11th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer

June 11–12, 2010

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 11th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer, participants should be able to:

- Discuss the health consequences of obesity
- Explain obesity as a disorder of energy balance
- Describe the role of the neuroendocrine system in energy balance
- Identify the monogenic causes of obesity
- Discuss the roles of insulin and gastrointestinal peptide hormones in energy balance
- Explain the roles of adiponectin and ghrelin in appetite regulation
- Describe the role of the endocannabinoid system in energy balance
- Discuss the methods for measurement of energy expenditure
- Identify the components of an exercise intervention
- Discuss the role of pharmacologic intervention for the management of obesity
- Discuss the role of bariatric surgery in the management of obesity

Participants

Participants will include, but not limited to US and international practitioners involved in the interdisciplinary fields of medical, surgical, pediatric hematology/oncology, radiation oncology, counseling, clinical researchers 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 10, 2010 for registration. In addition, the registration desk will be open at the following times:

Friday, June 11, 2010	7:00 AM-2:00 PM
Saturday, June 12, 2010	8:00 AM-2:00 PM

Registration fee includes the *Program/Proceedings*, Welcome Reception (June 10), admission to all scientific sessions, poster session, conference materials, breakfast, lunch, refreshment breaks, dinner (Friday, June 11).

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 is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians, and designates this educational activity 11th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer, June 11–12, 2010) for a maximum of 12.5 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 activity to disclose any real or apparent conflict of interest they may have as related to the content of this CME activity. All identified 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 Preview (Thursday, June 10)

Poster preview (no attendance of presenter), Virginia Room ABCD and Piedmont Room will be held Thursday, June 10 from 7:00 PM to 10:00 PM.

Poster Exhibition (Friday, June 11)

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 throughout the conference beginning Thursday, June 10 (Preview) through Saturday, June 12 at noon.

Welcome Reception Oval Garden, lower level

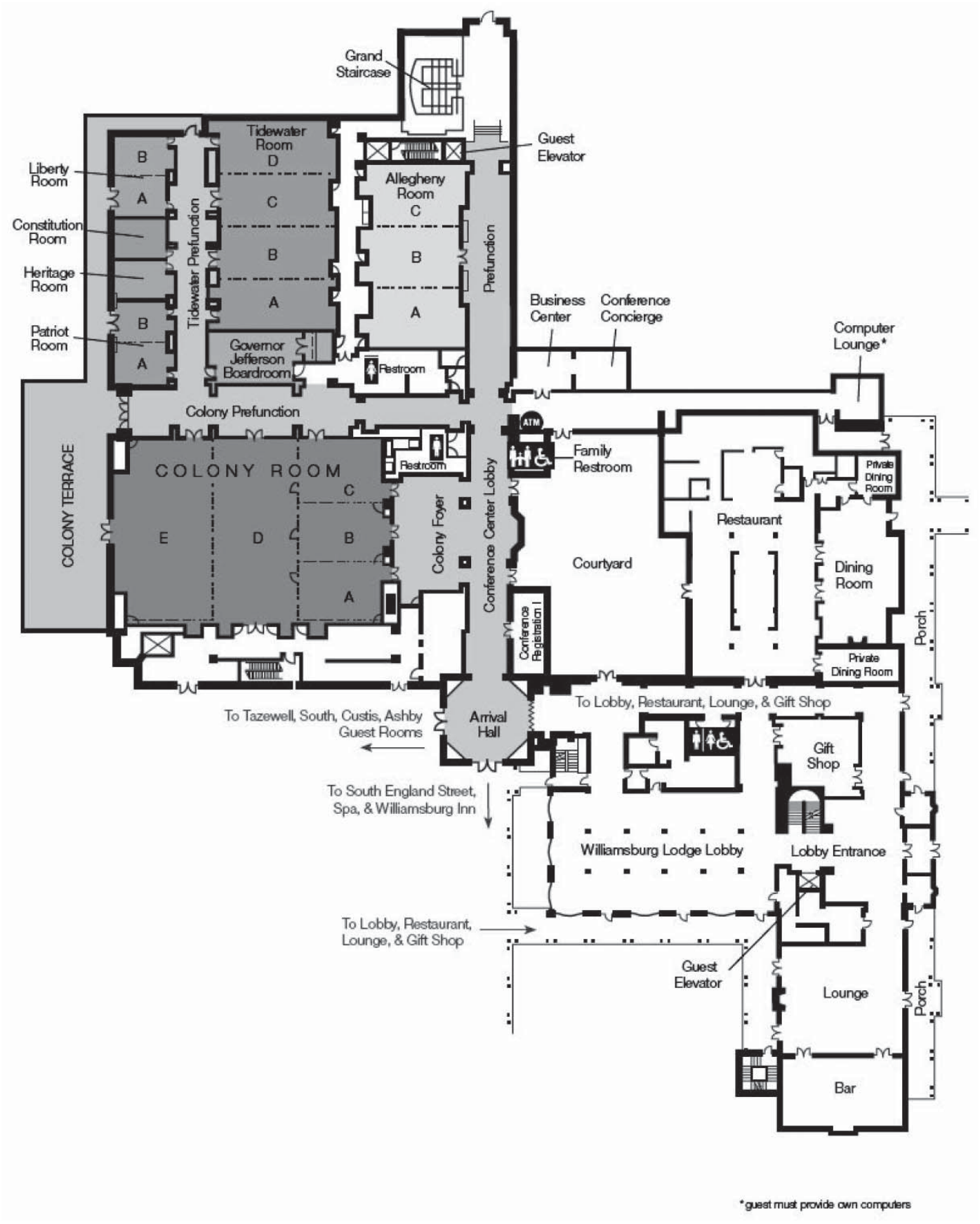
The Welcome Reception will be held on Thursday, June 11 in the Oval Garden (lower level). This will be held from 6:00 to 8:00 pm and will include wine and appetizers. The cost of this function is included in your registration fee.

Sponsor Acknowledgement

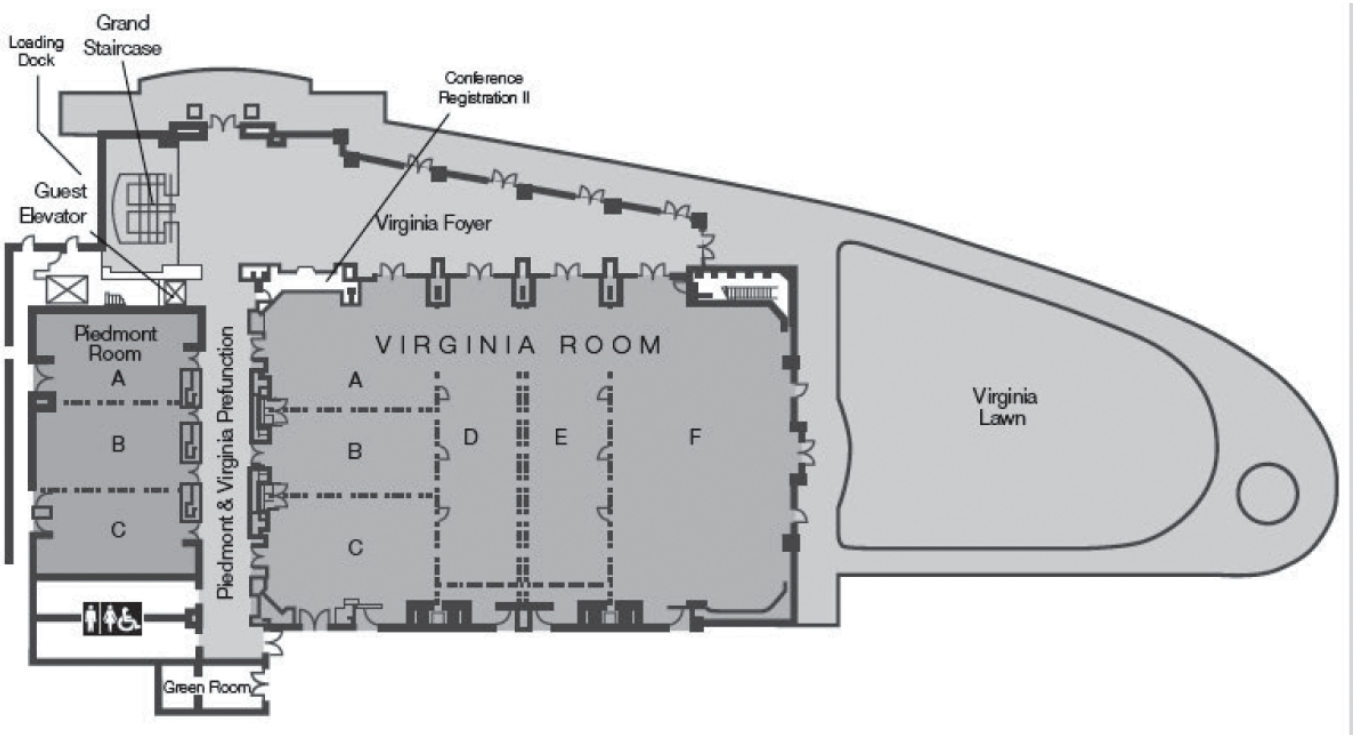
The 11th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer gratefully wishes to acknowledge support from St. Jude Children's Research Hospital and financial support of the National Cancer Institute.

Conference Center Map

Williamsburg Lodge Conference Center Main Level



Williamsburg Lodge Conference Center Lower Level



Invited Speakers

Gerald Berenson, MD

Department of Epidemiology, Tulane University, New Orleans, LA

Wendy K. Chung, MD, PhD

Herbert Irving Assistant Professor of Pediatrics in Medicine, Director of Clinical Genetics, Columbia University, New York NY

James DeLany, PhD

Research Associate Professor of Medicine, Division of Endocrinology and Metabolism, University of Pittsburgh, Pittsburgh, PA

Susan S. Deusinger, PT, PhD, FAPTA

Director, Program in Physical Therapy, Professor, Neurology and Physical Therapy, Washington University School of Medicine in St. Louis, St. Louis, MO

Robert F. Kushner, MD, MS

Clinical Director, Northwestern University Comprehensive Center on Obesity, Professor of Medicine, Division of General Internal Medicine, Northwestern University, Chicago, IL

Aron H. Lichtman, PhD

Associate Professor, Pharmacology & Toxicology, Virginia Commonwealth University, Richmond, VA

Kevin Dean Niswender, MD, PhD

Assistant Professor, Division of Diabetes, Endocrinology & Metabolism, Vanderbilt University, Nashville, TN

Eric Ravussin, PhD

Chief, Division of Health and Performance Enhancement, Douglas L. Gordon Chair in Diabetes and Metabolism, Professor, Pennington Biomedical Research Center, Baton Rouge, LA

Randy Seeley, PhD

Professor, Genome Research Institute, University of Cincinnati, Cincinnati, OH

Steven Teich, MD

Surgical Director of the Bariatric Surgery Program, Clinical Associate Professor of Surgery, Nationwide Children's Hospital, Columbus, OH

Matthias H. Tschöp, MD

Associate Professor, Departments of Psychiatry and Medicine , Obesity Research Centre/Genome Research Institute, University of Cincinnati, College of Medicine, Cincinnati, OH

Conference Program

Thursday, June 10

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 11

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: Giulio J. D'Angio, MD, University of Pennsylvania, Philadelphia, PA
8:30 AM	*Health Consequences of Obesity: The Bogalusa Heart Study* Gerald Berenson, MD, Tulane University, New Orleans, LA
9:00 AM	*Energy Balance: An Overview* Eric Ravussin, PhD, Pennington Biomedical Research Center, Baton Rouge, LA
9:30 AM	*Neuroendocrine Regulation of Food Intake* Kevin Niswender, MD, PhD, Vanderbilt University School of Medicine, Nashville, TN
10:00 AM	**Refreshment break**
10:15 AM	*Monogenic Causes of Obesity* Wendy K. Chung, MD, Columbia University, New York, NY
10:45 AM	*Novel Communication Between Adipose Tissue and the Brain to Regulate Energy Balance* Randy J. Seeley, PhD, University of Cincinnati, Cincinnati, OH
11:15 AM	*Adiponectin and Ghrelin* Mathias Tschoep, MD, University of Cincinnati, Cincinnati, OH
11:45 AM	**Discussion**
12:00 PM	**Lunch** (Colony Room DE, main level)

Session II

1:30 PM – 5:00 PM	**Platform Presentations**—Moderator: Jacqueline Casillas, MD, David Geffen School of Medicine at UCLA, Los Angeles, CA
1:30 PM	*Components of the Metabolic Syndrome in 500 Adult Long-Term Survivors of Childhood Cancer* Marjolein van Waas
1:45 PM	*Characteristics of Insulin Resistance (IR) and Cardiovascular Risk After Hematopoietic Cell Transplant (HCT) for Childhood Hematologic Maliganancies* K. Scott Baker
2:00 PM	*Insulin Resistance and Vascular Stiffness in Survivors of Childhood Hematologic Malignancies* Daniel A. Mulrooney
2:15 PM	*Correlates of Insulin Resistance Among Adult Survivors of Childhood Acute Lymphoblastic Leukemia (ALL)* ES Tonorezos

2:30 PM	*Improvement in Insulin Resistance Among Adult Survivors of Childhood ALL Following a 12-Month Lifestyle Intervention* Kevin C. Oeffinger
2:45 PM	*Resistance Exercise Intervention Improves Insulin Resistance and Fitness in Survivors of Childhood Bone Marrow Transplant (BMT) With Total Body Irradiation (TBI)* Nikki L Davis
3:00 PM	**Refreshment break**
3:15 PM	*Long-Term Outcomes After Cancer in Infancy: A Report From the Childhood Cancer Survivor Study (CCSS)* Lynda Vrooman
3:30 PM	*The General Health and Psychosocial Functioning of Adult Survivors of Retinoblastoma* Ira Dunkel
3:45 PM	*Twenty-Five Year Follow-Up Among Survivors of Childhood Wilms Tumor: A Report From the Childhood Cancer Survivor Study (CCSS)* Amanda M. Termuhlen
4:00 PM	*Renal Dysfunction and Hypertension in Long-Term Childhood Cancer Survivors* Sebastiaan L. Kninenburg
4:15 PM	*Executive Functions in Aging Adult Survivors of Childhood Leukemia* Kevin R. Krull
4:30 PM	*Signs and Symptoms of Peripheral Neuropathy in Adult Survivors of Childhood Acute Lymphoblastic Leukemia (ALL): Associations With Physical Performance and Chemotherapy Doses* Kiri K. Ness
4:45 PM	*Endocrinopathy in Survivors of Childhood Cancer: A Study From the British Childhood Cancer Survivor Study (BCCSS)* AA Toogood
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 12

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: Wendy Hobbie, RN, MSN, FAAN, University of Pennsylvania, Philadelphia, PA
8:45 AM	*Long-Term Population-Based Risks of Specific Causes of Death After Childhood Cancer: the British Childhood Cancer Survivor Study* Raoul C. Reulin
9:00 AM	*Cardiovascular Disease in Long-Term Survivors of Childhood Cancer* Helena JH van der Pal
9:15 AM	*Radiation Dose as a Risk Factor for Cardiac Diseases Following Childhood Cancer: a Case-Control Study* Florent de Vathaire
9:30 AM	*Coronary Heart Disease Events 50+ Years After Thoracic Irradiation: Preliminary Results* (Michael) Jacob Adams

9:45 AM	*Yield of Screening for Cardiovascular Risk Factors and Cardiac Dysfunction in Childhood Cancer Survivors Using the Children's Oncology Group (COG) Long-Term Follow-Up (LTFU) Guidelines: City of Hope Experience* Saro H. Armenian
10:00 AM	*Anthracycline-Related Cardiomyopathy (AC) in Childhood Cancer Survivors: Dose-Specific Role of Genetic Polymorphisms in the Carbonyl Reductase (CBR) Genes—a Children's Oncology Group Study* C.L. Sun
10:15 AM	**Refreshment break**
10:30 AM	*Long Term Population-Based Risks of Second Primary Neoplasms After Childhood Cancer: British Childhood Cancer Survivor Study (BCCSS)* Mike Hawkins
10:45 AM	*Multiple Subsequent Neoplasms in the Childhood Cancer Survivor Study (CCSS) Cohort* Gregory T. Armstrong
11:00 AM	*Gastrointestinal Malignancies as a Subsequent Malignant Neoplasm in Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study* TO Henderson
11:15 AM	*Radiation Dose as a Risk Factor for Second Neoplasms in Digestive System Following Childhood Cancer: A Case-Control Study* Florent de Vathaire
11:30 AM	*Breast Cancer After Childhood Cancer: an International Collaborative Case-Control Study* Raoul C. Reulen
11:45 AM	*Pharmacogenetic Risk Factors for Altered Bone Mineral Density and Body Composition in Pediatric Acute Lymphoblastic Leukemia* Mariel L. te Winkel
12:00 PM	**Lunch** (Colony Room DE, main level)

Session IV

1:30 PM – 4:15 PM	**Invited Speakers**—Moderator: Lisa Diller, MD, Dana-Farber Cancer Institute, Boston, MA
1:30 PM	*The Endocannabinoid System—Role in Energy Regulation* Aron H. Lichtman, PhD, Virginia Commonwealth University, Richmond, VA
2:00 PM	*Measurement of Energy Expenditure* James DeLany, PhD, University of Pittsburgh, Pittsburgh, PA
2:30 PM	*Exercise Intervention for Management of Obesity* Susan S. Deusinger, PT, PhD, FAPTA, Washington University School of Medicine, St. Louis, MO
3:00 PM	*Pharmacologic Management of Obesity* Robert F. Kushner, MD, Northwestern University, Chicago, IL
3:30 PM	*Bariatric Surgery for Obesity Management* Steven Teich, MD, Nationwide Children's Hospital, Columbus, OH
4:00 PM	**Discussion**
4:15 PM	**Conference summary**
4:30 PM	**Refreshments** (Virginia Foyer, lower level)

Invited Speakers Abstracts

HEALTH CONSEQUENCES OF OBESITY: THE BOGALUSA HEART STUDY Gerald Berenson, MD, for the Bogalusa Heart Study Group. *New Orleans, Louisiana*

It is well known that cardiovascular (CV) risk factors occur in childhood. Childhood values track at high or low levels and are predictive of adult CV disease. Risk factors cluster in both childhood and adulthood and result in a high prevalence of the cardiometabolic syndrome. Although insulin resistance is the hallmark of this syndrome, childhood obesity precedes insulin resistance. Both carbohydrate-insulin metabolism and obesity are the driving forces of the syndrome. The worldwide obesity epidemic is now exaggerating the dire consequence of obesity – multi risk factors cardiometabolic syndrome – diabetes picture. Perhaps the most dramatic consequence of this picture has been documented by autopsy studies.

Atherosclerotic lesions of fatty streaks and collagen capped, raised fibrous plaques are noted in the aorta and coronary vessels in childhood, adolescence and at young adult ages. These silent asymptomatic lesions increase with increasing numbers of risk factors and occur with a very high prevalence in our population. Of the risk factors, childhood obesity is the most consistent to predict adult heart disease.

Non invasive methodology is now allowing much broader evidence of early CV disease in the general population. Such studies as Doppler echocardiography of carotid intima-media thickness, which is a surrogate measure of coronary artery disease, and radial pulse analyses indicating vascular stiffness are providing insight into "vascular age" complementing a biologic age by the Framingham score. Such observations are providing evidence that diagnoses like prehypertension and impaired fasting glucose or prediabetes should not be treated as innocuous.

