sequellae of normal aging, there is no recommendation from medical or neurological practice leadership for pharmacotherapy. A fringe group of some members of the neuroscience community has advocated the application of "cognitive enhancers" to asymptomatic individuals to improve attention, wakefulness, and memory but there is currently a lack of clinical data regarding safety and efficacy.

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**ACTIVITY-BASED INTERVENTIONS FOR COGNITIVE PROBLEMS** Elizabeth R. Skidmore, PhD, OTR/L. *Department of Occupational Therapy, University of Pittsburgh, Pittsburgh, PA, USA*

Several reviews have demonstrated that central nervous system childhood cancers and their treatments frequently culminate in long-term impairments in neurocognitive functions.[1-3] These impairments include deficits in information processing speed, attention, memory, visuospatial functions, and executive functions, and they impede the performance of everyday activities at school and at home.[3-5] Thus, not only are neurocognitive impairments problematic, they limit the ability to perform meaningful everyday activities critical to long-term independence and favorable quality of life.[6]

Similar impairments and activity limitations are also common after mild stroke and mild traumatic brain injury (in both children and adults), and have been the subject of extensive examination in the field of neurological rehabilitation. In the course of this research, neurological rehabilitation specialists have derived two intervention approaches to address neurocognitive impairments and related activity limitations: "bottom-up" and "top-down" approaches.[7]

Bottom-up approaches encourage improvements in specific neurocognitive operations through "drill and practice" exercises based on the premise that positive changes in neurocognitive operations may subsequently promote positive changes in the performance of everyday activities. "Drill and practice" exercises frequently take the form of simple tasks such as "find the hidden object," "learn and recall the following list," or "complete the following sequence," and can be delivered through paper-and-pencil or computerized methods. The combined evidence from four systematic reviews[8-11] and two meta-analyses[12-13] suggests that "drill and practice" exercises produce small to medium improvements in selected neurocognitive operations (i.e., attention, information processing speed) after stroke or traumatic brain injury.[8-13] However, evidence does not indicate that "drill and practice" exercises promote improvements in the performance of everyday activities after stroke or traumatic brain injury.[8-13] The feasibility of similar interventions have been examined in survivors of childhood cancer, but as of yet the efficacy of these interventions in this population remains unclear.[14-15]

Top-down approaches promote positive changes in the performance of everyday activities that have the potential to promote subsequent positive changes in underlying neurocognitive operations.[7] With top-down approaches, everyday activities are both the modality through which the intervention is delivered (intervention process), as well as intervention outcome, and thus are frequently referred to as "activity-based" interventions. Activity-based interventions involve the identification of problematic everyday activities; the derivation of goals, plans and iterative practice to address these problematic activities; and the development, evaluation, and modification of strategies to facilitate generalized application to a variety of everyday activities at school and at home. In doing so, activity-based interventions blend principles of activity analysis and adaptation (from neurological rehabilitation) with principles that promote meta-cognitive self-instruction (from cognitive and behavioral psychology) and learning (from developmental and educational psychology). Recent evidence suggests that activity-based interventions that incorporate each of these elements (activity analysis and adaptation, meta-cognitive self-instruction, and learning) are effective in improving performance of everyday activities,[16-23] and in some cases improving underlying neurocognitive operations critical to the performance of everyday activities after stroke or brain injury.[17,24-26] Furthermore, selected elements of activity-based interventions have been examined in survivors of childhood cancer, with similar results.[27-29] Although further empirical examination is warranted, activity-based interventions show promise for promoting independence and improving quality of life among individuals with neurocognitive impairments.

This presentation will review the current state of science examining the feasibility and efficacy of empirically-derived activity-based interventions for addressing neurocognitive impairments and the subsequent effects of these impairments on the performance of everyday activities at school and at home. We will discuss the growing body evidence examining activity-based interventions for survivors of childhood cancers, as well as lessons learned in neurological rehabilitation that may help inform future research and clinical practices.

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**PHYSICAL ACTIVITY, EXERCISE AND COGNITION** Arthur F. Kramer. *Beckman Institute, University of Illinois, Urbana, IL, USA*

Over the past several decades our society has become increasing sedentary. Whether this change is due, in part, to the rapid technological development, economic challenges to our society, or a host of other factors, decreases in physical activity have been associated with diseases such as hypertension, diabetes, osteoporosis and a number of different cancers. In my presentation I will cover what we currently know about physical activity and exercise and their influence on healthy minds and brains. I'll briefly cover animal research which has elucidated the molecular and cellular mechanisms that relate physical activity to brain function and cognition. My main focus will be on human exercise research across the lifespan, covering both epidemiological and intervention studies. Finally, I will conclude with a discussion of our knowledge gaps and how we might fill them with future research.

# Oral Platform Presentations

**1. LATE OCCURING STROKE AFTER CRANIAL RADIATION AND ASSOCIATION WITH ATHEROSCLEROTIC RISK FACTORS IN ADULT SURVIVORS OF PEDIATRIC CANCER: RESULTS FROM THE CHILDHOOD CANCER SURVIVOR STUDY** Sabine Mueller MD, PhD; Heather J. Fullerton MD, MAS; Kayla Stratton, MS; Wendy Leisenring, ScD; Rita E. Weathers, MS; Marilyn Stovall, PhD[3]; Gregory T. Armstrong, MD, MSCE; Robert E. Goldsby, MD; Roger J. Packer, MD; Charles A. Sklar, MD; Daniel C. Bowers, MD; Leslie L. Robison, PhD; Kevin R. Krull, PhD. *University of California, San Francisco, CA, USA; Fred Hutchison Cancer Research Center, Seattle, WA, USA; University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; St. Jude Children's Research Hospital, Memphis, TN, USA; Children's National Medical Center, Washington, DC, USA; Memorial Sloan-Kettering Cancer Center, New York, NY, USA; University of Texas Southwestern Medical School, Dallas, TX, USA*

**Context:** Radiation therapy has vascular sequelae including accelerated atherosclerosis. However, the impact of childhood cranial radiation therapy (CRT) on risk of stroke in adulthood, and the role of atherosclerotic risk factors, remains poorly defined.

**Objective:** To assess long-term incidence rates and risk factors for stroke in pediatric cancer survivors followed by the Childhood Cancer Survivor Study (CCSS).

**Methods:** CCSS is a longitudinal cohort study of 14,358 childhood cancer survivors diagnosed between 1970 and 1986, and 4,023 randomly selected sibling controls. The age-adjusted incidence rates of self-reported late-occurring first-stroke (≥ 5 years after cancer diagnosis) were calculated for survivors compared to siblings. Multivariable Cox Proportional Hazards models were used to identify independent stroke predictors.

**Results:** During a mean follow-up of 23.3 years, 292 survivors reported a late-occurring stroke. The age-adjusted stroke rate was 77 per 100,000 person-years (95% Confidence Interval [CI] 62-96) compared to 9.3 (95% CI 4-23) for siblings. Treatment with CRT increased stroke risk in a dose dependent manner: hazard ratio (HR) 5.9 (95% CI 3.5-9.9) for 30-49 Gy CRT, and 11.0 (7.4-17.0) for 50+ Gy CRT. The cumulative incidence of stroke in survivors treated with 50+ Gy CRT was 1.1% (95% CI 0.4-1.8) at 10 years post-diagnosis and 12% (95% CI 8.9-15.0) at 30 years. Hypertension (HTN) increased stroke hazard 4-fold (HR 4.0, 95% CI 2.8-5.5) and in black survivors 16-fold (HR 15.9, 95% CI 6.9-36.6). A subgroup analysis of central nervous system tumor survivors revealed that the combination of diabetes and HTN resulted in a stroke HR of 14.4 (95% CI 5.7-36.2), compared to 2.9 (95% CI 1.6-5.3) for HTN alone.

**Conclusion:** Young adult pediatric cancer survivors have an increased stroke risk that is associated with CRT in a dose dependent manner and increases with age. Atherosclerotic risk factors enhanced this risk and should be monitored carefully.

**2. NEUROCOGNITIVE FUNCTION AND BRAIN IMAGING IN ADULT SURVIVORS OF CHILDHOOD HODGKIN LYMPHOMA** Kevin R. Krull, PhD; Noah D. Sabin, MD; Wilburn E. Reddick, PhD; Liang Zhu, PhD; Gregory T. Armstrong, MD; Daniel M. Green, MD; Alex Arevalo, MD; Matthew J. Krasin, MD; Deo Kumar Srivastava, PhD; Leslie L. Robison, PhD; Melissa M. Hudson, MD. *Departments of Epidemiology and Cancer Control, Radiological Sciences, Biostatistics, and Oncology, St. Jude Children's Research Hospital, Memphis, TN, USA; Department of Pediatrics, Division of Cardiology, University of Tennessee Health Science Center, Memphis, TN USA*

**Purpose:** Long-term survivors of childhood Hodgkin Lymphoma (HL) are at risk for cardiopulmonary complications, as well as central nervous system (CNS) stroke, though neurocognitive function has not been well examined. The aim of the current study was to examine neurocognitive and brain imaging outcomes in adult survivors of childhood HL.

**Method:** 62 adult survivors (mean [SD] age=42.2 [4.77] years; range=34.4-55.4 years; age at diagnosis=15.1[3.30] years) were identified by stratified random selection from a large cohort treated with either high dose (≥ 30 Gy) thoracic radiation (n=38) or lower dose (< 30Gy) thoracic radiation combined with anthracycline (n=24). Patients underwent neurocognitive evaluations, brain magnetic resonance imaging (MRI), echocardiograms, pulmonary function tests, and physical exams. MRI techniques included T1/T2 and susceptibility weighted imaging (SWI). Images were objectively processed for regional cortical thickness. Images were also reviewed and systematically coded by a board certified neuroradiologist blind to treatment history and performance measures.

**Results:** Compared to national age-adjusted norms, HL survivors demonstrated lower performance on sustained attention (p=0.004), short-term memory (p=0.001), long-term memory (p=0.006), working memory (p<0.001), naming speed (p<0.001) and fluency (p=0.007). Brain MRI revealed leukoencephalopathy in 53% of survivors, 35% in frontal lobe regions and 13% in parietal lobe regions, and 37% had SWI suggestive of cerebrovascular injury. Attention problems were correlated with decreased cortical thickness in frontal brain regions (p=0.03), while survivors with leukoencephalopathy demonstrated reduced cognitive fluency (p=0.001). Working memory was associated with cardiac diastolic function (E/E'), while sustained attention and naming speed were associated with pulmonary function ($DLCO_{corr}$). Neurocognitive performance was associated with academic and vocational functioning.

**Conclusion:** These results suggest that adult long-term survivors of HL are at risk for neurocognitive impairment, which is associated with radiological indices suggestive of reduced brain integrity and occurs in the presence of symptoms of cardiopulmonary dysfunction.

**3. DEXAMETHASONE AND MEMORY FUNCTION IN ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA** Michelle N Edelmann, Robert J. Ogg, Matthew A. Scoggins, Noah Sabin, Ching-Hon Pui, Leslie L. Robison, Melissa M. Hudson, Kevin R. Krull. *St. Jude Children's Research Hospital, Memphis, TN USA*

**Background:** Dexamethasone is commonly used to treat childhood acute lymphoblastic leukemia (ALL), though long-term impact of prolonged repeated exposure on central nervous system function is unclear. As glucocorticoids influence hippocampal function, we questioned whether survivors who received dexamethasone were at a higher risk for memory deficits compared to survivors treated with prednisone.

**Methods:** We examined brain function in 38 adult survivors of childhood ALL randomly recruited from the St. Jude Lifetime Cohort study. Survivors were treated on one of two standard ALL therapy protocols, and were ≥18 years old and ≥ 10 years post diagnosis at assessment. The two therapy protocols differed in type of glucocorticoid given during the continuation phase (dexamethasone or prednisone), and none of the recruited survivors were treated with cranial radiation. Mean [SD] age at diagnosis was 10.2 [3.80] years and the age at evaluation was 25.1 [3.44] years. Direct neurocognitive assessment and functional magnetic resonance imaging (fMRI) were used to assess brain function.

**Results:** Compared to survivors treated with prednisone, survivors treated with dexamethasone demonstrated lower performance on multiple memory and learning measures, including: reading ($p=0.01$), math ($p=0.01$), and memory for stories ($p=0.008$). . Performance on these measures correlated with performance on fMRI activation tasks, e.g. assessment of reading and fMRI memory for words $r=0.58$, $p<0.001$. Memory for words was associated with altered activation in the left inferior frontal brain region. fMRI analysis demonstrated that survivors treated with dexamethasone had altered activity in the retrosplenial brain region, which (1) has dense reciprocal projections with the hippocampus, (2) is involved in memory function, and (3) is associated with the integrity of multiple neural networks.

**Conclusions**: These results suggest that adult survivors of ALL who received prolonged repeated dexamethasone treatment are at risk for memory deficits and appear to have decreased neural activity associated with memory networks.

**4. LONGITUDINAL PATTERNS OF PSYCHOLOGICAL DISTRESS IN ADULT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY** Tara M. Brinkman, PhD; Liang Zhu, PhD; Cara Kimberg, PhD; Nan Zhang, MS; Christopher J. Recklitis, PhD, MPH; Anna C. Muriel, MD, MPH; Lonnie K. Zeltzer, MD; Marilyn Stovall, PhD; Deo Kumar Srivastava, PhD; Leslie L. Robison, PhD; Kevin R. Krull, PhD. *St. Jude Children's Research Hospital, Memphis, TN, USA; Dana-Farber Cancer Institute, Boston, MA, USA; David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; M.D. Anderson Cancer Center, Houston, TX USA*

**Purpose:** Symptoms of psychological distress may persist or change over time in survivors of childhood cancer; yet longitudinal patterns of distress have not previously been examined in a large cohort of adult survivors of childhood cancer.

**Methods:** Participants included 4,569 adult survivors of childhood cancer who completed a measure of psychological distress (BSI-18) in 1994-1996 (baseline), 2003-2005, and 2007-2010 as part of the Childhood Cancer Survivor Study. Mean [SD] age at baseline = 27.4 years [6.1], age at diagnosis = 10.0 years [5.6], and time since diagnosis at baseline = 16.8 years [4.6]. Age-adjusted standard scores for psychological distress were calculated using national norms, with clinical impairment defined as scores >90th percentile. Latent profile analysis was performed to identify longitudinal classes of depression, anxiety, and somatization. Odds ratios (OR) and 95% confidence intervals (CI) were calculated using multivariable generalized logistic regression models to identify predictors of class membership.

**Results:** The final model indicated four longitudinal classes (e.g. trajectories) of depression: 1) survivors with elevated depressive symptoms at baseline that increased and exceeded clinical significance at both subsequent time points (11.4%); 2) survivors with average symptoms at baseline that increased then recovered over time (15.2%); 3) survivors with average symptoms at baseline and first follow-up, but elevated symptoms at second follow-up (8.0%); and 4) survivors with consistently average symptoms (65.5%). Compared to class 4, membership in class 1 was predicted by cancer related pain (OR=2.42, 95% CI= 1.68-3.49), poor physical health status (OR=3.16, 95% CI=2.19-4.56), and high dose cranial radiation (OR=1.89, 95% CI=1.37-2.60). Multiple classes were identified for symptoms of anxiety and somatization, with similar predictors of increasing symptoms over time.

**Conclusions:** Subgroups of adult survivors experience persistent and/or increasing symptoms of psychological distress over time. Identification of factors associated with changes in symptoms may inform targeted interventions to prevent or mitigate distress among survivors.

**5. SCARRING, DISFIGUREMENT AND QUALITY OF LIFE IN LONG-TERM SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY** Karen E. Kinahan, MS, PCNS-BC; Lisa K. Sharp, PhD; Aarati Didwania, MD; Kristy Seidel, MS; Wendy Leisenring ScD; Mario Lacouture, MD; Marilyn Stovall, PhD; Anand Haryani, BA; Leslie L. Robison, PhD; Kevin R. Krull, PhD. *Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, IL, USA; Department of Medicine, Northwestern University School of Medicine, Chicago, IL, USA; Department of Medicine, Section of Health Promotion Research, University of Illinois at Chicago, IL, USA; Clinical Statistics and Cancer Prevention Programs, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; Department of Medicine, Memorial Sloan Kettering Comprehensive Cancer Center, New York, NY, USA; Department of Radiation Physics, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN, USA*

**Purpose:** Childhood cancer survivors are at increased risk for adverse outcomes and chronic medical conditions. Treatment-related scarring, disfigurement and persistent hair loss, and their long-term impact on psychological distress or health-related quality of life (HRQOL) has received little attention.

**Methods:** Self-reported scarring/disfigurement and persistent hair loss were examined in 14,358 survivors and 4,023 siblings from the Childhood Cancer Survivor Study. Multivariable models were used to examine associations with demographic and cancer treatment. The impact of disfigurement and hair loss on HRQOL (i.e. Medical Outcomes Short Form–36) and emotional distress (i.e. Brief Symptom Inventory–18) was examined.

**Results:** Survivors reported a significantly higher rate of scarring/disfigurement compared to siblings for head/neck (25.1% vs. 8.4%), arms/legs (18.2% vs. 10.2%), chest/abdomen (38.1% vs. 9.1%) and hair loss (14.0% vs. 6.3%). In age-, sex-, and race-adjusted models, cranial radiation exposure ≥36 Gy increased risk for head/neck disfigurement (RR=2.50; 95% CI=2.29-2.73) and hair loss (RR=4.81; 95% CI=4.12-5.63). Adjusting for cranial radiation, age and sex, survivor hair loss increased risk of anxiety (RR=1.63; 95% CI=1.26-2.11), while head/neck disfigurement increased risk of depression (RR=1.26; 95% CI=1.07-1.49). Limitations due to emotional symptoms were associated with head/neck disfigurement (RR=1.28; 95% CI=1.13-1.44), arm/leg disfigurement (RR=1.21; 95% CI=1.06-1.37) and hair loss (RR=1.28; 95% CI=1.10-1.49).

**Conclusion:** Survivors of childhood cancer are at increased risk for disfigurement and persistent hair loss, which is associated with future emotional distress and reduced quality of life. Future studies are needed to better identify and manage functional outcomes in these patients.

**6. PSYCHIATRIC DISEASE IN CHILDHOOD CANCER SURVIVORS AND THEIR SIBLINGS: A DANISH COHORT-COHORT POPULATION BASED REGISTRY STUDY** L.W. Lund, MD, PhD fellow; C. Johansen, Professor, MD, PhD, DMSc; S.O. Dalton, MD, PhD; K. Schmiegelow, Professor, MD, DMSc; C. Rechnitzer, MD, DMSc; Marie Hargreave, MSc, PhD; Allan, Jensen PhD, MSc; I. Deltour, PhD; K.K. Andersen, PhD, MSc.Eng; Luise Cederkvist, MScEng. *Departments of Survivorship; Virus, Lifestyle and Genes; and Statistics and Epidemiololgy, Danish Cancer Society Research Center, Copenhagen, Denmark; Pediatric Clinics, Juliane Marie Centre, University Hospital Rigshospitalet, Copenhagen, Denmark; Section of Environment and Radiation, International Agency for Research on Cancer, Lyon, France*

**Introduction:** The childhood cancer experience is stressful for the child and the family. Most of the previous studies in this area rely on self reported data and suffer from low response rates.

**Material and methods:** We identified all incident cases of cancer in children in the Danish Cancer Registry diagnosed 1975-2010 born in Denmark (n=7.141) and their siblings (n=13.036). We obtained information on psychiatric disease in the Danish Psychiatric Central Registry.

**Results:** Overall childhood cancer survivors were at an increased risk for psychiatric disease (men: RR 1.35; 95% CI: 1.2-1.5; women: RR 1.26; 95% CI: 1.1-1.4), mostly driven by survivors of CNS tumors and of leukemia and lymphoma.

No increased risk of psychiatric disease was observed in sibling survivors overall (brothers: RR 0.99; 95% CI: 0.9-1.1; sisters: RR 1.01; 95% CI: 0.9-1.1). As a secondary finding, younger age of the sister at diagnosis of the cancer child was associated with a statistically significant increased risk and sisters in their teens at diagnosis were at lower risk of psychiatric disease than background population (RR: 0.83; 95% CI: 0.7-1.0).

**Discussion:** In this up-to-date cohort with complete follow up and almost negligible bias we find lower estimates of severe psychiatric diseases in childhood cancer survivors compared to previous studies. The limitations include inability to adjust for life style, somatic disease, parental divorce, and socioeconomic status due to lack of power.

**Conclusion:** Despite more targeted treatment, follow up programs and free health care in Denmark, childhood cancer survivors are still at increased risk for severe psychiatric disease. Focus on survivors who are young at diagnosis, of male gender or following CNS tumors is needed. Siblings are in general not at an increased risk for severe psychiatric illness, which is reassuring. However, this area needs further investigations before any psychological effect of this major stressful life event is excluded.

**7. MALE INFERTILITY IN CHILDHOOD AND ADOLESCENT CANCER SURVIVORS DIAGNOSED FROM 1970-1986: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)** Karen Wasilewski-Masker, MD; Kristy D. Seidel, MS; Wendy Leisenring, ScD; Ann Mertens, PhD; Margarett Shnorhavorian, MD; Chad W. Ritenour, MD; Marilyn Stovall, MD; Daniel M. Green, MD; Charles A. Sklar, MD; Gregory T. Armstrong, MD; Leslie L. Robison, PhD; Lillian R. Meacham, MD. *The Aflac Cancer Center and Blood Disorders Service at Children's Healthcare of Atlanta, Atlanta, GA, USA; Departments of Pediatrics and Urology, Emory University School of Medicine, Atlanta, GA, USA; Clinical Statistics and Cancer Prevention Programs, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; Division of Pediatric Urology, Seattle Children's Hospital, University of Washington, Seattle, WA, USA; Department of Radiation Physics, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN, USA; Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, New York, NY, USA*

**Background:** The American Society of Reproductive Medicine describes "infertility" as, "a disease, defined by the failure to achieve a successful pregnancy after 12 months or more of regular unprotected intercourse." In this study we analyzed the inability of a female partner to conceive after 12 months of trying to become pregnant with adult male survivors of childhood cancer.

**Purpose:** To determine the prevalence of infertility and treatment-related risk factors for infertility in male survivors of childhood cancer.

**Methods:** Within the CCSS cohort, 1622 adult long-term survivors and 274 sibling controls completed the self-administered Male Health Questionnaire. The analysis was restricted to survivors (938/1622; 57.8%) and siblings (174/274; 63.5%) who responded positively to the question, "Have you and a partner ever tried to become pregnant". The prevalence of self-reported infertility, relative risk (RR) and 95% confidence intervals (CI) were calculated for associated demographic and treatment-related factors.

**Results:** The prevalence of infertility was 17.5% in sibling controls versus 46.0% in survivors ($p < 0.001$). Survivors were less likely to have all the children they wanted, with male infertility being the most common reason for not having more children, cited by 64% of survivors and 15% of siblings ($p < 0.001$). Among survivors, 53.6% reported being evaluated for infertility. In a multivariable analysis, risk factors for infertility included a summed alkylator score ≥ 3 (RR= 2.13, 95% CI 1.69-2.68), surgical excision of any organ of the genital tract (RR=1.63, 95% CI 1.20-2.21), testicular radiation dose ≥ 4Gy (RR=1.99, 95% CI 1.52-2.61), and exposure to bleomycin (RR=1.55, 95% CI 1.20-2.01).

**Conclusions:** Male survivors of childhood cancer are at significantly increased risk for infertility. This analysis confirms known risk factors of dose of exposure to alkylating agents, testicular radiation, and surgery with the novel finding of an association of infertility with bleomycin exposure.

**8. CHILDHOOD CANCER SURVIVORS EXPOSED TO TOTAL BODY IRRADIATION ARE AT SIGNIFICANT RISK FOR SLIPPED CAPITAL FEMORAL EPIPHYSIS DURING RECOMBINANT GROWTH HORMONE THERAPY** Sogol Mostoufi-Moab, MD, MSCE; Elizabeth Isaacoff, BS; Denise Gruccio, MSN, CRNP; Wendy Hobbie, MSN, CRNP; Claire Carlson BSN, RN; David Spiegel, MD; and Jill P. Ginsberg, MD. *Department of Pediatrics, Divisions of Oncology and Endocrinology, and Department of Surgery, Division of Orthopedics, The Children's Hospital of Philadelphia, Philadelphia, PA, USA*

**Background:** Survivors of childhood cancer treated with cranial or total body irradiation (TBI) are at risk for growth hormone deficiency (GHD). Recombinant growth hormone (rhGH) is used to improve growth and can result in unique orthopedic disorders such as slipped capital femoral epiphysis (SCFE). Specific cancer treatment modality contributing to SCFE in survivors has not been previously evaluated.

**Objective:** To compare the incidence of SCFE subsequent to TBI vs. cranial irradiation exposure (CI) in childhood cancer survivors on rhGH.

**Design:** Retrospective cohort study (1980-2010) of 119 survivors treated with rhGH for irradiation-induced GHD (47% TBI). SCFE cumulative incidence and incidence rate per irradiation treatment group were determined. For each treatment group, irradiation-exposure age, rhGH-start age, sex, and cancer diagnosis were compared.

**Results:** Median survivor follow-up on rhGH was 4.8 (range 0.2-18.3) years. SCFE was diagnosed in ten survivors (70% male) after TBI and none after CI ($p<0.001$). Within the TBI exposed group, there was no significant difference for developing SCFE based on sex, cancer diagnosis, age at irradiation, or age at initiation of rhGH. SCFE subjects' mean age ± SD at time of TBI exposure was 2.7 ± 1.7 (range 0.7-5.6), rhGH start 10.1 ± 2.5 (range 6.4-13.0) and SCFE diagnosis 12.3 ± 2.7 (range 8.0-16.0) years. All SCFE subjects were prepubertal at time of SCFE diagnosis with no sex differences in age at time of TBI exposure, rhGH start or SCFE age. None had untreated endocrinopathies. TBI-associated SCFE incidence rate was 35.9 per 1,000 person years. The incidence rate of SCFE after TBI was substantially greater when compared to GH registry data for subjects treated with rhGH for idiopathic GHD (0.17/1000 person years).

**Conclusion:** TBI exposure for childhood cancer therapy at a young age is a significant risk factor for SCFE during rhGH treatment for irradiation-induced GHD.

**9. GENITO-URINARY (GU) SECOND MALIGNANT NEOPLASMS (SMN) IN SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)** Margarett Shnorhavorian, MD, MPH; Wendy Leisenring, ScD; Pamela Goodman, MS, Debra L. Friedman, MD; Marilyn Stovall, MD; Lillian R. Meacham,MD; Eric J. Chow, MD; Charles A. Sklar, MD; Lisa R. Diller, MD; Fernando Ferrer, MD; Greg T. Armstrong,MD; Joseph P. Neglia, MD, MPH; Leslie L. Robison, PhD. *Department of Urology, University of Washington, Seattle, WA, USA; Clinical Statistics and Cancer Prevention Programs, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; Department of Pediatrics, Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; Department of Radiation Physics, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA; Department of Pediatrics, University of Washington, Seattle, WA, USA; Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Department of Pediatric Oncology, Dana Farber Cancer Institute, Boston, MA, USA; Department of Urology, University of Connecticut, Hartford, CT, USA; Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN, USA; Department of Pediatrics, University of Minnesota, Minneapolis, MN, USA*

**Purpose:** To describe the occurrence of GU SMNs among five year survivors in the CCSS cohort.

**Methods:** Among 14,358 five-year survivors, cumulative incidence of first GU SMN was calculated using death as a competing risk. Standardized Incidence Ratios (SIRs) were calculated using age- sex- year- specific rates from the SEER program.

**Results:** A total of 72 GU SMNs were identified among 68 subjects. Median age at diagnosis of first GU SMN was 31.0 years (range 9.0-51.0), occurring a median of 21.9 years (range 6.3-35.7) after primary cancer. Among GU SMN cases, 68.4% had received radiation therapy (RT) involving the GU system. Sites of first GU SMN included: 27 female reproductive (13.2% ovary, 11.8% endometrium, 7.4% cervix, 2.9 % uterus, 2.9% vulva), 24 kidney (35.3%), 10 bladder (14.7%) and 7 male reproductive (5.9% testes, 4.4% prostate). Most common histologies included: 24 renal cell carcinoma (24.3%), 7 adenocarcinoma (9.7%), 5 transitional cell carcinoma (6.9%), and 5 endometrioid carcinoma (6.9%).The overall cumulative incidence at 30 years post diagnosis was 0.6% (95% CI: 0.4-0.8%) and SIR was 11.6 (95% CI: 9.1-14.7). Cumulative incidence was significantly higher for females (0.7%; 95% CI: 0.5-1.0%) as compared to males (0.5%; 95% CI 0.2%-0.7%) ($p=0.01$) as were SIRs (females: 20.9; 95%CI 15.4-28.4; males: 6.5; 95% CI: 4.3-9.6; $p<0.001$). Cumulative incidence did not significantly differ between exposure levels of GU RT and risk was elevated in comparison to the general population among those with no GU RT (SIR 12.1; 95% CI: 7.5-19.6), <2000 cGY (SIR 8.4; 95% CI: 5.6-12.7), and RT ≥2000 (SIR 20.6; 95%CI 11.7-36.2)

**Conclusion:** Although the absolute cumulative incidence is low, survivors of childhood cancer are at significantly increased risk for a GU SMN. In particular, female survivors and survivors with GU RT ≥ 2000 cGy have highest elevated risk for a GU SMN.

**10. RENAL CARCINOMA FOLLOWING THERAPY FOR CANCER IN CHILDHOOD: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY** Carmen L. Wilson; Kirsten K. Ness, PhD, PT; Joe P. Neglia, MD, MPH; Sue Hammond, MD; Wendy Leisenring, ScD; Marilyn Stovall, PhD; Leslie L. Robison, PhD; Gregory T. Armstrong, MD, MSCE. *Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN, USA; Department of Pediatrics, University of Minnesota, Minneapolis, MN, USA; Department of Laboratory Medicine and Anatomic Pathology, Columbus Children's Hospital, Columbus, OH, USA; Clinical Statistics and Cancer Prevention, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; Department of Radiation Physics, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA*

**Background:** Limited data exist describing the incidence of and risk factors for subsequent renal carcinoma among long-term survivors of childhood cancer.

**Methods:** The study included 14,351 five-year survivors of childhood cancer diagnosed between 1970 and 1986 who participated in the Childhood Cancer Survivor Study. Chemotherapy and radiotherapy exposures were abstracted from medical records; total dose of radiation to the renal beds was estimated by a radiation physicist. Standardized incidence ratios (SIRs) were calculated using age-, sex-, and calendar-specific incidence data from the Surveillance, Epidemiology and End Results (SEER) program. Cumulative incidence was calculated treating death as a competing risk. Poisson regression analyses were used to assess associations between diagnosis and treatment characteristics and the risk of subsequent renal carcinoma while adjusting for changes in risk due to age.

**Results:** Twenty-six survivors were diagnosed with a renal carcinoma at a median follow-up of 19.3 years (range: 1 month to 34.3 years) from study entry at 5 years post diagnosis. Eight patients received ≥5Gy radiotherapy to a renal bed, 16 received chemotherapy, seven of whom seven received both radiotherapy ≥5Gy and chemotherapy. Cumulative incidence of renal carcinoma at 20 years was 0.16% (95% CI 0.12-0.20). The SIR was 8.1 (95% CI 5.3-11.8) comparing survivors to the general population. Highest risk for renal carcinoma was observed among survivors of neuroblastoma (SIR 87.1, 95% CI 38.4-175.2), non-Hodgkin lymphoma (SIR 9.3, 95% CI 1.9-27.4), and bone tumors (SIR 7.0, 95% CI 1.4-20.4). In multivariable analyses, the risk of subsequent renal carcinoma was elevated among survivors exposed to platinum-based chemotherapy (Rate Ratio 3.1, 95% CI 0.9-10.6) or renal bed radiotherapy ≥5Gy (RR 3.6, 95% CI 1.5-8.4).

**Conclusion:** While cumulative incidence is low, survivors of childhood cancer are at an eight-fold increased risk for subsequent renal carcinoma compared to the general population. In addition to a primary diagnosis of neuroblastoma, radiotherapy directed to the renal bed increased the risk for renal carcinoma.

**11. SECOND CANCER RISK FORTY YEARS AFTER CURE FOR HODGKIN LYMPHOMA** M. Schaapveld; B.M.P. Aleman; A.M. van Eggermond; C.P.M. Janus, A.D.G. Krol; L.C.M. Kremer; R.W.M. van der Maazen; J.M.M. Raemaekers; J.P. de Boer; G.W. van Imhoff; M. Beijert; J.M. Zijlstra, M.L. Lybeert; Ph.M.P. Poortmans; I. Mulder; O. Visser; M. Louwman; G.C.C. Sombroek; P.J. Lugtenburg; F.E. van Leeuwen. *Departments of Psychosocial Research and Epidemiology, Radiotherapy, and Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands; Comprehensive Cancer Centre The Netherlands, Utrecht, The Netherlands; Departments of Radiotherapy and Haematology, Daniel den Hoed Cancer Center/Erasmus MC, Rotterdam, The Netherlands; Department of Radiotherapy, Leiden University Medical Center, Leiden, The Netherlands; Department of Oncology, Emma Children's Hospital, Academic Medical Center, Amsterdam, The Netherlands; Departments of Radiotherapy and Haematology, Radboud University Medical Center, Nijmegen, The Netherlands; Department of Haematology and Radiotherapy, University Medical Center Groningen, Groningen, The Netherlands; Department of Haematology, VU University Medical Center Amsterdam, Amsterdam, The Netherlands; Department of Radiotherapy, Catharina Hospital, Eindhoven, The Netherlands; Department of Radiation Oncology, Dr. Bernard Verbeeten Institute, Tilburg, The Netherlands; Comprehensive Cancer Centre South Netherlands, Eindhoven, The Netherlands*

**Background:** Background: During the last decades Hodgkin Lymphoma (HL) treatment changed towards less toxic chemotherapy schemes and smaller radiation fields. The impact of these changes on second cancer (SC) risk is still unknown.

**Methods:** We compared SC risk after HL treatment with expected risk, based on cancer incidence in the general population, and over time and between treatment modalities, accounting for competing events, in a large Dutch multicenter cohort comprising 1,604 5-years HL survivors, aged ≤25 years at HL treatment (55% aged <21 years) and diagnosed between 1965-2000.

**Results:** The median follow-up was 19.7 years; 30% of the patients was followed ≥25 years. During follow-up 293 SCs, other than non-melanoma skin cancer, occurred. The standardized incidence rate (SIR) for any SC was 8.5 (95% confidence interval (95%CI) 7.5-9.6). SC risk was still elevated after 35 years of follow-up (SIR 4.5; 95%CI 2.5-7.4) and cumulative incidence reached 41.3% (95%CI 36.4-46.2) at 40 years follow-up. The cumulative incidence of solid tumors (ST) between 5-19 years after HL treatment did not differ for patients treated in the periods 1965-1979, 1980-1989 or 1990-2000 (P=0.242; 19-year cumulative incidence 6.0%, 8.3% and 8.3%, respectively). Radiotherapy (RT) above the diaphragm significantly increased risk of STs above the diaphragm (Relative Risk 5.2, P=0.001), while subdiaphragmatic RT was associated with a 5.0-fold increased risk of a subdiaphragmatic STs (P<0.001). An incomplete mantle field was associated with a significantly lower breast cancer risk (hazard ratio (HR) 0.3, 95%CI 0.0-0.7). A cumulative procarbazine dose >4.2 g/m2 was associated with increased risk of gastrointestinal cancer (HR 3.4, 95%CI 1.5-7.4) and a decreased breast cancer risk (HR 0.4, 95%CI 0.1-0.7). Anthracyclines did not affect ST risk.

**Conclusions:** Although HL treatment intensity has decreased over time, it appears to be too early yet to observe a decline of SC risk in more recent treatment periods.

**12. NEW INSIGHTS INTO THE RISK OF BREAST CANCER IN CHILDHOOD CANCER SURVIVORS TREATED WITH CHEST RADIATION: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS) AND THE WOMEN'S ENVIRONMENTAL CANCER AND RADIATION EPIDEMIOLOGY (WECARE) STUDY** Chaya S. Moskowitz, PhD; Joanne F. Chou, MPH; Suzanne L. Wolden, MD; Jonine L. Bernstein, PhD; Jyoti Malhotra MD, MPH; Danielle Novetsky Friedman, MD; Nidha Z. Mubdi, MPH; Tara O. Henderson, MD; Wendy M. Leisenring, ScD; Marilyn Stovall, PhD; Sue Hammond, MD; John D. Boice, ScD; Melissa M. Hudson, MD; Lisa R. Diller, MD; Smita Bhatia, MD, MPH; Joseph P. Neglia, MD, MPH; The WECARE Study Collaborative Group; Colin B. Begg, PhD; Leslie L. Robison, PhD; Kevin C. Oeffinger, MD. *Memorial Sloan-Kettering Cancer Center, New York, NY, USA; University of Chicago Medical Center, Chicago IL, USA; Fred Hutchinson Cancer Research Center, Seattle, WA, USA; The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; Nationwide Children's Hospital, Columbus, OH, USA; Vanderbilt-Ingram Cancer Center, Nashville, TN and the International Epidemiology Institute, Rockville, MD, USA; St. Jude Children's Research Hospital, Memphis, TN, USA; Dana-Farber Cancer Institute, Boston MA, USA; City of Hope Comprehensive Cancer Center, Duarte, CA, USA; University of Minnesota Masonic Cancer Center, Minneapolis, MN, USA*

**Purpose of Study:** The risk of breast cancer (BC) by age 50 among women treated for childhood cancer with chest radiation therapy (RT) and how this risk compares with that of BRCA1 and BRCA2 (BRCA1/2) mutation carriers is unknown.