Overall, these observations show the horrible consequences of obesity, and the need to begin prevention of adult heart disease in childhood.

ENERGY BALANCE: AN OVERVIEW Eric Ravussin, PhD. Pennington Biomedical Research Center, *Baton Rouge, LA, USA*

Idiopathic obesity, that is obesity having unknown cause, is a result of multi-behavioral and metabolic factors including energy intake and energy metabolism.

For true weight maintenance, not only is energy intake required to match energy expenditure but macronutrient intake must balance macronutrient oxidation. However, this equilibrium seems to be difficult to achieve for individuals with low fat oxidation, low energy expenditure, low sympathetic activity or low levels of spontaneous physical activity. Additionally, large variability in weight change is observed when energy excess is imposed experimentally or spontaneously. Numerous genetic association studies have provided evidence for associations between measures of energy metabolism and genetic polymorphisms. Together, the data clearly suggest an involvement of genetics in body weight regulation implying a "normal physiology in an obesogenic environment". Genes not only influence appetite and satiety control, the efficiency of nutrient digestion and absorption but also the efficiency of mitochondrial ATP synthesis.

This presentation will first review the principle of the energy balance equation and the consequences of small imbalances between intake and expenditure on weight gain or weight loss.

This presentation will review prospective studies showing: 1) The inter-subject variability of weight change in response to overfeeding or caloric restriction; 2) The association between energy expenditure, sympathetic activity or spontaneous physical activity and body weight change; 3) The impact of macronutrients on energy balance suggesting that carbohydrate balance may represent a potential signal to modulate energy intake.

Controlled studies of overfeeding have clearly shown that in response to a clamped constant surplus of energy intake, there is a large variation in weight gain. This is strong evidence that components of energy expenditure are responsible for this variability. For example, the gain in fat mass in response to a fixed overfeeding was inversely related to the level of spontaneous physical activity that the authors called non-exercise activity thermogenesis (NEAT). Well-controlled overfeeding studies will be discussed in light of the potential metabolic adaptation to counteract excess food intake and the potential of dietary protein content.

More than 30 years ago it was shown that overfeeding in response to a cafeteria diet in rodents led to a wide variability in weight gain which was mostly related to the capability of developing thermogenic mechanisms principally in the brown adipose tissue. It is however only last year that three papers published in the April 9th issue of the New England Journal of Medicine and one in the July issue of Diabetes suggested a potential role for brown adipose tissue to regulate not only human body temperature but possibly energy balance. Whether these recent studies implicate a role for BAT in the regulation of body temperature and possibly the regulation of adiposity will be discussed

Finally we will review some of the studies in which energy expenditure has been measured in children and the possible impact of energy expenditure on excessive weight gain and the development of obesity.

During the past 40 years large increases in the prevalence of obesity have been mostly caused by our sedentary adjustment to urban developments in which demand for physical activity is reduced and highly palatable, cheap food is ubiquitously available. Interestingly, in this obesogenic environment many people still appear resistant to obesity. Differences in the propensity to gain weight are due to cognitive factors (eg. cognition, emotion and restraint) and genetic factors impacting the "normal physiologic" regulation of food intake and energy metabolism.

NEUROENDOCRINE REGULATION OF FOOD INTAKE Kevin Niswender, MD, PhD. *Vanderbilt University School of Medicine, Department of Medicine, Division of Diabetes, Endocrinology and Metabolism, Department of Molecular Physiology and Biophysics, Nashville, TN*

Despite the current obesity epidemic, abundant experimental evidence indicates that body weight and adiposity can be extremely tightly regulated physiological variables. The process whereby intake is matched to energy expenditure over time in order to promote the stability of body energy stores (in the form of adipose) is termed energy homeostasis. Current models of energy homeostasis implicate a classic endocrine feedback loop wherein the hormones insulin and leptin function as adiposity negative feedback signals to the central nervous system. Both hormones are secreted and circulate in proportion to fat mass; deficiency leads to obesity and/or hyperphagia, and administration of either hormone into the brain reduces food intake and body weight. In the hypothalamus, insulin and leptin regulate the activity of "primary" neurons in parallel neural circuits whose function is to coordinate changes in the two key variables involved in energy homeostasis: food intake and energy expenditure. For example, neuropeptide Y (NPY) is a potent orexigenic neuropeptide that potently increases feeding, and is inhibited by insulin and leptin. Conversely, the proopiomelanocortin (POMC) expressing neuron releases alpha-melanocyte stimulating hormone (a-MSH) in response to insulin and leptin stimulation, and, via the melanocortin receptors, decreases food intake and increases energy expenditure. Thus, the concept of adiposity negative feedback signaling and an overview of the structure and function of this system will be developed and applied to several experimental paradigms.

Recognizing that feeding occurs in meals, a conceptual framework will be described for how long term adiposity signals, such as insulin and leptin, interact with other signals that coordinate the termination of a meal, such as cholecystikinin (CCK). Numerous gut peptides are released in response to nutrient ingestion and several, including CCK, act in the enteric nervous system and hindbrain to induce satiation and termination of a meal. Of course, in the situation where fat stores are depleted, a larger meal would be required to restore homeostasis, whereas in the presence of adequate fat stores, a smaller meal would be favored. The status of adipose stores, as indicated by insulin and leptin action in the hypothalamus, is communicated to hindbrain centers, where sensitivity to the meal terminating (satiation) effects of CCK is modulated. Thus, mechanisms by which long term signals such as insulin and leptin interact with short term satiety signals, such as CCK will be described and the implications for human obesity and related disorders discussed.

Finally, the hypothesis that typical human obesity represents pathological dysfunction in energy homeostasis will be presented in the context of the structure-function relationships presented throughout. Here, the effects of high-fat feeding on the neural circuitry and signal transduction involved in energy homeostasis will be highlighted and molecular mechanisms involved in the genesis of hypothalamic insulin and leptin resistance briefly presented.

MONOGENIC CAUSES OF OBESITY Wendy K. Chung, MD. *Division of Molecular Genetics, Department of Pediatrics, Columbia University, New York, NY*

Obesity has become an increasingly prevalent public health problem and represents the complex interaction of genetic, developmental, behavioral, and environmental influences. Although rare, the study of monogenic forms of obesity provides insight into underlying molecular and physiological mechanisms by which adiposity is regulated through food intake, energy expenditure, and partitioning of stored calories. The identification of the genetic basis for many forms of monogenic obesity has provided a group of candidate genes and molecular pathways for study the genetic control of energy homeostasis. Many of the genes identify relate to the development and function of the hypothalamus and central control of food intake and energy homeostasis. Allelic variations in these genes could contribute to non-syndromic forms of obesity.

NOVEL COMMUNICATION BETWEEN ADIPOSE TISSUE AND THE BRAIN TO REGULATE ENERGY BALANCE Randy J. Seeley, PhD. *University of Cincinnati, Cincinnati, OH*

Adult mammals, including humans, match their caloric intake to their caloric expenditure to maintain energy balance. To do so, the system must be able to monitor both the amount of stored fuel in adipose tissue but also the amount of available fuel. Consequently, key regions of the hypothalamus must be sensitive to signals that convey information about both stored and available fuel. Information about stored fuel is conveyed to key hypothalamic centers via cytokine hormones such as leptin. Unfortunately, over the past decade, there have been dozens of neuropeptide and neurotransmitter systems linked to the control of energy balance that might be involved. One way to begin organizing functional circuits is to identify which of these systems are the direct targets for afferent signals about the status of adipose mass in the periphery. Such "adiposity signals" (like leptin and insulin) have concentrations of receptors in

the arcuate nucleus of the hypothalamus. Thus, this anatomical region is a logical starting point for trying to make these functional circuits. One CNS system that is prominent in the arcuate nucleus is the melanocortin system. Several lines of evidence point to the melanocortin system as a critical inhibitor of food intake and weight gain and that its activity is carefully regulated by the actions of adiposity signals. The problem, however, is that the melanocortin system is itself redundantly regulated. A unique aspect of this CNS melanocortin system is the presence of endogenous receptor antagonists/inverse agonists. Cells making the antagonist are also found in an adjacent population to those making the agonist and are reciprocally regulated by adiposity signals. Given the several dozen other proteins involved, such compensation by this receptor antagonist is but one factor that makes it difficult to change body weight under normal circumstances. Such a highly redundant system also limits the efficacy of pharmacotherapy for obesity since increased activity at one population of receptors is likely to result in a myriad of other changes that work against further loss of weight.

Despite the large number of biological systems that work to regulate food intake and energy expenditure, large numbers of individuals still become obese. A key question revolves around why some individuals become obese while others manage to remain lean in our obesigenic environment. Recently we have hypothesized that differences in adipose tissue capacity may be a contributor to these individual differences. We have recently tested peptides developed to home to the endothelium of white adipose tissue and cause apoptosis. This peptide sequence that elicits apoptosis of endothelium in white fat potently reduced body weight. Lean and obese mice or rats were treated with proapoptotic peptide for 4 or 27 days. This proapoptotic peptide completely reversed high-fat diet (HFD)-induced obesity in mice and reduced body weight in mice and rats on a HFD, but not a LFD. Fat loss occurred with no change of energy expenditure, but reduced food intake that occurred without signs of illness and despite reduced circulating leptin. These results indicate that there are important differences between white-fat vasculature in lean versus obese animals. Consistent with this hypothesis, mice that are prone to become obese on a HFD have higher expression of pro-angiogenic factors than mice that are resistant to weight gain on a HFD. Thus, adipose tissue remodeling may represent an important capacity difference that contributes to the differences among individuals to gain weight when exposed to calorie-rich environments.

ADIPONECTIN AND GHRELIN Mathias Tschoep, MD. *University of Cincinnati, Cincinnati, OH*

THE ENDOCANNABINOID SYSTEM— ROLE IN ENERGY REGULATION Aron H. Lichtman, PhD. *Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA*

Cannabis sativa has been used since antiquity for the treatment of many ailments, including the alleviation of pain, rheumatoid arthritis, epilepsy, and eating disorders. Cannabis extracts were introduced into Western medicine in the mid 19th century, when it was noted to produce a “remarkable increase of appetite”. In more recent times, Δ9-tetrahydrocannabinol (THC) was indentified as the primary psychoactive constituent of this plant. The Food and Drug Administration approved oral THC (called marinol) to treat nausea and emesis related to cancer chemotherapeutic agents as well as to stimulate appetite in AIDS patients suffering from cachexia. During the last twenty years, it has been established that THC and other synthetic cannabinoids act upon the endogenous cannabinoid system (ECS). These compounds produce their pharmacological effects by binding to and activating two types of G-protein coupled receptors that have been named cannabinoid CB1 and CB2 receptors. The CB1 receptor is located extensively throughout the central and peripheral nervous systems and modulates the release of neurotransmitters and hormones. In contrast, the CB2 receptor is primarily expressed on cells of the immune system and is believed to play a role in dampening pro-inflammatory responses. The ECS is comprised of CB1 and CB2 receptors, the endogenous cannabinoid ligands, which include N-arachidonoyl ethanolamine (anandamide) and 2-arachidonoylglycerol (2-AG), and enzymes regulating these naturally occurring cannabinoids. The ECS modulates a variety of physiological processes, including the regulation of feeding behavior as well as lipid and glucose homeostasis. In the CNS, stimulation of central CB1 receptors by THC and other cannabinoids elicits orexigenic effects. Endocannabinoids act on peripheral CB1 receptors in adipose tissue, liver, and skeletal muscle to promote lipogenesis and limit energy expenditure. Thus, endocannabinoids promote anabolic processes, as they increase food intake, promote storage, and decrease energy expenditure. In preclinical models of diet-induced and genetic obesity, endocannabinoid levels are elevated and produce adverse effects on insulin-sensitive tissues and lead to fatty liver. These findings led to the proposal that over-activity of the endogenous cannabinoid system contributes to human obesity. Consistent with this notion, CB1 receptor blockade promotes weight loss, reduces appetite, and elicits beneficial effects on dyslipidemia and glucose homeostasis in preclinical models of obesity as well as in obese patients. Accordingly, the CB1 receptor antagonist, rimonabant, showed promising effects in reducing the metabolic syndrome and other risk factors related to cardiovascular disease and diabetes. Although this drug was previously approved in the European Union as a weight loss medication for obese patients, concerns related to its safety led to its eventual removal from the market and thwarted clinical development of this class of drugs. During this presentation, I will cover the following three objectives: 1) provide an overview of the ECS; 2) describe preclinical and clinical research investigating the role of the ECS on food intake, lipogenesis, and energy expenditure; and 3) discuss therapeutic targets of the ECS to treat disorders related to energy regulation.

MEASUREMENT OF ENERGY EXPENDITURE James DeLany, PhD. *University of Pittsburgh, Pittsburgh, PA*

A great deal of investigation of human energy expenditure has been conducted over the last 100 years.. Many energy expenditure issues that are currently being studied, such as gender differences, energy requirements of infants, the effect of different diets, caloric restriction and physical activity were first studied in the early 1900's. In spite of this, there remain unanswered questions regarding the role that individual components of energy expenditure play in human health and disease. However, with the widespread availability of indirect calorimetry and increased availability of ^{18}O-labeled water for the DLW method, we are beginning to gain a clearer picture of many of these issues. Using a combination of the techniques available today, each component can be reliably studied, and the role that each of these plays in the human health can be examined. Furthermore, advances in validated activity monitors should allow for fairly accurate assessment of physical activity in large epidemiological studies to examine the importance of physical activity and human health.

Recent and current applications of the assessment of energy expenditure include: 1) determine energy requirements of normal, healthy individuals to maintain healthy weight throughout the lifecycle; 2) understand the role of energy expenditure in obesity, including assessment of actual energy intake; 3) determine energy requirements of intense physical exertion; 4) determine energy requirements during illness or in disease states; and 5) determine relation between energy expenditure and healthy aging with emphasis on calorie restriction, physical function and mortality.

EXERCISE INTERVENTION FOR MANAGEMENT OF OBESITY Susan S. Deusinger PT, PhD, FAPTA. *Washington University School of Medicine, St. Louis, Missour*i

Obesity now touches the lives of most Americans regardless of age. The condition is having both direct and indirect effects on both the American population and the global health picture. The direct impact of obesity on health is seen in the increased risk for hypertension, diabetes, musculoskeletal injury/pain and some forms of cancer. In children, the rising prevalence of such health insults in this country is new to the horizon of health and health care and raises serious prospective concerns for the health and life of these children as they grow into adulthood. Indirectly, obesity is responsible for increased costs of health care, interference in work and play activities and significant social effects manifested by bullying, discrimination, and even frank abuse and neglect. These conditions mandate aggressive public health action to address the multi-faceted behavioral and environmental factors affecting the lifestyle of both children and adults. Considering the current, and projected future, prevalence of overweight and obesity in the US, both prevention and remedy are required to reduce the effects on adult health that will require massive medical intervention. Especially in children and adolescents, prevention is crucial, with family and community participation essential, if true change is to occur and persist throughout the lifespan.

Obesity is primarily a result of an imbalance in how energy is regulated in the human body. Recognizing that energy regulation is influenced by one's genetic profile, the intake (via eating/drinking) and output (via movement) of energy are primarily matters of an intimate interface between nutrition and activity-related behaviors. Although both components of the problem are critical, this presentation will focus on concepts, specific strategies, and expected outcomes of the physical activity component of the problem. A variety of options are recommended to address the multiple facets of fitness required for health (i.e. strength, cardiovascular endurance, flexibility, and agility/coordination). The imperative to tailor exercise regimens and physical activity outlets to individual preferences and environmental conditions is a requisite to the success of long term participation in physical activity – and attainment or maintenance of healthy weight. Although participation in exercise and physical activity is complicated by previous injury and acute and chronic medical conditions, the potential for positive outcomes from movement is compelling. Thus, attention to the physical activity habits and engagement of all patients in change toward engaging in regular movement, is an obligation of every health professional committed to controlling the detrimental effects of excess body weight in adults and children.

The lives of both children and adults in this country are characterized by low levels of physical activity and exercise. Current estimates are that nearly 60% of adults and 50% of children in the US are sedentary and thus at risk for becoming overweight or obese. A number of studies have shown the difficulty of losing weight with exercise alone. Although a study conducted in Japan using a twice daily protocol demonstrated body weight changes in obese children with this singular approach, most research show the need for a comprehensive lifestyle approach to ensure long term adherence to new behavioral patterns. Because low levels of activity (in children) have been associated with development of obesity, overcoming a sedentary lifestyle requires moderate-to-vigorous physical activity on most (if not all) days of the week to be effective. In a culture in which sedentary behavior is so firmly embedded, the challenge of meeting this goal is significant. Included in this presentation is description of a feasible group exercise intervention that offers potential for delivery in a naturalistic setting.

Many attitudinal factors complicate the potential to address the development or persistence of obesity by increasing activity level. Adult perceptions of what body size and configuration is appropriate for age (e.g. chubby is cute and healthy), what body mass index-for-age means (e.g., 95th percentile is "better" than 85th), and what evidence of early adiposity signifies (e.g., "baby fat" will disappear with growth), can influence expectations within the family of whether lifestyle change is needed. Even higher risks for exceeding the 85th body mass index-for-age percentile are encountered by children with activity limitations from disability, those receiving special

education (especially girls with learning disabilities) and those whose medical status has been compromised by disease or interventions targeting disease. For example, the obesity that may develop in children being treated for acute lymphocytic leukemia may be difficult to remedy after treatment without comprehensive diet and activity changes. Perceptions of priorities for action in the face of primary health issues may diminish motivation to incorporate physical activity and exercise into a child's life without appropriate guidance for frequency, duration and mode of activity.

Individual nutritional and activity behaviors are influenced by an array of social and environmental factors that make neither prevention nor remedy of the energy imbalance that leads to obesity a simple matter. The intrusion of energy dense foods into the diet of Americans, changes in family dynamics and scheduling of meals, and marketing strategies advocating the increased value of large portion sizes have been catalysts for changes in eating habits of both adults and children. Similarly, the activity habits in our culture have been negatively influenced by a decrease in required physical education in schools, technology innovation which has reduced the need for physical exertion in the home and at the workplace, and access to television and computers for leisure-time outlets. Public health interventions and policy development have been successful in reducing the prevalence of polio through immunization, decreasing smoking in some groups, and increasing the use of motorcycle and bicycle helmets. Optimistically, these successes suggest that social change that alters eating and activity habits can be achieved. To effectively influence the dual behavioral components of the obesity epidemic, change must occur at home, in the schools, in the design of communities and urban centers, in marketing, and in the approaches taken in the media to address the value of proper nutrition and physical activity for health.

Testing for exercise tolerance, which can be formalized in a number of ways depending on the needs and ability of the individual – is important to establish baseline performance. Submaximal treadmill tests, six-minute walk tests and bicycle ergometer assessments can be options for testing aerobic capacity. Tests for strength can use standardized protocols; functional activities such as sit-to-stand, single-leg balance and stair climbing can be useful proxies for flexibility and agility/coordination. Exercise prescription follows such testing but must accommodate for co-morbidities that compromise movement and activity. In obese individuals, endurance is often low and flexibility limited due to tissue bulk. Strength may be impaired in some segments and agility/coordination affected by inexperience with movement, especially if obesity emerged in childhood. In individuals whose obesity is associated with disease or treatment sequelae, fatigue, pain and cardiovascular compromise may complicate the picture—but not eliminate the need.

Encouraging directions for addressing the activity needs of children and adolescents (and adults) come from policy development in schools, faith-based programs that target communities and families in their own cultural milieu, camping organizations that offer healthful and socially protective experiences, and urban re-design to afford safe and available options for sports and physical activity. Continued efforts to understand the influence of culture on eating and exercise habits, the development of perceptions of health, the readiness of adults (e.g. parents and teachers) to implement change and the barriers that impede such change are required to substantially influence the prevalence of obesity in the US. Failure to reach the goals of Healthy People 2010 signifies the need for broad-based action to avoid an increasing prevalence of overweight and obesity in American children, adolescents, and adults.

PHARMACOLOGIC MANAGEMENT OF OBESITY Robert F. Kushner, MD. *Northwestern University, Chicago, IL*

Recent elucidation of the circuitry that underlies the neuro-endocrine regulation of appetite control and energy expenditure has provided an opportunity to develop a more targeted pharmacological approach to the treatment of obesity. This presentation will provide an updated review of appetite regulation and the pharmacological agents that are currently in development.

Oral Platform Presentations

1. COMPONENTS OF THE METABOLIC SYNDROME IN 500 ADULT LONG-TERM SURVIVORS OF CHILDHOOD CANCER Marjolein van Waas; Sebastian JCMM Neggers, MD; Rob Pieters, MD, PhD; Marry M. van den Heuvel-Eibrink, MD, PhD. *Department of Paediatric Oncology/Haematology, Erasmus MC–Sophia Children's Hospital, Rotterdam, The Netherlands; Department of Medicine, Section of Endocrinology, Erasmus University Medical Centre, Rotterdam, The Netherlands*

Background: Adult survivors of childhood cancer have been reported to have an increased risk of late sequelae. A cluster of abnormalities that contribute to the metabolic syndrome may be expressed at a higher level and therefore result in an increased risk for diabetes mellitus and cardiovascular diseases.

Patients and Methods: We investigated a single centre cohort of 500 adult survivors (228 females) of childhood cancer, median age 28 years (range 18–59 years) and median follow-up time 19 years (range 6–49 years). This cohort included 164 acute lymphoblastic leukaemia (ALL) survivors (75 females). We measured total cholesterol, high-density lipoprotein-cholesterol (HDL), systolic and diastolic blood pressure, body mass index and the prevalence of diabetes mellitus. Data from the Dutch epidemiologic MORGEN-study were used to calculate standard deviation scores as normative values.

Results: The criteria of the metabolic syndrome were met in 13% of the total cohort. ALL survivors treated with cranial irradiation had an increased risk of developing the metabolic syndrome compared to ALL survivors not treated with cranial irradiation (23% vs. 7%, P=0.011). ALL survivors who received CRT had higher total cholesterol levels compared to ALL survivors who did not (mean SDS 0.38 vs. mean SDS – 0.05, P=0.027), whereas their HDL levels did not differ. Also, ALL survivors treated with CRT were more often hypertensive (22% vs. 10%, P=0.036) and more often overweight (59% vs. 34%, P=0.003), compared to ALL survivors not treated with CRT, however they were not more often obese (12% vs. 9%, ns).

Conclusions: Adult survivors of childhood cancer, especially ALL survivors treated with cranial irradiation, are at increased risk of developing the metabolic syndrome. This increased risk is probably determined by higher prevalence of hypertension and hypercholesterolemia in these survivors.

2. CHARACTERISTICS OF INSULIN RESISTANCE (IR) AND CARDIOVASCULAR RISK AFTER HEMATOPOIETIC CELL TRANSPLANT (HCT) FOR CHILDHOOD HEMATOLOGIC MALIGNANCIES K. Scott Baker, Lyn M. Steffen, Xia Zhou, Aaron S. Kelly, Jill Lee, Anna Petryk, Alan R. Sinaiko, Donald R. Dengel, Daniel Mulrooney, Julia Steinberger. *Fred Hutchinson Cancer Research Center, Seattle, WA, USA; University of Minnesota Schools of Public Health and Kinesiology and Department of Pediatrics, Minneapolis, MN, USA*

Background: Cardiovascular disease (CVD) contributes to the increased risk of late mortality after HCT and a diminished life expectancy. Studies of indirect measures of insulin resistance (IR) in cancer survivors suggest a higher risk for IR and CVD.

Methods: Measures of IR (euglycemic hyperinsulinemic clamp adjusted for lean body mass [Mlbm]), fasting glucose, insulin, lipids, anthropometry, DEXA (% body fat), blood pressure and carotid artery compliance and distensibility were determined in 106 children and young adults (current age 26.6 yr, 60.4% male) who had HCT for hematologic malignancy during childhood (mean age at HCT 9.9 yr) and 72 healthy sibling controls (current age 23.7 yr, 51.4% male). All received myeloablative preparative regimens (allogeneic n=79, autologous n=27). Sixty two (58.5%) received TBI, 20 (18.9%) received cranial radiation (CRT) prior to TBI (TBI+CRT), and 24 (22.6%) received no radiation (noXRT) before or during HCT. Linear regression models were adjusted for age, gender, pubertal stage, body mass index (BMI) and carotid lumen diameter.

Results: Compared to siblings, there were no differences between groups for body fatness (BMI, waist circumference, percent body fat). Despite this, HCT survivors were significantly more IR (Mlbm 10.0 vs. 12.1, p=0.01) compared to controls. IR worsened with longer follow-up (time after HCT(Mlbm): 2–9 yrs(11.5), 10–15 yrs(11.0), >15 yrs(7.31); p=0.008). Those who received TBI or TBI+CRT had significantly higher cholesterol, LDL cholesterol, triglycerides and insulin than siblings, but there were no differences in those who did not receive XRT. Those receiving TBI+CRT had significantly lower HDL cholesterol and were also more IR compared to siblings. Carotid artery distensibility was decreased in survivors who received TBI compared to controls with even greater negative impact in those who received TBI+CRT.

Conclusions: HCT survivors have increased CVD risk factors that are associated with IR despite being independent of obesity, and are also associated with exposure to TBI±CRT.

		Treatment Groups, mean (SD)			P-values		
Cardiometabolic Risk Factors	Control	(A) TBI	(B) TBI +CRT	(C) no XRT	A vs. control	B vs. control	C vs. control
BMI (kg/m^2)	22.9(1.2)	21.5(1.1)	21.1(1.4)	23.4(1.4)	0.15	0.17	0.71
Waist circumference (cm)	78.9(1.2)	78.6(1.1)	79.4(1.4)	80.3(1.5)	0.69	0.7	0.3
Systolic BP (mmHG)	113.4(2.7)	112.9(2.5)	119.0(3.2)	110.4(3.3)	0.85	0.06	0.29
Fasting glucose (mg/dL)	88.5(2.3)	91.5(2.1)	92.3(2.7)	87.3(2.8)	0.11	0.14	0.62
Fasting insulin (mU/L)	13.9(2.4)	21.1(2.2)	26.1(2.8)	16.2(2.9)	<0.001	<0.001	0.38
Total cholesterol (md/dL)	155.5(7.8)	176.2(7.2)	199.8(9.4)	157.7(9.6)	0.001	<0.001	0.78
LDL-cholesterol (mg/dL)	89.1(6.7)	98.6(6.1)	114.6(8.6)	92.5(7.9)	0.07	<0.001	0.61
HDL-cholesterol (md/dL)	45.3(2.5)	43.8(2.3)	38.3(2.9)	44.2(3.0)	0.44	0.01	0.67
Triglyderides (md/dL)	113(26.3)	172(23.7)	266(30.9)	114(31.5)	0.006	<0.001	0.98
Insulin resistance [Mlbm]	12.2(1.1)	10.5(1.0)	8.0(1.4)	10.5(1.4)	0.07	0.002	0.17
Carotid distensibility (%)	12.1(0.6)	10.2(0.6)	8.5(0.7)	10.9(0.8)	<0.001	<0.001	0.14
Carotid compliance (mm^2/mmHg)	0.14(0.009)	0.13(0.008)	0.10(0.01)	0.14(0.01)	0.15	<0.001	0.85
Carotid compliance (mm^2/mmHg)	0.14(0.009)	0.13(0.008)	0.10(0.01)	0.14(0.01)	0.15	<0.001	0.85

3. INSULIN RESISTANCE AND VASCULAR STIFFNESS IN SURVIVORS OF CHILDHOOD HEMATOLOGIC MALIGNANCIES Daniel A. Mulrooney, MD; Andrew C. Dietz, MD; Aaron S. Kelly, PhD; K. Scott Baker, MD; Lyn M. Steffen PhD, Jill Lunsford-Lee PNP, Anna Petryk MD, Alan R. Sinaiko MD, Donald R. Dengel PhD, Joanna Perkins MD, Yoav Messinger MD, Xia Zhou, Julia Steinberger MD. *University of Minnesota Department of Pediatrics, School of Public Health, and School of Kinesiology, Minneapolis, MN, USA; Children's Hospitals and Clinics of Minnesota, Minneapolis, MN, USA; Fred Hutchinson Cancer Research Center, Seattle, WA, USA*

Background: Survival rates for childhood hematologic malignancies continue to improve. Research suggests an increased risk for late adverse cardiovascular outcomes.

Methods: This analysis includes children (n=118) who survived ≥5-yrs following diagnosis of acute lymphoblastic leukemia (ALL) (n=93), acute myeloid leukemia (AML) (n=6), and non-Hodgkin lymphoma (NHL) (n=19), compared to their frequency matched healthy siblings (n=176). Anthropometric measurements, blood pressure (BP), fasting glucose, insulin, and lipids were collected; insulin resistance was assessed by euglycemic hyperinsulinemic clamp, adjusted for lean body mass (low Mlbm represents insulin resistance); carotid artery stiffness (distensibility and compliance—low levels represent increased stiffness), adjusted for lumen diameter, assessed by ultrasound. Least squares means and standard errors, adjusted for age, gender, pubertal development, and body mass index (BMI) were compared.

Results: Survivors (63.6% male) mean age at diagnosis 4.6 yrs (0.3–11.8) and 14.8 yrs (9.8–18.0) at evaluation; siblings (54% male) were 13.5 yrs (9.0–18.0) at evaluation. All survivors received chemotherapy but only 13 (11%) received chemotherapy and cranial radiation. There were no differences between cases and siblings on measures of adiposity (BMI, waist circumference, % body fat, visceral fat), BP, fasting glucose, insulin, and lipids. However, survivors were significantly more insulin resistant and had stiffer carotid arteries compared to controls (Table).

Conclusion: Survivors of childhood hematologic malignancies have increased insulin resistance and vascular stiffness at a young age. This appears to be independent of adiposity and other usual risk factors, suggesting a potential relation to chemotherapeutic regimens.

	Survivors (n = 118)	Siblings (n = 176)	
	LS means (SE)	LS means (SE)	(p)
Body mass index (BMI) (kg/m^2)	21.5 (0.5)	21.1 (0.4)	0.5
Visceral fat (cm^3)	22.5 (0.8)	22.2 (0.8)	0.7
Insulin resistance [Mlbm (mg/kg/min)]	12.6 (0.5)	13.8 (0.4)	0.02
Carotid artery distensibility (%)	13.4 (0.4)	15.1 (0.3)	0.0001
Carotid artery compliance (mm^2/mmHg)	0.15 (0.005)	0.17 (0.004)	0.001

4. CORRELATES OF INSULIN RESISTANCE AMONG ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)
E.S. Tonorezos, MD MPH; G.L. Vega, PhD; C. Sklar, MD; J Chou, MPH; C. Moskowitz, PhD; Q. Mo, MPH; T. Church, MD PhD; R. Ross, PhD; P. Janiszewski, MPH; K. Oeffinger, MD. *Memorial Sloan-Kettering Cancer Center, New York, NY, USA University of Texas Southwestern Medical Center, Dallas, TX, USA, Pennington Biomedical Research Center, Baton Rouge, LA, USA, Queen's University, Kingston, ON, Canada*

Background: Following our previous reports of an increased prevalence of insulin resistance and adiposity among ALL survivors, particularly women treated with cranial radiotherapy (CRT), we aimed to (1) assess the relationship between adipokines (leptin and adiponectin) and CRT and (2) determine correlates of insulin resistance, by gender.

Methods: Cross-sectional evaluation of 116 ALL survivors (median age, 23.0 years; range, 18-37) was conducted and included fasting laboratory testing (adiponectin, leptin, insulin, glucose), anthropometric measurements (weight, height, waist circumference), DXA (total body fat, truncal-to-lower-body-fat ratio), and abdominal CT (visceral fat). Insulin resistance was estimated using the homeostatic model assessment for insulin resistance (HOMA-IR). Analytic approach included Spearman correlation coefficients, regression models, and Wilcoxon Rank Sum testing.

Results: CRT was associated with a higher leptin:adiponectin ratio among both women (CRT 3.0±2.1, no CRT 1.7±1.7, P<0.01) and men (CRT 2.2±3.0, no CRT 0.8±1.1, P=0.01) and this ratio was associated with HOMA-IR (females β=0.15, 95%CI=0.09–0.21, P<0.01; males β=0.17, 95%CI=0.11–0.22, P<0.01). However, visceral adiposity and truncal-to-lower-body-fat ratio were more strongly associated with HOMA-IR than leptin:adiponectin ratio (or BMI, waist circumference, waist:height ratio). When assessing HOMA-IR, there was not a significant interaction between CRT and the adipokines.

Conclusions: Among ALL survivors, visceral adiposity and truncal-to-lower-body-fat ratio are superior to serum adipokines and anthropomorphic measures in predicting insulin resistance. Importantly, though the cross-sectional design limits inferences regarding causality, it appears that the relationship between CRT and insulin resistance is largely accounted for by increased adiposity and not via other factors.

Table. Serum adipokines and measures of body fatness, stratified by treatment with cranial radiotherapy (CRT), among 116 adult survivors of childhood acute lymphoblastic leukemia (ALL).

	CRT N=39		No CRT N=77		
	Mean	(SD)	Mean	(SD)	p
Leptin: adiponectin ratio	2.6	2.5	1.2	1.5	<0.01
Adiponectin per kg fat mass (mcg/mL/kg)	0.5	0.5	0.8	0.6	<0.01
Leptin per kg fat mass (mcg/L/kg)	0.7	0.4	0.5	0.5	<0.01
Percent total body fat	37.0	8.8	28.1	10.3	<0.01
Truncal-to-lower-body-fat ratio	1.5	0.4	1.2	0.3	<0.01
Visceral fat (kg)	0.38	0.21	0.22	0.16	<0.01
Body mass index (m/kg2)	30.2	8.3	26.6	5.8	0.01
Waist circumference (cm)	95.8	16.3	89.5	14.3	0.04
Waist:height ratio	59.4	10.4	52.6	8.5	<0.01
HOMA-IR	5.1	3.0	3.8	2.1	0.01

5. IMPROVEMENT IN INSULIN RESISTANCE AMONG ADULT SURVIVORS OF CHILDHOOD ALL FOLLOWING A 12-MONTH LIFESTYLE INTERVENTION
Kevin C. Oeffinger, MD; Emily Tonorezos, MD, MPH; Andrea L. Dunn, PhD; Timothy S. Church, MD, PhD; Debra A. Eshelman-Kent, RN, CPNP; Robert Ross, PhD; Peter M. Janiszewski, MPH; Peter G. Snell, PhD; Gloria Lena Vega, PhD; Ronald G. Victor, MD; Beverley Adams-Huet, MS; Joanne F. Chou, MPH; Stephanie Smith, MPH; Chaya S. Moskowitz, PhD. *Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Klein Buendel, Inc, Golden, CO, USA; Pennington Biomedical Research Center, Baton Rouge, LA, USA; Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA; Queen's University, Kingston, Ontario, Canada; University of Texas Southwestern Medical Center, Dallas, TX, USA*

Background: Survivors of childhood acute lymphoblastic leukemia (ALL) have an increased risk of premature cardiovascular mortality, insulin resistance, and physical inactivity.

Methods: We aimed to determine the effectiveness of a behaviorally-based 12-month Lifestyle intervention compared with a standard control group on insulin resistance (homeostasis model for assessment of insulin resistance [HOMA-IR]), physical activity (one-week monitoring with SenseWear Pro-2 Armband) and cardiorespiratory fitness (maximal oxygen uptake [VO2 max] during a graded exercise test on a treadmill). A random sample of 66 ALL survivors (median age, 22.3 years; range 18.0–36.7) who were physically inactive (less than 150 minutes of moderate or vigorous physical activity per week) were enrolled (intervention, N=32; control, N=34).

Results: Among those completing the 12-month measurements (intervention group, 59.4%; control group, 79.4%), HOMA-IR was significantly lower for participants in the intervention group (P=0.001). Cardiorespiratory fitness and levels of physical activity energy expenditure were not significantly different between the two groups (Table).

Conclusions: A 12-month Lifestyle intervention was associated with an improvement in insulin resistance but only a modest increase in physical activity and no change in cardiorespiratory fitness.

Table. Intervention effects for all participants with complete baseline and 12-month follow-up measurements

	ALLIFE Participants	
	Difference in Means INT-CTRL (95% CI)¶	P-value¶
Insulin resistance (HOMA-IR)	-1.5 (-2.5, -0.4)	0.001
Physical activity energy expenditure, kcal/day	133.4 (-71.6, 338.5)	0.196
Maximum 02 consumed (Max V02)	1.1 (-1.1, 3.3)	0.307
Visceral adipose tissue (VAT), L4L5*	-7.0 (-19.6, 5.7)	0.057
Subcutaneous adipose tissue (SAT), L4L5*	-25.1 (-60.2, 10.1)	0.119
High-sensitivity C reactive protein (hsCRP)*	0.17 (-1.8, 2.2)	0.928

Abbreviations: INT=intervention group, CTRL=control group, CI=confidence interval

¶Least-mean squares and p-values for difference in means obtained from analysis of covariance (ANCOVA), adjusting for gender; *A natural log transformation was performed prior to analysis to adjust an initially skewed distribution (p-value from log-transformed model)

6. RESISTANCE EXERCISE INTERVENTION IMPROVES INSULIN RESISTANCE AND FITNESS IN SURVIVORS OF CHILDHOOD BONE MARROW TRANSPLANT (BMT) WITH TOTAL BODY IRRADIATION (TBI) Nikki L Davis, B Med Sci, BMBS; Keith Tolfrey, PhD; Ruth Elson; Adrian Kendrick , PhD; Claire Stewart, PhD; Andrew Moss, BSc, MSc; Jacqueline M Cornish, MBChB; Michael CG Stevens, MD; Elizabeth C Crowne, MBChB, MD. *Bristol Royal Hospital for Children, Bristol, UK; School of Sport and Exercise Sciences, Loughborough University, UK; Manchester Metropolitan University, Manchester, UK*

Objectives: We have investigated the impact of resistance exercise on aerobic fitness and metabolic risk factors, known to be abnormal in survivors of childhood BMT with TBI.

Method: Participants undertook six months twice weekly 45–60 minute supervised resistance and aerobic training sessions and measurement of the following outcomes:

1. Body composition (DEXA),
2. Fasting blood for glucose, insulin, leptin and adiponectin. HOMAR was calculated to assess insulin resistance.
3. Aerobic fitness using a V02 max test on an inclined treadmill.

Subjects: 22 BMT survivors (11M; 8 pubertal, 14 post-pubertal) completed the programme. Median(range) for age and time since BMT were 14(12.4–24.5)yrs and 8(2.3–20.0)yrs respectively.