**Summarized description of project:** We evaluated the risk of BC in a cohort of 1268 female 5-yr childhood cancer survivors treated with chest RT and estimated the cumulative incidence of BC non-parametrically treating death as a competing risk. The cumulative incidence of BC in BRCA1/2 mutation carriers was estimated with the kin-cohort method using data from 4570 female first-degree relatives of women diagnosed with unilateral BC (probands) participating in the WECARE Study. Absolute Excess Risks (AERs) were estimating using population-based data from the SEER program.

**Results and conclusions:** With a median follow-up of 26 yrs (range 5-39) for the CCSS cohort, 175 women were diagnosed with BC at a median age of 38 yrs (range 24-53) and a median latency of 23 yrs (range 7-38); the overall cumulative incidence of BC by age 50 was 24% (95% confidence interval [CI] 20-28%) and among Hodgkin lymphoma survivors was 30% (95% CI 25-35%). In comparison, among first-degree relatives of WECARE Study probands 324 were diagnosed with BC (median age at diagnosis, 55 yrs (range 26-90)). The estimated cumulative incidence by age 50 was 31% (95% CI 16-47%) and 10% (95% CI 2-23%) in carriers of BRCA1 and BRCA2 mutations, respectively. The population cumulative incidence of BC is 4% by age 50. Among the childhood cancer survivors, AERs for BCs diagnosed per 10,000 person years of observation were respectively 34 (95% CI 18-52), 27 (95% CI 11-45), and 95 (95% CI 78-112) among women treated with 10-19 Gy (23%), 20-29 Gy (17%), and 30+ Gy (56%) of chest RT. Women treated for childhood cancer with chest RT have a substantial risk of BC comparable to BRCA1/2 mutation carriers and considerably greater than that of the general population. Women treated with 10-19 Gy RT had an increased excess risk warranting consideration of breast cancer surveillance strategies similar to the current recommendations for women treated with > 20 Gy.

**13. INCREASING RISK OF CHRONIC HEALTH CONDITIONS IN AGING SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY** Gregory T. Armstrong, MD, MSCE; Toana Kawashima, MS; Wendy Leisenring, ScD; Marilyn Stovall, PhD; Charles A. Sklar, MD; Leslie L Robison, PhD; Kevin C. Oeffinger, MD. *Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN, USA; Cancer Prevention and Clinical Statistics Programs, Fred Hutchison Cancer Research Center, Seattle, WA, USA; Department of Radiation Physics, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; Departments of Pediatrics and Medicine, Memorial Sloan-Kettering Center, New York, NY, USA*

**Purpose:** The incidence, severity, and spectrum of chronic health conditions in the fourth and fifth decades of life among survivors of childhood cancer have not been well defined.

**Methods:** Analyses included 14,358 >5 yr survivors of childhood cancer (median age at last follow-up 32.3 yrs, range 8.0-58.0; 21.4% >40 years) and a sibling comparison group (n=4,031). Self-reported health conditions were classified using NCI CTCAE 4.0 grading system. Analyses focused on two primary outcomes: severe/life-threatening/fatal conditions (grades 3-5), and multiple (≥2) conditions. Cumulative incidence of a new chronic health condition was calculated from age 26 yrs. Cox proportional hazards models, adjusted for gender and race, were evaluated using age as the time scale.

**Results:** Among survivors with no previous health conditions through age 25, the cumulative incidence for a new grade 3-5 condition by age 50 compared to siblings was 45.9% (95% CI 45.9-45.9) vs. 13.9%, (95% CI 13.9-14.0) and for new onset of ≥ 2 conditions 33.0% (95% CI 33.0-33.1) vs. 24.9% (95% CI 24.8-24.9) . Survivors ≥40 yrs of age had a 5.8-fold (95% CI 5.3 – 6.5) increased risk of a grade 3-5 condition compared to same age siblings, in contrast to those <40 years of age (HR 2.7, 95% CI 2.5-3.0). In comparison to siblings, survivors >40 years of age had a significantly increased risk for: congestive heart failure (HR 15.7, 95% CI 9.2-26.7), myocardial infarction (HR 8.8, 95% CI 6.0-12.9), stroke (HR 8.6, 95% CI 5.6-13.2), joint replacement (HR 6.8, 95% CI 4.1-11.4), renal failure (HR 5.1, 95% CI 2.2-11.9), among other serious conditions.

**Conclusions:** As they age, adult survivors continue to develop new and serious health conditions at substantially higher rates than siblings. These data emphasize the importance of placing a greater focus on investigations of premature aging and organ senescence in this high risk population.

**14. LONGITUDINAL CHANGES IN HEALTH CARE UTILIZATION BY ADULT SURVIVORS OF CHILDHOOD CANCER IN THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)** Jacqueline Casillas, MD, MSHS; Qi Liu MS; Melissa Hudson, MD; Mark L. Greenberg, MB, ChB; Mark W. Yeazel, MD, MPH; Kirsten Ness PT, PhD; Leslie L. Robison, PhD; Gregory T. Armstrong, MD, MSCE; Wendy Leisenring, ScD; Yutaka Yasui, PhD; Kevin C. Oeffinger, MD; Paul C. Nathan, MD, MSc. *Department of Pediatrics, University of California, Los Angeles, Los Angeles, CA, USA; Department of Public Health Sciences, University of Alberta, Edmonton, Alberta, Canada; Departments of Epidemiology and Cancer Control and Oncology, St. Jude Children's Research Hospital, Memphis, TN, USA; Department of Paediatrics, The Hospital for Sick Children, Toronto, Ontario, Canada; Department of Family Medicine and Community Health, University of Minnesota Medical School, Minneapolis, MN, USA; Departments of Pediatrics and Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA*

**Purpose:** We assessed longitudinal changes in health care utilization in adult survivors of childhood cancer participating in the CCSS.

**Methods:** Utilization at baseline and most recent follow-up was classified into one of three mutually exclusive hierarchical categories: no health care, general medical care, or survivor-focused care. Relative risk (RR) and 95% confidence intervals (CI) were calculated for predictors of reduction in care over time from survivor-focused to general or no care. Multivariable models, adjusted for key treatment exposures, were created to assess risk factors for reductions in level of care over time.

**Results:** Among 8591 eligible survivors, mean age at last follow-up was 35.1 years (SD=7.8) with a mean of 11.6 years (SD=2.2) since baseline. Of 3993 (46%) survivors who reported survivor-focused care at baseline, 2383 (59.7%) reported a lower level of care at

follow-up. Among 4598 (54%) not receiving survivor-focused care at baseline, 915 (20%) reported survivor-focused care at follow-up. Baseline predictors of a decreased level of care were no health insurance (RR=1.5, 95% CI 1.2-1.9), male sex (RR=1.4, 95% CI 1.2-1.6), being 10-19 years from diagnosis compared with 20+ years (RR=1.4, 95% CI 1.1-1.7). Factors associated with a maintenance in survivor-focused care were Canadian residency compared to U.S. residency with insurance (RR=0.7, 95% CI 0.6-0.9), unemployment (RR=0.8, 95% CI 0.7-0.9), physical limitations (RR=0.7, 95% CI 0.6-0.9), cancer-related pain (RR=0.7, 95% CI 0.5-0.8), poor emotional health (RR=0.7, 95% CI 0.5-0.9), having mild-moderate (RR=0.5, 95% CI 0.4-0.6) or severe-disabling chronic health condition (RR=0.6, 95% CI 0.5-0.7).

**Conclusions:** Less than a third of adult survivors of childhood cancer report survivor-focused care. Rates decrease over time. Targeted interventions to maximize survivor-focused care should be tested so risk-reducing opportunities are not lost.

**15. IRON OVERLOAD IN CHILDHOOD CANCER SURVIVORS** K. Reddy, MD; J. Eng, MD, C.A. Carlson, RN, BSN; J. Ginsberg, MD; J.D. Fish, MD *Pediatric Hematology/Oncology and Stem Cell Transplantation, Steven and Alexandra Cohen Children's Medical Center of New York, New Hyde Park, NY, USA; Division of Oncology, Children's Hospital of Philadelphia, Philadelphia, PA, USA*

**Background:** Children with cancer often receive substantial packed red blood cell (pRBC) support. Although transfusion-associated iron overload likely influences morbidity in survivors, the prevalence of iron overload has not been comprehensively examined in this population.

**Purpose:** To determine the prevalence of iron overload in childhood cancer survivors using total pRBC volume received, ferritin, and liver and heart iron.

**Project Description:** Eligible Patients were > 6 years old and had AML, high-risk ALL, Ewing sarcoma, osteosarcoma, rhabdomyosarcoma, neuroblastoma, or received HSCT for malignancy. They were > one year off-therapy and from last pRBC transfusion, and received all therapy at CCMC or CHOP. Diagnosis, age, weight at diagnosis, cumulative chemotherapy received, and total pRBCs transfused were collected from medical records and blood bank databases. Patients receiving > 120ml/kg pRBCs or ferritin > 1,000mcg/L underwent hepatic R2 and cardiac T2* MRI for iron quantification, an ECHO, assessment of liver and endocrine function, and genetic analysis for hereditary hemochromatosis.

**Results:** 73 patients were evaluable to date. Initial labs for all patients included total iron, ferritin, TIBC, and iron saturation. As per study criteria, 45 patients qualified for second-order studies and 32 completed MRI scans. These 32 patients received an average of 8,283ml pRBCs (2,590-25,080mL), 335mL/kg pRBCs (85-819ml/kg), had average ferritin of 639mcg/L (9-2419mcg/L), and hepatic liver iron concentration (LIC) of 4.4mg/g dry weight (0-15.6mg/g). 44% had an LIC > 3mg/g, and 25% > 7mg/g. LIC correlated with both total volume of PRBCs and ferritin (Spearman correlation coefficients = 0.61846 and 0.84031, p-values = 0.0002 and <0.0001).

**Conclusion:** Transfusion-associated iron overload (LIC > 3mg/g) and severe iron overload (LIC > 7mg/g) are prevalent among survivors of childhood cancer. The strong correlation of serum ferritin and LIC suggests that ferritin may be a useful screen in this population for iron overload, a condition that likely contributes to morbidity and is highly treatable.

**16. SYMPTOM PROFILES ASSOCIATED WITH HEALTH-RELATED QUALITY OF LIFE IN ADULT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE ST. JUDE LIFETIME COHORT STUDY** I-Chan Huang, PhD; Kevin Krull, PhD; Leslie Robison, PhD; Melissa Hudson, MD. *Department of Health Outcomes and Policy and Institute for Child Health Policy, College of Medicine, University of Florida, Gainesville, FL, USA; Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN, USA*

**Introduction:** Evidence is limited concerning symptom profiles and their association with health-related quality of life (HRQOL) in long-term childhood cancer survivors. We aimed to investigate this association in adult survivors of childhood cancer (ASCC) enrolled in the St. Jude Lifetime Cohort (SJLIFE) study.

**Methods:** Eligibility criteria for participation in the SJLIFE study include diagnosis of childhood malignancy treated at St. Jude, survival >10 years from diagnosis and current age ≥18 years. Physical and psychological symptoms were self-reported by a health assessment questionnaire. We categorized symptoms into 14 problem areas: body image, sensation, motor/movement, cardiac symptoms, pulmonary symptoms, pain in head, pain in back/neck, pain in other areas, learning/memory problems, somatization, anxiety, depressive symptoms, stress, and self-efficacy. HRQOL was measured using the SF-36, and specific domain and physical/mental component scores (PCS/MCS) were generated. Multivariate regression analysis was performed to investigate associations between symptoms and HRQOL. Cumulative incidence of symptoms for time since diagnosis was estimated.

**Results:** The most prevalent symptoms were pain in other areas (58.7%), followed by body image (56.3%), and pain in back/neck (48.5%). Approximately 60% of ASCC reported >3 symptoms. Greater symptoms were associated with impaired HRQOL across all domains. In multivariate regression analysis, the inclusion of symptoms alone accounted for 61% and 63% of the variance in SF-36's PCS and MCS, respectively, whereas demographic (age, gender, race/ethnicity, and education) and clinical (treatment modality, second cancer, and year since diagnosis) variables only accounted for 2% and 1% of the variance, respectively. Increase in time since diagnosis

was associated with higher cumulative incidence across all symptoms. The 30-year cumulative incidence was 40% for pain in other areas and 40% for body imagine.

**Conclusion/implications:** A great proportion of ASCC suffered from a variety of symptoms, which was associated with impaired HRQOL. Interventions that target specific symptoms may improve ASCC's HRQOL.

**17. RISKS ASSOCIATED WITH LEVELS OF CARE PROPOSED BY THE NATIONAL CANCER SURVIVORSHIP INITIATIVE (NCSI) FOR CHILDHOOD CANCER SURVIVORS** Clare Frobisher, PhD; Adam Glaser, MD; Gill Levitt, MD; Emma R Lancashire, PhD; David L Winter, HNC; Kevin C Oeffinger, MD; Julie S Kelly, Diploma; David J Cutter, FRCR; Raoul C Reulen, PhD; Michael M Hawkins, DPhil; On behalf of the National Cancer Survivorship Initiative (NCSI) and the British Childhood Cancer Survivor Study (BCCSS) Steering Group. *Centre for Childhood Cancer Survivor Studies, School of Health and Population Sciences, University of Birmingham, Birmingham, UK; Paediatric Oncology and Haematology Department, Leeds General Infirmary, Leeds, UK; Department of Haematology/Oncology, Great Ormond Street Hospital for Children NHS Trust, London, UK; Departments of Pediatrics and Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Clinical Trial Service Unit,, University of Oxford, Oxford, UK*

**Introduction:** Extensive restructuring of clinical long term follow-up within the National Health Service (NHS) in England has been proposed as part of the National Cancer Survivorship Initiative (NCSI), evolving from the "one model fits all" philosophy. Using risk stratification, based on cancer type and treatment, survivors are assigned to one of three levels of care ranging from 1 (supported self-management) to 3 (complex, multidisciplinary).

**Aim:** Provide large-scale population-based risks of serious adverse health outcomes associated with the care levels proposed.

**Methods:** Second primary neoplasms (SPNs) and deaths were ascertained by linkage to the NHS Central Registers. Non-fatal non-neoplastic outcomes were evaluated from completed BCCSS questionnaires. Each outcome was graded using the NCI Common Terminology Criteria for Adverse Events, version 3. The cumulative incidence of fatal and non-fatal (≥grade 3) health outcomes of specific types were estimated by the proposed levels of care, separately after acute lymphoblastic leukaemia (ALL) and specific solid tumours.

**Results:** For ALL survivors (n=2,638) categorised to care levels 1, 2 and 3, by 20y from diagnosis: the risk of a SPN was 0.0%, 1.5% and 2.8%; the risk of death from a non-neoplastic cause was 0.0%, 0.1% and 1.0%; the risk of a non-fatal non-neoplastic condition was 5.4%, 9.5% and 13.3%, respectively.

Overall, for solid tumour survivors (n=8,898) according to levels of care of 1, 2 and 3, by 30y from diagnosis: the risk of a SPN was 2.8%, 6.5% and 7.5%; the risk of death from a non-neoplastic cause was 1.5%, 1.6% and 3.3%, respectively. The risk of a non-fatal non-neoplastic condition increased by 9.5%, 12.1% and 22.9% for levels 1, 2 and 3, respectively, between 5y and 35y from diagnosis.

**Conclusion:** This investigation provides clear and strong discrimination in terms of risk between the proposed levels of care.

**18. COST-EFFECTIVENESS OF THE CHILDREN'S ONCOLOGY GROUP (COG) LONG-TERM FOLLOW-UP (LTFU) GUIDELINES IN REDUCING THE RISK OF CONGESTIVE HEART FAILURE (CHF) IN LONG-TERM CHILDHOOD CANCER SURVIVORS (CCS)** F. Lennie Wong, PhD; Smita Bhatia, MD, MPH; Seira Kurian, MD, MS; Wendy Landier, PhD, RN; Liton Francisco, BS; Wendy Leisenring, ScD; Melissa M. Hudson, MD; Gregory T. Armstrong, MD; Ann Mertens, PhD; Marilyn Stovall, PhD; Leslie L. Robison, PhD; Steven E. Lipshultz, MD; Saro Armenian, DO, MPH. *City of Hope, Duarte, CA, USA; Fred Hutchinson Cancer Research Center, Seattle, WA, USA; St. Jude Children's Research Hospital, Memphis, TN, USA; Emory University School of Medicine, Atlanta, GA, USA; The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; University of Miami/Miller School of Medicine, Miami, FL, USA*

**Background:** COG LTFU guidelines use echocardiographic (ECHO) screening for early detection of left ventricular dysfunction (LVD) in anthracycline-exposed CCS, recommending ECHOs at a frequency ranging from 1-5y depending on anthracycline dose, chest radiation therapy (RT), and age at diagnosis. The cost-effectiveness of these consensus-based guidelines is unknown.

**Methods:** Life expectancy and age at CHF onset were projected in a simulated cohort of anthracycline-exposed CCS undergoing ECHO screening per COG LTFU guidelines stratified on age at diagnosis (1-4y; ≥5y), RT, and anthracycline dose. The hypothetical intervention for LVD (enalapril) was modeled to reduce annual CHF risk by 30%. Quality-adjusted life-years (QALYs) and lifetime costs with and without ECHO screening were calculated. Non-CHF mortality was estimated from the Childhood Cancer Survivor Study and US population rates. CHF incidence and mortality were derived from the extant literature. Costs (2010 US$) and quality-of-life adjustments were obtained from the Healthcare Cost and Utilization Project and medical literature. Screening was considered cost-effective if it resulted in a >6 month delay in CHF onset and <$50,000 per QALY gained.

**Results:** Recommended screening strategies (Table) were cost-effective in: i) CCS exposed to ≥300mg/m$^2$ of anthracyclines regardless of RT or age at diagnosis; and ii) CCS diagnosed at age 1-4y, exposed to RT and <300mg/m2 of anthracycline. Screening was most cost-effective for CCS diagnosed at age 1-4y exposed to RT and ≥300 mg/m2 of anthracycline (1.4y delay in CHF onset; $15,821 per QALY gained). Screening strategies were ineffective for other age/anthracycline-dose/RT combinations.

Conclusions: Recommended ECHO screening strategies are cost-effective for CCS exposed to ≥300 mg/m$^2$ of anthracycline irrespective of age or RT; among 1-4y-olds, screenings are also cost-effective for CCS exposed to <300 mg/m2 of anthracycline and RT. Alternate cost-effective screening strategies are needed for CCS with other exposure conditions.

| COG screening guidelines | | | | Cost-effectiveness results | |
|---|---|---|---|---|---|
| Age Dx | Chest RT | Anthracycline dose (mg/m$^2$) | Recommended ECHO interval (years) | Delay in CHF onset age (years) | Cost per QALY gained (2010 US$) |
| 1-4 years | Yes | Any | 1 | 1.08 | $30,048 |
| | | <300 | 1 | 0.79 | $49,750 |
| | | ≥300 | 1 | 1.44 | $15,821 |
| | No | <100 | 5 | 0.35 | $17,798 |
| | | 100 to < 300 | 2 | 0.36 | $29,415 |
| | | ≥300 | 1 | 1.17 | $25,065 |
| ≥5 years | Yes | <300 | 2 | 0.38 | $36,874 |
| | | ≥300 | 1 | 0.80 | $28,093 |
| | No | < 200 | 5 | 0.13 | $50,750 |
| | | 200 to <300 | 2 | 0.24 | $86,867 |
| | | ≥300 | 1 | 0.72 | $36,401 |

**19. LONGITUDINAL CHANGES IN BODY MASS INDEX AND BODY COMPOSITION AMONG 417 ADULT SURVIVORS OF CHILDHOOD CANCER** K. Blijdorp, MD; M.M. van den Heuvel-Eibrink, MD, PhD; R. Pieters, MD, PhD; A.M. Boot, MD, PhD; A.J. van der Lely, MD, PhD; S.J.C.M.M. Neggers, MD, PhD. *Department of Pediatric Oncology/Hematology, and Endocrinology Section, Department of Medicine, Erasmus MC–University, Rotterdam, The Netherlands; Department of Pediatric Endocrinology, University Medical Center Groningen (UMCG),The Netherlands*

**Introduction:** Obesity, represented by high body mass index (BMI), is a major complication after treatment for childhood cancer. High amount of total and visceral fat and low lean body mass are described as more reliable determinants, predicting the development of cardiovascular disease. In this study longitudinal changes of BMI and body composition in adult childhood cancer survivors were evaluated.

**Methods:** Data of 417 adult childhood cancer survivors, who had visited the late effects clinic twice, were analyzed retrospectively. Median follow up time was 16 years (interquartile range 11-21) and time between visits was 3.2 years (2.9-3.6). At both time points BMI was measured and body composition was assessed by dual X-ray absorptiometry (Lunar Prodigy). BMI and body composition measures were compared with those of healthy Dutch references and calculated as standard deviation scores (SDS). Pituitary dysfunction and hormonal replacement were evaluated in all survivors. Nineteen growth hormone deficient subjects treated with growth hormone replacement at time of follow up were excluded from further analyses.

**Results:** BMI SDS at first assessment was only significantly higher in female cranial radiotherapy (CRT) survivors as compared to healthy Dutch references (SDS=0.40, p=0.02). Increase of BMI over time (expressed as units per year) was only significantly higher in male survivors (0.27 versus 0.02 in controls (p<0.001)). Percentage fat was significantly higher than controls in both men (SDS 1.37, P<0.001) and women (SDS 1.05, P<0.001) in all therapy groups, with the highest SDS after CRT (mean SDS 1.73 in men, 1.48 in women, P<0.001). Only in men, increase in total fat percentage was significantly higher as compared to controls (ΔSDS=0.22, P<0.001). Lean body mass did not significantly change over time.

**Conclusion:** Adult survivors of childhood cancer, especially men, show a faster increase in BMI and total fat percentage as compared to the normal population.

**20. ATHEROGENIC LOW DENSITY LIPOPROTEIN (LDL) PHENOTYPE IN LONG-TERM SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA** Jyoti Malhotra, MD MPH; Emily S. Tonorezos, MD MPH; Marina Rozenberg, MD; Gloria L. Vega, PhD; Charles A. Sklar, MD; Joanne Chou, MPH; Chaya Moskowitz, PhD; Robert Ross, PhD; Peter Janiszewski, MPH; Kevin C. Oeffinger, MD. *Memorial Sloan-Kettering Cancer Center, New York, NY, USA; University of Texas Southwestern Medical Center, Dallas, TX, USA; Queen's University, Kingston, Ontario, Canada*

**Introduction:** Childhood acute lymphoblastic leukemia (ALL) survivors have increased risk of coronary artery disease. Small density lipoproteins (sdLDL) are atherogenic and have not been studied in this population.

**Aims:** 1) Determine prevalence of sdLDL phenotype in ALL survivors, and identify associated treatment factors. 2) Assess relationship between different measures of body fat and sdLDL.

**Methods:** We conducted a cross-sectional analysis of 110 ALL survivors (median age, 23.5 years). Lipid sub-fractions were measured with Vertical Auto Profile-II (Atherotech, Birmingham, AL). Patients with >50% of LDL-c in sdLDL fractions ($LDL_{3+4}$) were classified as having atherogenic pattern. Visceral and subcutaneous adipose tissue (VAT, SAT) volumes were measured by abdominal CT. Analyses were adjusted for age, gender, smoking and hypertension. Fischer's exact test and multivariate linear regression were used for statistical analyses.

**Results:** While the mean LDL-c was 108.7±26.8 mg/dl, 36.4% (40/110) ALL survivors had the atherogenic pattern. Atherogenic pattern was more common in males (26/47) than females (14/63; 55.3% vs 22.2%; P=0.01). Among the 32.7% (36/110) survivors who had a normal body mass index (BMI: 18.5 to 24.9 kg/m$^2$), 11.1% (4/36) had an atherogenic pattern. In contrast, among the 67.3% (74/110) survivors with BMI ≥25 kg/m$^2$, 48.7% (36/74) had an atherogenic pattern (P=<0.001). Visceral pattern of obesity (VAT/SAT ratio≥0.4) was associated with the atherogenic phenotype (14/19, 73.7%) as compared to those without visceral pattern of obesity (24/85, 28.2%; P=0.03). In a linear model including all survivors, VAT was strongly associated with $LD_{L3+4}$ (sdLDL), $\beta$=0.1; 95% CI 0.04-0.1; p<0.001. Controlling for BMI, waist circumference or SAT did not yield any additional information about the variation in $LDL_{3+4}$ with increasing VAT.

**Conclusion:** We report a high prevalence of atherogenic phenotype in ALL survivors. Prevalence of atherogenic pattern in young adults in the general population is 7.5% in females and 22.9% in males (Watson TD, Arterioscler Thromb, 1994). Further studies are warranted to elucidate underlying mechanisms associated with the development of sdLDL phenotype in this population.

**21. DIETARY INTAKE AND METABOLIC SYNDROME IN ADULT SURVIVORS OF CHILDHOOD CANCER** Webb Smith, MS; Chenghong Li, PhD; Kerri Nottage, MD; Jenny Lanctot, PhD; Melissa Hudson, MD; Daniel Green, MD; Vikki Nolan, DsC; Joseph Laver, MD; James Gurney, PhD; Leslie Robison, PhD; Kirsten Ness, PhD. *St. Jude Children's Research Hospital, Memphis, TN, USA; University of Memphis, School of Public Health, Memphis, TN, USA*

**Introduction:** Childhood cancer survivors (CCS) are at increased risk for metabolic syndrome (MetSyn) and increased morbidity and mortality from cardiovascular disease. Following a heart healthy diet may decrease this risk. The purpose of this investigation was to characterize dietary patterns and to evaluate the association between diet and MetSyn among CCS.

**Methods:** CCS who were 10$^+$ year survivors of childhood cancer, who were older than 18 years of age, and participating in the St. Jude Lifetime Cohort Study (SJLIFE). They completed a medical assessment based on Children's Oncology Group screening guidelines, and a food frequency questionnaire (FFQ). Laboratory and physical measures were obtained to determine MetSyn status using the NCEP-ATPIII criteria. Participants were classified as having MetSyn if they met the criteria for ≥3 components of MetSyn. Data from the FFQ were used to score dietary patterns according to WCRF/AICR recommendations. Those who met ≥4 of the 7 recommendations were classified as following a "healthy diet." A stratified analysis by sex using log-binomial regression models was undertaken to evaluate associations between diet and MetSyn, adjusted for age, age at diagnosis, cranial radiation, education, household income, and smoking status.

**Results:** Among 1421 participating CCS (49.3% male, median age 33.0 years, range, 18.9-60.0 years), 31.5% met the criteria for MetSyn and 25.8 % followed a healthy diet according to the WCRF/AICR recommendations. In multiple regression models stratified by sex, females who followed a "healthy diet" were 2.1 (95% CI 1.5-2.9) times less likely and males who followed a "healthy diet" were 2.2 (95%CI 1.5-3.1) times less likely to have MetSyn than those who reported following a "healthy diet".

**Conclusion:** Heart healthy diets in CCS are associated with decreased risk for MetSyn. Dietary interventions may be warranted in CCS with MetSyn.

**22. VALVULAR DISEASE DETECTED BY ECHOCARDIOGRAPHY IN 5-YEAR SURVIVORS OF CHILDHOOD CANCER: A LONG-TERM FOLLOW-UP STUDY** Helena J. van der Pal, MD PhD; Irma W. van Dijk, MSc; Elvira C. van Dalen, MD PhD; Marianne Koolen, MD; E.Sieswerda, MD MSc; Wouter E. Kok, MD PhD; Ronald B. Geskus, MSc PhD; Foppe Oldenburger, MD PhD; Caro C. Koning, MD PhD; Flora E. van Leeuwen, MSc PhD; Huib N. Caron, MD PhD; Leontien C. Kremer, MD PhD. *Departments of Medical Oncology, Pediatric Oncology, Radiation Oncology, Cardiology, Clinical Epidemiology, and Biostatistics and Bioinformatics, Emma Children's Hospital/Academic Medical Centre, Amsterdam, The Netherlands; Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands*

**Purpose:** To determine the prevalence of valvular disease after radiotherapy involving the heart region and/or treatment with anthracyclines and to identify associated risk factors in a large cohort of 5-year childhood cancer survivors (CCS).

**Patients and methods:** The study cohort consisted of all eligible 5-year CCS diagnosed between 1966 and 1996 in the Emma Children's Hospital/Academic Medical Center with childhood cancer and treated with radiotherapy involving the heart region and/or with anthracyclines. Echocardiograms were performed in CCS who visited our late effects outpatient clinic. We used multivariate logistic regression analyses to examine the association between treatment and valvular disease.

**Results:** We identified 225 echocardiographic valvular abnormalities in 169 survivors (31%) of 545 CCS with a cardiac assessment after a median follow-up time of 14.9 years (range 5.1-36.8) and at a median attained age of 22.0 years (range 7.0-49.7). Most common were tricuspid valve disorders (N=119; 21.8%) and mitral valve disorders (N=73; 13.4%). In the multivariable logistic regression models, development of a valvular abnormality was associated with higher cardiac irradiation dose (OR 1.44), irradiation fields involving the heart region, namely thoracic (OR1.60), and total body irradiation (OR 2.23) and congenital heart disease (OR 3.79).

**Conclusions:** Almost one third of CCS has developed one or more relevant valvular abnormalities after a median follow-up of nearly 15 years. The most important risk factors for developing a valvular abnormality are higher cardiac irradiation dose (especially thoracic irradiation, and TBI), and CHD.

**23. PREDICTING CARDIOVASCULAR DISEASE AFTER CANCER: A CHILDHOOD CANCER SURVIVOR STUDY REPORT** Eric J. Chow, MD, MPH; Yan Chen, MSc; Gregory T. Armstrong, MD, MSCE; K. Scott Baker, MD, MS; William L. Border, MBChB, MPH; Lillian Meacham, MD; Kathleen A. Meeske, PhD; Daniel A. Mulrooney, MD, MS; Kevin C. Oeffinger, MD; Charles A. Sklar, MD; Marilyn Stovall, PhD; Leslie L. Robison, PhD; Yutaka Yasui, PhD. *Fred Hutchinson Cancer Research Center, Seattle, WA, USA; Children's Hospital, University of Washington, Seattle, WA, USA; University of Alberta, Edmonton, Alberta, Canada; St. Jude Children's Research Hospital, Memphis, TN, USA; Children's Healthcare of Atlanta, Emory University, Atlanta, GA, USA; Children's Hospital of Los Angeles, University of Southern California, Los Angeles, CA, USA; Memorial Sloan-Kettering Cancer Center, New York, NY, USA; The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA*

**Background:** Various factors are associated with an increased risk of cardiovascular (CV) disease among childhood cancer survivors at the population level. Models that combine selected risk factors to estimate an individual's probability of developing such complications would be clinically important.

**Methods:** Cohort study of 14,138 childhood cancer survivors diagnosed 1970-1986, free of CV disease at cohort entry 5 yrs from cancer diagnosis, and followed through 2009. Poisson regression models estimated the risk of developing subsequent severe/life-threatening 1) congestive heart failure (CHF), 2) coronary heart disease (CHD), and 3) CV-related death, in association with sex, ethnicity, cancer diagnosis age, and select chemotherapy and radiotherapy exposures. Discrimination was assessed via the concordance (c) index.

**Results:** Over a median follow-up of 19 yrs (range 0-34), the cohort experienced 312 (2.2%) CHF, 285 (2.0%) CHD, and 132 (0.9%) CV-related deaths. The magnitude of associations with selected factors varied by outcome (Table), but included female sex (CHF), older diagnosis age (CHD, CV-related death), increased anthracyclines (CHF, CV-related death), increased chest radiotherapy (all outcomes), and any neck (CHF) or abdominal radiotherapy (CHD). Overall, models predicting CHF, CHD, and CV-related death risk at 30 yrs after cancer diagnosis had excellent discrimination (c index 0.81, 0.80, and 0.79, respectively). C indices of models based on the same factors for outcomes at 15 yrs varied only by 0.01.

**Conclusions:** Readily available clinical factors predicted individual risk of CHF, CHD, and CV-related death in childhood cancer survivors with good discrimination 30 yrs after diagnosis. If validated in other populations, this may lead to more personalized long-term surveillance and counseling of survivors.

| Predictive factors | Congestive heart failure | | Coronary heart disease | | Cardiovascular related death | |
|---|---|---|---|---|---|---|
| | RR | 95% CI | RR | 95% CI | RR | 95% CI |
| Female | 1.6 | 1.3-2.1 | 0.8 | 0.6-1.0 | 0.8 | 0.6-1.2 |
| Diagnosis age | | | | | | |
| <5 (ref) | | | | | | |
| 5-9 | 1.0 | 0.7-1.5 | 2.2 | 1.4-3.7 | 1.2 | 0.6-2.5 |
| 10-14 | 1.0 | 0.7-1.4 | 2.5 | 1.6-4.2 | 1.7 | 0.9-3.2 |
| ≥15 | 1.1 | 0.8-1.6 | 5.1 | 3.2-8.2 | 2.4 | 1.3-4.6 |
| Anthracycline*, mg/m$^2$ | | | | | | |
| None (ref) | | | | | | |
| <100 | 1.7 | 0.6-4.8 | | | 0.7 | 0.1-5.3 |
| 100-299 | 3.5 | 2.4-5.1 | | | 1.8 | 1.0-3.2 |
| ≥300 | 8.3 | 6.1-11.3 | | | 3.0 | 1.8-4.9 |
| Radiotherapy field | | | | | | |
| Chest, Gy | | | | | | |
| <1 (ref) | | | | | | |
| 1-9 | 0.8 | 0.5-1.4 | 1.0 | 0.5-1.8 | 1.1 | 0.5-2.7 |
| 10-19 | 1.8 | 1.1-3.0 | 1.7 | 0.9-3.5 | 2.0 | 0.7-5.8 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 20-34 | 1.7 | 1.0-2.7 | 2.8 | 1.8-4.4 | 2.8 | 1.3-5.8 |
| ≥35 | 3.9 | 2.5-6.1 | 5.1 | 3.5-7.5 | 8.8 | 5.2-14.7 |
| Neck, any* | 2.1 | 1.4-3.1 | | | | |
| Abdomen, any* | | | 1.5 | 1.1 - 2.1 | | |

*Only estimates meeting model selection criteria shown

**24. CARDIOVASCULAR DISEASE IN ADULT LIFE AFTER CHILDHOOD CANCER IN SCANDINAVIA (ALICCS)—A LARGE POPULATION-BASED PATIENT COHORT** Thorgerdur Gudmundsdottir, MD; Jeanette Falck Winther, MD; Klaus Kaae Andersen, MSc, PhD; Henrik Hasle, Professor, MD, PhD; Jørgen H Olsen, MD, DMSc. *Danish Cancer Society Research Center, Survivorship Unit, Copenhagen, Denmark; Aarhus University Hospital Skejby, Department of Paediatrics, Aarhus, Denmark*

**Introduction:** Major improvements of treatment resulting in a growing population of childhood cancer survivors have increased the awareness of adverse long-term sequelae of the life-saving treatments. In a large population-based study, we assessed the risk for cardiovascular disease in childhood cancer survivors, thus avoiding some of the shortcomings of previous studies.

**Patients and methods:** Hospitalizations for cardiovascular disease were evaluated in a cohort of 19,887 childhood cancer survivors and 126,061 population comparisons from Denmark, Iceland and Sweden. The nationwide cancer registries, central population registries and hospital registries were used to identify cancer patients, comparisons and hospitalizations. Survivors were diagnosed with cancer below age 20 and recruited from beginning of cancer registration in the 1940s through 2010. Cohort members were followed-up individually for cardiovascular diseases through register linkages and hospitalization rate ratios (HRRs) for selected cardiac outcomes in survivors were calculated using a Cox proportional hazards model with population comparisons as referent.

Results: Preliminary results show that survivors were significantly more likely to be diagnosed with ischemic heart disease (HRR 1.63, 95% CI 1.44-1.84, based on 308 survivor cases), heart failure (HRR 3.71, 3.36-4.09; 596 cases), cardiomyopathy (HRR 1.67, 1.50-1.87; 389 cases), valvular abnormality (HRR 4.25, 3.56-5.08; 190 cases) and cerebrovascular incidents (HRR 2.36, 2.04-2.73; 240 cases) than comparisons.

In general the highest risk was observed among survivors diagnosed in the youngest age group, the most recent treatment period and in those with hematologic cancers. The probability of being hospitalized for cardiovascular diseases continued to be higher among survivors than comparisons in the total follow-up period even >30 years since diagnosis.

**Conclusions:** Survivors of childhood cancer are at substantial risk for cardiovascular disease compared to the general population. Awareness of this excess risk is important for clinicians and the growing survivor population, and essential for optimizing patient counselling and follow-up care.