Results: Insulin, leptin/adiponectin ratio, and HOMAR are expressed as geometric mean(range) after log- transformation to normalise the distribution; other results as mean(SD). All were compared using paired t-tests.

	% body fat DEXA	Fasting Insulin (µIU/ml)	HOMAR (mmol*µIU/ml)	Leptin/adiponectin ratio (pg/ng)	V02 peak/kg body mass (ml/min/kg)
Before training	29.8(13.7)	17.5(1.48–72.8)*+	4.14(0.3–17.26)*+	2.87(0.23–29.14)	36.5(11.7)*+
After training	30.2(13.2)	12.7(1.0–55.0)*	2.73(0.22–12.89)*	2.65(0.53–27.58)	42.9(13.2)*
6 months follow-up	28.4(13.8)	12.0(0.8–80.4)+	2.69(0.2–16.67)+	3.19(0.42–36.76)	41.5(9.5)+

*p<0.05 before-after training

+p<0.05 before training–6 months follow up

There were significant improvement in aerobic fitness and insulin resistance after training, maintained at 6 months despite no significant changes in body composition. There was a trend for leptin/adiponectin ratio to decrease (p=0.058).

All insulin parameters and leptin but not adiponectin correlated highly with body fat parameters (r=0.56–0.91, p=0.010–0.000). There were no correlations between these parameters and V02max after adjustment for body fat.

Conclusions: Resistance exercise significantly improved aerobic fitness and insulin resistance before significant changes in body composition in childhood BMT survivors, suggesting a metabolic training effect on muscle. These data support the role of targeted physical rehabilitation services for this group at high risk of T2DM and cardiovascular disease.

7. LONG-TERM OUTCOMES AFTER CANCER IN INFANCY: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS) Lynda M. Vrooman, MD; Julie Najita, PhD; Pamela Goodman, MS; Gregory Armstrong, MD, MSCE; Melissa M. Hudson, MD; Lisa B. Kenney, MD MPH; Caroline Laverdière, MD; Wendy Leisenring, ScD; Rajen Mody, MD; Paul Nathan, MD, MSc; Kevin Oeffinger, MD; Charles Sklar, MD; Leslie L. Robison; PhD, Lisa Diller, MD. *Dana-Farber Cancer Institute, Boston, MA, USA; Fred Hutchinson Cancer Research Center, Seattle, WA, USA; St. Jude Children's Research Hospital, Memphis, TN, USA; Hospital Sainte Justine, Montreal, QC, Canada; University of Michigan, Ann Arbor, MI, USA; The Hospital for Sick Children, Toronto, ON, Canada; Memorial Sloan-Kettering Cancer Center, New York, NY, USA*

Background: Approximately 12% of pediatric cancer patients are diagnosed during the first year of life. Because of their developmental stage, survivors diagnosed in infancy represent a potentially vulnerable population.

Methods: Prevalence of adverse health status and chronic health conditions in CCSS participants diagnosed with cancer <1 year of age between 1970–86 were compared with the CCSS sibling-cohort (age at questionnaire-matched) and with survivors 1–1.99 years and 2–10 years of age at diagnosis, using univariate methods and multivariable regression models.

Results: 1,006 (7%) survivors were <1 year at diagnosis (mean age 15.7 years at questionnaire, range 5–28.) Underlying diagnoses included neuroblastoma (52%), Wilms tumor (18%), leukemia (9%), sarcoma (9%), brain tumor (7%), NHL (1%), bone tumor (<1%). 26% reported ≥1 impaired health status domain. 53% reported ≥1 chronic condition, and 21% reported a severe or life-threatening condition (grade 3–4). Compared with siblings, survivors were at higher risk for adverse health status (Functional Status: OR 5.0, 95% confidence interval (CI)=3.1–7.9, p<0.0001; Activity Limitation: OR 3.4, 95% CI=2.2–5.2, p<0.0001), and chronic health conditions (severe or life-threatening condition: adjusted OR 16.2, 95% CI=10.1–26.1, p<0.0001). The infant-group was less likely to report ≥1 adverse health status domain compared with those diagnosed 1–1.99 years (OR 0.7, 95% CI=0.5–0.8) and 2–10 years (OR 0.7, 95% CI=0.6-0.9). Adjusting for sex, race, diagnosis, and age-at-questionnaire, there was no significant difference in the risk of a grade 3-4 chronic condition compared with survivors diagnosed 2–10 years of age (OR 1.21, CI=0.99–1.48).

Conclusions: Overall, survivors of cancer in infancy are at risk for adverse health status and chronic health conditions, but may not be at significantly greater risk than those diagnosed later in childhood. Newer survivor cohorts may reflect a different distribution of cancers in infancy.

Analyses are underway to address treatment-related factors which may modify risk in the infant-group.

8. THE GENERAL HEALTH AND PSYCHOSOCIAL FUNCTIONING OF ADULT SURVIVORS OF RETINOBLASTOMA Ira Dunkel, MD; Jennifer Ford, PhD; Charles Sklar, MD; Kevin Oeffinger, MD; Rika Tanaka, BA; Sarah Shankman, MA; Mary McCabe, MA; Nancy Kline, PhD; Leslie Robison, PhD; Ruth Kleinerman, MPH; Brian Marr, MD; David Abramson, 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: Retinoblastoma (RB) is a rare pediatric cancer of the eye, typically diagnosed before age two. While a great deal is known about the acute management of RB patients, less is understood about the physical and psychosocial functioning of long-term RB survivors.

Methods: A self-report descriptive study was conducted to examine the medical and psychosocial morbidities of adult RB survivors who had been treated in the New York area. Thus far, 58.9% of survivors contacted have completed the assessment

Results: To date, we have assessed 412 RB survivors (female=52.7%; mean age=43.5 yrs, SD=11.0; mean age at diagnosis=1.3 yrs, SD=1.6). About half (54%) were diagnosed with bilateral RB. Most were currently employed (76.0%), married (59.6%), and had at least some college education (61.4%).

A majority endorsed having good overall health (94.6%) while more than half endorsed having good eyesight (60.8%). Many participants (63.1%) reported no physical disabilities while a minority (15%) reported difficulty obtaining health insurance. Additionally, more than a quarter (29.9%) reported a history of psychological dysfunction: More than one-third (37.7%) reported having anxiety as a result of their RB. A majority of survivors worried about passing RB to their children (53.9%), had concerns about their future health (69.1%), or developing a cancer (71.1%) and were dissatisfied with their facial appearance (78%).

Participants who reported any disability, poor health, difficulty obtaining health insurance, anxiety due to RB, worry about passing RB to their children, or concerns about future health were significantly more likely to have been diagnosed with bilateral than unilateral RB.

Conclusions: These findings suggest that overall, RB survivors are high functioning and healthy. Future multivariable analyses will be conducted to determine the factors related to the poorer outcomes reported by survivors of bilateral RB. These findings will inform future psychosocial care and interventions for RB survivors.

9. TWENTY-FIVE YEAR FOLLOW-UP AMONG SURVIVORS OF CHILDHOOD WILMS TUMOR: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS) Amanda M. Termuhlen MD; Jean Tersak MD; Qi Liu MS; Yutaka Yasui PhD; Marilyn Stovall PhD; Rita E. Weathers MS; Melvin Deutsch MD; Kevin Oeffinger MD; Charles A. Sklar MD; Greg Armstrong MD; Leslie L. Robison PhD; Daniel M. Green MD. *The Ohio State University College of Medicine, Nationwide Children's Hospital, Columbus, OH, USA; Children's Hospital of Pittsburgh, Pittsburgh, PA, USA; University of Alberta, Edmonton, AB, Canada; University of Texas MD Anderson Cancer Center, Houston, TX, USA; Memorial Sloan-Kettering Cancer Center, New York, NY USA; St. Jude Children's Research Hospital, Memphis, TN, USA*

Purpose: Wilms tumor (WT) is highly curable with surgery, chemotherapy, ± irradiation (RT). This study describes the 25-year outcomes of 5-year WT survivors.

Methods: Analysis included 1256 5-year WT survivors diagnosed 1970-1986. Comparison groups were the general population and a sibling group (n=4023). Mortality, second malignant neoplasms (SMNs), frequency of chronic medical conditions (CMCs), health status, health care practices, and socioeconomic status were assessed.

Results: Cumulative mortality was 6.1% (95% confidence interval [CI], 4.7–7.4%) and cumulative incidence of SMN was 3% (95%CI, 1.9–4.0%). The most common causes of death were: SMN (27), recurrence (22), and cardiac disease (11). 33 WT survivors had 35 SMNs including soft tissue sarcomas (6), breast cancers (5), bone tumors (4), and adenocarcinomas (4). Chest and abdominal RT increased the likelihood of SMN (Standardized Incidence Ratio [SIR] 9.00, 95%CI, 3.87–17.73 with doxorubicin and SIR 4.87, 95%CI, 1.78–10.6 without doxorubicin). WT survivors reported CMCs more commonly than the sibling group (51% any grade, Hazards Ratio [HR] 2.0, 95%CI, 1.8–2.3;11% severe/life-threatening, HR 4.7, 95%CI, 3.6–6.1). The HR of reporting congestive heart failure (CHF) was 23.6 (95%CI, 10.8–51.5), renal failure was 50.7 (95%CI, 14.5–177.4), and hypertension was 8.2 (95%CI, 6.4–10.5) vs. the sibling group. Heart RT increased the likelihood of reporting CHF without doxorubicin (HR 6.6, 95%CI, 1.6–28.3), with ≤250 mg/m^2 (HR 13.0, 95%CI, 1.9–89.7) and with >250 mg/m^2 (HR 18.3,95%CI, 3.8–88.2).

WT survivors reported more adverse general health status than the sibling group (Odds Ratio [OR] 1.7, p<.001) but no difference in mental health status. Health care practices were similar to siblings. A slightly higher proportion of the sibling group were college graduates (p=0.045) and reported employment (p=0.046). There were no differences in the proportion married or in the personal income of WT survivors and the sibling group.

Conclusion: Long-term survivors of WT remain at risk of mortality and morbidity.

10. RENAL DYSFUNCTION AND HYPERTENSION IN LONG-TERM CHILDHOOD CANCER SURVIVORS Sebastiaan L. Knijnenburg, MSc; Monique W. Jaspers, PhD; Antoinette Y. Schouten–van Meeteren, MD, PhD; Antonia H. Bouts, MD, PhD; Jan Lieverst, MSc; Arend Bökenkamp, MD, PhD; Flora E. van Leeuwen, MD, PhD; Heleen J.H. van der Pal, MD; Huib N. Caron, MD, PhD; Leontien C. Kremer, MD, PhD. *Departments of Paediatric Oncology and Paediatric Nephrology, Academic Medical Center/Emma Children's Hospital, Amsterdam, The Netherlands; Departments of Medical Informatics and Medical Oncology, Academic Medical Center, Amsterdam, The Netherlands; Department. of Paediatric Nephrology, VU University Medical Center, Amsterdam, The Netherlands, Dept. of Epidemiology, The Netherlands Cancer Institute, Amsterdam, The Netherlands*

Purpose: This study aims to evaluate the prevalence of long-term renal adverse effects and the related risk factors in a large cohort of childhood cancer survivors.

Patients and methods: At the first visit to the late effects clinic, renal assessment was performed in approximately 80% of a cohort of 1011 5-year survivors of childhood cancer who were treated with potential nephrotoxic treatment between 1966 and 2002.

Results: After a median follow-up time of 12.8 years, 28.2% of all survivors has at least one renal adverse effect. Glomerular dysfunction and hypertension were most prevalent with 15.4% and 16.8% respectively. Independent risk factors for glomerular dysfunction were nephrectomy, higher cumulative ifosfamide dose, higher age at diagnosis and a longer follow-up duration. Abdominal irradiation, nephrectomy, higher age at diagnosis, longer follow-up duration, male gender and BMI were significantly associated with hypertension in the multivariate analysis.

Conclusion: Even at the long term, nearly 30% of the survivors of childhood cancer treated with potential nephrotoxic treatment has renal adverse effects. Continuous monitoring of renal function and blood pressure is necessary to be able to treat childhood cancer survivors early and improve their health status.

11. EXECUTIVE FUNCTIONS IN AGING ADULT SURVIVORS OF CHILDHOOD LEUKEMIA Kevin R. Krull, PhD; Neelam Jain, PhD; Zhenyu Pan, MS; Katina Shine, PhD; Deo Kumar Srivastava, PhD; Deborah Stewart, MEd; Cindy Jones, MS; Leslie L. Robison, PhD; Melissa M. Hudson, MD. *St. Jude Children's Research Hospital, Memphis, TN, USA*

Background: Survivors of childhood ALL are at risk for deficits in basic cognitive skills (e.g., attention, processing speed and working memory), typically beginning within five years of diagnosis and associated with cranial radiation therapy (CRT). The degree of impairment in very long-term survivors is unknown.

Methods: We evaluated complex neurocognitive functions (i.e., executive functions [EF]), in 285 adult survivors of childhood ALL (mean [range] of current age=35.0 yrs [20.4–49.9], age at diagnosis=6.0 yrs [0.2–18.8], and time since diagnosis=28.9 yrs [12.0–45.3]. Survivors completed a comprehensive neuropsychological evaluation. Age-adjusted standard scores were calculated using national norms, with clinical impairment defined as scores ≤10th percentile. Analysis of variance and regression were used to examine associations between executive functions and CRT, sex, and age at diagnosis, as well as educational and vocational outcomes.

Results: 73.8% of survivors demonstrated impairment on at least one measure of EF. Rates of impairment were higher on measures of cognitive fluency (28%), flexibility (34%), and working memory (39%) compared to basic intelligence (14%) and processing speed (15%). CRT was associated with impairment on measures of EF (p's <.01), and basic cognitive skills (p's <.005). Female sex was associated with impairment on basic cognitive skills (p's <.01), but not measures of EF. Younger age at diagnosis was associated with poor cognitive flexibility (p=.007) and problem solving (p<.0001), as well as intelligence (p=.004). All measures of EF were associated with level of educational attainment (p's <.01) and employment status (p's<.005).

Conclusions: Survivors of childhood leukemia continue to be at risk for neurocognitive impairment well into adulthood. Impairment appears more common in complex executive functions such as fluency, flexibility, and problem solving, functions which typically develop throughout adolescence. Impairment on these executive functions is related to educational and vocational outcomes.

12. SIGNS AND SYMPTOMS OF PERIPHERAL NEUROPATHY IN ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL): ASSOCIATIONS WITH PHYSICAL PERFORMANCE AND CHEMOTHERAPY DOSES K.K. Ness, M.M. Hudson, C.-H. Pui, D.M. Green, R. Karlage, L.L. Robison, E.B. Morris. *St. Jude Children's Research Hospital, Memphis, TN, USA*

Background: Treatment regimens for childhood ALL continue to contain neurotoxic agents that may interfere with neuromuscular health and physical function. The purpose of this analysis was to examine associations between persistent signs and symptoms of peripheral neuropathy and physical function, and to determine dose response relationships between vincristine, methotrexate and neuromuscular impairments among survivors of childhood ALL.

Methods: Medical records were abstracted and neuromuscular function and physical performance evaluated in adults surviving 10+ years after ALL diagnoses. Associations were examined in regression models.

Results: Among 302 survivors (median age 35 years; range 20–57), 36.8% had absent Achilles tendon reflexes, 35.4% <5 degrees dorsiflexion range of motion (ROM), and 26.2% limited plantar flexion strength. Balance, mobility and six minute walk (6MW) distances were 2.5 or more standard deviations below age and gender expected values in 14.9%, 43.4% and 17.9% of participants, respectively. In age and sex adjusted models, impaired ankle ROM and strength were associated with limited balance, mobility and 6MW distances (p-values <0.01). In adjusted models (including cranial radiation), survivors treated with intrathecal methotrexate cumulative doses 1–132 mg/m^2 were 3.2 (95% CI 2.2–9.7) and those with doses 133+ mg/m^2 were 4.7 (95% CI 1.3–15.7) times more likely than patients who received no intrathecal methotrexate to have limited ROM. Those who received vincristine cumulative doses 33+ mg/m^2 were 2.1 (95% CI 1.2–3.6) times more likely than those who received lower doses to have limited ROM. Higher vincristine dose was also associated with a 2.1 fold (95% CI 1.1–4.0) increase in the likelihood of reduced ankle strength.

Conclusions: Signs and symptoms of peripheral neuropathy in childhood ALL survivors persist and eventually interfere with physical performance. Higher cumulative doses of vincristine and/or intrathecal methotrexate administration are associated with persistent neuromuscular impairments, which have implications on future physical performance as this population ages.

13. ENDOCRINOPATHY IN SURVIVORS OF CHILDHOOD CANCER: A STUDY FROM THE BRITISH CHILDHOOD CANCER SURVIVOR STUDY (BCCSS) A.A. Toogood, D.L. Winter, C. Frobisher, E.R. Lancashire, R.C. Reulen and M.M. Hawkins. *Department of Endocrinology, University Hospitals Birmingham NHS Foundation Trust, Edgbaston, Birmingham, UK; School of Health and Population Sciences, University of Birmingham, Edgbaston, Birmingham, UK*

Endocrine dysfunction is the most frequent long-term complication of therapy used to treat childhood cancer reported in limited clinical series of survivors. However, a comprehensive examination of the total burden of endocrinopathy within a population of cancer survivors is lacking. This study aims to determine the prevalence of endocrinopathy in adults treated for childhood cancer between 1941–1991.

Methods: The responses to questions relating to the presence of thyroid disease, diabetes mellitus, pituitary dysfunction, lack of growth hormone and puberty from 10,488 subjects were reviewed. In addition the medication history was also reviewed.

Results: Overall 3,502 (36%) of the 9700 patients with evaluable data reported one or more endocrinopathy. Those at greatest risk received treatment for CNS tumours (46%), Hodgkin's disease (HD) (43%) and leukaemia (41%). Thyroid disease was common; hypothyroidism (8%), hyperthyroidism (1%), thyroid nodules (2%), thyroid enlargement (1%) and thyroxine use (10%). The frequency of hypothyroidism was not affected by the age of the subject and was greatest amongst those treated for HD (20%). A lack of growth hormone (GH) was reported by 11%, and 10% reported receiving GH injections at some point. The relative frequency of reported GH deficiency declined as the age of the subject increased and was greatest amongst those treated for CNS tumours (23%), leukaemia (16%) and soft tissue sarcomas (8%). Diabetes mellitus was reported by 1.9% of which 0.4% were diet controlled, 0.6% on oral hypoglycaemic agents and 0.9% on insulin. Osteoporosis was reported by 3%. Testosterone replacement was reported by 7% of men. Sex steroid use was reported by 46% of women of which 42% was for contraception.

Conclusions: This is the first population based study of endocrinopathy in survivors of childhood cancer. Endocrine complications are common, affecting 36% of subjects. Adult endocrinologists should be engaged in the care of this patient population.