# Posters

**25. USE OF THE N-BACK TASK TO ASSESS WORKING MEMORY IN SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA** Joshua Luxton, Tara Brinkman, PhD; Cara Kimberg, PhD; Ching-Hon Pui, MD; Deo Kumar Srivastava, PhD; Melissa M. Hudson, MDI; Kevin R. Krull, PhD. *Departments of Epidemiology and Cancer Control, Oncology, and Biostatistics, St. Jude Children's Research Hospital, Memphis, TN, USA*

**Objective:** The N-Back task is often used in functional brain imaging studies to activate working memory networks, albeit its association with clinical outcomes has not been well studied in children. The purpose of this study was to compare performance on the N-Back to clinical indices of working memory, attention and processing speed in survivors of childhood acute lymphoblastic leukemia (ALL), who are at increased risk for impairment in these processes.

**Participants and methods:** Long-term survivors of childhood ALL (N=70; mean [SD] age=14.4 [4.7] years; mean time since diagnosis=6.4 [4.2] years) completed the N-Back task and clinical measures, including digit span, spatial span and the continuous performance test (CPT-II). Performance on the N-Back was compared to clinical measures and potential risk factors such as age, sex, and treatment intensity.

**Results:** Performance on the N-Back task was associated with digit span ($r=0.46$, $p=0.04$) and spatial span ($r=0.57$, $p=0.009$), albeit only in survivors $\geq$ 17 years of age. For survivors $<$ 17 years of age, performance on the N-Back was more closely associated with indices of sustained attention ($r=0.59$, $p=0.001$). Females demonstrated slower reactions times for 0- ($p=0.04$), 1- ($p=0.04$), and 2-Back tasks ($p=0.001$). Survivors diagnosed $<$ 6 years of age demonstrated worse performance on 0- ($p=0.04$), 1- ($p=0.006$), and 2-Back tasks ($p<0.001$). Treatment intensity was unrelated to N-Back performance.

**Conclusions:** Reduced performance on the N-Back is associated with common neurocognitive risk factors in survivors of ALL. However, the task appears to assess different constructs at different ages and, thus, further research is recommended.

**26. CONTENT AND CONCURRENT VALIDITY OF THE CHILDHOOD CANCER SURVIVOR STUDY-NEUROCOGNITIVE QUESTIONNAIRE: A REPORT FROM THE ST. JUDE LIFETIME COHORT (SJLIFE)** Kelly M. Kenzik, MS; I-Chan Huang, PhD; Tara Brinkman, PhD; Elizabeth A. Shenkman, PhD; Leslie L. Robison, PhD; Melissa M. Hudson, MD; Kevin R. Krull, PhD. *Department of Health Outcomes and Policy, and Institute for Child Health Policy, College of Medicine, University of Florida, Gainesville, FL, USA; Departments of Epidemiology and Cancer Control and Oncology, St. Jude Children's Research Hospital, Memphis, TN, USA*

**Objective:** Childhood cancer survivors are at risk of developing neurocognitive impairment, though monitoring such risk over time is often difficult. This study aimed to refine and further validate the CCSS-NCQ as a screening tool for use with long-term survivors.

**Method:** Data were collected from adult survivors of childhood cancer enrolled in the St. Jude Lifetime Cohort study (SJLIFE; n=833) who completed the CCSS-NCQ, the Behavior Rating Inventory of Executive Function (BRIEF), and who received a clinical neurocognitive assessment. The following steps were performed to refine and further validate the CCSS-NCQ: 1) establishment of content validity by mapping items from the CCSS-NCQ and BRIEF to common domains (memory, task efficiency, organization, and emotional regulation); 2) assessment of construct validity of the revised CCSS-NCQ; and 3) equating and selecting items within a specific domain using Item Response Theory (IRT) methodology. We evaluated known-groups validity of the revised CCSS-NCQ based on clinical neurocognitive assessments. We then identified clinical and demographic variables associated with each domain using multiple linear regression.

**Results:** Based on content and measurement properties, 32 items were retained (8 items in each domain of the revised CCSS-NCQ). IRT results suggested items in each domain were able to capture low to average levels of functioning. Impairment classification effect sizes (ES) for the CCSS-NCQ memory domain were large for direct assessment of short-term (ES=0.54) and long-term memory (ES=0.64). For the task efficiency domain, effect sizes were large for direct assessment of focused attention (ES=0.72), cognitive fluency (ES=0.73), and attention span (ES=0.54). Effect sizes for the organization and emotional regulation domains were moderate for multiple direct measures of executive function. The impact of cranial radiation on impairment was strong for memory ($p=0.001$), task efficiency ($p<0.001$) and emotional regulation ($p=0.008$) domains of the revised CCSS-NCQ.

**Conclusion:** The revised CCSS-NCQ demonstrates improved measurement properties for assessment of neurocognitive functioning, with good to excellent agreement with related direct assessment measures.

**27. BENEFITS ON BEHAVIOR AND HEALTH-RELATED QUALITY OF LIFE (HRQL) IN CHILDHOOD BRAIN TUMOR (BT) SURVIVORS RECEIVING DONEPEZIL** SM Castellino; JA Tooze; L Flowers; E Shaw; SK Parsons. *Wake University Health Sciences, Departments of*

*Pediatrics, Public Health Sciences, Neurology, and Radiation Oncology, Wake Forest University School of Medicine, Winston-Salem, NC, USA; Tufts University School of Medicine and Tufts Medical Center, Boston, MA, USA*

**Purpose:** To evaluated the impact of the acetylcholinesterase (AChe) inhibitor donepezil on behavior and HRQL in pediatric brain tumor (BT) survivors at risk for neurocognitive dysfunction.

**Project description:** A single institution open-label pilot study was conducted in childhood BT survivors who were > 1 year from cancer treatment and had received > 23.5 Gy cranial radiation therapy (RT). In addition to a thorough neurocognitive battery, parents reported on the child's behavior (Behavior Assessment System for Children, Second Edition (BASC-2)) and HRQL (PedsQL™) at baseline and serially during 24 weeks of donepezil. Changes were estimated using a longitudinal mixed model adjusted for age at radiation and baseline IQ. Changes are expressed as effect size (ES) based on the adjusted change in t score from baseline to 24 weeks divided by the population standard deviation.

**Results:** From a pool of subjects, 13 were successfully contacted and screened, and 11 were eligible to initiate donepezil at a median of 4.7 (1.9-11.9) years from RT. Parent report by the BASC-2 indicated improvements within the externalizing domain with a drop in conduct problems from baseline to week 24 (ES = -0.69, p = 0.01). There was also significant improvement in Internalizing problems (ES = -0.87, p = .02), reflecting decreases in anxiety (ES = -1.0, p = .02). Atypicality symptoms improved (ES= -0.66; p = 0.05). The adaptive skills composite showed improvement as well (ES. = 0.40; p = 0.04); functional communication improved significantly at 24 weeks relative to baseline (ES = 0.52, p=0.02). Changes in emotional functioning on the PedsQL™ will be forthcoming.

**Conclusions:** We have recently shown that donepezil is well tolerated and has benefits on executive function and memory performance among childhood BT survivors who received substantial prior therapy. We now show correlative parent-reported outcomes, indicating the functional benefits of this intervention.

### 28. THE UTILITY OF GLUTAMATE ANTAGONISTS FOR THE PREVENTION OR REVERSAL OF CHEMOTHERAPY-INDUCED COGNITIVE DYSFUNCTION

Peter D. Cole, MD; Veena Vijayanathan, PhD; Yan Li, PhD; Nafeeza Ali, Maria Gulinello, PhD. *Albert Einstein College of Medicine, Bronx, NY, USA*

**Purpose:** Previous preclinical and translational work from our laboratory suggests intrathecal methotrexate contributes to cognitive deficits among leukemia survivors by causing a persistent increase in excitotoxic glutamate analogs within the central nervous system. We therefore sought to test whether glutamate receptor antagonists could reverse or prevent methotrexate-induced cognitive dysfunction.

**Methods:** Clinically relevant doses of methotrexate were administered intrathecally to healthy rats, four times over two weeks, a schedule we have shown to induce persistent deficits in visual and spatial memory. Using this model, the efficacy of glutamate receptor antagonists to prevent or reverse cognitive deficits was tested.

**Results:** CSF concentrations of the excitotoxic glutamate analogs homocysteic acid and homocysteine sulfinic acid were increased relative to baseline for three months following the last intrathecal injection. Dextromethorphan, a noncompetitive NMDA antagonist did not prevent methotrexate-induced cognitive dysfunction at the dose and schedule used in our experiments. However, when given one month after the final methotrexate treatment, dextromethorphan restored normal memory function among rats with deficits. Although this improvement was transient, each repeated treatment with dextromethorphan was followed by normalization of cognitive function. No deleterious effects on memory were observed among control rats given intrathecal injections of artificial CSF followed by dextromethorphan. We are continuing to explore alternate therapeutic strategies to prevent cognitive toxicity in our animal model.

**Conclusions:** NMDA receptor antagonists can reverse persistent cognitive deficits, although deficits reappear when the antagonist is withdrawn. We are currently developing a clinical trial piloting the use of an oral NMDA antagonist among leukemia survivors with identified cognitive deficits. Alternate glutamate receptor antagonists and/or administration schedules may prove more effective at preventing the development of cognitive deficits among children treated for leukemia.

### 29. EARLY CHANGES IN SPECIFIC NEUROPSYCHOLOGICAL FUNCTIONS AND QUALITY OF LIFE IN CHILDREN WITH CNS TUMORS: PRELIMINARY RESULTS UP TO 24 MONTHS POST-RADIATION

Pam Wolters, PhD; Staci Martin, PhD; Mary Anne Toledo-Tamula, MA; Robyn Bent, RN, BSN; Kathy Warren, MD. *Pediatric Oncology Branch (POB), National Cancer Institute (NCI), National Institutes of Health, Bethesda, MD, USA; Clinical Research Directorate/CMRP, SAIC-Frederick, Inc., NCI-Frederick, Frederick, MD, USA*

**Background:** Radiation therapy (RT) is an integral part of treatment for pediatric brain tumors, but it is associated with long-term cognitive deficits. This study seeks to identify patterns of change in specific neuropsychological (NP) functions and quality of life (QOL) in children with CNS tumors after RT.

**Methods:** Children with any primary CNS tumor, ages <21 years, treated with standard RT, were eligible. Patients received NP evaluations prior to and 6 and 24 months post RT assessing specific cognitive functions, depression/anxiety, and QOL. Forty-three children

obtained baseline evaluations to date; 12 with pontine gliomas were excluded. Repeated measures ANOVAs were used to examine changes over time.

**Results:** Among 31 children (mean age=9.47 years, 3-16; 68% males), all selected mean cognitive and emotional scores were in the Average range. No significant changes were found from baseline to 6 months (n=22) or 6- and 24-months (n=13) post-RT on digit span, continuous performance test (CPT) omission errors, verbal learning composite/delayed recall, or Trails cognitive flexibility mean scores. Worsening mean scores were found on Symbol Search (processing speed) from baseline to 6-months ($p<.05$) and on CPT commission errors (attention) from 6- to 24-months ($p<.05$). Improvements were found on the Behavior Assessment System for Children-II-Parent depression subscale (baseline-6 months; $p<.05$) and overall QOL rated by parents (baseline-6-24 months; $p<.05$). Radiation dose was associated with 24-month BASC-II-P Attention subscale scores ($p<.05$).

**Conclusions:** Overall cognitive and emotional functioning are within normal limits. Mean test scores indicated stable cognitive functioning to 24 months post-RT except for visual processing speed and attention. Depressive symptoms lessened while QOL increased, likely related to the acute effects of RT and diagnosis that dissipated over time. Radiation dose is associated with attention ratings. Future directions include analyzing data to 36-months, examining factors affecting outcome, and exploring relationships of biomarkers to specific NP domains..

**30.** DEVELOPMENT OF A MULTICULTURAL COMPREHENSIVE PSYCHOEDUCATIONAL PROGRAM FOR SCHOOL-AGE SURVIVORS of ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) Laura Bava, PsyD; Sharon H. O'Neil, PhD; Betty-Gonzalez-Morkos, PsyD; Lisl Schweers, LCSW; Maki Okada, RN, MS, CPNP; Kathy Ruccione, MPH, RN, FAAN; Ernest Katz, PhD; David R. Freyer, DO, MS *Children's Center for Cancer and Blood Diseases at Children's Hospital Los Angeles and Keck School of Medicine at University of Southern California, Los Angeles, CA, USA*

**Purpose:** Children treated for ALL are at increased risk for poor academic achievement. Traditionally, research has emphasized assessing cognitive treatment effects rather than actual academic placement and functioning, parental efficacy and multicultural considerations. Our study examines the feasibility and preliminary outcomes of a multicultural model that combines psychoeducational assessment, parental advocacy training and academic intervention for pediatric ALL survivors.

**Methods:** Our interdisciplinary team developed a model for English and/or Spanish-speaking survivors of childhood ALL to (1) screen for neurocognitive/academic risk factors, (2) evaluate school-related parental knowledge and efficacy, (3) provide personalized interventions and parent advocacy training, and (4) evaluate early outcomes and service satisfaction. Bilingual instrumentation, educational materials and an intervention manual were developed. Using project criteria, participants are assigned either to standard or tailored intervention based on composite results of screening measures. The target population for this intervention is school-aged survivors of ALL undergoing initial evaluation in the LIFE Survivorship & Transition Program at Children's Hospital Los Angeles.

**Results:** Over a 10-month period, the project model, instruments, and intervention were developed and implemented. 22 patient-parent dyads have been recruited to date. Mean patient age is 12 years (range, 5-20). 11 (50%) are female; 16 (72%) are Hispanic. Mean interval post-treatment is 2.7 years (range, 0.7-7.0). 7 (31%) parents are monolingual in Spanish. 19 parents completed a project-specific parental school-related knowledge measure and 11 children have completed psychoeducational academic screening. 9/11 (82%) needed tailored, in-depth intervention. Satisfaction with content and culturally-sensitive presentation is high.

**Conclusions:** Our preliminary results substantiate that pediatric ALL survivors are at risk for adverse educational outcomes, and highlight the importance of other determinants including language, acculturation, parental knowledge/efficacy, and socioeconomic status. This study is expected to contribute to a more informed understanding of risk and effective interventions necessary for improving academic outcomes for this population.

**31. NEUROCOGNITIVE OUTCOMES AND SCHOOL PERFORMANCE IN SOLID TUMOR CANCER SURVIVORS** Caroline Mohrmann, RN, MSN, CPNP; Jennifer Henry, BA; Nicole Cruz, PhD; Marnie Hauff, BA; Robert J. Hayashi, MD. *Washington University School of Medicine, and St. Louis Children's Hospital, St. Louis, MO, USA*

**Purpose:** School performance in patients who have received therapy for childhood cancers has been studied in depth. Risk factors have historically included cranial radiation, intrathecal chemotherapy and high doses of chemotherapy including methotrexate and cytarabine. Patients without such risk factors would be expected to achieve normal school performance. It would be important to identify other additional variables that may impact these patients. Identification of such risk factors would target patients who would be in need of academic support.

**Summarized description of project:** We examined the medical records of 58 pediatric solid tumor patients whom lacked CNS therapy or other risk factors to evaluate the incidence of reported difficulties or abnormalities in neuropsychological testing. We included

positive responses to any of the following items: parent report of school difficulties, failed grade level, having a 504 plan, having an IEP, and deficiencies noted on neuropsychological examinations.

**Results:** Thirty-one percent of patients were found to have at least one positive response. Of note, 34% of patients with Wilms tumor possessed difficulties compared to 23% of patients with other solid tumors. The mean age of this population at diagnosis was 2.34 years, suggesting that a young age at diagnosis may be a contributing factor as described by other investigators. Statistical analysis failed to identify specific risk factors due to the small sample size. This observed incidence is in contrast to U.S. Department of Education statistics from 2008-2009, where 8% of students nationwide were considered to have specific learning disabilities, intellectual disabilities, other health impairments, or developmental delays.

**Conclusion:** Solid tumor cancer survivors without known risk factors for school performance difficulties appear to have a high incidence of problems. Further study of this patient population is needed and care providers should be sensitive to the potential needs of this population.

**32. PERCEPTUAL REASONING, VISUAL MEMORY AND PROCESSING SPEED IN SURVIVORS OF PEDIATRIC BRAIN TUMOURS, COMPARISON BETWEEN SUPRA AND INFRATENTORIAL LOCATION** Adriana González, Marcela Palladino, Daniel Alderete, Lucía Salvia, Liliana Bin, Héctor Waisburg. *Departments of Interdisciplinary Clinics, Pediatrics, Hematology-Oncology, and Mental Health, Pediatric Hospital Prof. Dr. J. Garrahan, Buenos Aires, Argentina*

**Purpose:** Pediatric brain tumour patients are at risk for neurocognitive sequelae following treatment. Location of tumour is critical as each structure is related with different functions.The aim of this study is to compare the neurocognitive profile of school-age patients survivors of infra and supratentorial brain tumours and analyze potential risk factors.

**Methodology:** Comparative cross-sectional study. Cognitive assessment (selected tests from WISC IV and TOMAL) was performed at median of 43.5 months (2 to 136) after ending oncology treatment. Cut off for deficit: z-score≥-1.6. Population: 30 patients recruited between May 2010-April 2011 (15 each localization group). Both populations were similar. Infratentorial/supratentorial (I/S): age 146±31/153±34months; male 53/40%; motor impairment 46/40%; hydrocephalus at diagnosis 33/27%. No differences in received treatment. Tests results (median z-score and ranges I/S): Perceptual Reasoning IQ:-1.92±0.89/-1.5±0.94 p:0.33. Deficit 80/53% p:0.12. Visual Memory:-0.9±1.21/-1.19±1.34 p:0.54. Deficit 47/60% p:0.46. Processing Speed:-2.21±0.75/-2.08±0.78 p:0.63. Deficit 87/73% p:0.36.

We explored, through multivariate analysis, the association of the following variables: diagnosis age <5y, hydrocephalus, radiotherapy, and tumour location with the deficits. IQ deficit was related with infratentorial location (ORa 10.5 CI95% 1.04 – 107). Visual Memory deficit was related with hydrocephalus (ORa 14.3 CI95% 1.37 – 150). We could not find relation with Processing Speed deficit.

**Conclusions:** Both groups show similar and significant neurocognitive deficits in studied domains. Perceptual Reasoning deficit is related with infratentorial location. Hydrocephalus is a risk factor for visual memory deficit. It would be neccesary to confirm these results with a larger sample in order to have more power and accurance.

**33. EDUCATIONAL PROBLEMS IN SCHOOL-AGED SURVIVORS AND SIBLINGS** Laura Wengenroth, Dipl-Soz, MSc; Corina Rueegg, MSc; Micòl Gianinazzi, MA, BSc; Gisela Michel, PhD; Eva Bergstraesser, MD; Nicolas von der Weid, MD; Claudia Kuehni, MD. *Swiss Childhood Cancer Registry, Institute of Social and Preventive Medicine, University of Bern, Switzerland; Department of Pediatric Oncology, University Children's Hospital Zurich, Switzerland; Pediatric Hematology/Oncology Unit, Children's University Hospital, University of Lausanne, Switzerland*

**Objectives:** Diagnosis and treatment of childhood cancer often occurs during school years and the patients may encounter educational problems. So far, few data are available on school problems in pediatric and adolescent cancer patients. We aimed to 1) describe how many childhood cancer survivors ever repeated a year in school compared to siblings; and 2) find risk factors associated with repeating a year in school in survivors.

**Methods:** As part of the Swiss Childhood Cancer Survivor Study we sent a detailed questionnaire to all survivors aged 8-21 years, ≥5 years after diagnosis and registered in the Swiss Childhood Cancer Registry. The same questionnaire was sent to siblings. We used multivariable logistic regression to determine clinical and socio-demographic characteristics associated with repeating a year in school.

**Results:** The sample included 812 survivors and 181 siblings, with a mean age of 15 years (range 8-21). Of these, 167 survivors (23%; varying by diagnosis (leukemia 25%, lymphoma 20%, CNS 31%, other tumors 17%)) and 25 siblings (14%) had repeated a class (p=0.012). Compared to siblings, survivors of leukemia (OR=2.3, CI=1.4-4.0, p=0.002) and CNS tumors (OR=2.7, CI=1.5-4.9, p=0.001) had an increased risk of repeating a year.

Within survivors, migration background (OR=3.6, CI=1.2-10.7, p=0.020), radiotherapy (OR=8.9, CI=2.7-29.5, p<0.001) and relapse

(OR=3.7, CI=1.4-9.7, p=0.009) were risk factors for repeating a class. Survivors of renal tumors had a lower risk (OR=0.2, CI=0.1-0.9, p=0.041) compared to leukemia survivors.

**Conclusion:** We found that a considerable proportion of survivors had had to repeat a year in school, particularly those with a prolonged (leukemia) or intensified (radiotherapy) treatment and those who had suffered a relapse. This knowledge might help to further improve educational support for pediatric cancer patients during and after treatment..

**34. SELF-REPORTED MEMORY IMPAIRMENTS IN CHILDHOOD CANCER SURVIVORS AND SIBLINGS** E. Micòl Gianinazzi, MA; Corina S. Rueegg, MSc; Michael A. Grotzer, MD; Claudia E. Kuehni, MD; Gisela Michel, PhD. *Swiss Childhood Cancer Registry, Institute of Social and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland; University Children's Hospital, Zurich, Switzerland*

**Purpose of study:** Memory plays an important role in many daily activities and impairments in memory functionality can be debilitating. Due to their cancer history survivors of childhood cancer may be at particular risk for developing memory impairments. We thus aimed to 1) describe self-reported memory impairments in adolescent and adult survivors of childhood cancer and siblings, and 2) determine risk factors associated with memory impairments in survivors only.

**Methods:** Within the Swiss Childhood Cancer Survivor Study (SCCSS) we sent postal questionnaires to all survivors aged <16 years at diagnosis (1976-2003), who had survived >5 years and were aged ≥ 16 years at time of study. We used a similar questionnaire for siblings. Survivors who indicated to suffer often or very often from memory problems were classified as having a memory impairment. Associations between potential risk factors (demographic, disease-related and socio-economic factors) and memory impairments were assessed using multivariable logistic regressions.

**Results:** We included 1534 survivors and 548 siblings (response rate 77% and 48% respectively). Overall, more survivors (n=632; 41%) than siblings (n=65; 30%) reported to suffer from memory impairments often or very often (p<0.001). In the multivariable regression, memory impairments were more likely in survivors of CNS tumor (OR=1.9; global p=0.018), treated with radiotherapy (OR=1.7; p=0.005) and who reported late effects (OR=1.8; p<0.001). Impairments were less likely in survivors of soft tissue sarcoma (OR=0.5; global p=0.018) and who were older at study (OR 0.3-0.4; global p<0.001).

**Conclusions:** Our findings are in line with results of studies, which measured memory impairments with standardized tests and further stress the importance of screening. Patients who might be at risk for memory deficits should be tested regularly to determine the gravity of the impairment. Targeted interventions should be developed to compensate or remediate the impairment and improve quality of life.

**35. CONCORDANCE BETWEEN PARENT AND CHILD BEHAVIORAL RATINGS AND A CONTINUOUS PERFORMANCE TEST IN SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA** Cara Kimberg, PhD; Tara Brinkman, PhD; Melissa M. Hudson, MD; Ching-Hon Pui, MD; Deo Kumar Srivastava, PhD; Kevin R. Krull, PhD. *Departments of Epidemiology and Cancer Control, Oncology, and Biostatistics, St. Jude Children's Research Hospital, Memphis, TN USA*

**Background:** 20-40% of long-term survivors of childhood acute lymphoblastic leukemia (ALL) are reported to demonstrate impairments in attention and processing speed, albeit classification procedures vary between behavioral ratings and direct assessment. The purpose of this study was to compare behavioral ratings across parent-child dyads with direct assessment of attention.

**Methods:** Long-term child survivors of ALL (≥ 5 years post diagnosis; and ≥ 8 years of age at assessment) treated at St. Jude Children's Research Hospital on the Total XV protocol were recruited for a comprehensive neuropsychological battery. Intra-class correlations (ICCs) were utilized to compare concordance between parent and child ratings of attention, hyperactivity and aggression. Multivariable linear regression models, adjusting for sex and age, were used to examine associations between ratings and assessment of attention on the Conners' Continuous Performance Test (CPT-II).

**Results:** To date, 65 parent-child dyads (54% female; mean child age = 13.6 years; mean age at diagnosis = 5.8 years) have completed all study measures. ICCs indicated moderate agreement between parent and child ratings of attention, hyperactivity, and aggression (r's=0.45, 0.40 and 0.55 respectively; all p's<0.05); concordance increased when analyses were restricted to children ≥ 11 years of age. Child ratings of aggression were the strongest predictor of direct assessment of attention (CPT-II Hit Rate: $B = 0.44$, $t(59) = 2.69$, $p = 0.009$; CPT-II Variability: $B = 0.56$, $t(59) = 3.73$, $p < 0.001$; CPT-II Perseverations $B = 0.44$, $t(59) = 2.71$, $p = 0.009$). Parent ratings did not predict child performance.

**Conclusion:** Preliminary data support the need for comprehensive assessment of attention in a survivorship population, including multi-informant ratings and performance based measures. Future research should explore factors related to differential associations, including treatment intensity, as well as child and family characteristics.

**36. CNS INJURY IN CHILDREN WITH BRAIN TUMORS TREATED WITH CHEMOTHERAPY** Mary Baron Nelson, MS, RN; Paul M. Macey, PhD; Sharon O'Neil, PhD; Sunita K. Patel, PhD; Ronald M. Harper, PhD, Eufemia Jacob, PhD; Jonathan Finlay, MD; Fred Dorey, PhD; Peggy Compton, PhD, RN, FAAN. *Children's Hospital Los Angeles, Keck School of Medicine of University of Southern California, David Geffen School of Medicine at UCLA, and UCLA School of Nursing, Los Angeles, CA, USA; City of Hope, Duarte, CA, USA*

**Purpose:** The objectives were to determine whether children with brain tumors, mean of 5.4 years off-treatment with chemotherapy alone, have neuronal injury in regions apart from the tumor location, whether such injury is related to memory or executive functioning deficits and decreased quality of life (QOL).

**Methods:** Seven brain tumor survivors (mean age 8.3 +/- 3 years), treated with high-dose chemotherapy and autologous stem cell rescue, and nine healthy controls (mean age 9.3 ±/- 2.5 years), received brain MRI scans, including anatomical and diffusion tensor imaging (DTI) sequences. All participants completed measures assessing QOL, executive functioning, and social-emotional functioning (PedsQL, BRIEF, BASC-2), and survivors completed additional memory and executive functioning (EF) tests (CVLT-C, NEPSY II Inhibition and Memory for Designs). DTI was used to calculate mean diffusivity, a measure reflecting increased water content which is associated with chronic injury throughout the brain.

**Results:** Higher mean diffusivity appeared in the patient group over controls ($p < 0.05$, corrected for multiple comparisons), with age and sex as covariates, and was especially apparent in the thalamus bilaterally, internal and external capsules, putamen, globus pallidus and pons. The patient group had lower brain-to-CSF ratio ($p < .026$), and although not significant, lower mean volumes of gray and white matter than controls.

There were no notable differences in BASC-2 and BRIEF scores between groups. Twenty-nine percent of survivors scored well below average in memory tests and Inhibition, while 71% scored average or above average. Survivors had significantly lower scores on total QOL ($p < .004$), physical ($p < .014$), school ($p < .002$) and psychosocial functioning ($p < 0.004$).

**Conclusion:** We conclude that children with brain tumors treated with chemotherapy display diffuse brain tissue injury, some memory and EF deficits, and decreased QOL 5 years after treatment. The exact variables responsible for injury remain unclear and require further investigation.

**37. HIGHEST EDUCATION ACHIEVED AMONG 5-YEAR SURVIVORS OF CHILDHOOD CANCER AND A POPULATION COMPARISON GROUP** Dongdong Li, MSc; Sharon Relova, MSc; Maria Lorenzi, MSc; Linda S. Siegel, PhD; S. Rod Rassekh, MD; Sheila Pritchard, MD; Karen Goddard, MD; Paul Rogers, MD; Chris Fryer, MD; Mary L. McBride, MSc. *Cancer Control Research Program, British Columbia Cancer Agency, Vancouver, British Columbia, Canada; Faculty of Education, University of British Columbia, Vancouver, British Columbia, Canada; Division of Hematology/Oncology, British Columbia Children's Hospital, Vancouver, British Columbia, Canada; Division of Radiation Oncology, British Columbia Cancer Agency, Vancouver, British Columbia, Canada*

**Background:** Improved survival for childhood cancer has led to more survivors within the education system. Although research indicates that some survivors may experience neurocognitive deficits, there is little information on long-term and highest educational attainment.

**Purpose:** To describe the highest level of education attained by survivors of childhood cancer in British Columbia (BC), Canada, and compare to a general student population sample.

**Methods:** 498 five-year childhood cancer survivors diagnosed aged 0-12 years from 1978-1999 in BC, alive and aged 16 to 24 years by 2002, were identified from the BC Cancer Registry. A 10-times age- and gender- matched comparison group (n=4980) was randomly selected from the kindergarten to grade 12 (K-12) education system roster. Subject records were linked to K-12 and post-secondary databases to 2007 from provincial Education Ministries.

**Results:** Overall, 104/498 (20.9%) survivors had academic post-secondary education (APSE) compared to 867/4980 (17.4%) controls (OR = 1.22, 95% CI= 0.97-1.54). Compared to controls, 15/118 (12.7%) central nervous system (CNS) survivors had APSE (OR = 0.63, 95% CI= 0.36-1.10); CNS survivors treated with radiation therapy were even less likely to achieve APSE (OR = 0.20, 95% CI = 0.05-0.88). A total of 29.3% (29/99) leukemia survivors treated without radiation had APSE (OR=1.91, 95% CI=1.22-2.97), and 22.6% (14/62) leukemia survivors treated with radiation had APSE (OR = 1.48, 95%CI = 0.81-2.72).

**Conclusion:** In general, survivors had similar rates of APSE to the general student population sample, although leukemia survivors were more likely than the general population to achieve APSE. There was no statistical difference in APSE achievement between leukemia survivors who were irradiated and those not. CNS survivors were less likely to achieve APSE than leukemia survivors. Reasons for differences in APSE, and implications for support, will be discussed.

**38. NEUROCOGNITIVE ASSESSMENT IN CHILDHOOD CANCER SURVIVORS—OUR EXPERIENCE IN TERTIARY CARE CANCER CENTER IN INDIA** Savita Goswami, Lekhika Sonkusare, Jayita Deodhar, Vandana Padgaonkar, Purna Kurkure. *Psychiatric Unit and Pediatric Oncology, Tata Memorial Hospital, Mumbai, Maharashtra, India*

**Purpose:** Neurocognitive problems are a frequent long-term outcome following treatment of pediatric cancer with cranial irradiation and/or antimetabolite chemotherapy. Cranial radiation is known to adversely affect the developing central nervous system (CNS), which subsequently leads to neurocognitive deficits. Existing researches have shown that impairments within the domains of memory, processing speed, and attention occur very commonly in pediatric cancer patients and this can adversely affect academic, social, and vocational success, thereby impacting quality of life from childhood to adulthood.

**Method:** This study is a retrospective analysis of childhood cancer survivors who were attended in multidisciplinary clinic on regular annual follow up. Those who had scholastic adjustment issues were assessed on neurocognitive testing. A proforma was designed to note demographic variables & referral patterns. Neurocognitive testing details were also evaluated. Descriptive statistics are used.

**Results:** A total of 90 childhood cancer survivors were assessed on neurocognitive tests between 5-19 years of age. All were assessed on standardized tests. Majority were referred by mainly for scholastic difficulties and adjustment issues. Overall, approximately 22(25%) patients had average intelligence and 21(24%) had mild to moderate retardation. 15(17%) patients were of borderline intelligence and 18(20%) with above average intelligence. Details of domain impairments are discussed.

**Conclusion:** Majority of survivors had scholastic difficulties along with adjustment and behavioral problems despite average and borderline intelligence.

**Research Implication:** Identification of particular domains in neuropsychological testing in different groups of children with childhood cancer, based on cancer type & location, gender, socio-cultural context and various modalities of treatment used need to be studied further.

**Clinical Implications:** Neurocognitive testing pre and post chemotherapy as well as radiation can be more helpful in assessment of functional status of children. Planning therapeutic interventions to address the difficulties and issues can improve the quality of life of the childhood cancer survivors.

**39. ASSESSMENT OF FAMILY PSYCHOSOCIAL ADJUSTMENT IN SURVIVORS OF PEDIATRIC CANCER** Jordan Gilleland, PhD; Bonney Reed-Knight, MS; Sarah Brand, PhD; Anya Griffin, PhD; Karen Wasilewski-Masker, MD; Lillian Meacham, MD; Ann Mertens, PhD. *Aflac Cancer Center and Blood Disorders Service at Children's Healthcare of Atlanta, Atlanta, GA, USA; Emory University School of Medicine, Atlanta, GA, USA; University of Georgia, Athens, GA, USA; Dana-Farber Cancer Institute, Boston, MA, USA*

**Purpose:** The goal of this investigation was to 1.) examine the psychometric properties of a screening measure for psychosocial risk, the Psychosocial Assessment Tool (PAT2.0), among pediatric cancer survivors, and 2.) identify percentages of families falling into lower distress (i.e., "Universal"), acute distress (i.e., "Targeted"), and persistent/escalating distress ("Clinical") categories outlined in the Pediatric Psychosocial Preventative Health Model (Kazak, 2006).

**Methods:** Caregivers (N=94) completed the PAT2.0 during their child's yearly survivorship clinic appointment. Participants reported on familial social stressors and psychological symptoms. On average, participants' children were 12.9 years old (SD=4.31 yrs) and 8.1 years from diagnosis (SD=3.62 yrs).

**Results:** The internal consistency of the PAT2.0 Total Score in this survivorship sample was good (Cronbach's $\alpha$=.95). With the exception of the Family Structure/Resources scale (Cronbach's $\alpha$=.39), each of the other six subscales demonstrated adequate to good internal consistencies (Cronbach's $\alpha$=.60 to .88). Psychology was consulted by the physician to see 58% of participant families during their annual survivor visit, and families with psychology consults reported significantly higher PAT2.0 Total Scores than families without psychology consults ($t$(93)=2.20, p=.030). Further, PAT2.0 Total Scores were higher for patients ($t$(74)=2.12, p=.037), as well as parents ($t$(24.13)=3.83, p=.001) enrolled in outpatient mental health treatment. Strikingly similar to use of the PAT2.0 with families with children newly diagnosed with cancer (Pai et al., 2008), 55.3% of families presenting for survivorship care fell into the "Universal" category, 31.9% fell into the "Targeted" category, and 12.8% fell into the "Clinical" category.

**Conclusions:** Data indicate that the overall proportions of families experiencing universal, targeted, and clinical levels of psychosocial stress may be constant from the time of diagnosis into survivorship care. Overall, the PAT2.0 demonstrated strong psychometric properties among survivors of pediatric cancer and shows promise as a screening measure to facilitate more effective family support in survivorship care.

**40. THE FREQUENCY OF NEWLY IDENTIFIED NEUROCOGNITIVE AND EMOTIONAL IMPAIRMENT IN PATIENTS ATTENDING THE YALE UNIVERSITY HEROS (HEALTH, EDUCATION, RESEARCH OUTCOMES FOR SURVIVORS) CLINIC, A REGIONAL CHILDHOOD CANCER SURVIVOR CLINIC** Mary-Jane S. Hogan, MD; Lyn Balsamo, PhD; Tonetta Christie, RN; Nina S Kadan-Lottick, MD, MSPH. *Yale Section of Pediatric Hematology-Oncology, New Haven, CT, USA; Yale Cancer Center, New Haven, CT, USA*

**Purpose:** The Children's Oncology Group Long-Term Follow-Up Guidelines recommend screening for neuropsychological impairment in cancer survivors, but the merit of this screening is unknown. We sought to determine the frequency of newly identified neuropsychological conditions in childhood cancer survivors undergoing surveillance at their initial visit to Yale HEROS clinic.

**Methods/Design:** This cohort analysis included patients in remission who were diagnosed with cancer at an age ≤21 years, were ≥3years since diagnosis and attended HEROS clinic between 2/2003-12/2009. All HEROS attendees were screened and if appropriate, referred within 1 year for additional psychological evaluation. The frequencies of previously known and newly discovered neuropsychological conditions as a result of the first HEROS clinic visit were ascertained.

**Results:** A total of 210 patients were eligible for analysis (median age 18.2 years, 56% female, median of 9.8 years since cancer diagnosis and 92% with regular primary care). Prior cancer diagnosis included leukemia (36%), non-CNS solid tumor (34%), lymphoma (21%) and CNS tumor (9%). The table displays the frequency of previously known, newly-identified, and total disorders. Prior to the HEROS visit, 109 (72%) neuropsychological disorders were identified in 150 patients through routine primary care, oncology care, and/or school assessment. Screening of all 210 HEROS patients resulted in few newly identified emotional issues (n=10, 5%) and neurocognitive impairment (n=10, 5%). A total of 100 (48%) patients were diagnosed with a total of 129 disorders. Gender, cancer type, age at cancer diagnosis, time since cancer diagnosis, median household income, health insurance and primary care provider status were not associated with identification of a disorder.

**Conclusions:** Although a large proportion of survivors experienced a neuropsychological disorder, few new conditions were detected as a result of HEROS clinic screening. Our data suggest that there is adequate neuropsychological assessment of childhood cancer survivors by primary care physicians and school staff.

| Prevalence of Emotional and Neurocognitive Disorders | | | |
|---|---|---|---|
| Disorder | Previous (N)* | New (N)# | Total (N) |
| Emotional | 33% (50) | 5% (10) | 28% (60) |
| Neurocognitive | 39% (59) | 5% (10) | 33% (69) |
| Total | 72% (109) | 10% (20) | 61% (129) |

*previously screened N=150, #newly screened N=210

**41. NEUROCOGNITIVE AND FAMILY FUNCTIONING AMONG SURVIVORS OF CHILDHOOD BRAIN TUMORS AND THEIR MOTHERS** Matthew C. Hocking, PhD; Wendy L. Hobbie, CRNP, FAAN; Janet A. Deatrick, PhD, FAAN; Thomas Hardie, EdD, RN; Christina O. Nash, MS; Lamia P. Barakat, PhD. *The Children's Hospital of Philadelphia, Philadelphia, PA, USA; University of Pennsylvania School of Nursing, Philadelphia, PA, USA; Drexel University, Philadelphia, PA, USA; Department of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA, USA*

**Purpose/Background:** Childhood brain tumor (BT) survivors experience significant neurocognitive late effects across multiple domains that negatively influence psychosocial functioning and health-related quality of life (HRQOL). A theoretical model of childhood cancer survivorship suggests that survivor neurocognitive late effects and family functioning reciprocally interact to influence survivor, caregiver, and family functioning yet little research has explored these relations. This study examines the concurrent associations between survivor neurocognitive functioning, family functioning and survivor and caregiver HRQOL and the indirect effects of neurocognitive functioning on survivor and caregiver HRQOL through family functioning (mediation).

**Methods:** Participants include young adult (age 18-30) BT survivors (n = 22) and their mothers. Another 20 survivor-mother dyads will participate by the conference. Survivors were administered a brief neuropsychological battery assessing working memory, processing speed, verbal memory and executive functioning. Survivors and their mothers completed measures of family functioning and HRQOL.

**Results and Conclusions:** Pearson bivariate correlations tested the strength of the associations between indices of survivor neurocognitive functioning and concurrent family functioning and survivor and caregiver HRQOL. Poorer survivor working memory, processing speed, verbal memory and executive function were significantly associated with worse survivor- and caregiver-reported family functioning (r's range .34 - .61) and lower caregiver HRQOL (r's range .32 - .61). Additionally, worse survivor processing speed and executive function skills were significantly associated with poorer survivor HRQOL (r's range .30 - .45). Bootstrapping procedures for mediation provided evidence for the indirect effects of neurocognitive functioning on survivor and caregiver HRQOL through family functioning. These findings suggest that family functioning is an important factor that contributes to the variability in HRQOL outcomes in pediatric BT survivors and their caregivers. Moreover, interventions that target family functioning may mitigate the negative influence of neurocognitive late effects on survivor and caregiver HRQOL.

**42. COMPETENCE OF MOTHERS AS CAREGIVERS: ADOLESCENT AND YOUNG ADULT BRAIN TUMOR SURVIVORS LIVING AT HOME**
Janet A. Deatrick, PhD, FAAN; Wendy L. Hobbie, MSN, CRNP, FAAN; Sue Ogle, MSN, CRNP; Michael J. Fisher, MD; Lamia P. Barakat, PhD; Thomas Hardie, EdD, RN; Yimei Li, PhD; Jill Ginsberg, MD. *The Children's Hospital of Philadelphia, Philadelphia, PA, USA; Department of Family and Community Health, University of Pennsylvania School of Nursing, Philadelphia, PA, USA; College of Nursing and Health Professionals, Drexel University, Philadelphia, PA, USA; Department of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA, USA*

**Purpose:** Pediatric brain tumors patients have benefited significantly from treatment advances but may face significant physical, cognitive, and psychosocial late effects. Brain tumor survivors compared to survivors of other pediatric cancers are at the greatest risk for long-term cancer-related morbidities. Their mothers often lead dramatically altered lives, as they strive to support survivors to overcome significant neurocognitive late effects especially when must they remain at home into adulthood. The demands placed on mothers can challenge their sense of competence.

The aim of this study was to explore survivor, caregiver (mother), and family functioning predictors of the caregivers' perceived competence.

**Methods:** A model of Perceived Competence for Caregivers of Brain Tumor Survivors guided the study hypothesis: decreased caregiver competence would be predicted by increased caregiver demands, worse caregiver health, worse survivor health, and worse family functioning. Telephone interviews using structured self-report questionnaires were conducted in this cross-sectional study with a sample of 187 caregivers. Structural equation modeling was used to assess the hypothesized model.

**Results:** A path model explained that decreased caregiver competence is predicted by worse survivor health or worse family functioning, however, worse caregiver health only predicts decreased caregiver competence when there is increased caregiver demands and worse family functioning. Overall, the model showed adequate fit (CF I= 0.905, TFI = 0.880 and RMSEA = 0.081). All of the paths in the final model are significant at $P < 0.05$, and the final model accounted for 47% of variance in the perceived caregiver competence.

**Conclusions:** Based on the findings, we recommend targeting reducing caregiver demands and improving family functioning through family-based interventions to support improvement in caregiver competence. We also recommend that interventions targeted to survivor's health should consider the contribution of caregiver competence.

**43. MOTHER'S FUNCTIONAL EXPECTATIONS FOR SURVIVORS OF CHILDHOOD BRAIN TUMORS: PRELIMINARY ANALYSES**
Matthew S. Lucas, MS, MA, RN; Lamia P. Barakat, PhD; Wendy L. Hobbie, MSN, CRNP, FAAN; Janet A. Deatrick, PhD, RN, FAAN. *University of Pennsylvania School of Nursing, Philadelphia, PA, USA; The Children's Hospital of Philadelphia, Philadelphia, PA, USA; Department of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA, USA*

**Purpose:** When treatments for childhood brain tumors are explained to parents, they form expectations for their child's recovery from treatment. Here we examine previous (diagnosis/treatment) and current mothers' expectations of child functioning.

**Methods:** As part of a larger project investigating caregiving competence/demand, 40 mother-survivor dyads were interviewed face-to-face in their home using qualitative descriptive methods to better understand caregiver expectations for survivor function. All survivors (14-39 years, mean 20.9) lived at home with their mothers (30-69 years, mean 50.6). Data were analyzed using qualitative content analysis, performed by two readers to ensure rigor. The study also maintained conceptual, methodologic, and analytic documentation.

**Results/Conclusion:** Preliminary analysis revealed themes regarding the mothers' early expectations for the survivors' function. Functional expectations were described as physical (including longevity and activities of daily living), psychological (including anger management, anxieties, and changes in routine/transitions), social (lack of friends/significant others), and cognitive (educational performance/attainment). Consequences of these expectations include mothers' descriptions of the demands/responsibilities of caregiving, such as struggles or triumphs, caregiver worry, and how caregiver assists survivor. Expectations for function are woven throughout the mothers' survivorship experience including how providers helped to shape the expectations. Further analysis will develop dyadic narrative profiles concerning caregiver expectations. Previous work revealed that caregivers understand their children's lives in a division of 'before' and 'after'. An appreciation of caregiver expectations may help us better understand how expectations change over time as well how they may be related to survivor and caregiver outcomes. Implications for these findings include providers explicitly acknowledging the parents' concerns about expectations. There may be potential to change the interaction between providers and families at multiple points during and after treatment regarding expectations, thereby anchoring family management with the most realistic expectations based upon scientific evidence and assisting caregivers in (re)negotiating the goals of their caregiving.

**44. COGNITIVE PROCESSES AND SOCIAL OUTCOMES IN SURVIVORS OF CHILDHOOD MEDULLOBLASTOMA** Tanya Diver, PhD; Peter Manley, MD; Jessica Blais; Cori Liptak, PhD; Christine Chordas, PNP; Brian Delaney, PsyD; Celiane Rey-Casserly, PhD. *Departments of Psychiatry and Hematology/Oncology, Children's Hospital Boston, Boston, MA, USA; and Pediatric Neuro-Oncology and Pediatric Psychosocial Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; Colby College, Waterville, ME, USA*

**Introduction:** Children treated for medulloblastoma commonly demonstrate declines in neurocognitive skills over time, with risk factors including younger age at diagnosis, radiation treatment and other medically-related factors. This population is also at risk for significant social dysfunction, with some associations reported between neurocognitive status and social functioning.

**Purpose:** To examine neurocognitive domains of functioning in individuals treated for childhood medulloblastoma; examine specific patterns of change in intellectual processes over time; identify medical and treatment-related risk factors associated with different outcomes; examine current social status.

**Methods/Participants:** Retrospective chart review was conducted. Eighty-three individuals diagnosed with medulloblastoma between 1986 and 2008 were seen for neuropsychological assessment. Median age at diagnosis was 6.58 years and median age at initial neuropsychological assessment was 13.6 years. Forty-two individuals had multiple neuropsychological evaluations; median age at most recent evaluation was 16.25 years. Relevant medical factors, neurocognitive functioning (at the initial evaluation well as the most recent follow-up evaluation when available) and current social functioning were examined.

**Results:** Treatment-related effects were evident, with children treated with higher (versus standard) doses of craniospinal radiation therapy demonstrating significantly lower nonverbal reasoning scores. Large percentages of our sample experienced decline across neurocognitive domains over time (Verbal 56%, Nonverbal 42%, Working Memory 61%, and Processing Speed 51%). Children diagnosed at a younger age were more likely to demonstrate greater decline in nonverbal reasoning skills and processing speed over time. Greater decline in nonverbal reasoning skills was evident in those with current social problems.

**Conclusions:** Nonverbal reasoning skills and speed of processing appear to be particularly vulnerable neurocognitive processes to decline over time in survivors of childhood medulloblastoma. Those experiencing the greatest decline in nonverbal reasoning skills are demonstrating increased social difficulties at present. These data highlight the need to understand the multifactorial nature of cognitive late effects and impact on functioning.

**45. QUALITY OF LIFE IN CHILDREN WITH CANCER OR BRAIN TUMORS: SOCIOECONOMIC DISPARITIES AND THE MEDIATING ROLE OF FAMILY FACTORS** Kristin Litzelman, BA; Emily Barker, BS; Kristine Catrine, MD; Diane Puccetti, MD; Peggy Possin, RN; Whitney P Witt, PhD, MPH. *Department of Population Health Sciences, School of Medicine and Public Health, University of Wisconsin, Madison, WI, USA; American Family Children's Hospital, University of Wisconsin, Madison, Madison, WI, USA*

**Objective:** This study aimed to determine if and to what extent: (1) socioeconomic disparities exist in the health-related quality of life (QOL) of children with cancer or brain tumors and healthy children; and (2) family functioning and burden mediate the relationship between socioeconomic status and children's QOL.

**Methods:** In this cross-sectional study, parents of 71 children with and 135 children without cancer or brain tumors completed in-person interviewer-assisted surveys assessing sociodemographics, child QOL, family functioning and burden. For children with cancer, clinical characteristics were captured through medical record abstraction. Multiple linear regression was used to determine the relationship between socioeconomic demographics and child QOL; the interaction between group status and income was assessed. Staged multivariate regression models were used to assess the role of family factors in this relationship among children with cancer.

**Results:** Lower income was associated with worse child QOL. The effect of income differed by case status; income was more strongly associated with QOL in children with cancer than healthy children. Among children with cancer, log income was significantly associated with child QOL; this relationship was significantly attenuated by family functioning and family burden.

**Conclusions:** Significant socioeconomic disparities exist in the QOL of children with cancer. Family factors partially explain the relationship between low socioeconomic status and poor QOL outcomes among these children. Lower income families may have fewer resources to cope with their child's cancer. Increased support, monitoring, and referrals to reduce burden for lower income families may lead to improved QOL in children with cancer.

**46. RISING PHOENIX: PSYCHOSOCIAL FUNCTIONING OF INDIVIDUALS TREATED FOR PEDIATRIC CANCER** Deborah Dwelle, MS; Nahal Zakerani, PhD; Susan Lindemulder, MD, MCR; Kelly Anderson, MSN, FNP; Kitt Swartz, MPH; Michael A. Harris, PhD. *Oregon Health and Science University, Portland, Oregon, USA*

**Purpose:** Prior research suggests most survivors of pediatric cancer experience lingering psychosocial effects. This study examines the psychosocial adjustment of a sample of individuals treated for pediatric cancer.

**Methods:** Participants were patients seen in a multidisciplinary "survivorship clinic." Patients completed questionnaires assessing

psychosocial functioning, including perceived well-being (WHO-5), psychological stress (PSS), post-traumatic symptoms (PTSD), and behavioral symptoms (PSC). Of the 106 patients, 48% were female, mean age was 15.6 years, and mean years off treatment was 7.7.

| Cancer Type | Percent of Sample | Treatment Type | Percent of Sample |
|---|---|---|---|
| Blood | 43% | Chemotherapy | 98% |
| Bone | 13% | Surgery | 46% |
| Other | 13% | Radiation | 43% |
| Brain | 12% | Intrathecals | 34% |
| Lymph System | 11% | BMT | 21% |
| Kidney/Liver | 8% | Relapse | 14% |

**Results:** Findings revealed the patients in this clinic had few if any significant problems with psychosocial functioning. There were no significant differences in scores based on type of cancer. While not statistically significant, those treated for kidney/liver cancer had lower WHO-5, higher PSS, and higher PSC scores; PTSD scores were higher for brain cancers. Correlations between years off treatment and psychosocial functioning were non-significant across all measures (WHO-5, r = .11; PTSD, r = -.01; PSC, r = .05; and PSS, r = -.09).

| Psychosocial Functioning | Mean (SD) | Range | Cut-Off | Percent Above Cut-Off |
|---|---|---|---|---|
| PSC | 15.8 (12.3) | 0-42 | >28 | 22% |
| WHO-5 | 16.9 (4.4) | 6-25 | <13 | 19% |
| PSS | 14.2 (7.6) | 1-32 | >20 | 18% |
| PTSD | 28.1 (10.8) | 15-73 | >50 | 4% |

**Conclusions:** Though children treated for cancer may still be at risk for psychosocial maladjustment, results from this heterogeneous sample suggest psychosocial functioning was commensurate with the general population. Neither type of cancer nor years off treatment significantly differentiated psychosocial functioning in this sample. These findings are counter to some extant research demonstrating psychosocial difficulties in this population. Differences could be attributed to variation in domains assessed, assessment tools, and/or sample characteristics.

### 47. DEPRESSION AND POSTTTRAUMTIC STRESS AMONG HISPANIC AND NON-HISPANIC PARENTS OF ADULT SURVIVORS OF CHILDHOOD CANCER

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**Purpose:** Mothers of pediatric cancer survivors report higher rates of posttraumatic stress (PTS) symptoms than their children. It is unknown if parental distress varies among ethnic groups. This study examines parental distress, specifically PTS and depression, comparing Hispanic and non-Hispanic parents of adolescent/young adult (AYA) survivors of childhood cancer.

**Description:** English and Spanish-speaking parents of AYA childhood cancer survivors (aged 14-25, off treatment ≥2 years) completed a questionnaire assessing parental demographics, depression (CES-D), PTS (IES-R), perceived stress and child's health status/quality of life (QOL). Hispanic and non-Hispanic comparisons were conducted using Chi-square and t-tests. Regression procedures were used to identify independent risk factors associated with parental PTS and depression.

**Results:** Participants included 79 Hispanic and 60 non-Hispanic parents. Univariate analyses revealed Hispanic parents were significantly younger, had less education, lower incomes and higher levels of PTS and depressive symptoms compared to non-Hispanic parents (61% Hispanic, 23% non-Hispanic met criteria for PTS; 51% Hispanic, 25% non-Hispanic met screening criteria for depression (p- values<0.0001). No significant group differences were found for child's disease/treatment factors or for parents' rating of their child's health-related quality of life or chronic health problems. Multivariable analyses revealed a significant relationship between PTS and Hispanic ethnicity ($p<0.05$), birth outside the US ($p<0.01$), lower education ($p<0.001$), being single ($p=0.01$), higher perceived stress ($p<0.01$), lower child's psychosocial functioning ($p<0.01$) and greater intensity of child's cancer treatment ($p<0.01$). In contrast, depressive symptoms were associated only with lower income ($p<0.001$), higher perceived stress ($p<0.0001$) and lower child's psychosocial functioning ($p<0.01$).

**Conclusions:** Hispanic parents of AYA childhood cancer survivors report significantly higher symptoms of PTS and depression compared to non-Hispanic parents. Hispanic ethnicity and birth outside the US were independent risk factors for PTS. Further research is needed to understand how ethnic-specific factors (e.g., acculturation and immigration status) influence a parent's response/adjustment to his/her child's cancer diagnosis.

**48. THE INFLUENCE OF PSYCHOLOGICAL CONSTRUCTS ON KNOWLEDGE OF PAST DIAGNOSIS AND TREATMENT IN ADOLESCENT AND YOUNG ADULT CANCER SURVIVORS** Alicia Kunin-Batson, PhD; Jeanne Steele, PhD; Nora Erickson, BA; Ann Mertens, PhD; Joseph Neglia, MD. *University of Minnesota Medical School, Minneapolis, MN, USA; Minnesota Department of Health, Minneapolis, MN, USA; Emory University School of Medicine, Atlanta, GA, USA*

**Background:** Previous studies have found that childhood cancer survivors are not knowledgeable about their cancer health histories or continuing health risks resulting from their past diagnosis and therapy. Investigation of factors that influence cancer-knowledge may permit the development of interventions that improve knowledge and health behaviors. We examined the relationship between psychological constructs and cancer knowledge in adolescent and young adult cancer survivors.

**Methods:** 52 survivors of childhood cancer, ages 15-28 (mean 21.7 years), who were off treatment and in remission (mean 7.7 years) completed questionnaires measuring health locus of control, anxiety, cancer knowledge and quality of life as part of their baseline participation in a web-based intervention study to promote cancer knowledge.

**Results:** Few survivors accurately reported their chemotherapy history with detail (11%) and only 40% acknowledged that previous treatments they received for cancer could cause serious future health problems. 19.2% responded that they did not know what they could do to reduce their risk of complications from their cancer treatments. Independent samples t-tests found that these individuals had higher levels of state ($t(50)=-3.22$, $p = .002$) and trait anxiety ($t(50)= -3.15$, $p = .003$), and were less likely to report confidence in the role physicians and others play in their health ($t(50)=2.86$, $p = .006$) when compared to survivors who reported that they know what to do to reduce their risk for complications from cancer treatment.

**Conclusions:** Knowledge deficits exist among adolescent and young adult survivors regarding basic aspects of their diagnosis and treatment. Anxiety and health beliefs impact survivors' knowledge about cancer, including knowledge of steps they could take to mitigate their risks of late effects. Deficits in cancer knowledge may also contribute to anxiety. Interventions targeting maladaptive health beliefs and anxiety (e.g., cognitive-behavioral therapy) may be avenues through which cancer knowledge could be improved.

**49. NEUROCOGNITIVE FUNCTIONING CONTRIBUTES TO QUALITY OF LIFE (QOL) AFTER CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)** Alicia Kunin-Batson, PhD; Nina Kadan-Lottick, MD; Qing Cao, MS; Pim Brouwers, PhD; Joseph Neglia, MD. *University of Minnesota Medical School, Minneapolis, MN, USA; Yale University School of Medicine, New Haven, CT, USA; National Institute of Health, Rockville, MD, USA*

**Purpose:** Survivors of ALL treated without cranial radiation (CRT) are known to have modest impairment in neurocognitive functioning, but the implications of these for QOL are not known. This study examines the role of neurocognitive late effects in QOL after chemotherapy for ALL in childhood.

**Methods:** 263 survivors (46% female, mean of 3.9 years at diagnosis, and mean of 9.1 years since diagnosis) of standard risk ALL treated without CRT, underwent comprehensive neuropsychological evaluations, including performance measures of sustained attention, working memory, processing speed, and visual-motor integration, as well as parent and child report of physical and psychosocial (school, emotion, social) QOL (PedsQL). Hierarchical linear regression analyses were used to identify demographic, treatment, and neurocognitive contributors to QOL.

**Results:** Parent and child ratings of QOL were lower than population norms on scales of child's psychosocial functioning (child-report: 77.51 (15.2) vs. 81.83 (14.0), $p=.01$; parent report: 76.02 (17.9) vs. 81.24 (15.3), $p=.01$). Physical QOL ratings were consistent with population norms. Neurocognitive factors (working memory index, processing speed index, visual-motor integration, Conners CPT II) accounted for 7.8% ($p=.002$) of the variance in parent-reported school QOL and 11.9% ($p=.000$) of the variance in child-reported school QOL after demographic factors (age at diagnosis, time since diagnosis, sex, race, income, maternal education) and treatment factors had been accounted for. Neurocognitive factors also contributed to parent-report of child social QOL (5.5% of the variance, $p = .034$) beyond demographic and treatment factors. Treatment factors, specifically intrathecal regimen (triple intrathecal therapy versus intrathecal methotrexate) and steroid regimen (dexamethasome versus prednisone) did not contribute significantly to physical or psychosocial QOL.

**Conclusions:** Neurocognitive difficulties play a significant role in psychosocial QOL after chemotherapy for ALL. Interventions directed towards supporting neurocognitive functioning in childhood cancer survivors may be an important avenue for optimizing QOL after treatment.

**50. SOCIAL REINTEGRATION AFTER CENTRAL NERVOUS SYSTEM TUMORS IN CHILDHOOD** M. Peretz-Nahum, MD; E Krivoy; R Rosenkranz; M. Weyl Ben Arush, MD. *Pediatric Hemato-Oncology Department, Meyer Children Hospital, Rambam Health Care Center, Haifa, Israel*

**Objectives:** This study was designed to assess the overall morbidity burden of survival from central nervous system (CNS) tumors and its impact on return to a normal lifestyle.

**Methods:** Economical status, health, physical and social well-being were evaluated in CNS survivors aged minimum 18 years.

**Results:** Forty patients (pts) were evaluated, 23 (57.5%) males and 17 (42.5%) females, mean age was 28.5 (18-38) years (y), mean age on diagnosis was 7 y (1-19), mean y of FU was 19 y (8-29). Fourteen pts had medulloblastoma/primary neuroectodermal tumor, 20 pts glioma, 3 pts ependymoma, 3 pts germinoma. Thirty six pts (90%) received cranial radiotherapy (CSP), 14 pts (35%) cranio-spinal irradiation. Eleven pts (28%) lived with partner, 22 pts (55%) studied now at high school or university. Twenty three pts (58%) had good social relations, 18 pts (45%) satisfying economic level, 19 pts (48%) felt in good health status, 24 pts (60%) in good psychological status. Psychological status was significantly higher for pts with social or sportive activities (p=0.06). Social or sportive activities and relationship with partner are significantly correlated (p= 0.008). Male compared to female had less psychomotor delay (31% versus 70 %) and better QOL (48% versus 30%). In comparison the 27 pts diagnosed at age older than 6 y to the 13 younger pts had less mental retardation (30% versus 69%), better QOL, higher instruction level and better occupational status (44% versus 23%). Nine out of 14 pts treated by CSP had severe mental delay, 13/14 pts had poor QOL.

**Conclusion:** More than 50% of the CNS survivors have relatively good psychosocial status and instruction level. Risk of mental sequellae was correlated to female sex, young age on diagnosis, tumor type and cranio-spinal irradiation.

**51. LONG-TERM CHANGES IN PSYCHOLOGICAL DISTRESS IN CHILDHOOD CANCER SURVIVORS** Gisela Michel, PhD; Micòl Gianinazzi, MA; Corina S. Rueegg, MSc; Eva Bergstraesser, MD; Claudia E. Kuehni MD, MSc. *Swiss Childhood Cancer Registry, Institute of Social and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland and University Children's Hospital, Zurich, Switzerland*

**Purpose:** To evaluate change of psychological distress over time in survivors of childhood cancer and describe factors associated with change.

**Method:** Childhood cancer survivors aged <16 years when diagnosed 1990-2002, who had survived for ≥5 years and were aged ≥16 years received a postal questionnaire from the Swiss Childhood Cancer Survivors Study (SCCSS) in 2007-2009. A second questionnaire on childhood cancer follow-up (CCFU) was sent in 2010-2011. In both surveys, psychological distress was measured using the Brief Symptom Inventory-18 (BSI) assessing somatization, depression, anxiety and a Global Severity Index (GSI). Sum scores for each scale were transformed into T-scores. Survivor with T≥57 in two scales or the GSI were considered having significant psychological distress. We used paired t-test to analyze changes in sum scores and multinomial logistic regressions to describe factors associated with change in significant distress (improve, decline, stable distress, stable non-distress).

**Results:** We included 253 survivors who completed the BSI in both surveys. The mean sum-scores increased indicating higher distress in the second assessment (somatization: $mean_{SCCSS}$=1.24, $mean_{CCFU}$=2.03, p<0.001; depression: $mean_{SCCSS}$=1.81, $mean_{CCFU}$=2.55, p<0.001; anxiety: $mean_{SCCSS}$=1.92, $mean_{CCFU}$=2.36, p=0.016; GSI: $mean_{SCCSS}$=4.96, $mean_{CCFU}$=6.93, p<0.001). Regarding significant distress, 179 (70.8%) never reported any distress, in 13 (5.1%) distress improved, in 19 (6.3%) distress remained significant and in 45 (17.8%) distress became significant. In female survivors psychological distress was more likely to both improve (RRR=2.22) or decline (RRR=2.03), but also more likely to remain high (RRR=2.71; p=0.042). Also survivors of central nervous system tumors were more likely to remain distressed (RRR=6.11) or become significantly distressed (RRR=4.53; P=0.008). There was no association with current age, education, employment, age at diagnosis, or treatment.

**Conclusion:** Our results show that many survivors suffer from psychological distress, which does not improve over time. These findings underscore the need for regular long-term follow-up including a focus on psychological distress.

**52. EMOTIONAL DISTRESS IN 652 DUTCH VERY LONG-TERM SURVIVORS OF CHILDHOOD CANCER, USING THE HOSPITAL ANXIETY AND DEPRESSION SCALE (HADS)** I.M.M. van der Geest, BSc; W. van Dorp, MD; W.C.J. Hop, PhD; S.J.C.M.M. Neggers, PhD, MD; A.C.H. de Vries, MD; R. Pieters, PhD, MD; F. Aarsen, MSc; M.M. van den Heuvel-Eibrink, PhD, MD. *Departments of Pediatric Oncology/Hematology and Medical Psychology, Erasmus Medical Center–Sophia's Children's Hospital; Departments of Reproductive Medicine, Obstetrics and Gynecology, and Internal Medicine, Section Endocrinology, Erasmus Medical Center; Department of Biostatistics, Erasmus-MC University Medical Center, Rotterdam, The Netherlands*

**Introduction:** Following more successful treatment of pediatric cancer, the number of childhood cancer survivors is progressively increasing. Consequently, awareness of not only physical but also psychological late sequelae is important.

**Aim:** To identify survivors which suffer from emotional distress that may benefit from future psychological intervention.

**Method:** The two subscales of the Hospital Anxiety and Depression scale (HADS-anxiety and HADS-depression), were combined into one single scale, the total HADS score, and used as a screening tool for emotional distress in a single centre cohort of 652 childhood cancer survivors (Median age 23.3 range [15.0-46.0], median follow-up time 15.5 years range [5.0-41.5]). Higher HADS scores linearly reflect a higher level of emotional distress. HADS scores were compared with historical controls.

**Results:** Mean HADS score of the childhood cancer survivors was not different from the control group (p=0.38). None of the diagnostic subgroups had higher HADS scores than the control group. In survivors who received any kind of radiotherapy (7.7±6.3, p=0.03) and especially in the nested cohort of central nervous system (CNS) irradiated survivors of leukemia or lymphoma, HADS scores were

significantly higher than the control group (8.3±6.6, p=0.05). Using a previously described clinically relevant cut-off score of 15, forty-three survivors (7%) had a HADS score ≥15. The proportion of CNS irradiated survivors of leukemia or a lymphoma (n=9/76) was higher in the group with a score ≥15, than in the group with a score <15 ($\chi$2=3.85, p=0.05). Multivariate regression analysis showed that only educational achievement ($\beta$=-0.91, p=0.01) was independently associated with the HADS score.

**Conclusion:** Emotional distress does not occur more often in childhood cancer survivors than in the healthy population. Although the proportion of CNS irradiated survivors of leukemia or a lymphoma was higher in the group with a score ≥15, this is not an independent predictor of mental suffering.

**53. FATIGUE-RELATED QUALITY OF LIFE IN A COHORT OF PEDIATRIC CANCER SURVIVORS** Rose Lucey Schroedl, MA, MS; Kristin Bingen; Denise Gardner, MS; Debra Schmidt, MSN, APNP; Louise Leuthner, RN, BSN; Heather Christiansen, PsyD; Jacquelyn Smith, PhD; Mary Jo Kupst, PhD; and Lynnette Anderson, MSN, APNP. *Medical College of Wisconsin, Milwaukee, WI, USA; Marquette University, Milwaukee, WI, USA; Children's Hospital of Wisconsin, Milwaukee, Wisconsin, USA; Children's Hospitals and Clinics of Minnesota, Minneapolis, Minnesota, USA*

**Introduction:** Fatigue is a commonly reported symptom in pediatric cancer survivors that may affect quality of life (QOL). Research related to survivor fatigue is limited, though physical and psychosocial factors likely are contributors. Our objective was to evaluate the association between demographic, medical and psychosocial variables and QOL specific to fatigue symptoms in a cohort of pediatric cancer survivors. It was hypothesized that fatigue-related QOL would be related to treatment intensity and frequency/severity of late effects (LE).

**Methods:** As part of a larger study, survivors seen in a survivorship clinic completed the pedsFACIT-F (a measure of fatigue-related QOL) and were interviewed with their caregiver by a psychologist to assess psychosocial and cognitive functioning. Audiotaped interviews were transcribed and responses relevant to sleep or fatigue were coded. Demographic and LE data were collected via chart review.

**Results:** The sample consisted of 26 survivors between 7 and 20 years (M =12.50, SD =3.58), predominantly Caucasian (73.1%) and female (53.8%). Approximately 54% were diagnosed with acute lymphocytic leukemia, 23.1% had a bone marrow transplant, and 42.3% received radiation. Participants with >2 LEs reported worse QOL due to fatigue than participants who had 0-1 LE, $F(2, 22) = 3.40$, $p < .05$. Survivors with severe to life-threatening LEs reported worse QOL due to fatigue, $t(23) = 2.31$, $p < .05$. Treatment intensity and demographics were not related to fatigue. Of survivors/caregivers interviewed, 28.6% reported fatigue or sleep problems, described as difficulty sleeping or lack of energy/feeling tired. Of those reporting fatigue, 2/3 of fatigue problems were related to mood or anxiety, while the remaining 1/3 attributed it to treatment-related LEs.

**Conclusion:** Frequency and severity of LEs and psychosocial functioning may be contributing factors to fatigue-related QOL that warrant further investigation. Understanding fatigue is essential for developing interventions aimed at maximizing survivors' QOL.

**54. YIELD OF SCREENING VITAMIN D LEVELS IN A PEDIATRIC SURVIVORSHIP CLINIC** Adam J Esbenshade, MD, MSCI; Jenna Sopfe, BS; Jill H Simmons, MD; Travis Bowles, MD; Kristin Campbell, PNP; Debra L. Friedman, MD. *Departments of Pediatrics and Internal Medicine, Vanderbilt School of Medicine, Nashville, TN, USA; Vanderbilt-Ingram Cancer Center, Nashville TN, USA*

**Purpose of study:** Corticosteroid exposure increases risk for osteoporosis, which can be worsened by vitamin D deficiency (VDD). This study evaluated the utility of screening serum 25-OH vitamin D levels (VDL) in a survivorship clinic.

**Summarized description of project:** We evaluated all cancer survivors, aged < 23 years, attending the REACH for Survivorship Clinic between 1/2006-10/2011, screened for VDD (N = 182).

**Results and conclusions:** The cohort was 57% male, 87% Caucasian, a median age of 11 years (4-22), and a median of 2.9 years (0.1-10.8) from end of treatment. Diagnoses included acute lymphoblastic leukemia (63%), acute myeloid leukemia/lymphoma (20%), central nervous system tumor (6%), solid organ tumor (3%), and Langerhans cell histiocytosis (8%). VDD (< 20 ng/ml) was seen in 29/182 (15.9%), and vitamin D insufficiency (VDI) (<30 ng/ml) in 90/182 (65.1%). BMI >85th percentile was associated with VDI (Odds ratio = 3.1; 95% confidence interval [CI] 1.6 – 6.2 p=0.001) when controlled for cumulative steroid dose, time off therapy, age, and sex, which were not associated with VDI. VDL were not correlated with serum calcium levels or osteopenia on DEXA. After vitamin D supplementation and/or advice to increase dairy intake and sun exposure, improvement was noted in VDL in 20/25 (80%) patients with available repeat levels. Patients with elevated BMI may be less active and thus spend less time outside with sun exposure. Interventions targeted towards BMI reduction, increasing dietary vitamin D intake and safe sun exposure may decrease risk of vitamin D abnormalities in cancer survivors. These data suggest utility for vitamin D screening, particularly in those with elevated BMI. Prospective studies are indicated to develop preventive and treatment interventions.

**55. VITAMIN D LEVELS AND BONE MINERAL DENSITY IN MINORITY SURVIVORS** Colin Orr; Alison Fernbach, PNP; Solimar Curumi; Jennifer Levine, MD. *College of Physicians and Surgeons, Columbia University, New York, NY, USA; Division of Pediatric Oncology, Columbia University Medical Center, New York, NY, USA*

**Background:** Adequate Vitamin D levels are critical for the development of optimal bone mineral density, however vitamin D insufficiency is commonly seen in pediatric clinics, particularly in non-white ethnic groups. Survivors of childhood malignancies are at risk for vitamin D deficiency and bone mineral density (BMD) deficits related to their disease process, treatment, reduction in physical activity and poor nutrition. Despite the increased prevalence of vitamin D insufficiency, recent studies have reported higher BMD in African Americans compared to Caucasians. A limitation of current studies examining vitamin D and BMD in survivor populations is the lack of minority data.

**Methods:** Retrospective study assessing the vitamin D status and BMD of survivors of pediatric malignancies at a single institution.

**Results:** One hundred twenty five patients were eligible for review: 72 (57.6%) female, 65 (52%) white, 43 (34.4%) Hispanic, 7 (5.6%) African American, and 10 (8%) "other" or unreported. Median age at diagnosis for white patients was 6yrs (1yr-29yrs); 8yrs (1month-23yr) for minority patients. A total of 86 patients (68.8%) were vitamin D deficient or insufficient. Median Vitamin D 25(OH) levels for white patients was 29 (range: 6-63) and 22 (range: 5-56) for minority patients. Four (6.1%) white and 16 (32%) minority patients were Vitamin D deficient (OR=7; p= < 0.01) ; 36 (55.3%) white and 30 (60%) minority patients were Vitamin D insufficient (OR=1.2, p=0.7). Thirteen white and 8 minority patients had some form of BMD assessment. All minority patients BMD surveys were within limits; 1 white patient's assessment revealed osteopenia (z=-2.11) at the lumbar spine.

**Conclusions:** Minority patients are more likely to be vitamin D deficient relative to white patients; however, BMD surveys were similar between the two groups with one white patient showing evidence of osteopenia at the lumbar spine.

**56. GLUCOCORTICOIDS AND INSULIN RESISTANCE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA** Eric J. Chow, MD MPH; Catherine Pihoker, MD; Debra L. Friedman, MD, MS; Stephanie J. Lee, MD, MPH; Jeannine McCune, PharmD; Claire Wharton, BS; Christian L. Roth, MD; K. Scott Baker, MD, MS. *Department of Pediatrics, Seattle Children's Hospital, University of Washington, Seattle, WA, USA; Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; Vanderbilt University School of Medicine, Vanderbilt-Ingram Cancer Center, Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville TN, USA; Department of Pharmacology, University of Washington, Seattle, WA, USA*

**Background:** Children treated for acute lymphoblastic leukemia (ALL) are at increased risk of becoming overweight. Prolonged exposure to high-dose glucocorticoids (GC) may cause insulin resistance and facilitate development of this phenotype.

**Methods:** Body mass indices (BMI) and insulin resistance (HOMA-IR) were measured among on- (n=31) and off-therapy participants (n=29). On-therapy participants were assessed prior to and while on GCs, with a subset (n=10) receiving an intravenous glucose tolerance test (IVGTT).

**Results:** BMI z-scores increased significantly following diagnosis in both groups. Increased HOMA-IR values were associated with increased BMI, and were further increased with GC exposure ($p<0.05$; Table). Among those with IVGTT data, HOMA estimates in general correlated with values derived from a minimal model analysis ($r\sim0.7$). In multivariate analysis, among all participants, increased current BMI z-score was independently associated with current HOMA-IR (coeff 0.42, 95% CI 0.15, 0.69), BMI z-score at leukemia diagnosis (coeff 0.39, 95% CI 0.20, 0.58), and current on-therapy status (coeff 0.93, 95% CI 0.28, 1.59).

**Conclusions:** Children treated for ALL experienced significant weight gain during therapy. Exposure to high-dose GC was associated with a significantly increased insulin resistant state and may be an important contributor to the development of therapy-related obesity.