14. LONG-TERM POPULATION-BASED RISKS OF SPECIFIC CAUSES OF DEATH AFTER CHILDHOOD CANCER: THE BRITISH CHILDHOOD CANCER SURVIVOR STUDY Raoul C. Reulen, PhD; David L. Winter, HNC; Clare Frobisher, PhD; Emma R. Lancashire, PhD; Charles A. Stiller, MSc; Meriel E. Jenney, MD; Roderick Skinner, MD; Michael C. Stevens, MD; Michael M. Hawkins, DPhil. *Centre for Childhood Cancer Survivor Studies, School of Health and Population Sciences, Public Health Building, University of Birmingham, Birmingham, UK; Childhood Cancer Research Group, Richards Building, University of Oxford ,Oxford, UK; Children's Hospital for Wales, Cardiff, UK; Department of Paediatric and Adolescent Oncology, Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; Department of Oncology, Bristol Royal Hospital for Children, Bristol, UK*

Background: To quantify the risk of long-term cause-specific mortality with longer follow-up and more than three times the number of deaths and person-years beyond 25 years from diagnosis than previously available to any study.

Methods: Cause-specific standardized mortality ratios (SMR=Observed/Expected) and absolute excess risks (AER=excess deaths per 10,000 survivors per year) were calculated within the British Childhood Cancer Survivor Study, a population-based cohort of 17,981 5-year survivors of childhood cancer diagnosed with cancer prior to age 15 years between 1940 and 1991, in Britain.

Results: A total of 3,056 deaths were ascertained yielding an overall SMR of 11-fold expected. The SMR declined with follow-up, but was still 3-fold expected beyond 45 years from diagnosis. The AER was greatest in the first 10 years after 5-year survival (AER=115), declined to roughly 40 in subsequent years, but then increased again to 114 beyond 45 years from diagnosis. The SMRs of second primary tumors, circulatory, and respiratory deaths declined sharply with increasing time from diagnosis but were still 3 to 4-fold that expected subsequent to 45 years from diagnosis. By contrast, the AERs of second primary tumors, circulatory, and respiratory deaths increased rapidly with time from diagnosis and were 58, 29, and 9 respectively, beyond 45 years from diagnosis. Cumulative mortality from all death causes, other than recurrence, was 27% by 55 years from diagnosis, whereas from rates in the general population this would have been 9%.

Conclusions: The findings from this largest ever population-based study indicate that there is a rapid increase in AER and cumulative mortality of second primary tumour and non-neoplastic deaths beyond 25 years from diagnosis which suggests a substantial number of survivors are dying prematurely. This confirms the importance of very long-term outcome data and that survivors should be able to access health care programmes even decades from treatment.

15. CARDIOVASCULAR DISEASE IN LONG-TERM SURVIVORS OF CHILDHOOD CANCER Helena J.H. van der Pal, MD; Evelien van Delden; Elvira C. van Dalen, MD, PhD; Ronald B. Geskus, MSc, PhD; Wouter E. Kok, MD, PhD; Caro C. Koning, MD, PhD; Flora E. van Leeuwen, MSc, PhD; Huib N. Caron, MD, PhD; Leontien C. Kremer, MD, PhD. *Department of Pediatric Oncology, Department of Medical Oncology, Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Department of Cardiology, Department of Radiation Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands; Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands*

Background: To evaluate the risk of various clinical cardiovascular diseases (CVDs) and associated risk factors in 5-year childhood cancer survivors (CCS).

Summarized description of the project: The study population consists of all 5-year CCS treated in the Emma Children's Hospital/Academic Medical Center (EKZ/AMC) between 1966 and 1996 (n=1362). A case of CVD was defined as grade ≥3 arrhythmia, cardiac ischemia, ventricular dysfunction, pericarditis and valvular disease (Common Terminology Criteria for Adverse Events v3.0).

Results: We obtained complete information on clinical status up to at least January 2006 for 1230 patients (90.3%). The mean age at diagnosis was 6.9 years; mean follow-up time was 21.6 years, and mean attained age 28.5 years. In total 719 survivors (52.8%) received potentially cardiotoxic therapy (anthracyclines, cardiac irradiation, and/or cardiac surgery). We observed 47 CVDs (29 grade

3 (severe), 13 grade 4 (life-threatening) and 5 grade 5 (death) in 40 patients, of whom 37 received cardiotoxic therapy (5.6%) and 3 no cardiotoxic therapy (0.5%). In the Kaplan-Meier analyses, 25 years after diagnosis the estimated risks of developing CVD for CCS treated with anthracyclines and radiotherapy combined, with anthracyclines only, with cardiac irradiation only or with no cardiotoxic therapy were 18.3%, 6.3%, 4.4%, and 0.6%, respectively. In the multivariate Cox regression analyses anthracyclines and cardiac irradiation were significantly associated with developing CVD.

Conclusions: CCS have a high risk of severe clinical CVD. In CCS treated with cardiotoxic therapy the cumulative risk is 5.6% and 0.5% in survivors not treated with cardiotoxic therapy. After 25 years of follow-up, the risk of developing CVD is highest in the group of CCS treated with both anthracyclines and cardiac irradiation.

16. RADIATION DOSE AS A RISK FACTOR FOR CARDIAC DISEASES FOLLOWING CHILDHOOD CANCER: A CASE-CONTROL STUDY

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Purpose: Cardiac diseases are probably one of the most important long term iatrogenic effects of childhood cancer treatments. Nevertheless, very little is still known about the shape of the dose response with radiation dose to the heart, and on the role of chemotherapy, with the exception of Adriamycin.

Methods: A cohort of 3 073 5-year survivors of a childhood solid cancer in five French centres diagnosed between 1945 and 1985 was constituted between 1990 and 1995. Detailed information on clinic and treatment was collected. Between 1995 and 2000, the radiation dose received by the 2185 children who received radiotherapy was estimated in 8 sites in the heart. From 2006 to 2009 an auto-questionnaire was sent to patients still alive. This auto-questionnaire concerned all the aspects of social and professional lives, and potential long term iatrogenic effects of cancer treatments. The overall response rate was 70%. Cardiac diseases reported in the questionnaire were validated by obtaining the copies of the radiological documents. Medical records of patients dead from a cardiac disease were obtained for validation.

Results: A total of 180 patients developed a validated cardiac disease: 11 myocardial infarction, 12 angina pectoris, 97 heart failure and cardiomyopathies, 14 pericarditis, 46 valvular diseases. Survivors from a lymphoma were at cardiac disease risk 2.0 (95%CI: 1.4–3.0) times higher than the others. As compared to the patients who did not received radiotherapy, those who received an average heart radiation dose between 5 and 15 Gy had a 2.0 (95%CI: IC 95%=1.1–3.8) times higher risk of developing cardiac disease, those who received a heart radiation dose between 15 and 30 Gy had a 4.6 (95%CI; 2.7–8.1) times higher, and those who received a heart radiation dose higher than 30 Gy had a add 6.3 (95%CI: 3.2–12.6) times higher risk. Anthracyclines and vinca-alkaloids (RR=3.3, 95%CI=2.2–4.9), were also associated to an increased risk of cardiac disease.

Conclusion: In conclusion, this study confirms that radiation dose received to the heart during radiotherapy for a childhood cancer increases the risk of cardiac disease.

17. CORONARY HEART DISEASE EVENTS 50+ YEARS AFTER THORACIC IRRADIATION: PRELIMINARY RESULTS

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Background: Thoracic radiotherapy (RT) for the treatment of childhood cancer increases myocardial infarction (MI) incidence and mortality. Much of the evidence comes from studies of Hodgkin lymphoma survivors treated with older RT techniques that exposed the heart to the full dose of therapeutic irradiation. Current regimens limit the cardiac dose and volume, but longer follow-up is necessary to determine whether these modifications will eliminate the increased risk or simply delay it.

Methods: A population-based, longitudinal cohort of subjects exposed to irradiation for an enlarged thymus during infancy from 1926 to 1957 and of their non-irradiated siblings was reestablished between 2004 and 2008. Coronary heart disease (CHD) events were assessed using a mailed survey and checking cause of death in the National Death Index. We used Poisson regression methods to compare incidence rates by irradiation status and cardiac radiation dose.

Results: Subject's median age and length of follow-up was 57.5 years (range 41.2–88.8 yrs) among both irradiated and non-irradiated siblings. Eighty-four irradiated individuals (mean cardiac dose 1.45 Gy; range 0.17–20.20 Gy) had a MI during 124,631 person-years of follow-up compared to 131 non-irradiated siblings with a MI during 210,604 person-years. This resulted in a rate ratio of 0.99 (95%CI: 0.75–1.30) after adjustment for attained age and gender. The adjusted rate ratio for all CHD events (MI, bypass surgery and angioplasty) was 1.09 (95%CI: 0.88–1.35). No significant dose-effect association was observed for incidence of MI or all CHD events.

Conclusions: Although further analysis, including adjustment for other risk factors, needs to be performed, our preliminary results suggest that if cardiac radiation doses from childhood cancer therapy can be reduced to around 1.5 Gy, the average dose in our cohort, without increasing other cardiotoxic therapies, the increased MI risk may be nearly eliminated or at least delayed into the 7th decade of life.

18. YIELD OF SCREENING FOR CARDIOVASCULAR RISK FACTORS AND CARDIAC DYSFUNCTION IN CHILDHOOD CANCER SURVIVORS USING THE CHILDREN'S ONCOLOGY GROUP (COG) LONG-TERM FOLLOW-UP (LTFU) GUIDELINES: CITY OF HOPE EXPERIENCE Saro H. Armenian, DO, MPH; Wendy Landier RN, MSN, CPNP; Can-Lan Sun, PhD; Jin Lee, MPH; Meghan Zomorodi, BA; Liton Francisco, BS; Karla Wilson, RN, MSN, FNP-C; Smita Bhatia, MD, MPH. *Department of Population Sciences, City of Hope, Duarte, CA, USA*

Background: Childhood cancer survivors are at risk for cardiac dysfunction (CD) due to exposure to anthracyclines and chest radiation. This risk is further compounded by development of cardiovascular (CV) risk factors (hypertension, dyslipidemia, insulin resistance, and overweight/obesity) in this population. COG Guidelines use a consensus-based approach to recommend screening due to absence of randomized trials for guidance. The utility and yield of these recommendations need to be evaluated.

Methods: Survivors were screened for CV risk factors or CD per COG Guidelines. Screening outcomes: CD (ejection fraction [EF] <55%); CV risk factors (dyslipidemia [triglyceride >150 mg/dl and/or total cholesterol >200 mg/dl]; hypertension [>18 y.o: >130/>85; <18 y.o: >90th% age]; insulin resistance [HOMA-IR >2.86]; overweight/obese [BMI ≥25kg/m^2]).

Results: 310 survivors underwent screening (47% female; median age at diagnosis: 11.4 years; at screening: 24.1 years; time from diagnosis: 10.9 years; leukemia [44%], lymphoma [28%], solid tumor [28%]; median anthracycline dose: 225 mg/m^2 (25–642). Cardiac dysfunction: among those with ≥2 echocardiograms (n=129), 18.5% were identified with previously undiagnosed CD (45.8% on first screen and 54.2% on subsequent screening). The prevalence was highest (25.0%) for anthracycline exposure ≥250 mg/m^2 with radiation, and lowest (13.3%) for anthracycline exposure <250 mg/m^2 without radiation. CV risk factors: 30.1% of survivors screened had multiple (≥2) CV risk factors. Males (OR: 3.5, p<0.01), age at screening (OR: 1.1/yr increment, p=0.02), and cranial radiation >18Gy (OR: 3.1, p=0.04) were associated with increased risk. Males treated with >18Gy cranial radiation were at highest risk (OR: 17.1, p<0.01).

Conclusions: Screening per COG LTFU Guidelines helped identify previously unrecognized CD or CV risk factors in up to 30% of "at risk" survivors, reinforcing the critical need for long-term cardiac surveillance in this population. This study also attempts to refine consensus-based screening recommendations by identifying sub-groups with highest or lowest yield per current screening recommendations.

19. ANTHRACYCLINE-RELATED CARDIOMYOPATHY (AC) IN CHILDHOOD CANCER SURVIVORS: DOSE-SPECIFIC ROLE OF GENETIC POLYMORPHISMS IN THE CARBONYL REDUCTASE (CBR) GENES—A CHILDREN'S ONCOLOGY GROUP STUDY C.-L. Sun, J.G. Blanco, W. Landier, L. Chen, D. Esparaza-Duran, D.L. Friedman, J.P. Ginsberg, F. Keller, M.M. Hudson, J.P. Neglia, K. Oeffinger, K. Ritchey, D. Villaluna, M.V. Relling, S. Bhatia. *Department of Population Sciences, City of Hope, Duarte, CA, USA; State University of New York at Buffalo, Buffalo, NY, USA; Children's Oncology Group, Arcadia, CA, USA, Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; Children's Hospital of Philadelphia, Philadelphia, PA; Children's Healthcare of Atlanta, Atlanta, GA, USA, Emory University School of Medicine, Atlanta, GA, USA Departments of Oncology, Epidemiology and Cancer Control, Behavioral Medicine and Pharmaceutical Sciences, St. Jude Children's Research Hospital, Memphis, TN, USA; University of Minnesota Cancer Center, Minneapolis, MN, USA; Memorial Sloan-Kettering Cancer Center, New York, NY, USA University of Pittsburgh School of Medicine, Pittsburgh, PA, USA*

Background: Anthracycline-related cardiomyopathy (AC) is a well-recognized dose-limiting complication. Significant inter-individual variability in AC risk exists, potentially due to genetic susceptibility. Myocardial CBRs catalyze the reduction of anthracyclines to cardiotoxic alcohol metabolites. Polymorphisms in CBR3 V244M and CBR1 G1096A impact CBR activity. Our goal was to examine the role of functional polymorphisms in CBR3/1 on AC risk.

Methods: Using a case-control design, 165 cases with documented cardiomyopathy and 323 matched controls (cancer survivors without cardiomyopathy; matched on: primary diagnosis, year of diagnosis, follow-up, race/ethnicity) provided germline DNA. Detailed therapeutic exposures were abstracted.

Results: Primary diagnoses included acute leukemia (164), lymphoma (111), sarcoma (120) and others (93); 51% females; 77% whites; median age at cancer diagnosis: 7.5 years (0–21); time to cardiomyopathy: 7.1 years; median anthracycline dose–cases: 300mg/m^2; controls: 140mg/m^2. Multivariate analysis revealed anthracycline dose (per 100mg/m2: OR=1.75, p<0.001), and chest radiation (OR=3.13, p=0.05) to be associated with AC. The role of polymorphisms in CBR3/CBR1 was examined by stratifying cases and controls

by anthracycline dose, and adjusting for chest radiation. For the entire cohort, there was a borderline association between CBR3 V244M and cardiomyopathy (OR=1.49, p=0.08 for GG vs. GA/A); and no association for CBR1 G1096A (OR=1.01, p=0.97). The CBR3 V244M-AC association became stronger among subjects exposed to ≤250mg/m^2 of anthracycline (OR=6.38, p=0.006), but disappeared for those exposed to >250mg/m^2 (OR=0.90, p=0.83). Similar but non-significant associations were observed for CBR1 (OR=3.32, p=0.10; OR=0.78, p=0.65, respectively).

Conclusion: In the largest cohort of documented cardiomyopathy ever studied, this report demonstrates the following: i) a clear dose-response relationship between anthracyclines and cardiomyopathy; ii) the selectively greater impact of CBR3 on AC risk among those exposed to low-dose anthracycline. These data identify a definable subset of patients that may benefit from cardioprotection, surveillance and/or pharmacologic interventions.

20. LONG-TERM POPULATION-BASED RISKS OF SECOND PRIMARY NEOPLASMS AFTER CHILDHOOD CANCER: BRITISH CHILDHOOD CANCER SURVIVOR STUDY (BCCSS) Clare Frobisher, PhD; David L. Winter, HNC; Charles A. Stiller, MSc; Emma R. Lancashire, PhD; Helen C. Jenkinson, PhD; Raoul C. Reulen, PhD; Michael M. Hawkins, DPhil on behalf of the British Childhood Cancer Survivor Study. *Centre for Childhood Cancer Survivor Studies (CCCSS), School of Health and Population Sciences, Public Health Building, University of Birmingham, Edgbaston, Birmingham, UK; Childhood Cancer Research Group, University of Oxford, Oxford, UK; Department of Paediatric Oncology, Birmingham Children's Hospital NHS Trust, Birmingham, UK.*

Background: Estimate the risks of second primary neoplasms (SPNs) within the BCCSS; compare the observed numbers with that expected from the general population; investigate variation in risks by specific demographic factors, first and second primary neoplasm types, and treatment types.

Methods: The analysis included 17,980 individuals diagnosed with childhood cancer, 1940–91, in Britain and surviving at least 5 years. Ascertainment of any SPN diagnosed to 31/12/2004 was through linkage to the National Health Service Central Registers.

Results: Follow-up subsequent to 5-year survival accumulated 334,871 person-years; with a mean of 18.6 years (range 0.0–59.6 years). 3,388 survivors were aged ≥40 years at exit and contributed 115,675 person-years beyond this age. Overall 1,060 SPNs were observed, the most common were of the: central nervous system (274); non-melanoma skin cancer (208); bone (86), breast (72); and digestive system (72). The cumulative incidence of a SPN developing by age 20, 30, 40 and 50 years were 2.1%, 4.3%, 8.2% and 13.6%, respectively. Overall the observed number of SPNs was 4.2 (95% CI: 3.9-4.5) times that expected; whilst the absolute excess risk (AER) of a SPN was 1.6 cases/1,000 survivors/year. The standardised incidence ratio decreased significantly (P<0.0001) from 5.1 among those aged 20–29 years to 2.0 in those aged ≥40 years. The AER increased from 1.3 cases/1,000 survivors/year among those aged 20–29 years to 2.7 cases/1,000 survivors/year for those aged ≥40 years (P<0.0001).

Conclusion: Among those aged at least 40 years, for which there are greatest concerns and uncertainty relating to excess risk of a second neoplasm, there was a 2-fold excess risk for a SPN and this corresponded to 2.7 extra cancer cases per 1000 survivors per year. Further details from this rich resource would be presented.

21. MULTIPLE SUBSEQUENT NEOPLASMS IN THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS) COHORT Gregory T. Armstrong, MD, MSCE; Wei Liu, MS, PhD; Sue Hammond, MD; Smita Bhatia, MD; Joseph P. Neglia, MD, MPH; Marilyn Stovall, PhD; Wendy Leisenring, ScD; Yutaka Yasui, PhD; Deokumar Srivastava, PhD; Leslie L. Robison, PhD. *Departments of Epidemiology and Cancer Control and Biostatistics, St. Jude Children's Research Hospital, Memphis, TN, USA*

Background: Childhood cancer survivors demonstrate an increased incidence of subsequent neoplasms (SNs). Those surviving the first SN remain at risk to develop multiple SNs. As SNs are a common cause of late-morbidity and mortality, characterization of risk for multiple SNs is needed.

Methods: Analysis included 14,358 >5 yr survivors of childhood cancer diagnosed 1970–86 (median age at follow-up 30.9 yrs, range 5.6–56.3; median follow-up 18.0 yrs, range 0–32.6). Among survivors with a subsequent neoplasm (SN1), the 15-yr cumulative incidence of second subsequent neoplasm (SN2) or subsequent malignant neoplasm (SMN) other than non-melanoma skin cancer (NMSC) was calculated with death as a competing risk. Hazard ratios (HR) were calculated from multivariable regression models that included age at diagnosis, age at SN1, treatment era, radiation therapy (RT) exposure, and family history of cancer.