**57. YIELD OF SCREENING LIPID PROFILES USING CURRENT INDICATIONS PLUS PROLONGED STEROID EXPOSURE IN A SURVIVORSHIP CLINIC** Adam J Esbenshade, MD, MSCI; Jenna Sopfe, BS; Jill H Simmons, MD; Travis Bowles, MD; Kristin Campbell, PNP; Debra L. Friedman, MD. *Departments of Pediatrics and Internal Medicine, Vanderbilt School of Medicine, Nashville, TN, USA; Vanderbilt-Ingram Cancer Center, Nashville,TN, USA*

**Purpose of study:** The Children's Oncology Group Survivorship Guidelines recommend a fasting lipid profile (FLP) in patients with platinum or cranial radiation exposure.

**Methods:** This study evaluated utility of a non-fasting lipid profile as a preliminary screen to assess corticosteroid exposure as an indication for lipid screening. All cancer survivors, age <23 years, attending the REACH for Survivorship clinic between 1/2006-9/2011 with lipid screening (N = 226) were identified via chart review.

**Results:** The cohort was 56% male, 88% Caucasian, median age 11 years (2-22), and median of 3 years off therapy (0.1-15). Hypertriglyceridemia (> 110mg/dl) was noted in 9/27 (33.3%) and low HDL (< 40 mg/dl) in 4/27 (14.8%) patients with platinum exposure. In patients with corticosteroid exposure, 56/176 (31.8%) had hypertriglyceridemia and 43/176 (24.4%) had low HDL.

In patients with corticosteroid exposure, adjusted for systolic blood pressure z-score, gender, age, and time off therapy HDL was inversely associated with BMI-z score (beta -0.214; p=0.006) and age (beta -0.17; p= 0.042). A non-significant association was noted between triglycerides and BMI z-score (beta 0.141; p=0.072). In patients with platinum exposure, neither triglycerides nor HDL were associated with any of the above factors. Cumulative platinum doses were not correlated with triglyceride or HDL levels. Of 97 patients with initial dyslipidemia, only 10 patients returned for a fasting evaluation and 7/10 still met dyslipidemia criteria. Despite diet and exercise recommendations, minimal improvement in lipids were seen in patients with follow-up evaluations (N = 13).

**Conclusions:** Patients with corticosteroid exposure and elevated BMI are at risk for dyslipidemia and non-fasting lipid screening appears informative as an initial screen. Recommendation for diet/exercise modification may be insufficient to correct dyslipidemia, suggesting the need to evaluate a more active intervention. A prospective study may inform screening and preventive interventions.

**58. LIPID PROFILE ABNORMALITY IN CHILDHOOD CANCER SURVIVORS: A POTENTIAL TREATABLE TARGET FOR PREVENTION OF CARDIOVASCULAR DISEASE** Angela Yarbrough, RN, FNP; Sung Kim, RN, FNP; Colette Badeaux, RN; Angela Xu, MPH; Joann Ater, MD. *The Children's Cancer Hospital at The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA*

**Purpose:** Some survivors of childhood cancer are at increased risk of cardiovascular disease, stroke, and metabolic syndrome. This study was performed to evaluate patterns of abnormal lipid profiles related to patient characteristics and body mass index (BMI) and to identify the magnitude of this problem within our patient population.

**Methods:** We performed a chart review of patients seen in our Childhood Cancer Survivor Clinic over a 2 year period to identify patients who had lipid panels performed in our laboratory. Lipid panels and associated BMI on the date of the lipid panel were collected in a database along with patient characteristics.

**Results:** We identified 215 patients (126 females). Median age at diagnosis of cancer was 5.9 (range 0-20.9) years. Current median age of the patients at time of lipid profile was 26 (range 7 to 56) years. In the children < 19 years, 42.4% were > 85th % for age for BMI%, and BMI% correlated significantly with triglycerides (p=0.03), cholesterol (p=0.05), HDL (p=0.039), LDL (p=0.012), and very LDL (p=0.029). HDL (NL>60) was low in 71.2% and LDL high (> 100) in 36.6%. For adults, triglycerides were abnormal in 30.9%, cholesterol in 30.9%, HDL low in 65.8%, and LDL high in 53.7%. Only triglycerides (p=0.025) and LDL (p=0.004) had a significant correlation with BMI in adults.

**Conclusions:** In our clinic population, the most common lipid abnormality is low HDL. Since this factor is protective in preventing cardiovascular disease and improved by diet, it appears that this may be a good target for nutritional intervention and education. The high incidence of suboptimal levels in both adults and children indicate that the education should begin at an early age. Lipid panels may be a good objective measure to identify children for study of nutritional interventions to improve cardiovascular health.

**59. DO CHILDHOOD CANCER SURVIVORS AND THEIR PROVIDERS CORRECTLY IDENTIFY ABNORMALITIES IN BMI?** Swati V. Elchuri, MD; Briana C. Patterson, MD, MSc; Karen Wasilewski-Masker, MD, MSc; Ann Mertens, PhD; Lillian R. Meacham, MD. *Department of Pediatrics, Emory University and Aflac Cancer Center and Blood Services of Children's Healthcare of Atlanta, Atlanta, GA, USA*

**Purpose:** Ascertain survivor and provider perceptions of BMI status

**Background:** Pediatric cancer survivors may have abnormal body mass index (BMI) and with that, risk of health sequelae. Provider recognition and survivor self-awareness of abnormal BMI are key to making health changes that can normalize BMI.

**Methods:** BMI was calculated from measured height and weight from the survivor clinic visit and classified as underweight, normal, overweight or obese by Center for Disease Control guidelines. Providers' assessment of BMI was defined by documenting underweight, overweight or obese in the medical record problem list. Survivor self-assessment of BMI (low, normal or high [overweight/obese]) was abstracted from a questionnaire in which survivors self-report lifestyle and health data. BMI classifications were compared to survivors' perceptions and providers' problem lists. Proportions were compared with the Chi-Square test, with adjustment for multiple comparisons (SAS v9.2).

**Results:** Data was available from 325 survivors with 48% female and a mean age of 13.4 years (SD 4.3 yrs). BMI status of survivors: 6% were underweight, 56% were normal, 20% were overweight and 17.5% were obese. The overweight/obese survivors were correctly categorized 48% by self-report and 70% of the time by providers (sensitivity). Correct classification of overweight/obese survivors by self-report was significantly less than normal weight survivors. Correct classification of overweight survivors by providers was significantly less than other BMI groups.

| Sensitivity | Underweight | Normal | Overweight/Obese | Overweight | Obese |
|---|---|---|---|---|---|
| Survivor's Assessment | 65% | 85%[a] | 48%[a] | | |
| Provider's assessment | 75%[b] | 80%[c] | | 37%[b,c,d] | 77%[d] |

[a]p<0.001, [b]p=0.016, [c]p<0.001, [d]p<0.001

For survivors not identified as having increased BMI, this was accurate 76% of the time (self-report) and 84% of the time (provider report) (negative predictive value).

**Conclusions:** Childhood cancer survivors were not accurate in identifying overweight/obese status. Providers only identified 37% of overweight patients. Early recognition, counseling, and receptive intervention are necessary to correct BMI disorders.

**60. BODY COMPOSITION IN LONG-TERM CHILDHOOD CANCER SURVIVORS: APPLICABILITY OF ANTHROPOMETRIC MEASURES**
Robyn E. Karlage, MS; Sue C. Kaste, DO; Nan Zhang; Daniel M. Green, MD; Gregory T. Armstrong, MD; Leslie L. Robison, PhD; Joseph H. Laver, MD; Melissa M. Hudson, MD; Kirsten K. Ness, PT, PhD. *Departments of Epidemiology and Cancer Control, Radiological Sciences, Biostatistics, and Oncology, St. Jude Children's Research Hospital, Memphis, TN, USA*

**Background:** Many survivors of childhood cancer (CCS) are at risk for body composition abnormalities, including obesity and increased fat mass. The purpose of this study was to determine if anthropometric measures accurately predicted body composition of long-term CCS when body fat determined by dual energy x-ray absorption (DXA) was used as the standard.

**Methods:** Participants (n=1,063) were treated at St. Jude Children's Research Hospital, at least 10 years post-diagnosis, and at least 18 years of age. Persons with amputation were excluded from analysis. Participants underwent a musculoskeletal assessment to ascertain physical function and received a DXA. Height, weight, waist and hip circumference, and skinfold thickness were measured during the musculoskeletal assessment by an exercise specialist. A whole-body DXA scan was obtained to determine body composition. Mean body fat percentage determined by skinfolds ($BF_{SF}$) was 23.2% ± 7.6 for males and 32.0% ± 8.2 for females.

**Results:** Mean body fat percentage determined by DXA ($BF_{DXA}$) was 26.5 %± 7.3 for males and 38.0% ± 7.8 for females. Pearson correlations between $BF_{SF}$ and $BF_{DXA}$ were high for men (R=0.814) and women (R=0.845), and were greater than correlations between $BF_{SF}$ and body mass index (BMI) (men; R=0.762; women; R=0.829) and BFDXA and BMI (men; R=0.717; women; R=0.820). Using DXA as the gold standard to dichotomize the high risk group, the sensitivity and specificity for BMI are 63.14% and 92.34%, respectively; the sensitivity and specificity for $BF_{SF}$ are 52.91% and 96.77%. Using DXA as the gold standard to dichotomize the elevated risk group, the sensitivity and specificity for BMI are 81.14% and 86.38%, respectively; the sensitivity and specificity for $BF_{SF}$ are 72.70% and 97.67%.

**Conclusion:** BMI and skinfold measures are safe and inexpensive alternatives to DXA to estimate body composition of CCS when DXA is unavailable or too costly.

**61. TRENDS IN BODY MASS INDEX (BMI) DURING AND AFTER TREATMENT FOR STANDARD RISK (SR) ACUTE LYMPHOBLASTIC LEUKEMIA (ALL): A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP (COG)**
Susan J. Lindemulder, Linda C. Stork, Bruce Bostrom, Xiaomin Lu, Meenakshi Devidas, Joseph P. Neglia, Nina S. Kadan-Lottick

**Background:** Limited data exist regarding timing of BMI changes and risk of obesity in long-term survivors of ALL treated without cranial radiation (CRT). This study describes temporal trends in BMI during and after therapy for SR-ALL and identifies associated factors.

**Methods:** We conducted a retrospective cohort study of children with SR-ALL enrolled on sequential clinical trials between 1993 and 2000 and on the COG ALTE02C2 follow-up study. Therapy included prednisone or dexamethasone during induction, same steroid in maintenance, and no CRT. Standing height and weight were ascertained at diagnosis (dx), start of consolidation, maintenance, last cycle of maintenance, and at least one year off therapy. Age and gender-specific BMI percentiles (BMI%) were calculated using 2000 CDC growth charts for patients 2-20 years.

**Results:** The 269 subjects were a median of 3.5 years at dx, 46.7% female, 82.3% white, and a median of 9.1 years since dx at last timepoint. The BMI% was associated with time since dx. BMI% increased between dx and consolidation (50.9%-68.3%, $p < 0.0001$), remained stably elevated until the end of maintenance, and then decreased somewhat from end of maintenance to the last timepoint (74.1%-70.6%, $p = 0.03$). After therapy, 18.1% of survivors were overweight (BMI% 85-95) and 20.9% were obese (BMI% ≥ 95). By unadjusted linear regression, higher dx BMI% was positively associated with BMI% post-therapy ($p < 0.0001$). The association between dx BMI% and post therapy BMI% was significantly greater for the dexamethasone vs the prednisone group (p=0.01); no association with age at dx, gender, or race.

**Conclusions:** We found that in SR-ALL survivors BMI% increased significantly in the month after dx and remained substantially elevated even several years after the end of therapy. Dx BMI% was highly associated with off-therapy BMI%, particularly in patients who had received dexamethasone rather than prednisone.

**62. ASSOCIATION OF BONE MINERAL DENSITY WITH INCIDENTAL RENAL STONE IN LONG-TERM SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA**
Prasad Gawade, PhD; Kirsten K. Ness, PT, PhD; Shelly Sharma, MD; Zhenghong Li, MS; Kumar Srivastava, PhD; Sheri Spunt, MD; Kerri Nottage, MD; Matthew Krasin, MD; Melissa Hudson, MD; Sue C. Kaste, DO. *Departments of Epidemiology and Cancer Control, Radiological Sciences, Biostatistics, and Oncology, St. Jude Children's Research Hospital, Memphis, TN, USA*

**Background:** With 5-year survival of childhood acute lymphoblastic leukemia (ALL) now exceeding 90%, long term morbidities are of growing concern. Both low bone mineral density (BMD) and renal dysfunction have been reported in ALL survivors. Our objective was to evaluate the association between low BMD and incidental renal stones, a known predictor of renal dysfunction.

**Methods:** Adult participants who were 10+ year survivors of childhood ALL and members of St. Jude Lifetime Cohort study were recruited between 12/2007 and 3/2011. During their risk-based medical evaluations they underwent quantitative computed tomography (QCT) to evaluate BMD. Incidental renal stones were identified by radiologists' review of axial QCT source images. Demographic information was abstracted from responses to health surveys and dietary intake from a Block food frequency questionnaire. Association between BMD and renal stones was evaluated in a multivariable logistic regression model. Confounding variables were selected using directed acyclic graphs and change in effect estimates strategy.

**Results:** At a median of 26.1 years from diagnosis, BMD Z score of > 1 standard deviation (SD) was detected in 77/662 (11.6%) and renal stones in 73/662 (11%) participants. In a multivariable model adjusted for age, dietary vitamin D and renal radiation, when compared to BMD Z score > 1 SD, the risk of renal stones increased with a decrease in BMD Z-score; 1 to 0 SD (Odds Ratio (OR), 1.93; 95% confidence interval (CI), 0.69 to 5.41), 0 to -1 SD (OR, 1.46; 95% CI, 0.52 to 4.05), -1 to -2 SD (OR, 2.72; 95% CI, 0.81 to 6.41), and ≤ -2 SD (OR, 4.96; 95% CI, 1.43 to 17.13). Older age (45-54 vs.18-24 y; OR, 3.66; 95% CI, 1.10 to 12.15), renal radiation (OR, 1.97; 95% CI, 0.59 to 6.50) and > 141.5 IU intake of vitamin D (OR, 1.65; 95% CI, 0.98 to 2.77) were also associated with renal stone formation.

**Conclusions:** Our results not only help us recognize survivors at risk, but also informs radiologists to be vigilant of incidental renal stones among older ALL survivors with low BMD

### 63. INITIAL HYPOTHALAMIC INVOLVEMENT IS THE MAJOR RISK FACTOR FOR IMPAIRED PROGNOSIS AND QUALITY OF LIFE IN CHILDHOOD CRANIOPHARYNGIOMA REGARDLESS OF CHOSEN TREATMENT STRATEGIES—RESULTS OF KRANIOPHARYNGEOM 2000

Hermann L. Müller*, Ursel Gebhardt, Monika Warmuth-Metz, Rolf-Dieter Kortmann, Andreas Falldum, Torsten Pietsch, Gabriele Calaminus, Niels Sörensen. *Department of Pediatrics, Klinikum Oldenburg; Department of Neuroradiology, University Hospital, Würzburg; Department of Radiooncology, University Hospital, Leipzig, Germany; Institute for Medical Biostatistics and Informatics (IMBEI), University of Mainz, Mainz, Germany; Institute for Neuropathology, University Hospital, Bonn, Germany; Department of Pediatric Oncology, University Hospital, Münster, Germany; Department of Neurosurgery, Evangelisches Krankenhaus Oldenburg, Germany*

*on behalf of the study committee of KRANIOPHARYNGEOM 2007

**Background**: Hypothalamic obesity has major impact on prognosis and quality of life (QoL) in childhood craniopharyngioma (CP). The pathogenic relevance of initial hypothalamic involvement versus treatment-related hypothalamic lesions is a matter of controversy.

**Methods:** 120 patients were recruited prospectively (2001-2007) and evaluated after 3 yrs of follow-up. Body mass index (BMI) and QoL at diagnosis and 36 mo after diagnosis were analyzed based on reference assessment of tumour localization and post-surgical hypothalamic lesions using a standardized grading system (no, anterior, posterior involvement/lesion). Treatment was analyzed regarding neurosurgical strategy of 50 participating neurosurgical centres and the centre sizes. Based on patient load during the 6-year recruitment period, participating centres were categorized as small (1 pt / 6yrs), middle (2-5 pts /6yrs) or large-sized centres (>5 pts /6yrs).

**Results:** BMI SDS at diagnosis was similar in patients with or without hypothalamic involvement. Surgical lesions of anterior and posterior hypothalamic areas were associated with higher increases in BMI SDS during 36 mo post-diagnosis compared to patients without or only anterior lesion (+1.8BMISD, p=0.033;+2.1BMISD, p=0.011), negatively impacting QoL in patients with posterior hypothalamic lesions. Surgical strategies varied between the 50 neurosurgical centres (3 large, 24 middle, 23 small centres). Patients treated in small centres presented with a higher rate of hypothalamic involvement compared to middle and large-sized centres. Treatment in large centres was less radical, the rates of complete resection and hypothalamic surgical lesions lower than those of middle-sized and small centres. However, multivariable analysis showed that pre-operative hypothalamic involvement was the only independent risk factor for severe obesity (p=0.002).

**Conclusions:** Radical strategies leading to posterior hypothalamic lesions are not recommended due to potential to exacerbate hypothalamic obesity and impaired QoL. Because our results show that initial hypothalamic involvement has an a priori effect on the clinical course, our recommendations are based on recognizing CP as a chronic disease.

### 64. NO LONG-TERM WEIGHT REDUCTION AFTER GASTRIC BANDING (LAGB) IN OBESE PATIENTS WITH CRANIOPHARYNGIOMA INVOLVING HYPOTHALAMIC STRUCTURES—EXPERIENCES FROM KRANIOPHARYNGEOM 2000

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**Background**: Craniopharyngiomas are embryogenic malformations which lead to eating disorders and morbid obesity due to hypothalamic involvement. The experience with laparoscopic adjustable gastric banding (LAGB) in obese craniopharyngioma patients is limited especially in regard to long-term effects and tolerability.

**Patients and methods:** We are reporting on four patients with childhood craniopharyngioma diagnosed at age 2, 13, 12, and 20 years.

**Results:** Body mass index (BMI-SDS) at diagnosis was -0.9, +4.5, +4.7 and +0.23 SD. All patients developed morbid obesity (BMI-SDS: +10,87, +10.36, +11.4, +6,2) so that 11, 5, 9 and 3 years after diagnosis LAGB were performed. LAGB was well tolerated. During long-term follow-up, the nadir BMI SDS (+6.9, +9.5, +7.8, +4.9) were reached 2.0, 0.5, 1.0, 0.8 years after LAGB. At last evaluation 9.1, 5.3, 7.1, 7.1 years after LAGB, the patients BMI (BMI SDS at last evaluation: +10.2, +13.9, +10.2, +6.3) had increased again but remained at a constant level comparable with baseline BMI SDS at the time of LABG. Quality of life was not decreased due to LAGB and tolerability was sufficient.

**Conclusions:** We conclude that LAGB is feasible and could have clinical relevant effects on long-term weight stabilization of obese craniopharyngioma patients with hypothalamic syndrome. However, a significant weight reduction was not achieved after LAGB in patients with childhood craniopharyngioma. Non-reversible bariatric procedures such as gastric bypass are not recommended for treatment of obese children and adolescents with craniopharyngioma due to ethical considerations.

**65. CHANGES OF PERIPHERAL ALPHA-MELANOCORTIN STIMULATING HORMONE ($\alpha$-MSH) IN CHILDHOOD CRANIOPHARYNGIOMA PATIENTS IN COMPARISON WITH OTHER FORMS OF CHILDHOOD OBESITY** Hermann L. Müller, Pablo J. Enriori, Ursel Gebhardt, Anke Hinney, Johannes Hebebrand, Thomas Reinehr, Michael A. Cowley, Christian L. Roth. *Department of Pediatrics, Klinikum Oldenburg, Oldenburg, Germany; Division of Neurosciences, National Primate Research Center, Oregon Health and Science University, Beaverton, Oregon, USA; Department of Physiology, Faculty of Medicine, Monash University, Clayton, Victoria, Australia; Department of Child and Adolescent Psychiatry, Rheinische Kliniken Essen, University of Duisburg-Essen, Essen, Germany; Department of Paediatric Nutrition Medicine, Vestische Children Hospital Datteln, University of Witten, Herdecke, Germany; Seattle Children's Hospital Research Institute, Seattle, WA, USA*

**Objective:** Relationships of blood circulating melanocortins to childhood obesity are not well established. We evaluated serum $\alpha$-melanocyte stimulating hormone ($\alpha$-MSH) in lean children and different study groups of childhood obesity.

**Methods:** We examined serum $\alpha$-MSH in 52 otherwise healthy children with childhood obesity (Ob, mean age 11 years, 32 girls/20 boys), 27 normal-weight children of same age, 7 additional obese patients with reduced melanocortin-4 receptor function (MC4Rmut), and 22 patients with craniopharyngioma (CP). Fasting serum $\alpha$-MSH and leptin were measured by RIA. Serum $\alpha$-MSH was also evaluated one hour after 500 kcal liquid meal (CP and Ob) and at the end of one year lifestyle intervention in 24 Ob patients.

**Results:** $\alpha$-MSH levels were similar in obese vs. lean children but significantly lower in CP ($p<0.001$) and significantly higher ($p<0.05$) in MC4Rmut patients compared to Ob. One hour after liquid meal, $\alpha$-MSH increased in patients with SO but not with CP. After one year, $\alpha$-MSH levels increased significantly in the successful weight reduction Ob subgroup despite unchanged cortisol levels. $\alpha$-MSH changes correlated to weight status changes ($r=0.67$; $p=0.0003$) but not to changes of cortisol, insulin or insulin resistance index HOMA.

**Conclusions:** Persistently low $\alpha$-MSH levels in CP patients are suspected to be due to pituitary or hypothalamic damage. High peripheral levels in MC4Rmut carriers indicate up-regulation of $\alpha$-MSH. Changes of weight status are associated with changes of peripheral $\alpha$-MSH. Synthetic $\alpha$-MSH analogues might offer a promising therapeutic option for treatment of hypothalamic obesity in craniopharyngioma patients.

**66. EPIDEMIOLOGY OF LATE ONSET ANTHRACYCLINE INDUCED MYOCARDIAL DYSFUNCTION IN CHILDHOOD CANCER SURVIVORS** S. Seth, R. Seth, K. Verma. *Departments of Pediatrics and Cardiology, All India Institute of Medical Sciences, New Delhi*

**Objective:** To characterize anthracycline induced myocardial dysfunction in childhood cancer survivors.

**Methods:** Records of all children attending the Pediatric Cancer Survivor Clinic (PCSC) were screened. Children treated with anthracycline based chemotherapeutic regimes were eligible. Myocardial function was assessed by conventional echocardiography at baseline, at completion of chemotherapy and at 6 months interval subsequently.

**Results:** 483 records from PCSC were screened and 319 children were treated with anthracycline based regimes. Details of echocardiography were available in 203 patients. Mean age was 7.8 yrs. All patients were asymptomatic on completion of chemotherapy. The cumulative dose of anthracycline received was calculated [ALL (230mg/m2), AML (450mg/m2), HL (250mg/m2), Neuroblastoma (170mg/m2)]. Baseline myocardial function was normal in all. 27 survivors (13.3%) had myocardial dysfunction. Of these 3 occurred during chemotherapy and after completion of chemotherapy in 24 cases. Highest prevalence of myocardial dysfunction was seen in children with AML (31.25% of patients with LV dysfunction) who also received the highest cumulative dose of anthracycline. This was followed by ALL (15.8%) and then HL (8.7%). There was wide variation in the onset of myocardial dysfunction with earliest onset in AML patients who also got the maximum cumulative dose.

**Conclusions:** With improved survival focus is now on long term effects of cancer therapy. Myocardial dysfunction can be a late effect of cancer therapy and can manifest even after chemotherapy is over. There is a need for continued follow up of children after completion of chemotherapy even if they are asymptomatic.

**67. DEFINING LATE ONSET CARDIOMYOPATHY IN CANCER SURVIVORS TREATED WITH ANTHRACYCLINE** Olga Salazar, MD PI; Kerry Moss, MD; Georgina Burke, PhD; Lucy Prantis, RN; Eileen Gillan, MD. *Divisions of Pediatric Cardiology, Hematology/Oncology, and Clinical Research, Connecticut Children's Medical Center, Hartford, CT, USA*

**Introduction:** Anthracycline cardiomyopathy is a potentially devastating complication affecting childhood cancer survivors. The Children's Oncology Group defines cardiomyopathy as echocardiographically-determined fractional shortening <29%. Unfortunately, this measure is a late marker of disease and treatments options are limited. The purpose of this study is to identify the incidence of adverse cardiac outcomes, including heart transplantation, cardiac death, and systolic dysfunction as defined as FS <29% in childhood cancer survivors treated with anthracycline.

**Methods:** Since 1985, over 1,200 children have been diagnosed with cancers at our center. Of these, 460 patients received anthracyclines as part of their chemotherapy. One patient received a heart transplant. There were 2 cardiac deaths, 3 deaths from cancer with cardiac disease, and 50 non-cardiac related deaths. Clinical and echocardiographic parameters were analyzed in 136 of the 460 patients who received anthracyclines. Patients were stratified into three cohorts according to length of follow-up after initial chemotherapy.

**Results:** Overall incidence of cardiomyopathy in this group was 11%. There were no significant differences in age at diagnosis, gender or cumulative dose of anthracyclines between groups. However, there were significant differences in percentages of patients who had echocardiographic evidence of cardiotoxicity. Univariate analysis revealed that time of follow-up in years after chemotherapy served as a predictor of decreased shortening fraction over time ($P = 0.0006$).

**Conclusions:** Incidence of cardiomyopathy significantly increased over time in the 136 patients analyzed, independent of additional risk factors. The correlation between delayed diagnosis and increased severity of illness suggests the role for novel screening modalities. Such modalities include advanced cardiac MRI (cMRI) techniques that are capable of identifying occult asymptomatic cardiotoxicity. A current study utilizing cMRI to detect subclinical cardiotoxicity is currently being performed in this patient population.

**68. AN INSTITUTIONAL ASSESSMENT OF CURRENT SCREENING PRACTICES FOR CARDIOVASCULAR RISK FACTORS (CVRF) IN YOUNG SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)** Maria H. Lin, MD; Jamie R. Wood, MD; David R. Freyer, DO, MS. *Center for Endocrinology, Diabetes, and Metabolism and Children's Center for Cancer and Blood Diseases at Children's Hospital Los Angeles, Keck School of Medicine at University of Southern California, Los Angeles, CA*

**Purpose:** ALL survivors have increased risk for long-term cardiovascular complications. While the American Academy of Pediatrics has published guidelines for CVRF screening in the general population, there is no comparable guideline specific to pediatric ALL survivors. This study examined current screening practices and their results in the LIFE Cancer Survivorship & Transition Clinic at Children's Hospital Los Angeles.

**Patients/Methods:** For this retrospective study, subjects with ALL currently aged 2-21 years with ≥ 1 survivorship evaluation between 1/1/2009 and 9/30/2011 were identified. Data from most recent LIFE Clinic visits were abstracted. Demographic and CVRF characteristics collected included age, sex, race/ethnicity, physical activity level, tobacco exposure, diabetes history, cardiovascular family history, BMI, BP, and triglyceride/HDL.

**Results:** This cohort (n=194) had mean age of 15.5 years (range 6.7-21.5 years); 88 (45%) females and 130 (67%) Hispanics. Median interval since therapy completion was 8.2 years (range 2.3-15.8 years). Fifteen subjects received cranial irradiation. All received anthracyclines (mean cumulative dose 173 mg/m2, range 75-570 mg/m$^2$). Family history was positive for hypertension in 20 subjects, diabetes in 17, and hyperlipidemia in 13. While physical activity level was frequently assessed, tobacco exposure was not. Forty (21%) were overweight; 60 (31%) obese. Twenty (10%) subjects were pre-hypertensive; 7 (4%), hypertensive. Because survivors were not routinely seen under fasting conditions, only 11 had lipid profiles (7 with elevated triglyceride; 2 with low HDL). 176 subjects (90%) had serum glucose values (random for all but 3). Of these, only 1 was >200 mg/dL in the one survivor with type 2 diabetes.

**Conclusions:** Pediatric/adolescent survivors of childhood ALL have high prevalence of overweight/obesity. While BP and physical activity are assessed routinely, evaluation of hyperlipidemia, diabetes, and tobacco exposure are suboptimal when compared to current general pediatric recommendations. Development of standardized guidelines and more effective systems for CVRF screening are indicated.

**69. RETROSPECTIVE REVIEW OF CARDIOVASCULAR HEALTH IN PEDIATRIC CANCER SURVIVORS IN SOUTH TEXAS** Gregory J. Aune, MD, PhD; Forrestine Dickson, BA; and Gail E. Tomlinson MD, PhD. *Greehey Children's Cancer Research Institute and The University of Texas Health Science Center at San Antonio, San Antonio, TX, USA*

**Background and study purpose:** The most currently available statistics indicate 75-80% of all pediatric cancer patients will survive longer than five years. Unfortunately, exposure to chemotherapy and radiation is now known to cause a wide array of late health effects including cardiovascular disease, endocrinopathies, and secondary malignancies. Survivors with Hispanic ethnicity are underrepresented in survivorship research. Therefore, we completed a retrospective chart review of pediatric cancer survivors seen in the South Texas

Pediatric Cancer Survivorship Clinic, with particular focus on cardiovascular health and disease. We sought patients who had received treatment with either anthracyclines or radiation and had available follow-up echocardiogram data for review. We then completed a chart review collecting demographics, cancer diagnosis, BMI, history of diabetes, and compiled echocardiogram data including shortening fraction (SF), ejection fraction (EF), and structural abnormalities.

**Results and conclusions:** The study population consisted of 60 patients with age at diagnosis ranging from infancy to 20 years. There were 37 males (62%), 23 females (38%), 40 (67%) had been treated for either leukemia or lymphoma, and 47 (78%) were treated with chemotherapy only. The study population included 38 patients of Hispanic ethnicity (63%) and 21 Caucasians (35%). In the total study population, 28 (47%) were classified as obese with BMI greater than 85th percentile for age, 7 (12%) carried a diagnosis of diabetes mellitus, and 5 (8%) had elevated serum cholesterol. 33 patients (55%) had abnormalities in echocardiogram measurements: 28 in SF (47%) and 5 in EF (8%). The above findings describe cardiovascular health measurements and possible modifying factors, such as BMI, in a subset of mostly Hispanic patients followed in our survivorship clinic. The high rates of obesity and abnormalities in echocardiograms suggest efforts should be undertaken to expand the study population and to perform a more detailed assessment of cardiovascular health in patients seen in the South Texas Pediatric Cancer Survivorship Clinic.

**70. EVALUATION OF RADIATION-INDUCED VASCULOPATHY BY TRANSCRANIAL DOPPLER (TCD) AMONG SURVIVORS OF CHILDHOOD BRAIN TUMORS TREATED WITH CRANIAL RADIATION THERAPY** Daniel C. Bowers, MD; Sheetal Schneider; Mark Johnson, MD. *UT Southwestern Medical School, Dallas, TX, USA*

**Background:** The purpose of this study is to describe the prevalence of asymptomatic cerebrovascular disease among childhood brain tumor survivors who have received prior treatment with cranial radiation therapy.

**Methods:** > 5 year survivors of childhood brain tumors who were treated with > 30 Gy craniospinal radiation therapy were invited to participate in this study including a history, physical and neurological exam, laboratory markers of cerebrovascular disease (cholesterol, HDL, LDL, high sensitivity CRP, hemoglobin A1C, Apoprotein A and Apoprotein B) and transcranial doppler ultrasonography (TCD) of the cerebral arteries.

**Results:** 164 cerebral arteries from 13 patients (medulloblastoma = 10, germ cell tumor = 3; females = 5; mean age at diagnosis = 8.02 years; mean age at time of study = 20.9 years) were examined. 28 of 164 (17%) were considered abnormal by our pre-specified criteria. 113 cerebral arteries from 13 patients were assessed for >50% stenosis velocities. Arteries most likely to be considered abnormal included the distal bilateral vertebral arteries (right 38%, left 30%), basilar artery 30%, bilateral siphon internal carotid arteries (right 30%, left 23%), bilateral middle cerebral arteries (23% bilaterally), and bilateral anterior cerebral arteries (7% bilaterally). 2 vessels had mean flow velocities consistent with > 50% stenosis (1.8%). No vessels were found to have either > 80% stenosis (prespecified) or greater than 70% stenosis on the ones with standardized criteria.

**Conclusions:** This is the first study demonstrating a high prevalence of asymptomatic cerebrovascular disease among childhood brain tumor survivors treated with cranial radiation therapy. Posterior circulation vessels appear to be the ones with highest burden of disease in this group. TCD presents as a practical alternative for the follow up of patients in this population. More work is necessary to better understand the mechanism and risk factors for cerebrovascular disease as well as consideration of intervention strategies for this population.

**71. A PREDICTIVE BIOMARKER OF VASCULOPATHY IN SURVIVORS OF CHILDHOOD MALIGNANCIES** K. Pradhan, MBBS, MS; H. Claussen, CCRP; T. Vik, MD; C. Calley, MS; J. Mund, MS; J. Case, PhD. *Department of Pediatric Hematology-Oncology, Riley Hospital for Children, Indianapolis, IN, USA; Department of Bio-Statistics, Indiana University School of Medicine, Indianapolis, IN, USA; Herman B. Wells Center for Pediatric Research, Indiana University School of Medicine, Indianapolis, IN, USA*

**Background:** Cardiovascular and cerebrovascular late-effects occur in survivors of childhood cancer at an increased frequency at least two-decades after their cancer treatment. These late-effects are typically seen in survivors of leukemia, brain-tumors and Hodgkin's lymphoma, with radiotherapy and anthracyclines causing the vasculopathy. Although multiple screening modalities for these side effects have been recommended, there are no established peripheral blood (PB) biomarkers that correlate with vasculopathy. Our exploratory study was designed to detect the frequency of circulating cellular biomarkers of angiogenesis in cancer survivors, with the goal to eventually establish them as biomarkers of vasculopathy.

**Methods:** Based on our previous published findings, we elected to study circulating hematopoietic stem and progenitor cells (CHSPCs) and their subsets using polychromatic flow cytometry (PFC). Utilizing PFC, CHSPCs were further characterized into two subsets, pro-angiogenic and non-angiogenic ($CD31^{+}CD34^{bright}CD45^{dim}AC133^{+}$ and $CD31^{+}CD34^{bright}CD45^{dim}AC133^{-}$ cells respectively). We have recently shown that the ratio of the pro-angiogenic to the non-angiogenic CHSPCs (CPC: n-CPC) is significantly decreased in patients with peripheral arterial disease when compared to normal subjects (p=0.0001). Our hypothesis was that CHSPCs and the CPC: n-CPC ratio would also be lower in cancer-survivors compared to normal subjects. We studied twelve patients with leukemia, brain-tumors

or Hodgkin's lymphoma who were at least three years post–treatment (5-18 years). Baseline levels of CHSPCs and their subsets were compared to normal subjects using the Kruskal-Wallis test. Non-parametric analyses were done because the data was not normally distributed.

**Results:** In the survivors, the median CHSPCs and CPC: n-CPC ratio was 0.001% (±0.002) and 0.2% (±0.6) respectively. In normal subjects, the median CHSPCs and CPC: n-CPC ratio was increased to 0.06% (±0.044) and 1.26% (±0.2) respectively. Pair-wise comparisons indicated that cancer survivors had significantly lower CHSPCs (p=0.0003), and CPC: n-CPC ratio (p=0.0009) compared to normal subjects.

**Conclusions:** Utilizing PFC, the CHSPCs and their subsets detected in PB of cancer-survivors may serve as predictive biomarkers for early detection of vascular late-effects.

**72. CANCER PREVENTION AND SCREENING PRACTICES OF SIBLINGS OF CHILDHOOD CANCER SURVIVORS: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY** David Buchbinder, Ann C. Mertens, Lonnie K. Zeltzer, Wendy Leisenring,Pam Goodman, E. Anne Lown, Melissa A. Alderfer, Christopher Recklitis, Kevin Oeffinger, Gregory T. Armstrong, Melissa M. Hudson, Leslie L. Robison, Jacqueline Casillas. *Department of Pediatrics and Division of Hematology at Children's Hospital of Orange County, Orange, CA, USA; Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA; Department of Pediatrics, Division of Hematology-Oncology, and Division of Cancer Prevention and Control Research, David Geffen School of Medicine at University of California at Los Angeles (UCLA) and UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA; Cancer Prevention Program at Fred Hutchinson Cancer Research Center, Seattle, WA, USA; Alcohol Research Group, Emeryville, CA, USA; Division of Oncology, The Children's Hospital of Philadelphia and Department of Pediatrics, Perelman School of Medicine, The University of Pennsylvania, Philadelphia, PA, USA; Perini Family Survivors' Center, Dana-Farber Cancer Institute, Boston, MA, USA; Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Department of Epidemiology and Cancer Control and Oncology, St. Jude Children's Research Hospital, Memphis, TN, USA*

**Objective:** To compare the skin cancer prevention practices and breast/cervical cancer screening practices of adult siblings of childhood cancer survivors with the general population and to identify modifying factors for these practices.

**Methods:** Cross-sectional, self-report data from 2,861 adult siblings of 5+ year survivors of childhood cancer were analyzed. An age, sex and race/ethnicity-matched sample (n=5,915) from the Behavioral Risk Factor Surveillance System served as the comparison population. Sociodemographic and cancer-related data reported by the siblings and their familial cancer survivors were explored as modifying factors for sibling prevention/screening practices through multivariable logistic regression.