Results: 1383 (9.6%) survivors developed SN1, of whom 384 (27.8%) developed SN2. Of those with SN2, 153 (39.8%) developed >2 SNs. Cumulative incidence of SN2 was 38.8% (95% CI 35.1–42.5) 15 yrs after SN1. Cumulative incidence of SN2 was highest in those with a primary diagnosis of Hodgkin lymphoma (50.3%, 44.1–56.6), CNS malignancy (44.5%, 33.3–55.6), and osteosarcoma (40.9%, 21.5-60.4). Among those experiencing an SN1, multivariable analysis identified older age at SN1 (HR 2.21, p<0.0001) and RT for the initial cancer (HR 1.83, p=0.003) as independent risk factors for SN2. Cumulative incidence of SN2 among RT-exposed survivors was

41.3% (95% CI 37.2–45.4). For those RT-exposed with SN1 of NMSC, the cumulative incidence of SMN (excluding NMSC) was 19.4% (95% CI 12.1–26.5). In SN1 survivors not exposed to RT for their initial cancer, the 15-yr cumulative incidence of SMN (excluding NMSC) was 18.6% (95% CI 10.6–26.5).

Conclusion: Multiple SNs are common among aging survivors of childhood cancer who experience and survive SN1. Exposure to RT and increased age at SN1 place survivors at significantly higher risk. SN1 of NMSC identifies a population at high risk for invasive SMN. Multiple SNs among non-RT exposed patients reflect a population of interest for genetic susceptibility to neoplasia.

22. GASTROINTESTINAL MALIGNANCIES AS A SUBSEQUENT MALIGNANT NEOPLASM IN SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY TO Henderson, MD, MPH; J Whitton, MS; W Leisenring, PhD; J Neglia MD, MPH; A Meadows, MD; C Crotty, MPH; KC Oeffinger, MD; L Diller, MD; P Inskip, ScD; M Stovall, PhD; GT Armstrong, MD, MSCE; LL Robison, PhD, PC Nathan, MD, MSc. *University of Chicago, Chicago, IL, USA; Fred Hutchinson Cancer Research Center, Seattle, WA, USA; University of Minnesota, Minneapolis, MN, USA; Children's Hospital of Philadelphia, Philadelphia, PA, USA; Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Dana-Farber Cancer Institute/Children's Hospital Boston, Boston, MA, USA; National Cancer Institute, Bethesda, MD, USA; MD Anderson Cancer Center, Houston, TX, USA; St. Jude Children's Research Hospital, Memphis, TN, USA; The Hospital for Sick Children, Toronto, ON, Canada*

Background: There is emerging evidence that childhood cancer survivors (CCS) develop gastrointestinal (GI) malignancies more frequently and earlier than the general population. We determined the risk of GI subsequent malignant neoplasms (SMN) and described factors associated with their development to inform surveillance recommendations.

Methods: We assessed the risk of GI SMN in a cohort of 14,372 5-year CCS and compared that to population-based data from the Surveillance, Epidemiology and End Results (SEER) program. Multivariate Cox regression models identified associations between key risk factors and GI SMN development.

Results: 45 CCS developed GI SMN at a median age of 33.5 years (range: 9.7–44.8) and a median of 22.8 years (range: 5.5–30.2) from their original diagnoses. The 30-year cumulative incidence of a GI SMN was 0.64% (95% confidence interval [CI]: 0.43–0.86). The most frequent SMN locations were colorectal (n=24; 53%), stomach (n=7; 16%), and hepatobiliary system (n=4, 9%). CCS with a GI SMN were more likely to be deceased than those without (51.1 vs. 13.8%, $p<0.05$). 60.9% of deceased died of their GI SMN. The risk of GI SMN was almost 5-fold higher in CCS than the general population (standardized incidence ratio [SIR]=4.6, 95% CI: 3.5–6.1) with absolute excess risk (AER) of 14 per 100,000 person-years (py). Colorectal SMN SIR was 4.19 (95% CI: 2.7806.30), AER was 7/100,000 py. Survivors of Wilms' tumor, Hodgkin's lymphoma and bone tumors were at highest risk. The multivariate model revealed abdominal radiation (RR=5.32, 95% CI: 2.74–10.32), alkylating agents (RR=2.60, 95% CI: 1.06-6.37) and platinum drugs (RR=4.73, 95% CI: 1.49–15.14) increased the risk of GI SMN.

Conclusions: While the overall incidence is low, CCS are at increased risk for developing a GI SMN with an associated elevated risk of mortality. Surveillance in at-risk survivors should commence at a younger age than is recommended for the general population.

23. RADIATION DOSE AS A RISK FACTOR FOR SECOND NEOPLASMS IN DIGESTIVE SYSTEM FOLLOWING CHILDHOOD CANCER: A CASE-CONTROL STUDY Markhaba Tukenova, MD; Ibrahima Diallo, PhD; Harald Anderson; Gudrun Svahn-Tapper; Mike Hawkins PhD; Garwicz Stanislaw, PhD; Risto Sankila; Chiraz El Fayech, MD; Dave Winter; Odile Oberlin, MD; Torgil Moller, PhD; Froydis Langmark; Laufey Tryggvadottir; Hélène Pacquement, MD; Jorgen H. Olsen, MD; Florent de Vathaire, PhD. *INSERM UMR 1018 Villejuif, France; Institut Gustave Roussy, Villejuif, France; University Paris XI, Villejuif, France; Lund University, Sweden; University of Birmingham, UK; University Children's Hospital, Lund, Sweden; Finnish Cancer Registry, Helsinki, Finland; Norwegian Cancer Registry, Oslo, Norway; Institute of Cancer Epidemiology, Danish Cancer Society, Copenhagen, Denmark; Institut Curie, Paris, France*

Purpose: Digestive system cancers count for half of the excess of cancer diagnosed in atomic bomb survivors. Therefore it is expected that these cancers will be a major issue in childhood cancer survivors treated by radiotherapy when attaining adulthood. The aim of this study was to determine therapy-related risk factors for the development of second malignancy in the digestive system after childhood cancer.

Method: Among 4,226 5-year survivors of a childhood solid cancer in eight French and British centres diagnosed before 17 years and 25 120 patients younger than 20 years old at first malignant neoplasm extracted from the Nordic Cancer Registries, and followed 28 years in average, 58 cases of digestive tract cancer were diagnosed: 27 in colon-rectum, 14 in oesophagus or stomach, 10 in liver, 6 in pancreas. Each case was matched with 3 controls in each respective cohort according to sex, age at the first cancer, the calendar year of occurrence of the first cancer and length of follow-up. Complete clinical, chemotherapy, and radiotherapy data were recorded for each case and control. Radiation dose received to the site of each second malignancy and to the corresponding site of its matched controls was estimated.

Results: The mean local dose received to the at the site of the SMN was 20.1 Grays (Gy) for cases (range 0–71) and 7.5 Gy for controls (range 0–57.5). A very strong ($p<0.001$) dose-response relationship was estimated between the radiation dose and the risk of developing a cancer of the digestive system SMN. As compared to the survivors who did not received radiotherapy, the relative risk was 5.21 (95% CI: 1.70 to 16.01) for local radiation doses between 10 and 29 Gy, 9.62 (95% CI: 2.63 to 35.20) for radiation dose higher than 30 Gy. Chemotherapy was also associated to a higher risk of digestive system SMN, the highest risks being observed following alkylating agents and anthracyclines.

Conclusion: This study confirms that childhood cancer treatments strongly increase the risk of digestive tract cancer, which occurred only after a very long latency period.

24. BREAST CANCER AFTER CHILDHOOD CANCER: AN INTERNATIONAL COLLABORATIVE CASE-CONTROL STUDY Raoul C Reulen, PhD; Ibrahima Diallo, PhD; Florent de Vathaire, PhD; Monica Terenziani, PhD; Flora E van Leeuwen, PhD; Ricardo Haupt, PhD; Corrado Magnani, PhD; Vanessa Tenet; Elisabeth Cardis, PhD; Ausrele Kesminiene, MD; Michael M Hawkins, DPhil. *Centre for Childhood Cancer Survivor Studies, School of Health and Population Sciences, Public Health Building, University of Birmingham, Birmingham, UK; Research Unit of Cancer Epidemiology (U351 INSERM), Institut Gustave Roussy, Villejuif, France; Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands; Epidemiology and Biostatistics Section, Gaslini Children Hospital, Genova, Italy; Childhood Cancer Registry of Piedmont, CPO Piemonte, Torino, Italy; Radiation Group, International Agency for Research on Cancer, Lyon, France; Centre for Research in Environmental Epidemiology, Barcelona, Spain*

Background: To investigate the risks of breast cancer subsequent to therapeutic radiation and chemotherapy among childhood cancer survivors within a large international collaborative study.

Methods: This matched case-control study was part of an international collaborative study (Gene-Rad-Risk) examining the risks of breast cancer in women exposed to therapeutic and diagnostic irradiation prior to age 35. The current case-control study was nested within cohorts of childhood cancer survivors across four European countries. Cases were individually matched to two controls for interval from first primary cancer, age at first primary cancer (±1 year), and calendar year of first primary cancer (±3 years). Information on radiotherapy and chemotherapy exposure was abstracted from available medical records. Radiation doses to the breast cancer site for cases and to the same site for matched controls were estimated individually. Variations in the odds ratio (OR) of breast cancer by level of exposure to radiation dose and chemotherapy were investigated by means of conditional logistic regression models.

Results: In total, 203 breast cancers were identified from six centres across Europe. Survivors treated with any radiotherapy had a 2.7-fold increased OR compared to those who had not received radiotherapy, and the OR increased linearly with increasing radiation exposure (Gy) ($P_{trend}<.0001$) with no departure from linearity ($P_{nonlinearity}=0.66$). Among survivors treated with any anthracycline, the risk of breast cancer was significantly elevated (OR=2.5, 95%CI: 1.3–4.9). Similarly, the risk was significantly increased among survivors treated with other cytotoxic antibiotics (principally actinomycin-D) (OR=2.3, 95%CI: 1.3–4.1). No other chemotherapeutic drug group was associated with a significantly increased risk.

Conclusions: These preliminary results indicate a linear increase in breast cancer risk with increasing radiation dose. Exposure to anthracyclines or other cytotoxic antibiotics also appears to increase the risk of breast cancer.

25. PHARMACOGENETIC RISK FACTORS FOR ALTERED BONE MINERAL DENSITY AND BODY COMPOSITION IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA Mariël L. te Winkel, MD; Robert D. van Beek, MD; Sabine M.P.F. de Muinck Keizer-Schrama, MD, PhD; André G. Uitterlinden, Prof; Wim C.J. Hop, MD, PhD; Rob Pieters, Prof; and Marry M. van den Heuvel-Eibrink, MD, PhD. *Departments of Pediatric Oncology/Hematology and Pediatric Endocrinology, Erasmus MC–Sophia Children's Hospital; Departments of Internal Medicine and Biostatistics, Erasmus MC–University Medical Center; Rotterdam, The Netherlands*

Background: As the survival of pediatric acute lymphoblastic leukemia (ALL) improves, research on treatment-related morbidity, like osteogenic toxicity, is required. This study investigates pharmacogenetic risk factors for low BMD and disturbed body composition, in order to identify pediatric ALL patients who may benefit from interventions to prevent long-term complications.

Methods: We determined the influence of SNPs in 4 genes [*vitamin-D receptor* (*VDR:BsmI/ApaI/TaqI* and *Cdx-2/GATA*), *collagen type I alpha 1* (*SpI*), *estrogen receptor 1* (*ESR1:PvuII/XbaI*), *glucocorticoid receptor* (*BclI*)] on body composition and BMD during dexamethasone-based pediatric ALL treatment. Anthropometry data of 69 patients treated with the DCOG-ALL9 protocol were evaluated. In patients ≥4 years body composition, BMD of the total body (BMD-TB) and the lumbar spine (BMD-LS) were measured repeatedly using dual-energy X-ray absorptiometry. Values were expressed as standard deviation scores (SDS). Repeated measurements analysis (ANOVA) was used.

Results: Non-carriers of *VDR* 5'-end (*Cdx-2/GATA*) haplotype 3 revealed more fat gain than carriers (Δ%fat: non-carriers:+1.76SDS, carriers:+0.77SDS, p<0.001). At diagnosis and during therapy, BMD-LS was significantly higher in non-carriers of *VDR* 5'-end (*Cdx-2/GATA*) haplotype 3 than in carriers. The other SNPs did not influence BMD during/after treatment. The year after treatment discontinuation, lean body mass increased in non-carriers of *ESR1* (*PvuII/XbaI*) haplotype 3 and decreased in carriers (Δlean body mass: non-carriers:+0.28SDS, carriers:-0.55SDS, p<0.01).

Conclusion: This is the first study investigating the influence of genetic variation of the *VDR*, *COLIA1*, *ESR1* and *GR* on body composition and BMD in pediatric ALL. We found the *VDR* 5'-end (*Cdx-2/GATA*) haplotype 3 as a protective factor for excessive fat gain during therapy. Moreover, this haplotype 3 of the *VDR* 5'-promoter was determined as a risk factor for lower BMD-LS at diagnosis that remained during treatment. Carriage of *ESR1* (*PvuII/XbaI*) haplotype 3 negatively influenced recovery of lean body mass after treatment discontinuation.

Posters

1. ATHEROSCLEROTIC DISEASE BURDEN AND FUTURE RISK IN CHILDHOOD CANCER SURVIVORS David C. Landy, MPH, Tracie L. Miller MD, MS; Gabriela Lopez-Mitnik, MS; Stuart R. Lipsitz, ScD; Andrea Hinkle, MD; Louis Constine, MD; Carol A. French, MPH; Amy Rovitelli, MS; Cindy Proukou, RN, PNP; M. Jacob Adams, MD; Steven E. Lipshultz, MD. *University of Miami Miller School of Medicine, Miami, FL, USA; Harvard Medical School, Boston, MA, USA; University of Rochester School of Medicine and Dentistry, Rochester, NY, USA*

Background: Concerns that survivors are at increased risk of atherosclerotic disease and particularly susceptible to future cardiac damage have elicited recommendations for early testing of atherosclerotic disease risk factors and their aggressive management. These recommendations, however, provide no method for aggregating risk factors or identifying survivors with the highest cumulative risk though both may be possible using two recently developed measures from NIH studies. The Pathobiological Determinants of Atherosclerosis Study's score (PDAY) predicts risk of a coronary artery atherosclerotic disease lesion in 15–34 year olds. The Framingham Heart Study's calculator (FHSC) predicts 30-year risk of coronary death, myocardial infarction, or stroke in those over 20-years old.

METHODS: Risk factors were measured in a representative sample of 110 survivors and 32 siblings over 15 years old in a NCI prospective cohort study in Rochester, NY from 1999-2004. Risk factors were aggregated using PDAY and FHSC measures which are weighted combinations of age, sex, total cholesterol, HDL-cholesterol, smoking, systolic BP, insulin, and BMI or hypertensive treatment. Survivors were compared to siblings after controlling for age and sex.

Results: Survivors were a mean 15 years post-diagnosis, ranged in age from 15–46 years of age, and 56% received anthracyclines, 46% cardiac radiation, 44% cranial radiation, and 5% total body radiation.

Method (n)	Mean (Range) Risk for Survivors by Age-Group and Sex			
PDAY (101)	15–24 yr old females	15–24 yr old males	25–34 yr old females	25–34 yr old males
	<1% (0–8%)	3% (0–24%)	9% (3–26%)	18% (7–42%)
FHCS (73)	20–29 yr old females	20–29 yr old males	30–39 yr old females	30–39 yr old males
	2.1% (1–9%)	3.3% (1–12%)	2.9% (1–5%)	15.6% (5–35%)

Survivors had similar PDAY risk (p=.83) and 52% higher FHCS risk (p=.22) versus siblings. FHSC risk appears comparable to NCI CCSS event rates.

Conclusions: PDAY and FHSC measures provide clinicians caring for survivors new ways of interpreting the multiple results from recommended atherosclerotic disease risk factor testing. These easy to use and cost-effective, single measures of atherosclerotic disease risk may help identify survivors with the highest cumulative risk and greatest need for medical assessment and intervention while also increasing survivor understanding of atherosclerotic disease risk.

2. ELEVATED PULMONARY ARTERY PRESSURE AMONG SURVIVORS OF HODGKIN LYMPHOMA E.S. Tonorezos, MD, MPH; S. Martin, MD; W. Schaffer, MD, PhD; R. Kaplan, MD; K. Oeffinger, MD. *Memorial Sloan-Kettering Cancer Center, New York, NY, USA*

Background: Many survivors of Hodgkin Lymphoma have risk factors for pulmonary hypertension, including a history of splenectomy, but few studies have examined pulmonary artery pressures in this population.

Methods: We retrospectively reviewed medical records of twenty survivors of Hodgkin Lymphoma seen in our practice. All subjects underwent echocardiography as part of routine long-term follow-up screening, and all had left ventricular EF >50%. We defined elevated pulmonary artery systolic pressure in the following way: borderline, 36–40 mm Hg; mild, 41–50 mmHg; moderate 51–69 mmHg; severe, ≥70 mmHg. We performed chi square and logistic regression for associations between variables.

Results: All subjects had received radiation therapy (mantle, n=15; mediastinal, n=3; low neck, n=2). Eight subjects had received bleomycin. Ten subjects were asplenic (surgical, n=9; radiation-induced functional asplenia, n=1). Four subjects (20%) did not have pulmonary artery pressure measured by echocardiogram due to testing characteristics. Of the remaining sixteen subjects, four (25%) had borderline, mild, or moderate elevation in pulmonary artery pressure by echocardiography (borderline, n=2; mild, n=1, moderate, n=1). The finding of elevated pulmonary artery pressure was not associated with either splenectomy (p=0.14) or history of treatment with bleomycin (p=0.78).

Conclusions: In this small retrospective study of survivors of Hodgkin Lymphoma, we noted a high prevalence (13%) of mild or moderate increases in pulmonary artery pressure. We were not able to identify treatment factors associated with elevated pulmonary artery pressure, possibly due to small sample size. Further investigation of this potentially serious late effect is warranted, as treatment of pulmonary hypertension relies on early diagnosis.

3. CARDIOVASCULAR SCREENING AND CUMULATIVE ANTHRACYCLINE DOSE DO NOT PREDICT CARDIAC DYSFUNCTION IN SURVIVORS OF CHILDHOOD CANCER Dava Szalda, MD; Anna T. Meadows, MD; Donna Pucci, MHK; Joseph Carver MD. *Abramson Cancer Center, University of Pennsylvania, Children's Hospital of Philadelphia, Philadelphia, PA, USA*

Background: Approximately 80% of childhood cancer patients are likely to survive for more than five years and most are cured. One of the most serious long term complications of treatment is cardiac dysfunction. Children's Oncology Group guidelines for screening of survivors prompted us to study cardiac function following treatment with anthracyclines in a cohort of adult survivors of childhood cancer. We related current cardiac status to previous therapy and previous screening echocardiograms.

Methods: Charts of patients attending the Transition Clinic of the LiveStrong Program at the Abramson Cancer Center were reviewed with attention to variables such as age, years since treatment, anthracycline dose and thoracic radiation. Screening results prior to transition were also recorded. At initial visit, survivors who had received any anthracycline with or without thoracic radiation (RT) were examined by an adult cardiologist. Comparisons were made between history, physical exam and findings on adult echocardiograms to patient and treatment specific variables.