**Results:** Compared to controls, siblings were more likely to practice skin cancer prevention behaviors: protective clothing use (OR 3.07, 95% 2.60-3.64), shade use (OR 2.20, 95% 1.97-2.46), sunscreen use (OR 1.30, 95% 1.17-1.43), and hat use (OR 1.83, 95% 1.64-2.04). No differences were noted for breast/cervical cancer screening practices (mammography and Pap testing). Older age at time of study was associated with greater skin and breast/cervical cancer prevention/screening behaviors: sunscreen use (OR 1.33, 95% 1.02-1.75), protective clothing use (OR 1.55, 95% 1.12-2.12), hat use (OR 1.53, 95% 1.10-2.13), shade use (OR 1.57, 95% 1.24-2.00), mammography (OR 2.72, 95% 1.60-4.77), and Pap testing (OR 4.16, 95% CI 2.79-6.35). Being older than the cancer survivor was associated with greater skin and cervical cancer prevention behaviors: sunscreen use (OR 1.24, 95% 1.01-1.52), hat use (OR 1.33, 95% 1.07-1.67), and Pap testing (OR 1.68, 95% 1.05-2.73). Survivor diagnosis, treatment intensity, and survivor complications (adverse health, chronic health conditions, second cancers) were not consistently associated with sibling behaviors.

**Conclusions:** Siblings of childhood cancer survivors report greater skin cancer prevention practices when compared with controls; however, no differences were noted for breast/cervical cancer prevention practices. Research should be directed at understanding the impact of the childhood cancer experience on sibling health behaviors.

**73. REPORTED HEALTH PROBLEMS AND HEALTHCARE SPECIALIST NEEDS OF CHILDHOOD CANCER SURVIVORS TRANSITIONING TO ADULT-BASED-CARE** Kristen Vangile, MPH; Leann Hassen-Schilling, MPH; Jordan Gilleland, PhD; Brooke O. Cherven, RN, MPH, CPON; Ann Mertens, PhD; Lillian Meacham, MD; Karen Wasilewski-Masker, MD, MsC. *Aflac Cancer Center and Blood Disorder Service at Children's Healthcare of Atlanta, Atlanta, GA, USA; Emory School of Medicine, Atlanta, GA, USA*

**Background:** Adolescent and young adult (AYA) survivors of childhood cancer have an increased risk of treatment related late-effects. Late-effects often manifest during young-adulthood when many survivors are lost to healthcare follow-up. As patients transition to adult-based-care, they often cannot access survivorship care and are forced to navigate the healthcare system independently. Prior to transitioning to adult-based-care, both provider and patient should understand the patient's healthcare needs and proactively plan to ensure those needs will be met by the correct adult specialists.

**Purpose:** To determine the health problems and specialist needs of patients transitioning from pediatric survivorship to adult-based-care.

**Methods:** Baseline surveys were completed by 357 survivors as part of the Children's Healthcare of Atlanta (CHOA) institutional cohort study Childhood, Adolescent and Young Adult Cancer Survivor Study (CHOA-CAYACSS). This analysis included survivors aged 15 and older.

**Results:** Of 157 surveys, respondents ranged from 15 to 28 years old. 52% were male; 75% were white; 62% had a diagnosis of leukemia or lymphoma; and 59% were diagnosed before the age of 8. The five most commonly self-reported problems were vision (34%), headaches (31%), tiredness (20%), dental (19%) and being overweight (18%). The five most commonly reported provider visits were Dentist (94%), PCP (89%), Hematologist/Oncologist (65%), Endocrinologist (36%) and Cardiologist (36%). Of the most commonly reported problems, three did not show a relationship between having the problem and seeing the specialist.

| Problem (n) | Provider | OR(95%CI) |
|---|---|---|
| Headaches (49) | Neurologist | 1.42 (0.502-4.009) |
| Dental (30) | Dentist | 0.29 (0.061-1.369) |
| Overweight (28) | Endocrinologist | 1.19 (0.502-2.817) |

**Conclusions:** AYA childhood cancer survivors have treatment-related medical problems and medical needs as they transition to adult-based care. To develop a model of care to facilitate the transition for AYA survivors as they move to adult-based-care, it is important to understand their healthcare and specialist provider needs. Additional information is needed to determine the reason for specialist visits.

**74. MORBIDITY PROFILE OF CHILDHOOD CANCER SURVIVORS IN INDIA: A NEED FOR CANCER SURVIVOR CLINICS** R Seth, S Saharan, L Narayan, S Seth, S Sapra, K Verma. *Departments of Pediatrics and Cardiology, All India Institute of Medical Sciences, New Delhi, India*

**Background:** With refinements in diagnostics and advances in therapeutics the overall survival of childhood cancer has increased. This is at the cost of increased morbidity in the form of various long/late effects of cancer treatment. We report data from our cohort of childhood cancer survivors being followed at the pediatric cancer survivor clinic.

**Methodology:** A detailed evaluation including treatment details is done. Investigations pertaining to the primary disease are done. Growth is monitored on growth charts. Transfusion related hazards are assessed. A detailed psychosocial and IQ assessment is done. Systemic evaluation is done. Myocardial function and thyroid profile are done when required.

**Results:** This clinic is ongoing and the current data reflect that of 300 patients. The median age at evaluation was 9 years and of follow up were 3.5 years. Male to female ratio was 4.6:1. 25% patients had height less than 3rd centile and 26% patients had weights less than 3rd centile. 6 had transaminitis and one patient died of liver failure. 110 patients had received some form of blood component of which 22 patients were found to be positive for Hepatitis B antigen. Eleven patients relapsed on follow up of which five expired. There were no second malignancy IQ and Psychosocial assessment was done for patients with acute lymphoblastic leukemia Myocardial dysfunction was identified in 4%.

**Conclusion:** This clinic reflects a need for multimodal evaluation. Longer follow will highlight the morbidity profile, identify patients at risk, develop programs for educating survivors on positive lifestyles patterns.

**75. BENEFITS OF A SUPPORT GROUP FOR ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA LIVING WITH COGNITIVE LATE EFFECTS** Colleen Dibden, BA, BSW, RSW; Maureen DiSciglio, BScN; Maria Spavor, MD, FRCPC. *Kids With Cancer Society Survivor Program, Stollery Children's Hospital, Division of Pediatric Oncology, Edmonton, Alberta, Canada*

**Background:** Cognitive functioning in adult survivors of Acute Lymphoblastic Leukemia who received cranial radiation can be significantly compromised. These individuals report difficulties with memory loss, slow processing speed, problem solving and decision-making. These problems can have a negative impact on quality of life and result in challenges in: self-esteem, relationships, communication, depression, post-secondary studies and finding a job. The social worker in the Kids With Cancer Society Survivor Program has established a monthly support group to help these individuals develop coping strategies to more effectively manage the challenges of daily living.

**Project description:** Six adult ALL survivors aged 34-47 years old attend the sessions. Cranial radiation doses varied between a minimum of 2000 cGy and a maximum of 3337 cGy. The survivors were between 1 and 12 years old when they received the radiation. Support group sessions have included: talking and sharing experiences, memory improvement strategies, stress reduction techniques, money management, organizational skills, nutrition and exercise. All participants have responded favorably to the group and improvements in skills have been noted by the facilitator.

**Conclusion:** Adult survivors of Childhood ALL who received cranial radiation can face significant cognitive challenges which greatly effect activities of daily living. Establishing formal support systems can help these survivors improve their cognitive skills and enhance their quality of life.

**76. A SYSTEMATIC REVIEW OF SUBSEQUENT NEOPLASMS OF THE CENTRAL NERVOUS SYSTEM AMONG SURVIVORS OF CHILDHOOD CANCER** Daniel C. Bowers, MD; Paul C. Nathan, MD; Louis Constine, MD; Catherine Woodman, MD; Smita Bhatia, MD, MPH; Lisa Bashore, PhD, CPNP, CPON. *UT Southwestern Medical School, Dallas, TX, USA; Hospital for Sick Children, Toronto, Ontario, Canada; University of Rochester, Rochester, NY, USA; University of Iowa Hospitals and Clinics, Iowa City, IA, USA; City of Hope, Duarte, CA, USA; Cook-Children's Medical Center, Ft. Worth, TX, USA*

**Background:** Children treated with therapeutic radiation that directly or incidentally exposes the brain may develop subsequent central nervous system (CNS) tumors. The aim of this study is to summarize the risk of subsequent CNS neoplasms among childhood cancer survivors.

**Methods:** A systematic review of the literature was conducted to examine subsequent CNS neoplasms among childhood cancer survivors. Articles were identified through queries of MEDLINE, EMBASE, CancerLit, and the Cochrane Library (1966 – present). Two investigators independently abstracted data and assessed study quality. Articles were selected that addressed at least one of 3 questions: (1) What is the incidence and relative risk of subseqeunt CNS neoplasms (especially meningiomas/gliomas) among childhood cancer survivors treated with radiation therapy to the brain?; (2) What are the clinical characteristics and outcomes of these neoplasms?; (3) Is it possible to establish recommendations for surveillance neuro-imaging for subsequent CNS neoplasms in this population and to describe the potential risks and benefits associated with surveillance?

**Results:** 54 abstracts were reviewed and 13 retrospective cohort studies met eligibility criteria for this review. The median standardized incidence ratio of subsequent CNS neoplasms in survivors was 10.4 (range = 8.1 – 52.3), with a median absolute excess risk of 3.1 (range = 1.9 – 72.8 per 10,000 patient years). The cumulative incidence of subsequent CNS neoplasms ranged from 1.4%– 7.1%. Risk factors included exposure of the brain to radiation therapy, cumulative dose of radiation therapy and a first neoplasm of acute lymphoblastic leukemia (ALL) or brain tumor. Median interval from first cancer to diagnosis of a subsequent glioma was 6.0 – 17.4 years. Survival was poor in patients with a subsequent glioma. The interval to diagnosis of a subsequent meningioma was 20.6 – 23.1 years, although a recent study suggests the risk of meningioma does not appear to plateau. Patients with subsequent meningiomas often had prolonged subsequent survival.

**Conclusions:** Survivors of childhood ALL and CNS tumors who were treated with radiation therapy involving the brain have an elevated risk for subsequent CNS neoplasms. The current literature is insufficient to inform about the potential harms and benefits of routine surveillance.

**77. CANCER SURVIVORLINK™: RECRUITMENT STRATEGIES FOR WEBSITE UTILIZATION** Leann Hassen-Schilling, MPH; Brooke O. Cherven, RN MPH; Lillian Meacham, MD; Paula Edwards, PhD; Sofia Espinoza, MSHS; Mike Palgon; Ann Mertens, PhD. *Aflac Cancer Center and Blood Disorders Service, Children's Healthcare of Atlanta(CHOA), Atlanta, GA, USA; Emory University, Atlanta, GA, USA; Himformatics, Atlanta, GA, USA; Georgia Institute of Technology, Atlanta, GA, USA*

**Background:** With an 80% cure rate in pediatric cancer, there is a need to empower survivors to seek lifelong individualized surveillance and treatment for late effects to improve quality and length of life. Cancer SurvivorLink™(CSL) (*www.cancerSurvivorLink.org*) is a website designed to increase awareness and educate survivors, families and healthcare providers about survivorship care.

**Purpose:** Determine the most effective method to increase website awareness and registration in patients/parents through three recruitment strategies.

**Methods:** Standard mailing: 218 randomized pediatric cancer patients from CHOA received CSL information via standard mail. Patients/parents not registered after the mailings received a phone call from CSL staff. Community event: five survivor focused events were attended by CSL staff that provided individualized discussions and demonstration of CSL to attendees. Social media: creation of a Facebook page. Website traffic volumes were tracked using Google Analytics.

**Findings:** 23 survivors (11%) registered for CSL after standard mail contact; and 49 (22%) after a standard mail contact and follow-up call. Individuals that previously attended a cancer survivor clinic visit were more likely to register on CSL vs. non-attendees (47% vs 25%; p=.037); while no-association was found between parent vs. survivor and registration (p=.18). 22% of patients/parents engaged by CSL staff at community events registered on CSL. Number of unique visits to CSL were increased post-community event (averaged 44.4 users per/week) vs non-event weeks (19.5 users/week). Over the first 4 months, CSL Facebook received 645 page views. 58 people have 'liked' CSL from 4 countries, 78% were female, 47% under age of 35.

**Conclusions:** Community engagement is the most efficient/ effective method to increase awareness and website registration, with minimum staff time and budget. Standard mailings require the most staff time, but demonstrated similar registrants with a follow-up call. Facebook offers an affordable and easily accessible marketing tool to increase awareness, but is difficult to encourage user registration.

**78. PARTNERSHIP FOR ACADEMIC SUPPORT AND SUCCESS (PASS): USING COMMUNITY-BASED PARTICIPATORY RESEARCH TO FACILITATE SCHOOL RE-INTEGRATION IN PEDIATRIC CANCER PATIENTS AND SURVIVORS** Amanda L. Thompson, PhD; Kristina K. Hardy, PhD; Sarah A. Hostetter, BA; Katherine Kelly, PhD, RN. *Children's National Medical Center, Washington, DC, USA*

**Background and purpose:** As a result of prolonged absences and neurocognitive effects, children with cancer are at significant risk for academic difficulties during and after treatment. Because success in school is a major determinant of a child's future quality of life, it is imperative to ensure optimal school experiences for these children. Recent studies support the role of the school nurse in advocating and providing case management services for children with chronic illness; however, formal school-based intervention programs for children with cancer are rare.

**Methods:** PASS is using community participatory research methods to cultivate a partnership among stakeholders from hospital, school, family, and community environments and to develop an evidence-based school-nurse led intervention. In the inaugural meeting, a 20 member Advisory Board consisting of hospital clinicians and researchers; school nurses and educators; parents of children with chronic illness; and community advocacy members met to discuss student goals and potential barriers to achieving goals. Ideas were documented verbatim, and then coded for related content and themes.

**Results and conclusions:** The use of community-based participatory research methods resulted in rich data from the multiple systems of the patient-student's environment (e.g., hospital, school, family, community). Goals and barriers were identified that might have been missed if not for the inclusion of Board members outside of the hospital. The overarching goal identified by the community partners was for students to be able to learn and achieve their academic potential in a safe and supportive environment, thereby maximizing their quality of life and hope for their future. Key barriers included limited resources and the need for patient- and school- specific individualization of intervention. Data will be utilized to guide future intervention development. We will present outcomes from subsequent community partner meetings, including intervention components developed to date and plans for evaluation.

**79. A NATIONAL SURVEY OF GENERAL INTERNIST'S PREFERENCES AND KNOWLEDGE GAPS REGARDING THE CARE OF CHILDHOOD CANCER SURVIVORS** T.O. Henderson, MD, MPH; P.C. Nathan, MD, MSc; K.A. Rasinski, PhD; E. Suh, MD; M. Kigin, BA, K.E. Wroblewski, MS; J. Ford, PhD; E.S. Tonorezos, MD, MPH; K.C. Oeffinger, MD; C.K. Daugherty, MD. *University of Chicago, Chicago, IL, USA; Hospital for Sick Children, Toronto, Ontario, Canada; Memorial Sloan Kettering Cancer Center, New York, NY, USA*

**Background:** Although most childhood cancer survivors (CCS) report obtaining health care in the community, primary care physicians' views and knowledge regarding the long-term follow-up (LTFU) care of CCS are largely unknown.

**Methods:** Surveys were mailed to a random sample of 1,907 general internists under age 65 years from the American Medical Association Physician Masterfile in November 2011. A second mailing to non-responders is ongoing.

**Results:** 892 (47%) physicians have responded. Respondents have practiced a median of 10 years (range: 3-20), and see a median of 70 patients/week (range: 40-100). 46% are in solo/group practice, 17% in multi-specialty practice, and 14% in academic practice. In the last five years, 53% have seen at least one CCS, 71% of whom have never received a treatment summary. 85% prefer to care for CCS in consultation with a cancer center based physician. A vignette of a 29-year-old female treated for Hodgkin lymphoma with mantle radiation at age 16 was provided and participants were asked a series of questions regarding monitoring for late effects. The percentage of responses that were concordant with available LTFU Surveillance Guidelines were: breast cancer, 29%; cardiac, 15%; thyroid, 77%; and all three recommendations, only 5%. By logistic regression, greater likelihood of concordance with at least one surveillance recommendation was associated with being female (OR=2.0 95% CI 1.3-3.1), seeing more patients/week (OR=1.4 per SD increase, 95% CI 1.1-1.7) and more years in practice (OR=1.3 per SD increase, 95% CI 1.0-1.6). The two modalities felt to be most useful for independent care of CCS by internists were access to LTFU guidelines and receiving a patient-specific care plan from the cancer center.

**Conclusion:** Although the majority of internists are willing to follow CCS, they appear unfamiliar with the available LTFU guidelines and prefer to care for patients in collaboration with a cancer center based physician.

**80. PATIENT-PERCEIVED FACILITATORS TO THE TRANSITION OF SURVIVORSHIP CARE FROM THE PEDIATRIC TO ADULT CARE-SETTING** Karim Thomas Sadak, MD, MSE; Amanda DiNofia, MD; Gregory Reaman, MD. *Children's National Medical Center, Washington, DC, USA*

**Purpose:** Survival rates in childhood cancer continue to rise. A new challenge has emerged in optimizing the transition of pediatric survivorship care to similarly focused programs that are age-appropriate. The purpose of this study is to identify components of a clinical survivorship program that facilitate the transition of care for adult survivors of childhood cancer from the pediatric to adult care-setting.

**Description:** A descriptive study of childhood cancer survivors was conducted using a cross-sectional study design. A questionnaire was used to identify which clinical components of a survivorship program most influenced the decision to transition care to an adult medical center. Data were collected through the mail, online and in-person during survivorship clinic visits. 140 survivors were eligible.

129 had valid addresses and received the questionnaire. The study endpoint was achieved when the response rate reached 80% (n=103). A descriptive review of clinical program components was performed using a frequency analysis.

**Results:** Of 129 invited survivors, 103 participated (80%). Their mean and median age-range was 20-24 years. There were 49 males (48%) and 54 females (52%). The most common diagnosis was leukemia (40/103) followed by lymphoma (20/103). When asked if the participant was willing to transition their survivorship care to an adult facility, 97 (95%) responded affirmatively. The clinical component most frequently rated "Very Important" in the decision to transition survivorship care was the acceptance of insurance (80/103, 78%). The clinical components most frequently rated "Very Important" or "Important" in this decision were the availability of flexible scheduling (102/103, 99%) followed by comprehensive care being offered (101/103, 98%).

**Conclusions:** Issues related to insurance, clinical team composition, and scheduling appear to be most important for young adult survivors when making the decision to transition survivorship care to age-appropriate care-settings

**81. IMPLEMENTATION AND EVALUATION OF A TRANSITION CLINIC FOR ADULT SURVIVORS OF PEDIATRIC CANCER** Brian Greffe, MD; Linda Overholser, MD, MPH; Betsy Risendal, PhD; Timothy Garrington, MD; Kristen Leonardi-Warren, RN, ND; Allison Faust-Jones, RN, ND; Kristin Kilbourn, PhD, MPH, Traci Yamashita, MS; Jean Kutner, MD, MSPH. *Center for Cancer and Blood Disorders, Children's Hospital Colorado; Division of General Internal Medicine, University of Colorado Denver School of Medicine, University of Colorado Cancer Center, Cancer Prevention and Control, Aurora, CO, USA*

**Background:** Childhood cancer has become a curable disease with survival rates now surpassing 80%. Successful transition to adult care for these survivors however can be difficult due to lack of understanding of potential long-term problems secondary to therapy, post-traumatic stress issues, and/or anxiety over follow-up.

**Methods:** In 2008 we implemented a transition clinic for adult survivors of pediatric cancer in order to facilitate seamless transition from a children's hospital cancer setting to an internal medicine setting. Known as TACTIC (Thriving After Cancer Therapy is Complete), the clinic consists of pediatric oncologists, a general internist, health psychologist, and cancer center nurse. Patients must be 21 years older or greater and be at least 5 years from diagnosis and 2 years off therapy. As part of an IRB approved study, patients are asked to complete a survey at baseline and at 2 and 8 weeks following their clinic visit. The survey assesses patient satisfaction, self-efficacy with managing one's health, health behaviors, and uptake of provider recommendations.

**Results:** The clinic has seen 77 patients since its inception in July 2008. Twenty-four patients have consented to be part of the study. Median age of consenting survivors is 28 with an average of 17.9 years since diagnosis. Comorbid conditions reported included diabetes, hypertension, obesity, high cholesterol, and kidney disease. Survey results indicated that patients preferred the adult care setting to the pediatric setting. From baseline to 8 weeks after receiving their survivorship care plan, respondents demonstrated statistically significant improvements in ability to access cancer survivorship resources, knowing who to talk to about specific medical issues, and identifying unique health risks associated with their cancer diagnosis.

**Conclusions:** Our results indicate that successful transition to adult care for pediatric cancer survivors is both possible and beneficial.

**82. UNIVERSITY HEATLHCARE PROVIDERS AS PARTNERS IN TRANSITION OF CHIDHOOD CANCER SURVIVORS** Lillian R. Meacham MD; Ronald L. Forehand MD; Maureen L. Olson MD; Michael J. Huey MD; Brian M. DeLoach MD; Paula J. Edwards PhD; Brooke O. Cherven RN MPH; Leann Hassen-Schilling MPH; Ann C. Mertens PhD. *Department of Pediatrics, Emory University and Aflac Cancer Center–Children's Healthcare of Atlanta, Atlanta, GA, USA; Medical Services University Health Center, University of Georgia, Athens, GA, USA; Stamps Health Services, Georgia Institute of Technology and Student Health and Counseling Service, Emory University, Atlanta, GA, USA; Student Health Services, Georgia Southern University, Statesboro, GA, USA; Himformatics-Healthcare Information Technology Consultants, Atlanta, GA, USA*

**Background:** At age 18, pediatric cancer survivors (pedCS) begin to face many transitions. These may include: legal responsibility for their care, changing to adult healthcare providers (HCP) and leaving home to attend college. College student health centers are an ideal scenario to utilize Cancer SurvivorLink™ (*www.cancersurvivorlink.org*™) a web-based patient controlled communication tool to expedite sharing of key survivor health documents.

**Purpose:** To partner with student health centers as medical homes for pedCS

**Methods:** Lectures on survivor care were given at key Georgia colleges and HCPs were asked to register on Cancer SurvivorLink™. A baseline assessment of knowledge and willingness to provide survivor care was ascertained.

**Results:**

| College/University in Georgia Location | Student body | Clinic visit/yr | # HCPs | SurvivorLink registered HCPs |
|---|---|---|---|---|
| University of Georgia Athens | 34,885 | 75,566 | MD 16.0 Mid levels 11.9 | 7 |
| Georgia Institute of Technology Atlanta | 22,000 | 34,042 | MD 11.0 Mid level 3.75 | 5 |
| Georgia Southern University Statesboro | 20,212 | 24,786 | MD 2.0 Mid levels 6.1 | 4 |
| Emory University Atlanta | 13,500 | 23,127 | MD 7.2 Mid level 2.7 | 7 |

Post-lecture, 23 student health care providers have registered on Cancer SurvivorLink™ and completed the baseline survey. Providers reported moderate familiarity with survivor care (30%) and a survivor healthcare plan (43%). There were no differences in responses comparing schools in large cities (Atlanta) and close proximity to a survivor clinic vs not. 52% felt a primary care provider should be responsible for late effects surveillance but 48% did not feel comfortable in this role.

**Conclusions:** The transition to college is an opportunity to establish transition to adult HCPs. Student health centers often function as the medical home for survivors during college and transition may be aided by access to key health documents and educational material on Cancer SurvivorLink™. One year follow up surveys to assess knowledge and comfort providing survivor care are planned.

**83. PRIMARY CARE INVOLVEMENT IN THE CARE OF ADULT SURVIVORS OF YOUNG PEOPLE'S CANCER** Adam Glaser MD; Jennifer Dutton; Heather Berry RGN; Naseem Sarwar RGN; Elizabeth Brown; Geraint Hughes BSc; Bryan Power, MD; Marlous Van Laar MSc; Lorna Fraser MD; Richard Feltbower PhD; Una MacLeod MD. *Long Term Follow-Up, St. James's Institute of Oncology, Leeds, UK; Yorkshire Cancer Network, Harrogate, UK; H3 Clinical Commissioning Group, Leeds, UK; Paediatric Epidemiology Group, University of Leeds LS1, Leeds, UK; Department of Primary Care, Hull and York Medical School, York, UK*

**Introduction:** Supported self management of adult survivors of childhood cancer has been proposed.

**Aim:** To identify components of nationally recommended follow-up that Primary Care Providers (PCPs) would deliver and which they would prefer to be managed by a specialist long term follow-up service (LTFU).

**Methods:** All LTFU users, aged 18+, attending a regional LTFU between January-March 2011 were included (n=207). On the basis of the cancer, treatments received, co-morbidities and psychosocial factors, we identified those suitable for remote management/PCP led support along with required surveillance examinations and investigations according to national best practice (CCLG Guidelines). Patients' named PCPs were asked to identify components of care they would be willing to deliver. Subsequent survey of initial respondents asked PCPs about knowledge, skills, resource and financial factors underlying their responses.

**Results:** 179 of 207 (86%) PCPs responded to initial survey, 134 of these (75%) responded to the follow-up survey.

3% of patients, whose PCPs responded, were classified as Wallace level 1 (low risk), 64% level 2 and 33% level 3. 79% were suitable for remote monitoring. For the 178 PCPs responding, 1088 clinical examinations or surveillance investigations over a 5 year period were identified.

Summary of all responses from survey participants

| Examinations Requested | Total requested | PCP willing to do | % PCPs willing to do |
|---|---|---|---|
| Blood Pressure | 46 | 42 | 91% |
| Clinical Examinations | 106 | 47 | 44% |
| Bloods | 618 | 477 | 77% |
| Tests (other than bloods and radiology) | 213 | 90 | 42% |
| Radiology | 105 | 49 | 47% |
| Total | 1088 | 705 | 65% |

60% of PCPs reported having the necessary skills for the proposed supported management, whilst 29% felt they had the capacity. 26% did not have access to appropriate investigations and 76% required additional funding to do them.

4% (n=5) of practices wished to take over all care, 65% (n=79) preferred to take over some aspects of care whilst a further 31% (n=37) preferred all care to be delivered by LTFU.

**Conclusion:** PCPs are willing to take on some aspects of care traditionally delivered by specialist LTFU. The majority wish to manage survivors in partnership with specialist support and would require additional funding.

**84. PRIMARY AND HOSPITAL CARE IN THE CLINICAL FOLLOW-UP OF CHILDHOOD CANCER SURVIVORS** Joyeeta Guha, MSc; Clare Frobisher, PhD; Andrew Toogood, MD; Adam Glaser, MD; David Winter, HNC; Julie Kelly, Diploma; Raoul Reulen, PhD; Michael Hawkins, DPhil; On behalf of the National Cancer Survivorship Initiative (NCSI) and the British Childhood Cancer Survivor Study (BCCSS) Steering Group. *Centre for Childhood Cancer Survivor Studies, School of Health and Population Sciences, Public Health Building, University of Birmingham, Birmingham UK; Department of Endocrinology, University Hospitals Birmingham NHS Foundation Trust, Edgbaston, Birmingham, UK; Regional Paediatric Oncology Unit, St. James' University Hospital, Beckett Street, Leeds UK*

**Background:** Extensive restructuring of clinical long-term follow-up within the National Health Service (NHS) in England has been proposed as part of the National Cancer Survivorship Initiative (NCSI), moving away from the single model of care. Using risk stratification, based on cancer type and treatment, survivors are assigned to one of three levels of care ranging from 1 (supported self-management) to 3 (complex, multidisciplinary). It is anticipated that primary care physicians (PCPs) will be increasingly involved in the care of intermediate risk survivors.

**Aims:** Quantify the extent to which: 1) childhood cancer survivors are on regular long-term hospital follow-up in relation to their childhood cancer and its treatment; 2) PCPs are willing to discuss survivorship issues with survivors.

**Methods:** Within the British Childhood Cancer Survivor Study almost 13,000 PCPs returned a form indicating: 1) Whether their patient was still on regular long-term hospital follow-up in relation to their childhood cancer? 2) Whether they would be prepared to discuss personal medical questions which might arise as a result of their patient completing the questionnaire?

**Results:** PCPs indicated that 36% (4707/12978) of survivors were still on regular hospital follow-up. However this percentage varied substantially by region (ranging from 31% in the South West and East of England to 46% in the North West) and attained age (ranging from 62% in those under 20 years to 9% in those 50 years or older). Similar substantial reductions with attained age were observed irrespective of cancer or treatment subgroup considered. PCPs returns indicated that 74% (9595/12978) were willing to discuss survivorship issues with survivors.

**Conclusion:** Systems for potential recalls need consideration because of the evidence that substantial numbers of higher risk survivors have been discharged from an appropriate level of NHS follow-up. Three-quarters of PCPs are content to discuss survivorship issues with survivors, which is encouraging.

**85. CHILDHOOD CANCER SURVIVAL IN IRELAND: TEMPORAL, REGIONAL AND DEPRIVATION-RELATED PATTERNS** Paul M Walsh, PhD; Julianne Byrne, PhD; Michael Capra, FRCPCH; Harry Comber, PhD MB BCh BAO. *National Cancer Registry, Cork, Ireland; Boyne Research Institute, Drogheda, Ireland; Our Lady's Children's Hospital, Crumlin, Dublin, Ireland*

**Introduction:** Survival after childhood cancer varies across Europe, but national/regional studies have so far shown no survival differences related to socio-economic disparity. The relationship of childhood cancer survival to disparity has not been studied in Ireland.

**Aims:** To determine if Irish children from deprived backgrounds have poorer survival rates after cancer compared to children from advantaged backgrounds.

**Methods:** We assessed survival for Irish children (ages 0-14 years) diagnosed with cancer during the period 1994-2005, overall and for three main diagnostic groups - leukaemias, lymphomas, and central nervous system tumours. Comparisons were made between two diagnosis periods (1994-1999 and 2000-2005), between four regions of residence, and between five area-based deprivation categories.

**Results:** There was only limited evidence of improvements in survival over time. No clear evidence was found of deprivation-related influences, overall or for the three main diagnostic groups examined, although a weak trend was apparent for lymphoid leukaemias. Regional variation in survival was likewise not clear-cut, with the possible exception of CNS tumours (significantly higher survival among patients resident in the Western region).

**Conclusions:** The absence of clear trends for regional- or deprivation-related variation in survival may reflect a high degree of application, coordination and uniformity of treatment, and perhaps diagnostic services.

**86. SURVIVING CHILDHOOD CANCER—WHAT NEXT?** Vandana Dhamankar, P Kurkure, S Goswami, N Dalvi. *ACT Clinic, Division of Pediatric Oncology, Tata Memorial Hospital, Mumbai, India*

**Background, aims and objectives:** Advances in treatment of childhood cancer have greatly improved survival outcomes. As number of childhood cancer survivors continue to rise this has brought into focus the problem of late effects of therapy. Conventionally, treatment of childhood cancers has included intensive chemotherapy regimens/radiotherapy which has led to significant organ damage in a developing child leading to major long term sequelae. Identification of these late effects of therapy has brought into focus the

urgent need to redesign treatment protocols in order to minimize late effects without compromising on therapeutic efficacy. To address this issue, long term follow-up clinic [After Completion of Therapy (ACT) Clinic] for survivors of childhood cancer was initiated at Tata Memorial Hospital in February 1991 with aim to monitor growth, development, puberty and somatic late effects of therapy and make appropriate interventions.

**Methods:** Prospective database of 1250 survivors (off therapy and disease free for >2 years) registered in ACT Clinic from Feb 1991 to Oct 2011 was analysed for identification of late effects of therapy.

**Results:** Of 1250 survivors, 73% are males, 27% females. Haematolymphoid malignancies: Solid tumors-578:672. Median age at diagnosis is 6 yrs (0-19 yrs). Median time to follow up since cessation of therapy is 8 yrs (2-36 yrs). Median duration of follow up in ACT Clinic is 4 yrs (1-20 yrs). 46% did not have any evidence of late effects. 18% had Grade I toxicity (Abnormal Lab report-no intervention), 10% had Grade II toxicity (requiring simple intervention), 21% Grade III toxicity (required complex intervention). Five percent developed second malignancies or Life threatening complications. Survivors of solid tumours had greater sequelae (Grade III-30%) compared to survivors of haematolymphoid malignancies (Grade III-10%) highlighting need for organ preservation protocols.

**Conclusions:** Cancer survivors would be better served if oncology treatment centers were equipped to offer them a comprehensive followup care through a structured programme. Early identification of late effects and appropriate interventions allow for childhood cancer survivors to not only function optimally as an individual but also integrate better into society. Our ACT model provides longitudinal care at a tertiary care centre, ensures continuity of follow up through communication with primary care providers and also promotes education and empowerment of survivors through a voluntary support group.

**87. CHALLENGES OF INTERVENTION RESEARCH IN CHILDREN DIAGNOSED WITH CANCER** Carrie Howell, MS; Kirsten Ness, PT, PhD. *St. Jude Children's Research Hospital, Memphis, TN, USA*

**Background:** Children diagnosed with cancer may benefit from exercise; however, randomized intervention trials are few, with small sample sizes. Research needs to be conducted with larger sample sizes and different diagnostic groups before we can evaluate the timing and dose of exercise necessary to produce positive health outcomes. We examined enrollment and compliance on two pilot studies conducted at St. Jude Children's Research Hospital (SJCRH) to provide insight into the challenges encountered when enrolling children with cancer on non-therapeutic interventions.

**Methods:** Enrollment and compliance data were examined. The first study was a 16 week home based aerobic and strengthening intervention (5 times per week) conducted among 5-10 year old children during maintenance therapy for childhood ALL (XRCISL). The second study (VIBE) randomized children to a low magnitude, high frequency vibrating plate or a placebo device. Participants were required to stand on the device for 10 minutes, twice per day for one year. Participant/parent and staff feedback regarding feasibility and ease of compliance were recorded.

**Results:** Five institutions participated and enrolled 20 participants on XRCISL. At SJRCH, the participation rate was 54% (N=13) with 9 patients completing the intervention. Overall compliance with exercise was 83.2%. The major challenge reported was difficulty contacting the study participants to progress the exercise program. On VIBE, the acceptance rate was 60% (N=103), with 68 patients eligible and enrolled after pre-study screening. Overall compliance for active and completed patients is 67 ± 27%. The major challenge for the VIBE study was difficulty contacting the participants to monitor compliance. Participants who were older (high school age), and whose families faced social challenges had difficulty completing the intervention.

**Conclusion:** Participation and compliance rates for intervention studies with children diagnosed with cancer show early promise. Enrollment and compliance challenges need to be taken into consideration when designing prospective trials.

**88. LONGITUDINAL PROGRAM EVALUATION OF AN EDUCATIONAL INTERVENTION FOR ADOLESCENT AND YOUNG ADULT SURVIVORS OF CHILDHOOD CANCER** Constance Connor, MSW, LCSW; Holly DeLuca, MSN, PNP-BC; Karim Thomas Sadak, MD, MSE; Kate Shafer, MSW, LICSW. *Life with Cancer-Inova Cancer Services, Fairfax, VA, USA; Children's National Medical Center, Washington, DC, USA; The George Washington Cancer Institute, Washington, DC, USA*

**Purpose:** Evaluate the ability of an educational conference to change self-reported fitness/nutrition knowledge and health practices in adolescent and young adult survivors of childhood cancer as measured by pre- and post-intervention survey responses with longitudinal follow-up.

**Description:** Life with Cancer and its institutional partners conducted an all-day educational conference for adolescent and young adult survivors of childhood cancer. Many survivorship topics were covered including long-term complications of childhood cancer treatments and the importance of a healthy lifestyle. A subset of questions from the *Health Protective Behaviors Questionnaire (HPBQ)* was used to collect baseline information prior to the start of the conference on participant knowledge and practice, specifically related to nutrition and fitness. The same questions from the HPBQ were administered again immediately following the conference and were repeated 6 months later. The intervention for this study was the educational conference which included a series of talks on nutrition

and lifetime fitness for the childhood cancer survivor. The talks were given by healthcare providers knowledgeable in childhood cancer survivorship.

**Results/Conclusions:** Twenty-eight survivors were invited to participate. Of these, all 28 completed the modified HPBQ prior to the intervention. Twenty-three (83%) completed the modified HPBQ after the intervention. The collection of 6 month follow-up data is ongoing. Student's t-test will be used to determine statistically significant differences between the pre- and post-intervention survey responses. The conclusions will report if an educational conference has the potential to positively change self-reported fitness/nutrition knowledge and health practices in adolescent and young adult survivors of childhood cancer immediately after an intervention and again in longitudinal follow-up 6 months later.

**89. SURVIVOR AND PARENT EVALUATION OF AN EDUCATION PACKAGE RECEIVED AT A LATE EFFECTS CLINIC** Maria Spavor MD, FRCPC; Maureen Disciglio BScN; Colleen Dibden BSW, RSW. *Kids with Cancer Society Survivor Program, Stollery Children's Hospital, Division of Pediatric Oncology, Edmonton, Alberta, Canada*

**Background:** Educating survivors and parents of survivors of childhood cancer about their diagnosis, treatment and risk for late effects is an essential part of long term follow up care. At the *Kids with Cancer Society* Survivor Program in Edmonton, Alberta, Canada a personalized education package is given once to each survivor. The package contains a diagnosis and treatment summary, a welcome letter explaining the purpose of the program and educational handouts regarding specific late complications the survivor is at risk for. This study was done to determine whether survivors and their families found this education package to be a good resource and a valuable part of follow-up care.

**Methods and results:** A survey evaluating the package was given to all survivors aged > 13 or parents of survivors at their subsequent follow-up visit. 63 survivors of 18 different malignancies (age range 13 years to 48 years) and 56 parents of survivors of 16 different malignancies (age range: 4 years to 25 years) agreed to complete the survey. 45 (72%) survivors and 45 (80%) parents of survivors remembered receiving the package at their prior visit. 39/45 (87%) survivors and 38/45 (84%) parents knew the current location of the package in their home. 42/45 (93%) survivors and 45/45 (100%) parents had read the package. 29/45 (64%) survivors and 30/45 (67%) parents recalled the survivors actually receiving all of the therapy included on the treatment summary. Overall 43/45 (96%) survivors and 41/45 (91%) parents thought the package was useful. 45/45 (100%) of survivors and 45/45 (100%) of parents thought the package should continue to be given to new patients.

**Conclusion:** The development and use of a formal education package in a long term follow-up program regarding diagnosis, treatment and late complications is a valued and useful resource for survivors and their families.

**90. CONTRIBUTION OF DIET AND PHYSICAL ACTIVITY TO METABOLIC PARAMETERS AMONG LEUKEMIA SURVIVORS** Emily S. Tonorezos, MD MPH; Debra Eshelman-Kent, RN MSN CNP; Chaya Moskowitz, PhD; Kevin C. Oeffinger, MD. *Departments of Medicine, Biostatistics and Pediatrics, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Division of Hematology Oncology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA*

**Background:** Survivors of childhood acute lymphoblastic leukemia (ALL) are at increased risk for obesity, insulin resistance and increased visceral adiposity. A history of cranial radiation therapy (CRT) worsens this risk. In non-cancer populations, adherence to a Mediterranean Diet has been shown to improve metabolic parameters and risk of diabetes mellitus. Whether diet may contribute to insulin resistance and increased adiposity in ALL survivors is not known.

**Methods:** We surveyed 117 adult survivors of childhood ALL using the Harvard Food Frequency Questionnaire. Physical activity energy expenditure (PAEE) was measured with the SenseWear Pro2 Armband. Fasting blood was obtained on all subjects and insulin resistance was estimated using the Homeostasis Model for Insulin Resistance (HOMA-IR). Visceral adiposity was measured by abdominal CT. Adherence to a Mediterranean Diet pattern was calculated using the index developed by Trichopoulou. Subjects were compared using univariate analysis.

**Results:** Subjects were majority female (56%); 25% were minority or Hispanic white. A history of CRT was present in 15 (29%) men and 25 (38%) women. Among all subjects, greater adherence to a Mediterranean diet pattern was associated with improved HOMA-IR ($p=0.14$), visceral adiposity ($p=0.03$), subcutaneous adiposity ($p=0.005$), waist circumference ($p=0.02$), and body mass index ($p=0.03$) (all unadjusted analyses). The effect of adherence to a Mediterranean diet on insulin resistance was especially notable in men who did not receive CRT ($p=0.06$). Higher dairy intake was found to worsen HOMA-IR ($p=0.014$), but other individual components of the Mediterranean diet, such as low intake of meat and high intake of fruits and vegetables, were not significant. Inclusion of PAEE did not alter our findings, although higher PAEE was associated with lower body mass index.

**Conclusions:** Adherence to a Mediterranean diet pattern, especially low consumption of dairy products, may improve insulin resistance in survivors of childhood ALL. Further study is warranted.

**91. DAILY LIFE PHYSICAL ACTIVITY IN DUTCH ADULT LONG-TERM SURVIVORS OF NEPHROBLASTOMA AND NEUROBLASTOMA** M. van Waas, M. Wijnen, A. Hartman, A.C.H. de Vries, R. Pieters, S.J.C.M.M. Neggers, M.M. van den Heuvel-Eibrink. *Department of Pediatric Oncology/Hematology, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands; Department of Pediatric Physiotherapy, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands; Department of Medicine, Section Endocrinology, Erasmus University Medical Center, Rotterdam, The Netherlands*

**Background:** The risk of metabolic late effects after childhood cancer, such as obesity, hypertension and diabetes, can be positively influenced by a healthy lifestyle with sufficient physical activity. Nevertheless, studies on physical activity in adult survivors of childhood cancer are scarce and involve different and often non-validated questionnaires. For this study, we used the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH), which was developed and validated to assess daily life physical activity in the Dutch adult population.

**Objective:** To assess daily life physical activity in Dutch adult long-term nephroblastoma and neuroblastoma survivors using the SQUASH.

**Methods:** Sixty-seven nephroblastoma and 36 neuroblastoma survivors (median age 30 years, range 18-51 years) and 60 socio-demographically similar healthy control subjects (median age 32 years, range 18-61 years) were asked to complete the SQUASH during their regular follow-up visit.

**Results:** The adjusted mean physical activity score in male neuroblastoma survivors was significantly lower compared with male controls (mean 7767 vs. mean 10341, P=0.028). Physical activity score in male nephroblastoma survivors was not significantly lower compared with male controls (mean 8980 vs. mean 10341, P=0.121). Adjusted means for physical activity scores in females were not different from their controls.

**Conclusions:** Male neuroblastoma survivors were identified as performing less daily physical activity.

**92. PHYSICAL PERFORMANCE LIMITATIONS IN ADOLESCENT AND ADULT SURVIVORS OF CHILDHOOD CANCER AND SIBLINGS** C.S. Rueegg, G. Michel, M.E. Gianinazzi, L. Wengenroth, N.X. von der Weid, E. Bergstraesser, C.E. Kuehni for the Swiss Pediatric Oncology Group (SPOG). *Institute of Social- and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland; Pediatric Hematology/Oncology Unit, University Children's Hospital, University of Lausanne, Lausanne, Switzerland; Department of Oncology, University Children's Hospital Zurich, Zurich, Switzerland*

**Objectives:** None of the population-based studies on physical performance limitations included recently diagnosed survivors. We aimed to 1) describe performance limitations in survivors compared to siblings, and 2) identify predictors of performance limitations in survivors.

**Methods:** As part of the Swiss Childhood Cancer Survivor Study (SCCSS) we sent a detailed questionnaire to all survivors (≥16years) registered in the Swiss Childhood Cancer Registry who were diagnosed between 1976-2003 at an age <16years. The same questionnaires were sent to siblings. We assessed two types of performance limitations: 1) limitations in sporting activities; 2) limitations in daily activities such as vigorous or moderate activities, walking, bending, or washing using the SF-36 (physical function score; population mean=50; SD=10). Subgroup analysis was performed for survivors diagnosed ≥1990. Predictors (age, sex, parents' education, clinical factors) of both types of performance limitations in survivors were assessed using multivariable logistic regression models.

**Results:** The sample included 1038 survivors and 534 siblings (response rates 78% and 41%, respectively). Overall, 96 (9.5%) survivors reported a limitation in sporting activities compared to 7 siblings (1.1%; p<0.001). Mean physical function score for limitations in daily activities was 49.1 in survivors and 53.1 siblings (p<0.001; table 1). Of survivors diagnosed ≥1990 (n=536), 52 (10.1%) reported a limitation in sporting activities. They reached a mean physical function score of 48.9.

In the multivariable regression, the strongest predictors for both types of limitations were type of treatment (both p<0.001) and diagnosis (both p<0.001). Most affected were survivors treated with radiotherapy, survivors of bone tumors, CNS tumors, and retinoblastoma.

**Conclusions:** Survivors of childhood cancer, even when diagnosed recently and treated according to new protocols are at high risk of suffering from performance limitations. More research should be invested in modern treatments and interventions to preserve long-term functionality.

Table 1: Description of limitations in sporting activities (proportions) and daily activities (physical function score SF-36) in survivors and siblings

| | Survivors | | | Siblings | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Limitation for sporting activities | | | | | | | | | |
| | N | % | 95% CI | N | % | 95% CI | OR | 95% CI | p-value |
| Total | 96 | 9.5 | 7.8-11.4 | 7 | 1.1 | 0.6-2.1 | 5.5 | 2.9-10.4 | <0.001 |
| Musculoskeletal problems | 43 | 4.2 | 3.2-5.7 | 3 | 0.5 | 0.2-1.2 | | | |
| Neurological problems | 27 | 2.7 | 1.8-3.9 | 2 | 0.3 | 0.1-1.1 | | | |
| Pain and fatigue syndromes | 7 | 0.7 | 0.3-1.4 | 0 | 0 | - | | | |
| Weight and endurance problems | 5 | 0.5 | 0.2-1.2 | 0 | 0 | - | | | |
| Cardio-pulmonary problems | 3 | 0.3 | 0.1-0.9 | 1 | 0.2 | 0.02-1.1 | | | |
| Visual impairment | 3 | 0.3 | 0.1-0.9 | 0 | 0 | - | | | |
| Psychological problems | 2 | 0.2 | 0.1-0.8 | 0 | 0 | - | | | |
| Problem unknown | 6 | 0.6 | 0.3-1.3 | 1 | 0.2 | 0.02-1.2 | | | <0.001 |
| Limitations for daily activities | | | | | | | | | |
| | | Mean | 95% CI | | Mean | 95% CI | Coef. | | p-value |
| Physical function score SF-36 | | 49.6 | 48.9-50.4 | | 53.1 | 52.5-53.7 | -3.3 | -4.5--2.1 | <0.001 |

**93. MOTOR PERFORMANCE AND FUNCTIONAL EXERCISE CAPACITY IN SURVIVORS OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA** A. Hartman, W. Hop, T. Takken, R. Pieters, M.M. van den Heuvel-Eibrink. *Department of Pediatric Oncology/Hematology, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands; Department of Pediatric Physiotherapy, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands; Department of Biostatistics, Erasmus University Medical Center, Rotterdam, The Netherlands; Child Development and Exercise Center, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands*

**Background:** Cross-sectional studies have shown impaired motor performance and reduced maximum exercise capacity after treatment of acute lymphoblastic leukemia (ALL). However, no longitudinal study monitoring motor performance after stop treatment has been published. Whether functional sub-maximal exercise capacity is reduced has not yet been investigated.

**Methods:** Motor performance of pediatric ALL survivors, treated with ALL-9 protocol of the Dutch Childhood Oncology Group were measured with the movement-ABC at stop treatment and ≥ 5 years later. At the latter time functional exercise capacity was also investigated, using the 6-Minute Walk Test (6MWT).

**Results:** Nineteen boys and fourteen girls, median age 12.3 years (range 9.0-18.7), median time since completion of chemotherapy 5.2 years (5.0-7.1), participated. Mean height/age did not differ from the norm nor did mean weight/age, whereas mean BMI/age was significantly increased (mean SDS 0.38, SEM 0.17 p=0.04). Five years after stop treatment 97% of children achieved movement-ABC scores within the norm with a median percentile score of 56.5, versus 52% within the norm with median score of 19.5 at cessation of treatment (p< 0.001). In contrast, SD scores of 6MWT were significantly lower than normative values (mean SDS -2.05, SEM 0.13, p < 0.001).

**Conclusion:** Five years after completion of ALL treatment motor performance had improved significantly with 97% of the children obtaining a score within the norm. In contrast, functional exercise capacity was significantly impaired, for which no single underlying cause could be identified. The exact underlying cause of this late effect needs further study.

**94. DECREASED SERUM TESTOSTERONE LEVELS IN LONG-TERM ADULT SURVIVORS WITH FATTY LIVER AFTER CHILDHOOD STEM CELL TRANSPLANT** Hiroyuki Ishiguro, MD; Hiromi Hyodo, MD; Yuichiro Tomita, MD; Hiromitsu Takakura, MD; Takashi Koike, MD; Takashi Shimizu, MD; Tsuyoshi Morimoto, MD; Hiromasa Yabe, MD; Miharu Yabe, MD; and Shunichi Kato, MD. *Departments of Pediatrics, Cell Transplantation and Regenerative Medicine, and Clinical Laboratory, Tokai University School of Medicine, Tokai, Japan*

**Introduction:** Fatty liver and gonadal dysfunction have been identified as potential late effects of therapy in adult survivors treated with SCT. Obesity and metabolic syndrome are also associated with low testosterone levels in general population. However, the relationship between fatty liver and testosterone levels in adult survivors is not fully elucidated.

**Aims:** Our objective was to determine the relationship between fatty liver and testosterone levels in adult survivors.

**Methods:** We reviewed the clinical records of 34 male patients who received allogeneic SCT at Tokai University Hospital. The median age of the 34 patients at SCT was 10.0 years, the median age at the last evaluation was 25.5 years, and the median follow-up duration after SCT was 15.9 years. The study population was categorized into 4 groups according to the conditioning regimens they had received: cranial irradiation (CRT)+TBI, TBI, TAI, and Chemo groups.

**Results:** One patient treated with only chemotherapy was obese. On the other hand, 11patients were underweight. Fatty liver was diagnosed in 15 patients by ultrasound during the follow-up period. Patients who had fatty liver did not tend to be overweight/obese. A greater number of patients who received CRT+TBI developed fatty liver compared with among remaining groups. Patients in CRT+TBI group were statistically associated with decreased testosterone levels compared with among remaining groups ($p<0.001$, respectively), although testosterone levels in all patients were within normal range during follow-up period. Moreover, severe fatty liver was statistically associated with decreased testosterone levels compared with among moderate, mild and non-fatty liver ($p<0.001$, median 273ng/dL, 333 ng/dL, 345 ng/dL, and 530 ng/dL, respectively).

**Conclusion:** Even patients who are not overweight/obese may develop fatty liver, and degree of fatty liver was associated with decreased testosterone levels in adult survivors.

**95. GONADAL FUNCTION RECOVERY IN VERY LONG-TERM MALE SURVIVORS OF CHILDHOOD CANCER** Wendy van Dorp, MD; Ivana M.M. van der Geest, BSc; Joop S.E. Laven, MD, PhD; Wim C.J. Hop, PhD; Sebastian J.C.M.M. Neggers, MD, PhD; Andrica C.H. de Vries, MD; Rob Pieters, MD, PhD; Marry M. van den Heuvel-Eibrink, MD, PhD. *Department of Pediatric Oncology/Hematology, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands; Division of Reproductive Medicine, Department of Obstetrics and Gynaecology, Erasmus MC-University Medical Center Rotterdam, Rotterdam, The Netherlands; Department of Biostatistics, Erasmus-MC University Medical Center Rotterdam, Rotterdam, The Netherlands; Department of Internal Medicine/Endocrinology, Erasmus MC–University Medical Center Rotterdam, Rotterdam, The Netherlands*

**Context:** Gonadal toxicity is a major complication after specific treatment for childhood cancer, such as gonadal irradiation and alkylating agents.

**Objective:** We performed this retrospective study with data from our outpatient late effects clinic for childhood cancer survivors to evaluate possible recovery of gonadal dysfunction over time in a large single center cohort of male long-term childhood cancer survivors (n=203) using Inhibin B as a first marker for gonadal function.

**Results:** Median age at diagnosis was 5.9 years (range 0.0-17.5) and discontinuation of treatment was reached at a median age of 8.2 years (range 0.0-20.8). Inhibin B levels were first measured after a median follow-up time of 15.7 years (range 3.0-37.0). Median interval between the first and second measurement was 3.3 years (range 0.7-11.3). Median Inhibin B level was 127 ng/L (range 5-366 ng/L) at first assessment and 155 ng/L (range 10-507 ng/L) at second assessment. The prediction model suggests that Inhibin B levels do not normalize in survivors with a very low Inhibin B level at the first follow-up time point. This group included mainly survivors of Hodgkin lymphoma treated with MOPP and rhabdomyosarcoma or survivors treated with pelvic irradiation or Alkylating Agent Dose scores $\geq 3$, which is an important threshold for alkylating agent dose.

**Conclusion:** In general, Inhibin B levels increase over time, which is suggestive for recovery of gonadal function long after discontinuation of cancer treatment. However, this increase does not seem to occur in survivors who already reached critically low Inhibin B levels at first assessment.

**96. REPRODUCTIVE OUTCOME IN MARRIED YOUNG ADULT SURVIVORS OF CHILDHOOD CANCERS ATTENDING AFTER COMPLETION THERAPY (ACT) CLINIC** P Kurkure, V Dhamankar, S Goswami, N Dalvi, D Bhartia. *ACT Clinic, Division of Pediatric Oncology, Department of Medical Oncology, Tata Memorial Hospital, Mumbai, India*

**Purpose:** To assess reproductive outcome in married young adult (Age>18 yrs) survivors of childhood cancers registered in After Completion of Therapy (ACT) Clinic between Feb 1991 to Jan 2012.

**Method:** ACT Clinic database was analyzed for reproductive outcome in married young adult survivors. Risk factors for infertility such as diagnosis, age at diagnosis, sex and treatment modalities were reviewed.

**Results:** 1275 survivors (>2 years off therapy and disease free) registered in ACT Clinic. 556/1275 (44%) are young adults. Male:female 3:1 (418:138). 329/556 (59%) are survivors of hematological malignancies, 227/556 (41%) are survivors of solid tumors. 74/556 (14%) are married. Further data obtained from 66/74 married survivors following up regularly. Male:female 3:1 (46/20). 47/66 (71%) are survivors of hematological malignancies majority (53%) being Hodgkins disease. 19/66 (29%) are survivors of solid tumors. Median age at diagnosis 8 yrs (1-16). Median time since cessation of treatment 21 yrs (10-36). Median duration of follow up in ACT Clinic15 yrs (1-20). Median age at last follow up is 29 yrs indicating they are at prime of reproductive life. 44/46 (95%) men are azoospermic, 2 (5%) have normal semen analysis. 19/44 (43%) have children through assisted reproduction. 1/44 (2%) has adopted while 24/44 (55%) are awaiting. All 20 female cancer survivors have normal menstrual cycles and 10/20 (50%) have conceived normally.

**Conclusion:** Gonadal failure and infertility are important sequelae of previous exposure to chemotherapy and radiotherapy during treatment of childhood cancers. Although our results are based on few cases, male survivors appear to be at greater risk for infertility as compared to female survivors. Premarital counseling about fertility and assisted reproduction should be incorporated as an essential part of survivor's follow-up. The effect of oncotherapy on embryonic-like stem cells in adult human testes which have been postulated to be primordial germ cells persisting in adulthood need to be explored for therapeutic potential towards fertility restoration in these survivors.

**97. GENETIC DISEASE IN THE CHILDREN OF DANISH SURVIVORS OF CHILDHOOD AND ADOLESCENT CANCER** Jeanette F. Winther, MD; Jørgen H. Olsen, MD, DMSc; Huiyun Wu, PhD; Yu Shyr, PhD; John J. Mulvihill, MD; Marilyn Stovall, PhD; Annelise Nielsen, DDS; Marianne Schmiegelow, MD, DMSc; Nea Malila, MD; John D. Boice Jr, ScD. *Danish Cancer Society Research Center, Copenhagen, Denmark; Vanderbilt University, Department of Medicine and Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; Vanderbilt University, Department of Biostatistics and Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; Department of Pediatrics, University of Oklahoma, Oklahoma City, OK, USA; Department of Radiation Physics, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; Clinic of Pediatrics, Copenhagen, Denmark; Mass Screening Registry, Finnish Cancer Registry, Helsinki, Finland; Tampere School of Health Sciences, University of Tampere, Tampere, Finland*

**Purpose:** Preconception radiation and chemotherapy have the potential to produce germ-cell mutations leading to genetic disease in the next generation. Dose-response relationships were evaluated between cancer treatments and untoward pregnancy outcomes.

**Methods:** A case-cohort study was conducted of 472 Danish survivors of childhood and adolescent cancer and their 1,037 pregnancies. Adverse outcomes included 159 congenital malformations, six chromosomal abnormalities, seven stillbirths, and nine neonatal deaths. Preconception radiation doses to the gonads, uterus, and pituitary gland and administered chemotherapy were quantified based on medical records and related to adverse outcomes using a generalized estimating equation model.

**Results:** No statistically significant associations were found between genetic disease in children and parental treatment with alkylating drugs or preconception radiation doses to the testes in male and ovaries in female cancer survivors. Specifically, the risk of genetic disease was similar among the children of irradiated survivors when compared with nonirradiated survivors (RR, 1.02; 95% CI, 0.59-1.44; p=.94). A statistically significant association between abdomino-pelvic irradiation and malformations, stillbirths and neonatal deaths was not seen in the children of female survivors overall (p=.07) or in the children of mothers receiving high uterine doses (mean, 13.5 Gy; max, 100 Gy; RR, 2.3; 95% CI, 0.95-5.56).

**Conclusion:** Mutagenic chemotherapy and radiotherapy doses to the gonads were not associated with genetic defects in children of cancer survivors. However, larger studies need to be conducted to further explore potential associations between high-dose pelvic irradiation and specific adverse pregnancy outcomes. In conjunction with an international study of trans-generational effects of cancer treatment (www.gcct.org), we have increased the sample size by adding offspring of cancer survivors diagnosed in early adulthood (< age 35) from both Denmark and Finland. The first results of this large case-cohort study based on a cohort of more than 23,000 children of 14,500 cancer survivors will be presented.

**98. OVARIAN FUNCTION (OVF) IN SURVIVORS OF MEDULLOBLASTOMA (MB): IMPACT OF REDUCED DOSE CRANIOSPINAL RADIATION (CSI) AND HIGH DOSE CHEMOTHERAPY WITH AUTOLOGOUS STEM CELL RESCUE (ASCR)** Sadana Balachandar, MD; Ira Dunkel, MD; Yasmin Khakoo, MD; Suzanne Wolden, MD; Jeffrey Allen, MD; Charles A. Sklar, MD. *Department of Pediatrics, Weill Cornell/New York Presbyterian Hospital, New York, NY, USA; Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Department of Pediatrics, New York University Medical Center, New York, NY, USA*

**Purpose of study:** Data on OvF in MB survivors is limited, with most studies describing outcomes in survivors treated with CSI doses > 2400 cGy +/- standard chemotherapy. The purpose of this study is to report on OvF 1) across a range of CSI doses and 2) following high dose chemotherapy with ASCR.

**Description of project:** Retrospective chart review of all MB female survivors who received treatment from 1980 to 2010, and are followed in the Long-Term Follow-Up Clinic at Memorial Sloan-Kettering Cancer Center. Subjects were divided into 3 groups based on treatment: CSI > 3500 cGy +/- standard chemotherapy (n=11); CSI ≤ 2400 cGy +/- standard chemotherapy (n=18); ASCR with (n=4) or without (n=2) CSI.

**Results:** 35 subjects were evaluated. Their median age at diagnosis of MB was 6.8 years (0.80-26.6) and median age at last evaluation was 16.5 years (4.0-33.2). In the > 3500 cGy group, 7 of 11 subjects had evidence of primary ovarian dysfunction (POD) (LH or FSH ≥ 15 mIU/mL). Of these 7 subjects, 4 normalized their ovarian function and/or developed spontaneous puberty, including 1 with precocious puberty, while 3 (27%) developed premature ovarian failure (POF) requiring hormone replacement therapy (HRT). In the ≤ 2400 cGy group, 8 of 18 subjects had evidence of POD. Of these 8 subjects, 7 normalized their ovarian function and/or experienced spontaneous

puberty, including 1 with precocious puberty, while 1 (5%) developed POF requiring HRT. In the ASCR group, 5 of 5 evaluable subjects had evidence of POD; 3 (60%) developed POF requiring HRT.

**Conclusion:** While POD is common in MB survivors who received CSI ≤ 2400 cGy +/- standard chemotherapy, in most cases it was transient and only a small minority required HRT. High dose chemotherapy with ASCR is associated with a high incidence of POF requiring HRT.

**99. OVARIAN TISSUE CRYOPRESERVATION: FEASIBILITY AND SAFETY** Jill P. Ginsberg, MD; Claire A. Carlson, BSN, RN; Maureen Prewitt,BSN, RN; Peter Mattei, MD; Clarisa R. Gracia, MD. *Division of Oncology, The Children's Hospital of Philadelphia, Philadelphia, PA, USA; Department of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA, USA; Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA, USA; Department of Surgery, The Children's Hospital of Philadelphia, Philadelphia, PA*

**Purpose:** Gonadotoxicity is an unfortunate consequence of pediatric cancer treatment. While embryo cryopreservation remains the standard option for adult females, ovarian tissue cryopreservation (OTC) has become an option for those without time to delay treatment for ovarian stimulation, for females without a partner and for prepubertal girls. We report on a novel experimental protocol that offers OTC to girls with malignancies or blood disorders whose therapy places them at high risk for ovarian failure. The primary aims were to determine the feasibility and safety of this procedure.

**Patients and methods:** Eligible pediatric subjects were at least one year of age and were limited to those at highest risk for long term ovarian dysfunction based on planned cumulative dose of alkylating agents, expected radiation exposure or stem cell transplant conditioning. Previous therapy was not an exclusion. A laparoscopic ovarian cortical biopsy was performed in the operating room. 80% of the biopsy was frozen for the subject's future use and the remainder used for laboratory research. Data on adverse intraoperative or post-operative sequelae were assessed by chart review.

**Results and conclusions:** Ten patients (range: 8-18 years) have cryopreserved ovarian tissue. Four patients had hematologic disorders (2 leukemia, 1 sickle cell anemia, 1 MDS) and 8 were anticipating stem cell transplantation. Nine had a concomitant surgical procedure, such as tumor resection or CVL placement, at the time of OTC. Three patients attempted another method of fertility preservation either prior to or at the time of OTC (2 underwent ovarian transposition along with OTC). No surgical or post-operative complications have occurred. Ovarian tissue cryopreservation protocols can be implemented at pediatric institutions through multidisciplinary collaborations.

**100. ADRENAL FUNCTION IN ADULT LONG-TERM SURVIVORS OF NEPHROBLASTOMA AND NEUROBLASTOMA**
Marjolein van Waas, Sebastian J.C.M.M. Neggers, Judith P. van Eck, Max M. van Noesel, Aart-Jan van der Lely, Frank H. de Jong, Rob Pieters, Marry M. van den Heuvel-Eibrink. *Department of Pediatric Oncology/Hematology, Erasmus MC-Sophia Children's Hospital Rotterdam, Rotterdam, The Netherlands; Department of Medicine, Section Endocrinology, Erasmus University Medical Centre Rotterdam, Rotterdam, The Netherlands*

**Background:** Adrenal insufficiency, or relative insufficiency, might partly explain increased mortality rates in nephroblastoma and neuroblastoma survivors after unilateral adrenalectomy.

**Objective:** To assess adrenal function and its metabolic effects in survivors after adrenalectomy.

**Methods:** In this cross-sectional study, 67 adult long-term survivors of nephroblastoma, 36 survivors of neuroblastoma and 49 control subjects participated. Adrenal function was assessed by a 1µg short Synacthen-test. Levels of cortisol, adrenocorticotrophic hormone (ACTH), low (LDL-C) and high-density lipoprotein-cholesterol (HDL-C), triglycerides, apolipoprotein-B, glucose and insulin were assessed in blood samples taken at baseline. In addition, cortisol levels were assessed after 30 (t=30) and 60 minutes. Homeostatic Model Assessment (HOMA) was calculated.

**Results:** Adrenal insufficiency was not present in survivors. Interestingly, baseline serum cortisol levels were higher in survivors after unilateral adrenalectomy (mean 503 nmol/l) (N=46) than in survivors with both adrenals intact (mean 393 nmol/l, P=0.002) (N=52), and than in controls (mean 399 nmol/l, P=0.013) (N=49). After correcting for age, sex, and use of oral estrogens, unilateral adrenalectomy was independently associated with elevated baseline cortisol and ACTH levels. Baseline cortisol levels were positively associated with triglycerides (P<0.001), LDL-C (P=0.004), apolipoprotein-B (P<0.001) and HOMA (P=0.008).

**Conclusions:** No adrenal insufficiency was observed in survivors of nephroblastoma and neuroblastoma. Survivors treated with unilateral adrenalectomy had relatively high basal cortisol and ACTH levels, indicating a higher central setpoint of the hypothalamic-pituitary-adrenal axis. This higher setpoint was associated with lipid concentrations and insulin resistance and can therefore influence the cardiovascular risk profile in long term survivors of nephroblastoma and neuroblastoma.

**101. ENDOCRINE LATE EFFECTS IN CHILDHOOD CANCER SURVIVORS IN THE NORDIC COUNTRIES—UNDER THE RESEARCH PROGRAM "ADULT LIFE AFTER CHILDHOOD CANCER IN SCANDINAVIA" (ALICCS)** Sofie de Fine Licht, MSc; Jeanette Falck Winther, MD; Klaus Kaae Andersen, MSc, PhD; Henrik Hasle, Professor, MD; Jørgen H Olsen, DMSc. *Danish Cancer Society, Danish Cancer Society Research Center, Copenhagen, Denmark; Aarhus University Hospital, Skejby, Department of Pediatrics, Aarhus, Denmark*

**Introduction:** With the remarkable improved survival of childhood cancer, late effects of the cancer and its treatment become more apparent. Using the unique population-based registries in the Nordic countries with long-term and virtually complete follow-up, we investigated if childhood cancer survivors are at increased risk of wide range of endocrine late effects compared to the general population.

**Methods:** We identified 19,793 children from Denmark, Iceland and Sweden diagnosed with cancer before the age of 20 from the beginning of cancer registration in the 1940s through 2008, who were alive at the start of the patient registries (Denmark 1977, Iceland 1999 and Sweden 1964). A population comparison cohort of 125,711 individuals were randomly selected from the central population registries and matched by gender, country and age. Study subjects were followed-up for a wide range of endocrine disorders in the national patient registries, which include all hospital-discharge diagnoses. Cox proportional hazard models were used to estimate the relative risks of endocrine late effects in childhood cancer survivors compared to the population cohort members.

**Results:** Preliminary results show that compared to the general population, survivors of childhood cancer are at increased risk of a broad range of endocrine disorders. Crude estimates show an increased risk of hypothyroidism (Hazard ratio (HR)=7.89, 95% CI:7.04-8.84), hyperthyroidism (HR=1.52, CI:1.24-1.86), diabetes mellitus (HR=1.95, CI:1.75-2.17), hypoparathyroidism (HR=11.95, CI:6.63-21.54), hyperparathyroidism (HR=5.48, CI:3.94-7.61), pituitary hypofunction (HR=69.36, 95% CI:57.34-83.91), pituitary hyperfunction (HR=11.59, CI:9.09-14.78), adrenocortical diseases (HR=19.23, CI:14.61-25.32), ovarian dysfunction (HR=3.58, CI:2.99-4.29) and testicular dysfunction (HR=28.24, CI:20.13-39.63). Relative risks adjusted for age at diagnosis and year of treatment will be presented.

**Conclusion:** Preliminary analyses show that children treated for childhood cancer are at a highly increased risk of a wide range of endocrine late effects.

**102. DIFFERENTIAL EFFECTS OF RADIOTHERAPY ON GROWTH AND ENDOCRINE FUNCTION AMONG ACUTE LEUKEMIA SURVIVORS: A CHILDHOOD CANCER SURVIVOR STUDY REPORT** Eric J. Chow, MD, MPH; Wei Liu, PhD; Kumar Srivastava, PhD; Wendy M. Leisenring, ScD; Robert J. Hayashi, MD; Charles A. Sklar, MD; Marilyn Stovall, PhD; Leslie L. Robison, PhD; K. Scott Baker, MD, MS. *Department of Pediatrics, Seattle Children's Hospital and University of Washington, Seattle, WA, USA; Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; Departments of Biostatistics and Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN, USA; Pediatric Hematology/Oncology, Washington University School of Medicine, St. Louis, MO, USA; Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Department of Radiation Physics, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA*

**Background:** The differential effects of cranial (CRT), craniospinal, and total body irradiation (TBI) on growth and endocrine outcomes have rarely been examined in combination among childhood acute leukemia survivors.

**Procedure:** Self-reported height/weight, hypothyroidism, and pregnancy/live birth were determined among acute lymphoblastic and myeloid leukemia survivors (n=3,483) participating in the Childhood Cancer Survivor Study, an ongoing cohort study of 5-year survivors of pediatric cancers diagnosed from 1970 to 1986.

**Results:** Compared with no radiotherapy, multivariate adjusted risk estimates were consistent across outcomes (adult short stature, hypothyroidism, absence of pregnancy/live birth) with CRT treatment associated with 2-3 fold increased risks, TBI associated with 5-10 fold increased risks, and CRT+TBI associated with >10 fold increased risks (Table). Exposure to any spinal radiotherapy further increased risk of these outcomes 2-3 fold. Changes in body composition were more nuanced as CRT only was associated with an increased risk of being overweight/obese (OR 1.6, 95% CI 1.3-1.9) whereas TBI only was associated with an increased risk of being underweight (OR 6.0, 95% CI 2.4-14.9).

| | Adjusted Odds Ratio (95% CI)* | | | | | |
|---|---|---|---|---|---|---|
| Radiotherapy | Short stature | Under-weight vs. normal | Overweight/ obese vs. normal | Hypo-thyroidism | Ever pregnant | Live birth |
| None (ref) | | | | | | |
| Cranial only | 2.9 (2.0, 4.2) | 1.3 (0.8-2.1) | 1.6 (1.3-1.9) | 1.6 (1.1, 2.3) | 0.5 (0.5-0.6) | 0.6 (0.5-0.7) |
| Total body only | 8.0 (3.7, 17.4) | 6.0 (2.4-14.9) | 1.0 (0.5-1.9) | 6.8 (3.4, 13.5) | 0.1 (0.04-0.2) | 0.07 (0.03-0.18) |
| Cranial + total body | 10.6 (4.5, 25.3) | 2.4 (0.7-7.6) | 0.6 (0.3-1.3) | 10.9 (5.3, 22.3) | 0.03 (0.01-0.14) | 0 |

*Adjusted for growth hormone supplementation (short stature and body mass categories only), sex, race/ethnicity, age at diagnosis and at follow-up, leukemia histology, and spinal radiotherapy

**Conclusions:** Although patients treated with CRT+TBI are at greatest risk for short stature, hypothyroidism, and a reduced likelihood of pregnancy/live birth, those treated with either modality alone have significantly increased risks as well, including altered body composition.

**103. GLUTATHIONE S-TRANSFERASE P1 SINGLE NUCLEOTIDE POLYMORPHISM PREDICTS OTOTOXICTY IN CHILDREN WITH MEDULLOBLASTOMA** Surya Rednam, MD; Michael E. Scheurer, PhD, MPH; Adekunle Adesina, MD, PhD; Ching Lau, MD, PhD; Mehmet Fatih Okcu, MD, MPH. *Baylor College of Medicine, Houston, TX, USA*

**Background:** Glutathione S-transferase (GST) enzymes are involved in detoxifying chemotherapy agents and clearing reactive oxygen species formed by radiation. In this study, we explored the relationship between the host *GSTP1-105* polymorphism (rs1695), tumor GSTpi protein expression, and clinical outcomes in pediatric medulloblastoma. We hypothesized that the *GSTP1-105* G-allele and increased tumor GSTpi expression would be associated with lower progression-free survival and fewer adverse events.

**Methods:** The study included 106 medulloblastoma/primitive neuroectodermal tumor (PNET) patients seen at Texas Children's Cancer Center. Genotyping was performed using an Illumina HumanOmni1-Quad BeadChip and tumor GSTpi expression was assessed using immunohistochemistry. We used the Kaplan-Meier method for survival analyses and multivariable logistic regression for toxicity comparisons.

**Results:** Patients with a *GSTP1-105* AG/GG genotype or who had received a higher dose of craniospinal radiation (median 36 Gy) had a greater risk of requiring hearing aids than their respective counterparts (OR 4.0, 95%CI 1.2 - 13.6, and OR 3.1, 95%CI 1.1 - 8.8, respectively). Additionally, there was a statistically significant interaction between the two variables. Compared with the lowest risk group (*GSTP1-105* AA-lower dose radiation) patients with a *GSTP1-105* AG/GG genotype who received a higher dose radiation were 8.4 times more likely to require hearing aids (95%CI 1.4 - 49.9, p-trend = 0.005). When adjusted for age, gender, and amifostine use, the association remained.

**Conclusions:** The *GSTP1-105* G-allele is associated with permanent ototoxicity in pediatric medulloblastoma/PNET and strongly interacts with radiation dose. A possible mechanism for this finding is that the *GSTP1-105* G-allele leads to reduced GSTpi free radical detoxification in the setting of multimodality therapy including cisplatin and radiation. Patients with this allele should be considered for clinical trials employing radiation dose modifications and more targeted cytoprotectant strategies than are currently being used with amifostine.

**104. MEDICAL INTERVENTIONS FOR THE PREVENTION OF PLATINUM-INDUCED HEARING LOSS IN CHILDREN WITH CANCER: A COCHRANE SYSTEMATIC REVIEW** Jorrit W. van Asl Henk van den Berg, MD, PhD, Elvira C van Dalen, MD, PhD. *Cochrane Childhood Cancer Group, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands; Department of Pediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands*

**Background:** One of the most important adverse effects of platinum-based therapy is hearing loss/ototoxicity. The objective of this systematic review was to assess the efficacy of different otoprotective drugs in preventing platinum-induced hearing loss in children with cancer.