Results: Patients (n=109) (mean age 30 years, mean 19.6 years since diagnosis) had been treated with doses of anthracycline ranging from 75 mg/m^2 to 500 mg/m^2 (mean 230 mg/m^2). RT had been given to 40 patients; 37 also had anthracyclines. There were five patients with documented cardiac dysfunction on adult echo. Of those all but one was documented to have symptoms (namely dyspnea on exertion) or an abnormal pediatric echo. The anthracycline doses in mg/m^2 patients received ranged from 150 to 280. There was no relation of an abnormal adult echo to the number of studies obtained during pediatric screening, such as Holter, stress test or symptoms such as palpitations or chest pain.

Conclusions: Our results suggest that cardiac dysfunction in adult survivors of pediatric cancer can be diagnosed by a thorough history, physical exam and review of pediatric echocardiograms. Testing in the absence of symptoms did not predict adult cardiac status up to 20 years from treatment. Late cardiotoxicity did not correlate with cumulative anthracycline doses. Cardiac follow up of adult survivors of childhood cancer should maximize patient outcome and cost effectiveness of screening. Survivors should recognize the value of follow-up. Adult practitioners should continue to study the cardiac status of childhood cancer survivors as they age.

4. THE USE OF LIPOSOMAL ANTHRACYCLINE ANALOGUES FOR CHILDHOOD MALIGNANCIES: A SYSTEMATIC REVIEW Elske Sieswerda, MD; Leontien C.M. Kremer, MD, PhD; Huib N. Caron, MD, PhD; Elvira C. van Dalen, MD, PhD. *Department of Pediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands*

Background: Currently, nearly 60% of children diagnosed with a malignancy receive anthracyclines as part of their treatment and are therefore at risk to develop anthracycline-induced cardiotoxicity. In an effort to prevent or reduce this cardiotoxicity, liposomal anthracyclines have been developed. They have been shown to decrease the risk of cardiotoxicity in adults with solid tumors while attaining similar anti-tumor efficacy compared to conventional anthracyclines.

Purpose of the study: We aimed to evaluate all available evidence on the benefits and harms of liposomal anthracyclines in childhood cancer patients.

Summarized description of project: We searched the databases of MEDLINE, EMBASE and CENTRAL as well as relevant reference lists and ongoing trial databases for studies reporting on the use of liposomal anthracyclines in childhood cancer patients. Two reviewers independently selected studies, extracted data on study characteristics and outcomes and performed quality-assessments of included studies.

Results: A total of 15 studies met our inclusion criteria. No randomized controlled trials were identified. Incidence of cardiotoxicity was evaluated in ten studies and ranged from 0% to 67%. The studies were heterogeneous and had methodological limitations. Almost all patients had a poor prognosis and had been treated extensively previously. Therefore, no conclusions could be made about risks of cardiotoxicity of liposomal anthracyclines alone. Similarly, no conclusions could be made about survival, anti-tumor efficacy and risks of other toxicities.

Conclusions: There is currently no evidence to support or discourage the use of liposomal anthracyclines in childhood cancer patients. There is an urgent need for well-designed randomized controlled studies that accurately evaluate if the benefits of liposomal anthracyclines found in adults also apply to children with cancer. The results of one ongoing randomized controlled trial and two other trials in children with acute myeloid leukemia are awaited and will contribute to the available evidence.

5. TREATMENT INCLUDING ANTHRACYCLINES VERSUS TREATMENT NOT INCLUDING ANTHRACYCLINES FOR CHILDHOOD CANCER: A COCHRANE SYSTEMATIC REVIEW Elvira C. van Dalen, MD, PhD; Martine F. Raphaël, MD; Huib N. Caron, MD, PhD; Leontien C.M. Kremer, MD, PhD. *Department of Pediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands; Department of Pediatric Hematology and Oncology, Wilhelmina Children's Hospital/University Medical Center of Utrecht, Utrecht, The Netherlands*

Background: One of the most important adverse effects of anthracyclines is cardiotoxicity. A well-informed decision on the use of anthracyclines in the treatment of childhood cancer should be based on the available evidence on both antitumor efficacy and cardiotoxicity. The objective of this systematic review was to compare antitumor efficacy of treatment including or not including anthracyclines in childhood cancer patients.

Methods: We searched the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE (all January 2007) for randomized controlled trials (RCTs) comparing treatment of childhood cancer with and without anthracyclines. In addition, reference lists, conference proceedings and ongoing-trial-databases were searched. Two reviewers independently performed study selection, quality assessment and data-extraction.

Results: We identified RCTs for acute lymphoblastic leukemia (ALL) (n=3), Wilms' tumor (n=1), rhabdomyosarcoma / undifferentiated sarcoma (n=1), Ewing's sarcoma (n=1), and non-Hodgkin lymphoma (NHL) (n=1). All studies had methodological limitations. For ALL no evidence of a significant difference in antitumor efficacy was identified in the meta-analyses, but in most individual studies there was a suggestion of better antitumor efficacy with anthracyclines. For both Wilms' tumor and Ewing's sarcoma a significant difference in survival in favor of anthracyclines was identified. For both rhabdomyosarcoma / undifferentiated sarcoma and NHL no difference in antitumor efficacy was identified.

Conclusions: At the moment no evidence from RCTs is available which underscores the use of anthracyclines in ALL. However, it should be noted that "no evidence of effect", as identified here, is not the same as "evidence of no effect". For Wilms' tumor, rhabdomyosarcoma/undifferentiated sarcoma, Ewing's sarcoma, and NHL only 1 RCT was available and therefore, no definitive conclusions can be made about the antitumor efficacy of treatment with or without anthracyclines in these tumors. For other childhood cancers no RCTs were identified. More high quality research is needed.

6. DIFFERENT DOSAGE SCHEDULES FOR REDUCING CARDIOTOXICITY IN CANCER PATIENTS RECEIVING ANTHRACYCLINE CHEMOTHERAPY: UPDATE OF A COCHRANE SYSTEMATIC REVIEW Elvira C. van Dalen, MD, PhD; Helena J.H. van der Pal, MD; Huib N. Caron, MD, PhD; Leontien C.M. Kremer, MD, PhD. *Department of Pediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands; Department of Medical Oncology, Academic Medical Center, Amsterdam, The Netherlands*

Background: The use of anthracycline chemotherapy is limited by the occurrence of cardiotoxicity.

Objective: To determine the cardiotoxicity of different anthracycline dosage schedules.

Methods: We searched CENTRAL (Cochrane Library, Issue 4, 2008), MEDLINE (1966–2008) and EMBASE (1980–2008) for randomized controlled trials (RCTs) comparing different anthracycline dosage schedules. We also searched reference lists of relevant articles, conference proceedings and ongoing-trial-databases.

Results: Seven RCTs addressed different infusion durations. The meta-analysis showed a significant decrease in clinical heart failure with an infusion duration of ≥6 hours as compared to a shorter duration (RR 0.27; 95% CI 0.09 to 0.81).

Two RCTs addressed a doxorubicin peak dose (defined as the maximal dose received in one week) of <60 mg/m^2 versus ≥60 mg/m^2, one RCT addressed a liposomal doxorubicin peak dose of 25 versus 50 mg/m^2 and one RCT addressed an epirubicin peak dose of 83 versus 110 mg/m^2. In none of these studies a significant difference in the occurrence of clinical heart failure was identified.

The majority of patients were adults with different solid tumors.

Conclusions: An infusion duration of ≥6 hours reduces the risk of clinical heart failure and it seems to reduce the risk of subclinical cardiac damage. Since there is only a small amount of data for children, different infusion durations should be further evaluated in children.

In patients treated with a doxorubicin peak dose of <60 mg/m^2 or ≥60 mg/m^2 no significant difference in the occurrence of clinical heart failure was identified. For the other identified peak doses only one RCT was available for each comparison, so no definitive conclusions can be made about the occurrence of cardiotoxicity. Before recommendations for the most optimal anthracycline peak dose can be given more high quality research is needed, both in children and adults.

7. SECOND MALIGNANT NEOPLASMS AFTER CHILDHOOD CANCER IN GERMANY - RESULTS FROM THE LONG-TERM FOLLOW-UP AT THE GERMAN CHILDHOOD CANCER REGISTRY P. Kaatsch, C. Spix, D. Grabow, M. Blettner. *German Childhood Cancer Registry (GCCR) at the Institute for Medical Biostatistics, Epidemiology and Informatics (IMBEI), University of Mainz, Germany*

Background: A cohort of long-term survivors has been established in the German Childhood Cancer Registry (GCCR). Within this cohort a nested case-control study was performed to investigate risk of second malignant neoplasms (SMN) associated with radio- and chemotherapy.

Methods: In Germany, 37,291 children younger than 15 years were diagnosed with cancer between 1980-2004. Until spring 2007, 8,896 children died. Overall, 629 patients with SMN were reported until 2007. A case-control study included patients with SMN until 2002. 328 children fulfilled the inclusion criteria for the case-control study, and 639 patients without SMN were randomly selected as controls. Detailed information on primary therapy was obtained from the clinics. Statistical analysis was performed using logistic regression analysis to estimate odds ratio (OR) and 95% confidence intervals (CI).

Results: The cumulative risk of all former childhood cancer patients by the end of 2007 to develop a SMN was 1.5% within 10 years after the primary cancer, and 2.0% within 15 years.

In the nested case-control study, the OR for SMN following any radiotherapy (adjusted for chemotherapy) is 2.1; (CI=1.8–3.3), following any chemotherapy (adjusted for radiotherapy) is 1.8; (CI:1.0–3.1).

The results of the case-control-study showed that SMN after solid tumours are associated with radiotherapy (adjusted OR=4.5; CI:2.5–8.0). Secondary acute myeloid leukaemia and myelodysplastic syndrome after any primary malignancy are associated with alkylating agents (OR=8.5; CI:0.97–74.8), asparaginase (OR=6.8; CI:2.3–20.6), and platinum derivatives (OR=4.5; CI:1.5–13.6).

Conclusion: Our study confirmed a clear association with risk of SMN with radiotherapy and chemotherapy. Detailed information on chemotherapy could be used to further distinguish the effect of different agents. However, numbers are yet too small for more specific comparisons.

8. SECOND TUMOURS IN PATIENTS TREATED FOR MALIGNANT NEOPLASMS IN CHILDHOOD I.P. Romashevskaya, MD; N.N. Savva, MD, PhD; M.V. Fridman, MD, PhD; A.A. Zborovskaya, MD, PhD; O.V. Aleinikova, MD, DSc. *The Republican Research Center for Pediatric Oncology and Hematology, Minsk, Belarus*

Background: To assess the epidemiology of second tumors (incidence, mortality and survival) in patients of Belarus received anti-cancer treatment in childhood (0–18 years old).

Methods: Population-based analysis was fulfilled using the data of Childhood Cancer Subregistry of Belarus for the period 1989-2007. Childhood population data were obtained in the Ministry of Statistics of Belarus. The methods recommended by IARC had been applied for analyses and interpretation.

Results: Totally, 5507 cases of cancer were registered in children and adolescents of Belarus in 1989–2007 y.y., 59 (1,07%) of them had second tumors: solid tumors—50/59 (85%), leukemia/lymphoma—9/59 (15%). Second tumors developed after treatment of leukemia/lymphoma in 39/59 (66%) and mainly after HD, after treatment of solid tumors in 20/59 (34%). Sex ratio m:f is 0,78. Median age at diagnosis of second tumor is 15 years old. 48/59 cases of second tumors were registered in children aged 0–19 y.o. Incidence of second tumors within 1989–2007 y.y. was 0.092 (0.066–0.118) per 100 000, mortality 0.027(0.012–0.047), 10-years overall survival 47%. 5-, 10-, 15-, and 19-years cumulative risks are 0.3, 1.51, 2.43 and 3.56. The main reasons of death were resistance of second tumor to the anticancer treatment and relapse/progression. 3 pts died because of third tumor.

Conclusions: New approaches are necessary for prophylactics and treatments of second tumors in children and adolescents as well as for distinguish of primary multiplies and therapy induced.

9. SECOND NEOPLASMS IN CHILDHOOD CANCER SURVIVORS IN BELARUS OVER THE PERIOD 1989–2006 A. Zborovskaya, N. Savva, I. Romashevskaya, M. Fridman. *Belarusian Research Center for Pediatric Oncology and Hematology, Belarusian Childhood Cancer Subregystry Minsk, Belarus*

Background: Existence of population cancer registry is an essential instrument of epidemiologic studies. The objective was to describe the pattern of second neoplasms in childhood cancer survivors on population level.

In Belarus Republic in years 1989–2006 there had been registered malignancies (group I–XII ICCC-3, 2005) in 5301 children. In 59 patients (1.1%) later the primary multiple and secondary neoplasm developed. Forty-eight (81.35%) out of 59 cases had developed in age group under 19 years. There had been predominance of leukemia and lymphomas in structure of primary tumors and brain tumors and thyroid cancer in second tumors group. Cumulative risk of second tumor development in dependency of type of primary tumor had been higher after treatment of Hodgkin disease (in 10 years, $p<0.001$) and ALL (in 15 years, $p<0.0001$), compared to other malignancies. We did not reveal evident difference in cumulative risk of development of certain type of second malignancy. One-year and five-year total

survival rate had been lower in patients with second malignancies, compared to population overall survival rate in primary malignancies. Main cause of death had been primary resistance of second tumor to the treatment and relapse/progression of second tumor, which emphasizes need in development of effective methods of treatment of secondary neoplasm, and new approaches in prevention, prediction and early detection of fatal disease.

10. SECOND MALIGNANT NEOPLASMS IN CHILDHOOD CANCER SURVIVORS: REPORT OF THREE RARE CASES M. Peretz-Nahum, MD; A. Ben Barak, MD; S. Postovsky MD; D. Harlev, MD; M. Weyl Ben Arush, MD. *Department of Pediatric Hematology Oncology, Meyer Children's Hospital, Rambam Health Care Campus, Haifa, Israel*

Background: The incidence of second malignant neoplasms (SMN) in survivors of pediatric malignancies ranges between 8–12% at 20 years. Common SMN include skin and thyroid neoplasms, bone and soft tissue sarcomas, lymphomas, acute myeloid leukemia, breast and brain tumors. We describe three uncommon cases of SMN in young adults.

Methods: The three uncommon SMN are: 1] post-radiation pulmonary synovial sarcoma in a Hodgkin lymphoma survivor; 2] contralateral renal cell carcinoma (RCC) in a Wilm's tumor survivor post chemo-radiotherapy; 3] abdominal desmoplastic small round cell tumor (DSCT) after chemotherapy for acute lymphoid leukemia (ALL). Age at diagnosis, histology, stage of disease and treatment modalities are outlined for both primary childhood cancer and SMN. A thorough literature review was performed to identify the type, occurrence and interval time from presentation of such SMN in survivors of Wilm's tumor and childhood ALL to resuming post-radiation soft tissue sarcoma (PRSTS) characteristics.

Results: Synovial sarcoma is a rare PRSTS, previously described in three cases; we report the fourth case in the literature. Increased SMN risk is well known after Wilm's tumor but RCC is not definitively listed as a late effect of therapy, despite the previously reported five cases of RCC in Wilm's tumor survivors and six cases of translocation RCC (TFE3/TFEB gene fusions) post-chemotherapy. We present another case of RCC in a Wilm's tumor survivor. DSCT, a very unusual SMN, has been described in survivors of adult testicular cancer or chronic leukemia and in survivors of pediatric brain glioma; we report the unique case of DSCT in a childhood ALL survivor.

Conclusion: Two rare and one unique cases of SMN in adult survivors of childhood cancer are described. The present cases along with the published data indicates the possibility of such an association that may lead in the future to re-evaluating long-term follow-up guidelines and primary therapeutic approach.

11. FOCAL NODULAR HYPERPLASIA OF THE LIVER FOLLOWING SOLID TUMORS IN CHILDHOOD Y. Goshen, MD; L. Kornreich, MD; J. Stein, MD; S. Ash, MD; I.J. Cohen, MBChB; M. Feinmesser, MD; I. Yaniv MD. *Departments of Hematology/Oncology and Imaging, Schneider Children's Medical Center of Israel, Pathology, Rabin Medical Center, Petach Tikva; Sackler Faculty of Medicine, Tel Aviv University, Israel*

Background: The detection of hepatic nodules during follow-up of survivors of solid tumors in childhood raises a diagnostic dilemma. Focal nodular hyperplasia (FNH) is an uncommon, benign tumor that must be differentiated from adenomas or late hepatic metastasis. The aim was to describe the clinical characteristics and the follow-up of FNH lesions.

Methods: We retrospectively analyzed patients, treated for pediatric solid tumors between January 1990 and December 2009, and performed abdominal imaging as part of the follow-up.

Results: Five survivors with asymptomatic FNH were detected, out of 450. All were female, median age at primary diagnosis was 6y (1.5–11), 2 had RMS, 1 germ cell tumor, 1 embryonal sarcoma of liver, 1 choroid plexus carcinoma. All received chemotherapy including alkylating agents, 2 underwent ABMT. Three received abdominal radiotherapy. Liver lesions were detected at median age of 21y (9–24). Two received oral contraceptive (OC), one for ovarian disorder. Abdominal ultrasound disclosed 3 to multiple nodular lesions. All underwent MRI; in 3/5 the radiological appearance was typical of FNH. Two underwent resection biopsy to exclude other diagnoses. During follow up lesions disappeared in one patient, and reduced in size in three others.

Discussion: The incidence of FNH is unknown as most cases are asymptomatic; the etiology is unknown but related to vascular damage including VOD associated with high dose chemotherapy. Two of our patients underwent ABMT but had no VOD. Imaging studies are not conclusive in about 30% of cases.

Conclusions: FNH of liver can be differentiated from other lesions by imaging; in questionable cases patients must have tissue diagnosis, close follow-up is recommended. Cancer in childhood, female gender, alkylating agents especially during BMT and OC may be regarded as risk factors.

12. OSTEOPOROSIS IN LONG TERM SURVIVORS OF CHILDHOOD CANCER Edit Bardi MD, PhD; Timea Bodo, MD; Laura Sándor, MD; Mariann Bende, MD; János Kappelmayer, MD, PhD, DSc; Csongor Kiss, MD, PhD, DSc. *Departments of Pediatric Hematology and Oncology; Clinical Biochemistry and Molecular Pathology, Medical and Health Science Center, University of Debrecen, Hungary*

Background: The aim of this study was to investigate osteoporosis in different cancer groups.

Methods: We enrolled 118 long term survivors (male: female=66:52, age±SD: 12±4 years), and 82 controls (male: female=38:44, age±SD: 12±2 years). Three subgroups of patients (pts) were analyzed: leukemia/lymphoma (LL) survivors (63 pts), Wilms tumor (WT) survivors (16 pts) and (other) solid tumor (ST) survivors (39 pts), as therapy intensity is different between these groups, but it is similar within the individual groups of patients. Serum osteocalcin, "crosslaps" (β-CTX), 25-OH-vitamin D, Calcium, Phosphate, Alkaline phosphatase (ALP), and plasma parathormone, calcitonin levels were determined according standard laboratory methods as well as the thyroid and sexual hormone levels. Bone mineral density parameters (Z score and BMD %) of the lumbar spine and femur were assessed by dual energy X-ray absorptiometry method.