**Methods:** An extensive literature search was performed (up till December 2011) for randomized controlled trials (RCTs) and controlled clinical trials (CCTs) evaluating platinum-based therapy together with an otoprotective drug versus platinum-based therapy with placebo, no additional treatment or another otoprotective drug in children with cancer. Two authors independently performed study selection, quality assessment and data extraction of included studies.

**Results:** Two RCTs and one CCT (including 149 children treated with different platinum-based protocols for osteosarcoma and hepatoblastoma) evaluated amifostine versus no additional treatment. All studies had methodological limitations. Pooling of results was not possible, but in all individual studies no significant difference in ototoxicity between both treatment groups was identified. For possible otoprotective drugs other than amifostine and other types of cancer no eligible studies were found.

**Conclusions:** At the moment there is no evidence from individual studies in children with osteosarcoma and hepatoblastoma treated with different platinum-based protocols which underscores the use of amifostine as an otoprotective drug as compared to no additional treatment. Since pooling of results was not possible and all studies had methodological limitations, no definitive conclusions can be made. It should be noted that 'no evidence of effect', as identified in this review, is not the same as 'evidence of no effect'. Based on the currently available evidence, we are not able to give recommendations for clinical practice. For other possible otoprotective drugs and other types of malignancies no eligible studies were identified, so no conclusions can be made about their efficacy in preventing ototoxicity in children treated with platinum-based therapy. More high quality research is needed.

**105. EFFICACY OF THE SPEECH INTELLIGIBILITY INDEX AS AN INTERVENTION TOOL WITH PEDIATRIC CANCER PATIENTS** Susan S. Hayashi, Megan Cahill, Jingnan Mao, Robert J. Hayashi, Roanne Karzon. *Department of Audiology, St. Louis Children's Hospital, St. Louis, MO, USA; The Moog Center for Deaf Education, St. Louis, MO, USA; Department of Pediatrics, Washington University School of Medicine, St. Louis, MO, USA*

**Purpose:** This study evaluated the Speech Intelligibility Index (SII) as a tool to describe hearing loss and predict when hearing aids would be appropriate for pediatric oncology patients with cisplatin associated hearing loss. The SII is compared to the Brock grading system, a commonly used scale for cisplatin ototoxicity.

**Methods:** A retrospective chart review was performed on pediatric oncology patients treated between August 1990 and April 2007 at St. Louis Children's Hospital. Seventy-eight met eligibility criteria for prior cisplatin exposure with an audiogram obtained at least 6 months after therapy. Patients with conductive hearing loss were excluded. SII values were calculated for both ears and compared to the Brock grade. Three experienced audiologists independently evaluated audiograms and rated the need for hearing aids.

**Results:** The SII provided a more concise numeric value of hearing loss than the Brock grade. SII values within a Brock grade varied from 18-53%. There was excellent agreement of audiologists' ratings of the audiograms. A SII cutoff value of 0.8 yielded high sensitivity (100% for the worse ear, 86% for the better ear) and specificity (100% for both ears) in identifying patients judged to need hearing aids.

**Conclusion:** The SII, which can be easily generated from the audiogram, results in a discrete measure that precisely reflects the child's functional hearing status and is highly correlated with the recommendation for hearing aids. The SII has great potential to guide clinicians and counsel families of children with high frequency hearing loss.

**106. FOLLOW-UP PROGRAMS FOR ADULT SURVIVORS OF CHILDHOOD CANCER IN EUROPE** Stefan Essig, MD; Roderick Skinner, FRCPCH; Claudia Kuehni, MD; Nicolas von der Weid, MD; Gisela Michel, PhD. *Swiss Childhood Cancer Registry, Institute of Social and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland; Department of Paediatric and Adolescent Oncology, and Children's BMT Unit, Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK; Centre Hospitalier Universitaire Vaudois, Pediatric Hematology-Oncology Unit, Lausanne, Switzerland*

**Purpose:** Regular long-term follow-up has been recommended for most childhood cancer survivors. Therefore, formal programs of comprehensive, evidence-based health care and education for childhood cancer survivors have been promoted in relevant guidelines. Little is known about how these recommendations have been implemented. We aimed to determine the availability and characteristics of formal follow-up programs (LTFU) for adult survivors in Europe.

**Methods:** We asked 179 pediatric oncology institutions in 20 European countries to complete an online survey on LTFU.

**Results:** 110 responses (62%) were received from 19 countries. 38% (n=35) stated that LTFU was available for adult survivors. This was most common in the UK and Ireland (67%), followed by Southern (45%), Western (39%), Eastern (17%) and Northern Europe (9%). Survivors started attending at a median age of 18 years (range: 16-40). LTFU took place in pediatric (56%; n=18), or adult hospitals (44%) and routinely included screening for late effects (91%; n=29), second cancer (87%) and psychosocial problems (84%), and educating survivors on health behavior and potential future problems (both 81%). Pediatric oncologists were routinely involved in 62% (n=20) of the programs, adult oncologists in 25%. Major barriers encountered were survivors' lack of interest in continuing follow up care (74%) and the providers' lack of personnel (74%) or dedicated time (71%). Survivors were eventually discharged in 45% of programs, most of them to GPs (64%) and adult oncologists (43%); the most common reason for discharge was a low risk for future late effects (44%). 86% of institutions without LTFU would like to offer it.

**Conclusion:** We conclude that despite general agreement on the need of continued follow-up for adult survivors of childhood cancer, 3 of 5 institutions do not have formal follow-up programs available. A qualitative study is needed to identify surmountable barriers to implementation in European health care systems.

**107. INTEGRATING PREVENTIVE DENTAL CARE IN A PEDIATRIC ONCOLOGY CLINIC** Erin Hartnett, DNP, APRN-BC, CPNP,
New York University Langone Medical Center, Hassenfeld Center for Children with Cancer and Blood Disorders, New York, NY, USA

**Purpose:** A collaborative program was developed between a university dental school and a pediatric oncology center which implemented an oral assessment and fluoride varnish treatment educational program for pediatric oncology providers in order to prevent both acute and long term dental effects of cancer treatment in children.

**Background:** Chemotherapy and radiation place the child at high risk for developing oral problems both during and after childhood cancer treatment, yet preventive dental care is not considered a priority at this time. Yeazel et al. (2004) reported that dental abnormalities occurred in about 30% of all childhood cancer survivors; however, in those who received certain treatments the dental abnormalities increased to 60-95%. The pediatric oncology provider in collaboration with the dental provider is in an optimal position to deliver preventive dental care to this population during oncology care in order to prevent present and future dental problems (daFonseca, 2004).

**Methods:** This project consisted of an interdisciplinary collaborative educational program between a university dental school and an urban outpatient pediatric oncology center for pediatric oncology providers who: (a) completed a pre-survey assessing oral health knowledge (b) attended an oral health educational intervention and fluoride varnish skills lab, and (c) performed an oral assessment and application of fluoride varnish on children being treated for cancer.

**Results:** The results indicated that the pediatric oncology providers increased their oral health knowledge and current practice in oral assessment and fluoride varnish. The program was easily incorporated into the oncology practice, was accepted by staff, parents and children

**Implications:** This project has implications for future practice, policy, education and research. It demonstrated that pediatric oncology providers can implement a preventive dental program, which may positively impact long-term dental problems of childhood cancer survivors.

**108. LOSS OF IMMUNITY TO VACCINE ANTIGENS FOLLOWING CANCER TREATMENT** Jennifer B. Dean, MD; Ramanand Arun Subramanian, PhD, CCRP; Alissa Mills, PA-C; Jeffrey S. Dome, MD, PhD. *Children's National Medical Center, Washington, DC, USA*

**Background:** In the United States each year approximately 14,000 children and adolescents are diagnosed with cancer. Approximately 80% of these children survive their cancer diagnosis after treatment with chemotherapy, surgery, and radiation therapy. Children who are being treated with chemotherapy typically have their immunizations held until they have completed therapy; however there is no consensus for re-immunizing or checking the immune titers after standard chemotherapy.

**Objective:** The purpose of this study was to identify the immune status of childhood cancer survivors after they have completed their treatment, specifically their immunity to polio, pertussis, measles, mumps, rubella, varicella, hepatitis B, diphtheria and tetanus.

**Method:** We performed a single institution retrospective, chart review of pediatric oncology patients, ages 2-18 years at diagnosis, who received chemotherapy between 2001 and 2010. Patients who had undergone bone marrow transplant were excluded. Patients had their immune titers drawn at six months or later from the end of therapy per our standard practice.

**Results:** Eighty-six patients with evaluable immune titers were identified. Of the eighty-six, 56% had leukemia, 18% lymphoma, and 22% solid tumors (including brain tumors). All eighty (100%) patients who had their immune titers drawn for polio had lost their immunity. Eighty-eight percent of patients had lost their immunity to pertussis and seventy-four percent had lost their immunity to hepatitis B. Forty-one patients (47%) had lost immunity to four or more vaccine preventable diseases.

**Conclusion:** A significant proportion of patients undergoing chemotherapy lose their immunity to vaccine preventable diseases. The relatively high rate of non-immune patients is concerning for the potential development of vaccine-preventable infections. Routine testing of immune titers with subsequent revaccination or simply revaccination after completion of chemotherapy for all types of pediatric cancer patients is warranted.

**109. INFECTIOUS COMPLICATIONS IN SURVIVORS OF CHILDHOOD AND ADOLESCENT CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)** Joanna L. Perkins, MD, MS; Yan Chen, MMath; Anne Harris, BA; Charles Sklar, MD; Lisa Diller, MD; Marilyn Stovall, MPH, PhD; Gregory T. Armstrong, MD, MSCE; Yutaka Yasui, PhD; Les Robison, PhD; on behalf of the Childhood Cancer Survivor Study. *The Children's Hospitals and Clinics of Minnesota, Minneapolis, MN, USA; University of Alberta, Edmonton, Alberta, Canada; Memorial Sloan Kettering Cancer Center, New York, NY, USA; Dana Farber Cancer Institute/Children's Hospital, Boston, MA, USA; University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; St. Jude Children's Research Hospital, Memphis, TN, USA*

**Purpose:** Little is known about the long-term risks of infectious complications in survivors of childhood cancer. This study reports on the prevalence of and risk factors for infectious complications in survivors of childhood cancer.

**Patients and methods:** CCSS is a large, retrospective cohort study of 5-year survivors of childhood cancer from 26 participating institutions in North America. We compared incidence of infectious complications between 5-year survivors and their siblings, and infection-related mortality between survivors and the U.S. population. Demographic and treatment variables were analyzed as factors potentially associated with the risk of infectious complications, using Poisson regression models.

**Results:** CCSS survivors (N=12,365) showed elevated rates, in comparison with sibling controls (N=4,023), for overall infectious complications (Rate Ratio (RR), 1.2; 95% CI, 1.2-1.3), pneumonia (RR, 4.2; 95% CI, 2.6-6.9), hepatitis (RR, 2.4; 95% CI, 1.8-3.1), sinusitis (RR,1.6; 95% CI, 1.4-1.7) and chronic gingivitis (RR, 1.5; 95% CI, 1.2-1.8). Factors associated with higher rates of overall late infectious complications included: female sex (RR, 1.7; 95% CI, 1.6-1.9), diagnosis of Hodgkin lymphoma (RR, 1.3; 95% CI, 1.1-1.5), and age at cancer diagnosis over 15 years old. Survivors who received steroids had an increased rate of chronic gingivitis (RR, 1.3; 95% CI, 1.1-1.6). Compared with the U.S. population, survivors were at an increased risk of death from infectious causes (RR, 2.5; 95% CI,1.9-3.2), with females (RR, 2.6; 95% CI, 1.5-4.5) and those exposed to abdominal radiation (RR, 2.4; 95% CI, 1.4-4.1) having the highest mortality.

**Conclusion:** Long-term survivors of childhood cancer remain at increased risk for infectious related complications including death from infectious causes years following completion of therapy. Interventions are needed to target those at highest risk.

**110. BLEOMYCIN ASSOCIATED LUNG TOXICITY IN CHILDHOOD CANCER SURVIVORS** Alexandra Zorzi, Connie L. Yang, Sharon Dell, Paul C. Nathan. *The Hospital for Sick Children, Department of Pediatrics, Division of Hematology/Oncology, University of Toronto, Toronto, Ontario, Canada; BC Children's Hospital, Department of Pediatrics, Division of Respirology, University of British Columbia, Vancouver, British Columbia, Canada; The Hospital for Sick Children, Department of Pediatrics, Division of Respirology, University of Toronto, Toronto, Ontario, Canada*

**Background:** Bleomycin has been established as a pulmonary toxin, but the risk for toxicity in survivors of childhood cancer is poorly characterized.

**Methods:** We conducted a cross-sectional study of lung function in survivors of childhood Hodgkin lymphoma and germ cell tumor treated with bleomycin at our institution between 1997 and 2010. We assessed their most recent post-therapy pulmonary function test (PFT). Spirometry and lung volumes were categorized as normal, restrictive, obstructive or mixed. Diffusing capacity of carbon monoxide (DLCO) was categorized as normal or abnormal.

**Results:** 195 patients were treated with bleomycin. Ten died of non-pulmonary causes. Of 185 survivors, 143 (77%) had complete data available for analysis. Median cumulative bleomycin dose was 60U/m 2 (IQR 30-60). Three patients (2%) had a history of acute bleomycin toxicity. PFTs were performed a median of 2.3 years (IQR 1.4-4.9) from completion of therapy. Spirometry was abnormal in 58 patients (41%), of whom 5 (9%) had respiratory symptoms. 42 (70%) had obstructive, 11 (18%) restrictive and 5 (9%) mixed ventilatory defects. Abnormalities were mild in 53 (91%), moderate in 3 (5%) and severe in 2 (4%). DLCO was abnormal in 27 patients, 26 (96%) of whom had mildly reduced DLCO and were asymptomatic. Univariate analysis did not demonstrate a significant association between gender, smoking, lung metastases, lung radiation, chemotherapy regimen, or autologous transplant and abnormal lung function. Disease relapse was associated with abnormal lung function (p=0.01). Smoking (p=0.04) and relapse (p=0.03) were associated with abnormal DLCO. The odds ratio of developing abnormal spirometry for each 1unit/m2 increase in bleomycin was 1.01 (95% CI 1.00-1.02, p=0.07).

**Conclusions:** Childhood cancer survivors treated with bleomycin frequently have evidence of asymptomatic abnormalities on PFT. The current recommendation for PFT in childhood cancer survivors appears justified.

**111. CORRELATION OF CLINICAL AND DOSIMETRIC FACTORS WITH ADVERSE PULMONARY OUTCOMES IN CHILDREN RECEIVING LUNG IRRADIATION** Rajkumar Venkatramani, Sunil Kamath, Kenneth Wong, Arthur Olch, Jemily Malvar, Richard Sposto, Fariba Goodarzian, Albert Yu, David Freyer, Thomas G. Keens, Leo Mascarenhas. *Children's Hospital Los Angeles, Los Angeles, CA, USA*

**Purpose:** To correlate the clinical and dosimetric factors with adverse pulmonary outcomes in children receiving contemporary lung irradiation.

**Methods:** Children receiving irradiation to the fields of interest, as defined by Children's Oncology Group long term follow-up guidelines, at Children's Hospital Los Angeles from 1999 to 2009 were identified from the radiation oncology database. Clinical features, radiographic findings, pulmonary function tests and dosimetric parameters were retrospectively ascertained.

**Results:** 139 patients (93 male) were identified. Median age at irradiation was 13 years (range 0.04-21 years) with a median follow-up of 3.4 years. Median prescribed radiation dose was 21 Gy (0.4-64.8 Gy). Diagnoses were equally distributed between lymphomas and other solid tumors. Pulmonary toxic chemotherapy included bleomycin in 46.7 % and cyclophosphamide in 78.4%. The following pulmonary outcomes were identified and graded; pneumonitis (7%), chronic cough (8%), pneumonia (32%), dyspnea (9%), supplemental oxygen requirement (3%), radiographic interstitial lung disease (33%), and chest wall deformity (9%). The cumulative incidence (CI) of any one of the above outcomes at 5 years was 62%. Two patients died due to progressive respiratory failure. Post-irradiation pulmonary function tests from 49 patients showed evidence of obstructive lung disease (39%), restrictive disease (15%), hyperinflation (29%), and abnormal diffusion capacity (14%). Thoracic surgery, bleomycin, mean lung dose (MLD), max dose, prescribed dose, and multiple dosimetric parameters starting from V22, were significant in univariate analysis. MLD was the only significant predictor of adverse pulmonary outcome in multivariate analysis (p=0.006).

**Conclusions:** With relatively short follow-up, we found significant pulmonary dysfunction in children receiving lung irradiation using contemporary techniques. MLD rather than prescribed dose should be used to risk stratify patients receiving lung irradiation.

**112. LATE MEDICAL OUTCOMES IN SURVIVORS OF EXTRA-OCULAR RETINOBLASTOMA: THE MEMORIAL SLOAN-KETTERING EXPERIENCE** Danielle Novetsky Friedman, MD; Charles A. Sklar, MD; Kevin C. Oeffinger, MD; Nancy A. Kernan, MD; Yasmin Khakoo, MD; Brain P. Marr, MD; Suzanne L. Wolden, MD; David H. Abramson, MD; Ira J. Dunkel, MD. *Department of Pediatrics, Ophthalmic Oncology Service, Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA*

**Background:** Data on long-term outcomes of survivors of extra-ocular retinoblastoma (RB) are limited. The authors sought to provide the first report characterizing chronic health conditions among survivors of extra-ocular RB.

**Methods:** Retrospective analysis of late medical outcomes in 19 survivors of extra-ocular RB diagnosed between 1990 and 2009. Late effects were graded using the CTCAE v4.0 scoring system. All patients received intensive multimodality therapy for extra-ocular disease

following local control of the primary intra-ocular disease, including conventional chemotherapy (n=19, 100%), radiotherapy (n=15, 69%), and/or high-dose chemotherapy with autologous stem cell transplant (n=17, 89%).

**Results:** The median follow-up was 7.5 years from diagnosis of extra-ocular RB (range 1.8-17.5 years). After excluding visual defects, which were present in all survivors, the most common long-term complications were hearing loss (n=15, 79%), short stature (n=7, 37%), and second malignant neoplasms (n=6, 31%). Sixty-eight percent of survivors exhibited ≥2 non-visual long-term effects of any grade. Except for short stature, which was not graded for severity, grade 3-4 toxicities were limited to: ototoxicity (n=8; n=4 require hearing aids), secondary malignancies (n=6), and unequal limb length (n=1). Secondary malignant neoplasms (SMNs) developed at a median of 11.1 years after initial diagnosis; two of the six patients died of their SMN. Long-term cardiac, pulmonary, hepatobiliary or renal toxicities were not identified in any survivors.

**Conclusion:** Late effects are commonly seen in extra-ocular RB survivors but the majority are mild-moderate in severity. Longer comprehensive follow-up is needed to fully assess treatment-related chronic health conditions in this population but the information collected to date may affect management decisions for children with extra-ocular disease.

**113. CHRONIC MEDICAL CONDITIONS AND HEALTH STATUS IN ADULT SURVIVORS OF RETINOBLASTOMA** Danielle Novetsky Friedman, MD; Jennifer S. Ford, PhD; Charles A. Sklar, MD; Kevin C. Oeffinger, MD; Yuelin Li, PhD; Joanne F. Chou, MPH; Mary McCabe, RN, MA; Leslie L. Robison, PhD; Ruth A. Kleinerman, MPH; Brian P. Marr, MD; David H. Abramson, MD; Ira J. Dunkel, MD. *Memorial Sloan-Kettering Cancer Center, New York, NY, USA; St. Jude Children's Research Hospital, Memphis, TN, USA; National Cancer Institute, Bethesda, MD, USA*

**Background:** Survival rates for retinoblastoma (RB) are approaching 95%. While the increased risk of second neoplasms is well documented, little is known about the burden of other non-ocular chronic medical conditions in survivors of RB.

**Methods:** A retrospective cohort study of adult RB survivors treated at one of several hospitals in New York City was conducted. Eligible survivors were asked to complete a comprehensive questionnaire, adapted from the Childhood Cancer Survivor Study surveys. Forty-nine percent of eligible survivors participated in the study.

**Results:** Four hundred seventy RB survivors (female, 52.1%; mean age at study 43.4+11.0 yrs) were included: 53.6% were survivors of bilateral RB. Twenty-six percent of patients had been treated with chemotherapy and 53.8% had received external beam radiotherapy.

The vast majority of patients reported having good overall health (94.4%). The most frequently described non-visual medical conditions were related to subsequent malignant neoplasms (19.4%), hypercholesterolemia (18.6%), hypertension (14.8%), and migraines (12%). Six percent of patients reported problems with learning and memory with 3.4% rating their impairment as mild and 3.2% as moderate. 3.6% of patients reported severe hearing loss requiring hearing aids. Less than 1% reported heart failure, history of myocardial infarction, pulmonary fibrosis, or dyspnea at rest.

Sixteen percent of patients reported difficulty conceiving for > 1 year. Five hundred sixty-seven pregnancies were reported among 253 survivors or their partners; 67.7% of those who had achieved successful pregnancy reported at least one live birth.

**Conclusion:** These findings suggest that the majority of RB survivors experience good overall health. Future analyses will compare outcomes to those of non-cancer controls and determine risk factors for adverse outcomes among RB survivors.

**114. RADIATION EXPOSURE ASSESSMENT IN LATE EFFECTS STUDIES: OVERVIEW OF AVAILABLE METHODS AND DESIGN/ RATIONALE OF THE DCOG LATER DOSIMETRY RESEARCH PROJECT** Judith L. Kok, MSc; Wil Dolsma, MD, PhD; Flora E. van Leeuwen, PhD; Marry M. van den Heuvel-Eibrink, MD, PhD; Wim Tissing, MD, PhD; Eline van Dulmen-den Broeder, PhD; Jacqueline Loonen, MD, PhD; Dorine Bresters, MD, PhD; Birgitta Versluys, MD; Irma W.M. van Dijk, MSc; Berthe Aleman, MD, PhD; Huib N. Caron, MD, PhD; Arjan van der Schaaf, PhD; Leontien C. Kremer, MD, PhD; Cécile M. Ronckers, PhD; for the Dutch Childhood Oncology Group (DCOG) LATER Dosimetry Research Group. *Department of Pediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands; Department of Radiation Oncology, University Medical Center Groningen, Groningen, The Netherlands; Department of Psychosocial Research and Epidemiology, Amsterdam, The Netherlands; Department of Pediatric Oncology, Sophia Children's Hospital/Erasmus Medical Center, Rotterdam, The Netherlands; Department of Pediatric Oncology and Hematology, University Medical Center Groningen, Groningen, The Netherlands; Department of Pediatric Oncology, Vrije Universiteit Medical Center, Amsterdam, The Netherlands; Department of Pediatric Oncology and Hematology, Radboud University Medical Center, Nijmegen, The Netherlands; Department of Pediatric Immunology, Oncology, Hematology and Bone Marrow Transplantation, Willem Alexander Children's Hospital, Leiden University Medical Center, Leiden, The Netherlands; Department of Pediatric Oncology and Hematology, University Medical Center Utrecht, Utrecht, The Netherlands; Department of Radiation Oncology, Academic Medical Center, Amsterdam, the Netherlands; Dutch Childhood Oncology Group–Late Effects after Childhood Cancer (DCOG-LATER) Consortium*

**Background:** Anticancer therapy is associated with adverse health effects. We are conducting a series of retrospective studies on medically assessed adverse events among long-term childhood cancer survivors in the Dutch DCOG LATER cohort, of whom ~3000 had

radiotherapy between 1963 and 2001. We aim to (1) provide a review of available methods to quantify radiation effects in existing late effects studies and (2) describe rationale for and design of our Dosimetry Research Program.

**Methods:** We conducted a review of available methods employed in studies on late effects of radiotherapy, including study design (i.e., cohort, case-control, patient series, etc.), methods to quantify radiation dose (patient chart based, type of dosimetry method employed, etc.), and the statistical/biological/mathematical models applied to derive quantitative risk estimates, including an assessment of pros and cons.

**Results:** The literature review results will be summarized in a concise table. Cohort-wide data collection for absorbed radiation doses for multiple organs-at-risk is warranted and feasible and should allow for (a) valid comparison of patients treated for different cancer types at different ages and affecting different body parts; and (b) investigation of the potential contribution of volume and fractionation to risk estimates, important parameters according to radiobiology, yet rarely studied epidemiologically. We propose to construct a radiation exposure matrix, for homogeneous patient groups treated with similar radiotherapy, with measures of: organ-in-beam (y/n); absorbed dose; volume; and fractionation; for relevant organs, where feasible. This is probably not possible for any combination of past therapy and organ-at-risk. Nevertheless, this effort will serve DCOG LATER late effects studies and will allow for a descriptive analysis of radiotherapy methods in pediatric oncology in the past 50 years.

**Conclusions:** The DCOG LATER Dosimetry Research Program is unique in scope and will provide a solid basis for current and future retrospective quantitative studies on radiotherapy-related adverse events.

**115. LONG-TERM FOLLOW-UP OF SURVIVORS OF CHILDHOOD AND YOUNG ADULT CANCER: A WORLDWIDE COLLABORATION TO HARMONIZE GUIDELINES** L.C.M. Kremer, MD, PhD; R.L. Mulder, MSc; K.C. Oeffinger, MD; S. Bhatia, MD, MPH; W. Landier, RN, PhD; G. Levitt, MD; L.S. Constine, MD; W.H. Wallace, MD; R. Skinner, MD, PhD; M.M. Hudson, MD. *Department of Pediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands; Departments of Pediatrics and Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Department of Population Sciences, City of Hope National Medical Center, Duarte, CA, USA: Department of Oncology/Haematology, Great Ormond Street Hospital for Children NHS Trust, London, UK; Departments of Radiation Oncology and Pediatrics, University of Rochester Medical Center, Rochester, NY, USA; Department of Pediatric Oncology, Royal Hospital for Sick Children, Edinburgh, UK; Department of Pediatric and Adolescent Oncology, Royal Victoria Infirmary, Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; Departments of Epidemiology and Cancer Control and Oncology, St. Jude Children's Research Hospital, Memphis, TN, USA*

**Purpose:** To establish a common vision and integrated strategy for the surveillance of late effects in survivors of childhood and young adult cancer throughout the world, and to prioritize topics for this international guideline harmonization effort.

**METHODS:** In 2010 the harmonization endeavor was initiated, directed by a core group of ten representatives from guideline groups in North America (COG), the Netherlands (DCOG), United Kingdom (UKCCLG) and Scotland (SIGN). The core group established the overall policy for the harmonization process and selected topics by means of a modified Delphi survey.

**Results:** We will apply evidence-based methods, consisting of the evaluation of concordance and discordance among existing recommendations, the formulation of clinical questions relevant to discordant areas, the performance of systematic literature searches and the organization of extensive evidence summaries. Recommendations will be formulated considering the quality of the evidence, the benefits versus harms of the screening intervention, and the need to maintain flexibility across health care systems. The core group selected the first two topics: secondary breast cancer and cardiomyopathy surveillance. As determined by the Delphi survey, gonadal dysfunction, coronary artery disease, central nervous system malignancies, growth hormone deficiency and neurocognitive deficits will be on the next harmonization agenda.

**Conclusions:** To reduce the consequences of late effects and to improve the quality of life in childhood cancer survivors, childhood cancer survivors should receive the optimum care. By international collaboration in guideline development we can achieve this goal. With the implementation of evidence-based methods we provide a framework for the harmonization of guidelines for the long-term follow-up of childhood and young adult cancer survivors.

**116. INTERNATIONAL HARMONIZATION OF BREAST CANCER SURVEILLANCE RECOMMENDATIONS FOR CHILDHOOD AND YOUNG ADULT CANCER SURVIVORS** R.L. Mulder, MSc; L.C.M. Kremer, MD; M.M. Hudson, MD; S. Bhatia, MD, MPH; W. Landier, RN, PhD; G. Levitt, MD; L.S. Constine, MD; W.H. Wallace, MD; F.E. van Leeuwen PhD; C.M. Ronckers, PhD; T.O. Henderson, MD, MPH; M. Dwyer, MD, PhD; R. Skinner, MD, PhD; K.C. Oeffinger, MD. *Department of Pediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands; Departments of Epidemiology and Cancer Control and Oncology, St. Jude Children's Research Hospital, Memphis, TN, USA; Department of Population Sciences, City of Hope National Medical Center, Duarte, CA, USA; Department of Oncology/Haematology, Great Ormond Street Hospital for Children NHS Trust, London, UK; Departments of Radiation Oncology and Pediatrics, University of Rochester Medical Center, Rochester, NY, USA; Department of Pediatric Oncology, Royal Hospital for Sick Children,*

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**Purpose:** To develop international harmonized guidelines for breast cancer surveillance among women treated with chest radiation for a pediatric malignancy.

**Methods:** A multidisciplinary guideline panel consisting of 31 experts was convened to evaluate three published guidelines that provide recommendations for breast cancer surveillance in this high risk population. Three members of the panel (RLM, LCK, and KCO) identified areas of concordance and discordance amongst the guidelines, formulated clinical questions relevant to discordant areas, performed systematic literature searches to answer the questions, and developed extensive evidence summaries. This information was provided to the expert panel and discussed at a meeting. The panel developed and categorized recommendations according to a 4-level color schema adapted from the 'Applying classification of recommendations and level of evidence' criteria of the American Heart Association and the Grading of Recommendations Assessment Development and Evaluation (GRADE) criteria.

**Results:** Green (strong) recommendations included: Providers and female survivors treated with chest radiation should be aware of breast cancer risk; breast cancer surveillance is recommended for female survivors treated with ≥20 Gy chest radiation; initiation of breast cancer surveillance is recommended at age 25 years or ≥8 years from radiation (whichever occurs last); annual breast cancer surveillance is recommended for female survivors treated with chest radiation until at least 50 years of age; mammography and/or MRI is recommended for at risk women. Yellow (reasonable) recommendations included: Breast cancer surveillance is reasonable for female survivors treated with 10-19 Gy chest radiation; and continuation of breast cancer surveillance (beyond that recommended by national health care systems) in female survivors > 50 years is reasonable.

**Conclusions:** The harmonized set of breast cancer surveillance recommendations is intended to be scientifically rigorous, to positively influence health outcomes, and to facilitate the care for female survivors of childhood cancer treated with chest radiation.

**117. DECREASED WHITE MATTER INTEGRITY AND ASSOCIATED COGNITIVE DYSFUNCTION 25 YEARS AFTER TREATMENT FOR CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA** Ilse Schuitema, Sabine Deprez, Wim van Hecke, Marita Daams, Anne Uyttebroeck, Stefan Sunaert,Cor van den Bos, Anjo Veerman, Leo de Sonneville. *Department of Child and Adolescent Studies, University of Leiden, Leiden, The Netherlands; Department of Pediatrics, Division of Pediatric Hematology/Oncology, VU University Medical Center, Amsterdam, The Netherlands; Department of Radiology, University Hospital Gasthuisberg of the K.U. Leuven, Leuven, Belgium; icoMetrix, Leuven, Belgium; Department of Radiology, VU University Medical Center, Amsterdam, The Netherlands; Department of Pediatric Hematology and Oncology, University Hospitals Leuven, Leuven, Belgium; Department of Pediatrics, Division of Pediatric Hematology and Oncology, Amsterdam Medical Center, Amsterdam, The Netherlands*

**Purpose of study:** Central nervous system (CNS) directed chemotherapy (CT) and radiotherapy (CRT) for childhood acute lymphoblastic leukemia (ALL) has neurotoxic properties. The aim of this study is to find the underlying mechanisms of neuropsychological sequelae in adulthood, 25 years after treatment.

**Description of project:** Twenty-four subjects treated with standard dose CT + CRT (2500 cGy), 29 subjects treated with standard dose CT only, 7 patients treated with high dose CT + CRT (for high risk of CNS relapse), 20 patients treated with high dose CT, 13 relapse patients treated with CT+CRT and 49 healthy controls have been assessed with subtests from the Amsterdam Neuropsychological Tasks program (ANT) and MR diffusion tensor imaging (DTI). Differences in fractional anisotropy (FA, DTI-measure describing white matter (WM) integrity) between groups were analysed using voxel-based statistical analysis.

**Results and conclusions:** Long-term survivors of ALL demonstrated significantly decreased FA (pFWE corrected < 0.05) in frontal (orbitofrontal, corpus callosum, cingulum), temporal (inferior longitudinal and fronto-occipital fasciculus) and parietal (cingulum and corpus callosum) WM tracts compared to controls. When contrasting patient groups separately with controls, a decrease in WM quality was mainly seen in the groups that received CRT. This effect was more extended for the high risk CT+CRT group. At a lower threshold ($p<0.001$ uncorrected for multiple comparisons), indications for lower WM integrity were seen for the group that received standard dose CT in frontal WM tracts, and for the group treated with high dose CT in the lemnisci.

Voxel-based correlation analysis between all subjects' FA maps and task performance revealed significant correlations in frontal, parietal and temporal WM tracts with indices for visuomotor control, visuospatial sequencing and sustained attention work pace, with lower FA values denoting worse cognitive performance. These results suggest a link between decreases in cerebral WM integrity and impaired cognition, which were both most prominent in the irradiated groups.

**118. GENDER AND SELF-REPORTED CHANGES IN ACADEMIC FUNCTIONING AMONG CHILDHOOD CANCER SURVIVORS** Jordan Gilleland, PhD; Kristen Vangile, MPH; Ann Mertens, PhD; Lillian R. Meacham, MD; Karen Wasilewski-Masker, MD, MsC. *Aflac Cancer Center and Blood Disorder Service at Children's Healthcare of Atlanta, Atlanta, GA, USA; Emory University School of Medicine, Atlanta, GA, USA*

**Purpose:** The goals of this investigation were to 1) examine self-reported changes in academic functioning before treatment, after treatment, and at survivorship care for childhood cancer survivors, and 2) explore potential gender differences in academic functioning over time.

**Methods:** Survey data were collected from patients ages 4-28 years old, as part of an institutional cohort study, the Children's Healthcare of Atlanta Childhood and Adolescent Young Adult Cancer Survivor Study (CHOA-CAYACSS). Participants reported on dichotomously coded variables related to academic functioning including involvement with special education (n=217), tutoring (n=223), and honors/advanced classes (n=208). Mixed factorial analyses of variance were conducted to explore main effects for time and gender differences in academic function, as well as interaction effects for gender differences over time.

**Results:** Significantly more patients utilized special education services after treatment (21%) or currently (18%) than prior to treatment (5%) ($F(1, 215)=29.67$, $p < .001$). Gender main effects and interaction effects were not significant for special education services.

Significantly more patients engaged in tutoring after treatment (28%) than before treatment (5%) or currently (13%)($F(1, 221)=37.86$, $p < .001$). Gender main effects were non-significant; however, interaction effects were significant ($F(1, 221)= 5.71$, $p= .018$), with equal participation in tutoring before treatment (males=3%, females=3%), and more females engaging in tutoring after treatment (males=9%, females=18%) and currently (males=5%, females=7%).

Significantly more patients completed advanced coursework after treatment (36%) than before (17%) or currently (26%)($F(1, 206)=20.70$, $p < .001$). Gender main effects were non-significant; however, interaction effects were significant ($F(1, 206)=7.94$, $p= .005$), with more females completing advanced courses prior to treatment (males=5%, females=12%) and more males completing advanced courses after treatment (males=19%, females=16%) and currently (males=15%, females=11%).

**Conclusions:** Data are consistent with previous survivorship outcome research and add to the literature by helping to clarify relationships between gender and academic functioning over time.

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**The Meeting Planners responded as follows:**

| **Faculty Name:** | **Commercial Interest(s):** |
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| Smita Bhatia | None |
| Jacqueline Casillas, MD, MSHS | None |
| Sarah Donaldson, MD | None |
| Daniel Green, MD | None |
| Wendy Hobbie, MSN, PNP | None |
| Melissa Hudson, MD | None |
| John J. Mulvihill, MD | Yes (Ownership Interest in Aetna and Bristol Myers Squibb) |
| Kevin Oeffinger, MD | None |
| David Poplack, MD | None |
| Leslie Robison, PhD | Yes (Advisory Board for Eli Lilly) |
| Flora van Leeuwen | None |
| Charles Sklar | None |
| Jeanette Falck Winther | None |

**The Oral Presenters responded as follows:**

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| Tara Brinkman, PhD | None |
| Jacqueline Casillas, MD, MSHS | None |
| Eric Chow, MD, MPH | None |
| Michelle N. Edelmann, PhD | None |
| Clare Frobisher, PhD | None |
| Thorgerdur Gudmundsdottir, MD | None |
| I-Chan Huang, PhD | None |
| Karen E. Kinahan, MS, PCNS-BC | None |
| Kevin Krull, PhD | None |
| Lasse Wegener Lund, MD | None |
| Jyoti Malhotra, MD, MPH | None |
| Sogol Mostoufi-Moab, MD, MSCE | None |
| Sabine Mueller, MD, PhD | None |
| Kiranmye Reddy, MD | Yes (Funding from Novartis for patient MRI Studies and lab work) |

**The Oral Presenters responded as follows (continued):**

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| Michael Schaapveld | None |
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| Bryan Kolb, PhD | None |
| Arthur Kramer, PhD | None |
| Scott M. Lynch, PhD | None |
| Rima Obeid | None |
| Elizabeth Skidmore, PhD | Yes (Supported/Contracted Research: NCMRR, NINDS, NIMH, University of Pittsburgh Medical Center Rehabilitation Institute; University of Pittsburgh Office of Research) |

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