Results: Significantly lower 25-OH-vitamin D (69±39 vs 82±23 nmol/L, p=0.08) and higher calcitonin levels (10.6±4 vs 7.4±1.6 ng/L, p<0.0001) could be measured in long term survivors than in controls. Only LL survivors had significantly lower 25-OH-vitamine D levels, than controls (64±36 vs 82±23 nmol/L), but calcitonin levels were significantly higher not only in LL but in WT, than in controls (11.3±4.3, 10.4±3.7 vs 7.4±1.6 ng/L, respectively). Values, indicating bone loss, like mean β-CTX values were significantly higher in ST (1.6±0.9 ug/L) than in LL (1.2±0.6 ug/L) as well as PTH levels (4.5±3.2 vs. 3.1±1.7 pmol/L). ALP, bone formation marker, was significantly lower in LL than in WT (499±217 vs. 725±382 U/L). Femur neck Z score values were significantly worse in ST than in LL (-1.9±1.47 vs -0.02±2.09).

Conclusion: Childhood cancer and its treatment profoundly affect bone homeostasis of long term childhood cancer survivors, most seriously ST survivors.

13. BONE MINERAL DENSITY IN CHILDHOOD CANCER SURVIVORS (CCS) Lynda Polgreen, Anna Petryk, Andrew C. Dietz, Wendy Leisenring, Pam Goodman, Anne Norris, Megan Hoffman, Daniel Mulrooney, Joanna Perkins, Lyn Steffen, Aaron Kelly, Alan Sinaiko, Antoinette Moran, Donald R. Dengel, K. Scott Baker, and Julia Steinberger. *Department of Pediatrics and Schools of Public Health and Kinesiology, University of Minnesota, Minneapolis, MN, USA; Fred Hutchinson Cancer Research Center, Seattle, WA, USA; Children's Hospitals and Clinics, Minneapolis, MN, USA*

Background: Decreased bone mineral density (BMD) has been reported in childhood cancer survivors (CCS). However, factors associated with low BMD in CCS are not well characterized.

Objective: To identify factors associated with low BMD (Z-score ≤-1) in CCS.

Methods: In a cross-sectional study of CCS. BMD was determined by dual-energy x-ray absorptiometry. All patients underwent growth hormone (GH) stimulation testing. Multivariable logistic regression was utilized to evaluate relations between anthropometrics, endocrine function, and treatment history with BMD, adjusted for bone age and gender.

Results: Of 284 CCS patients, 41 were excluded due to previous diagnosis of GH deficiency (GHD) and/or treatment with GH , leaving 243 subjects (54% males), median age 15.1 years (range 9.5–18.0 years), surviving 5.4–17.8 years after cancer diagnosis. 21% had GHD and 0.8% had gonadal failure. 21% had low lumbar spine (L2–L4) BMD and 6% had low total body less head (TBLH) BMD. Brain irradiation (yes vs. no; Odds ratio [OR] 3.8; 95% confidence interval [CI] [1.0, 15.6]), cumulative prednisone equivalent dose (≥ 6350 vs. 0 mg; OR 4.8; CI [1.7, 14.2]), lower lean body mass (LBM) Z-score (per standard deviation (SD); OR 1.8; CI [1.2, 3.0]), and GHD status (yes vs. no; OR 2.8; CI [1.1, 6.7]) were associated with low L2-L4 BMD (adjusted for height, Tanner stage, and age). Lower LBM Z-score (per SD; OR 4.5; CI [1.9, 12.5]) and increased time since diagnosis (>10 vs. 5-10 years; OR 3.8; CI [1.1, 14.3]) were associated with low TBLH BMD (adjusted for height).

Conclusions: In CCS, lower LBM, higher cumulative steroid exposure, history of brain irradiation, longer time since diagnosis, and GHD were associated with low BMD. LBM and GHD are the only modifiable risk factors for low BMD. Weight-bearing physical activities and early treatment of GHD to increase BMD are recommended in CCS.

14. MUSCULOSKELETAL SEQUELAE OF HIGH-RISK SOFT TISSUE SARCOMA OF CHILDREN TREATED WITH INTENSIVE CHEMOTHERAPY, SURGERY AND RADIATION THERAPY Anna Shvarova, MDsc; Nadeghda Ivanova; Galina Zajeva, MDsc; Natalya Koshechkina. *Departments of Childhood Bone and Soft Tissue Tumors, Polyclinic and Childhood Radiology, Institute of Pediatric Oncology and Hematology N.N. Blokhin Cancer Research Center Moscow, Russian Federation*

Survivors of childhood soft tissue sarcoma are at risk for long-term effects of disease and treatment. Recommendations for screening, prevention, and management of survivors are the aim of this study. 40 children and adolescents at the mean age of 9.9±4,0 years (17 males, 23 females) with synovial sarcoma and rhabdomyosarcoma were treated between 1999 and 2004 years. Histologically, 5 patients had the biphasic,12 had the monophasic, 2 patients had the poorly differentiated pattern SS, 6 had the embryonal

rhabdomyosarcoma and 15—alveolar rhabdomyosarcoma. The most often affected area was the area of the lower extremity—17 cases. According to the staging systems adopted, the size >5cm (TB) was reported in 30 cases. Twelve patients (non-staging) had relapse of disease. Thirteen patients had nodal involvement, and 11 had distant metastases.The general scheme of the treatment included: 8 courses of chemotherapy (used ifosfamide or cyclophosphamide, etoposide, carboplatin); the harvesting and preservation of the stem cells after the stimulation of the haemophoesis by G-CSF, the stage of the local control of the tumor consisting of the surgical ablation of the primary lesion (in 5 cases it was not available) and the radiotherapy of the initial tumor and metastasis left after the induction. 5-year disease-free survival was 66,1±11,3 %, overall 5-year survival, 75,6±10,6% for patients with SS, and 5-year disease-free survival was 29,1±12,0%, overall 5-year survival, 29,1±12,0% for patients with RMS. 18 patients are alive without disease at the present time, 6 survivors of RMS, 12 survivors of SS. The most common late effects we had observed were: muscular hypoplasia,in 14 cases, limb-length discrepancy, in 5 cases, poor joint movement, in 5 cases. Stump-prosthetic problems had experienced 3 girls (16, 5, 3 years old) and 1 boy (15 years old) after amputation.

15. MUSCULOSKELETAL SEQUELAE OF HIGH-RISK EWING SARCOMA OF CHILDREN TREATED WITH INTENSIVE CHEMOTHERAPY, SURGERY AND RADIATION THERAPY Anna Shvarova, MD; Nadeghda Ivanova; Galina Zajeva, MD; Natalya Koshechkina. *Departments of Childhood Bone and Soft Tissue Tumors, Polyclinic and Childhood Radiology, Institute of Pediatric Oncology and Hematology N.N. Blokhin Cancer Research Center Moscow, Russian Federation*

Background: Childhood Ewing's sarcoma family tumors survivors are known to be at risk for serious musculoskeletal late effects that may result in disability. Recommendations for screening, prevention, and management of survivors are the aim of this study.

Methods: 133 children and adolescents at the mean age of 10.99±3.56 years (55 males, 78 females) with Ewing sarcoma were treated between 1997 and 2004 years. The most often affected area was lower extremity, 32 cases, pelvis was affected in 32 cases, ribs, 27 cases. 42 patients had distant metastases. The general scheme of the treatment included: for local disease—10 courses of intensive chemotherapy (used vincristine, doxorubicin, cyclophosphamide, ifosfamide, etoposide); the stage of the local control of the tumor consisting of the limb salvage surgery (if it was available), and the radiotherapy of the initial tumor (35–57Gy) left after the induction; for children with initial metastasis—5 courses of intensive chemotherapy (used vincristine, doxorubicin, cyclophosphamide, ifosfamide, etoposide); the stage of the local control of the tumor consisting of the limb salvage surgery (if it was available), and the radiotherapy of the initial tumor and metastasis (35–57Gy) left after the induction; the harvesting and preservation of the stem cells, and high dose chemotherapy after the induction and RT. Thus, overall 5-year survival was 70.5±5,0% for patients with local disease, and 44.,0±8.3% for patients with metastases, 85 patients are alive without disease at the present time. The most common late effects we had observed were: muscular hypoplasia and osteopenia—in all cases, limb-length discrepancy in spite of usage of growing endoprosthesis—in 12 cases, scoliosis or deformation of chest wall—in 14 cases. Pathological fractures and slipped capitofemoral epiphysis were described in 7 and 1 cases, poor joint movement in 7 cases. Neurological disturbances were in 7 cases.

16. STRUCTURAL BONE DEFICITS AFTER BONE MARROW TRANSPLANTATION S. Mostoufi-Moab, MD; J.P. Ginsberg, MD; J. Shults, PhD; B.S. Zemel, PhD; R.M. Herskovitz, M.B. Leonard, MD. *Department of Pediatrics, Children's Hospital of Philadelphia, Department of Biostatistics and Epidemiology, University of Pennsylvania School of Medicine, Philadelphia, PA, USA*

Background: Children requiring bone marrow transplant (BMT) for childhood leukemia have multiple risk factors for impaired bone accrual. The long-term effects on volumetric bone mineral density (vBMD), bone structure, and muscle mass have not been established. The objective of this cross-sectional study was to assess musculoskeletal outcomes in children and young adult survivors after BMT using peripheral quantitative computed tomography (pQCT).

Methods: Tibia pQCT was performed in 29 BMT subjects (ages, 14.7±5.0 yrs) a median of 5 yrs (range 3–10) after BMT for childhood leukemia. pQCT outcomes were converted to sex-, race-, and age tibia length specific Z-scores based on reference data in over 650 controls.

Results: BMT survivors had significant deficits in trabecular vBMD (-1.1±-1.1; $p<0.001$) and, cortical stress strain index (SSI), a composite measure of bone geometry and strength (-0.4±0.8; $p=0.02$) Z-scores, compared with controls. The lower SSI was due to smaller endosteal and periosteal circumferences. Although BMI Z-scores did not differ between BMT survivors and controls, BMT survivors had significantly lower muscle (-0.50±1.5; $p=0.04$) and greater fat (0.6±1.3; $p<0.01$) mass Z-scores compared with controls. In addition, BMT survivors had significant growth impairment: height Z-scores averaged -1.1±1.3 and 31% were <3rd %ile for height relative to age and sex.

Conclusions: Substantial deficits in trabecular vBMD, cortical bone geometry, and muscle mass were observed in BMT survivors of childhood leukemia. Future studies are needed to determine fracture risk and to identify therapies to improve bone accrual in survivors of childhood leukemia after BMT.

17. VITAMIN D LEVELS AT DIAGNOSIS AND BONE LOSS DURING INDUCTION THERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA: PRELIMINARY RESULTS IN PRE-ADOLESCENTS AND TEENAGERS Anna Butturini, MD; Steve Mittelman, MD; Vincente Gilsanz, MD; David Freyer, DO, MS; Nancy Hart, MS, RN; Diandra Nuno, BS. *Childrens Hospital Los Angeles, Los Angeles, CA, USA*

Background: To assess the relationship between obesity, vitamin D levels and bone changes during the initial phases of the therapy for ALL.

Methods: Physical exam, laboratory tests (serum vitamin 25(OH)D, PTH, Alkaline Phosphatase and Calcium) and the DEXA scans were performed at diagnosis and at the end of Induction therapy per high-risk COG protocols (including Prednisone, 60 mg/m^2 for 28 days);

Results and Conclusions: Ten patients aged 11 to 19 years were enrolled: five were obese (BMI ≥95th percentile) and five lean (BMI 15th to 85th percentile). Seven were male and three female; two were Caucasian, two American-Asians, and six Hispanics; all but one were at the completion of their sexual development (Tanner stage IV or V). At diagnosis one patient had vitamin D sufficiency, while 9 were vitamin D deficient (serun vitamin 25(OH)D median 13, range 6–27 ng/ml): vitamin D levels correlated with the Fat-to-Lean ratio by DEXA (p=0.02) and, as a trend, with the bone density also by DEXA (p=0.1). PTH was low or normal (<70 pg/ml) in eight patients and increased in two (132 and135 pg/ml). By the end of induction, vitamin D levels and bone density decreased in all the patients, paralleling an increase in body fat and in serum PTH.

These data indicate that serum vitamin D deficit is almost universal at diagnosis of ALL: such deficit correlates with the amount of body fat and with the initial bone density by DEXA. The biological implications of these findings are unknown. Also our study shows the induction therapy causes further bone loss. Whether the initial changes predict the probability of long-term bone damage and whether they can be reversed by therapy with Vitamin D is unknown.

18. SIGNIFICANT 25-HYDROXYVITAMIN D DEFICIENCY IN PEDIATRIC ALL SURVIVORS: TREATMENT WITH CONVENTIONAL CHEMOTHERAPY COMPARED WITH ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT Jill H. Simmons, MD; Eric J. Chow, MD MPH; Elizabeth Koehler, MS; Adam Esbenshade, MD; Leslie-Ann Smith, BS; Debra Friedman, MD, MS. *Department of Pediatrics, Vanderbilt University School of Medicine and the Monroe Carell Jr. Children's Hospital at Vanderbilt, and Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; Fred Hutchinson Cancer Research Center and Seattle Children's Hospital, Seattle, WA, USA*

Background: There have been limited studies on the prevalence of 25-hydroxyvitamin D deficiency in survivors of childhood and adolescent ALL, and no studies comparing the prevalence of 25-hydroxyvitamin D abnormalities in subjects who received conventional chemotherapy versus those treated with allogeneic hematopoietic cell transplantation (HCT).

Methods: We evaluated 80 pediatric ALL survivors (53 chemotherapy-treated and 27 HCT-treated) to determine the prevalence of and risk factors for 25-hydroxyvitamin D insufficiency and deficiency. All patients had completed therapy and/or received their HCT at least 11 months earlier and were off chronic graft-versus-host disease medications at time of evaluation.

Results: There were no differences in serum 25-hydroxyvitamin D levels between ALL survivors treated with conventional chemotherapy and those treated with HCT [median 26 (21–33.2) vs. 25 (21–32.5) ng/ml, p=0.9]. Fifty-three percent of pediatric ALL survivors were 25-hydroxyvitamin D insufficient (15–29 ng/ml), and 14% were deficient (≤15 ng/ml). Only 28% of conventional chemotherapy-treated ALL survivors and 7% of HCT-treated ALL survivors met RDA for dietary vitamin D intake (p=0.03). Predictors of normal serum 25-hydroxyvitamin D levels included younger age, higher reported dietary vitamin D intake, and increased ambient ultraviolet light. Gender, race, time since treatment completion, and history of chronic graft-versus-host disease were not predictive of serum 25-hydroxyvitamin D levels.

Conclusions: The prevalence of vitamin D deficiency and insufficiency in ALL survivors was similar to that of the general pediatric population in the United States, with few survivors meeting RDA requirements. There were no differences in serum 25-hydroxyvitamin D status between those treated with conventional chemotherapy versus HCT. Given the beneficial effects of 25-hydroxyvitamin D on bone and general health, further studies are needed to develop dietary and behavioral interventions to improve the vitamin D status of ALL survivors.

19. ALLELIC VARIATION IN THE METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) AND METHIONINE SYNTHASE REDUCTASE (MTRR) GENES DETERMINES IMPAIRMENT OF BONE MINERAL DENSITY IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA M.L. te Winkel, MD; S.M.P.F. de Muinck Keizer-Schrama, MD, PhD; R. de Jonge, MD, PhD; R.D. van Beek, MD; W.C.J. Hop, MD, PhD; R. Pieters, Prof; M.M. van den Heuvel-Eibrink, MD, PhD. *Departments of Pediatric Oncology/Hematology and Pediatric Endocrinology, Erasmus MC–Sophia Children's Hospital; Department of Biostatistics, Erasmus MC–University Medical Center, Rotterdam, The Netherlands*

Background: Suboptimal bone formation may interfere with achievement of optimal peak bone mass. Therefore, concern exists about both short-term and long-term effects on bone mineral density (BMD) in children treated for acute lymphoblastic leukemia (ALL). This study aims to identify folate-metabolism-related genetic risk factors for low BMD during and after pediatric ALL treatment.

Methods: We investigated the influence of methylenetetrahydrofolate reductase (MTHFR 677C>T and 1298A>C) and methionine synthase reductase (MTRR 66A>G) single nucleotide polymorphisms (SNPs) on BMD of the total body (BMD-TB) and lumbar spine (BMD-LS) in 83 patients. Moreover, homocysteine, folate and vitamin B12 were determined. BMD was measured repeatedly using dual-energy x-ray absorptiometry in patients ≥4 years (n=68).

Results: Carriers of the MTHFR 677 T-allele showed a lower baseline BMD-TB than non-carriers (-0.38SDS vs. +0.55SDS, p=0.01) and BMD-TB remained lower during and after treatment. MTHFR 677C>T did not influence treatment-related loss of BMD-TB (p=0.39). The MTRR 66 G-allele carriers showed a trend towards a lower BMD-TB compared with non-carriers. Combining these two SNPs, patients carrying ≥2 risk alleles had a significantly lower BMD-TB (-1.40SDS) than patients with one (-0.80SDS) or no risk alleles (-0.31SDS). Although carriers of the MTHFR 1298A>C had higher homocysteine levels, this SNP was not related to BMD-TB. BMD-LS of carriers was similar to that of non-carriers of the three investigated SNPs.

Conclusion: MTHFR 677C>T and MTRR 66A>G SNPs were identified as determinants of impaired BMD-TB in children treated for ALL. We did not establish that effects of these genetic risk factors on BMD were carried out by differences in homocysteine levels. These findings may in the future be used to develop a prediction model for low BMD in pediatric ALL patients and survivors.

20. NEUROCOGNITIVE OUTCOMES IN ADULT SURVIVORS OF CHILDHOOD HODGKIN LYMPHOMA Neelam Jain, PhD; Kevin R. Krull, PhD; D. Kumar Srivastava, PhD; Brannon Morris, MD; Monika Metzger, MD; Kathleen J. Helton, MD; Leslie L. Robison, PhD; Melissa M. Hudson, MD. *Departments of Epidemiology and Cancer Control, Biostatistics, Oncology, and Radiological Sciences, St. Jude Children's Research Hospital, Memphis, TN, USA*

Background: Adult survivors of Hodgkin lymphoma (HL) diagnosed in childhood are at increased risk for cardiac morbidity as a consequence of previous treatment. Cardiovascular morbidity in non-cancer populations is associated with increased rates of neurocognitive deficits in attention, executive function, and memory.

Methods: Forty-eight adult survivors of childhood HL were randomly selected from a large cohort of childhood cancer survivors (≥18 yrs of age and >10 yrs post-diagnosis) recruited for participation in the St. Jude Lifetime Cohort Study. Treatment included high-dose chest radiation (≥30 Gy) in Cohort 1 (n=24) and anthracycline chemotherapy and chest radiation (any dose) in Cohort 2 (n=24). All survivors completed standardized neurocognitive, cardiac (echocardiogram and electrocardiogram), and brain magnetic resonance imaging examinations during a single visit. Cohorts 1 and 2 were similar in mean age and time since diagnosis (Cohort 1: age=43.5 yrs., range 37.4-52.4, time since diagnosis=29.1 yrs., range 21.8-27.3; Cohort 2: age=40.1 yrs., range 37-46.7, time since diagnosis=23.8 yrs., range 18.4-33.8). Compared to age-adjusted national normative values, significant differences in performance were observed on measures of verbal IQ ($p<.01$), cognitive processing speed ($p<.01$), verbal memory ($p<.05$), sustained attention ($p<.01$), and fine motor speed ($p<.01$). Between groups comparisons revealed significantly lower performance in Cohort 1 on measures of focused attention, sustained attention, cognitive processing speed, and fine motor speed, and lower performance in Cohort 2 on measures of short and long-term verbal memory (all comparisons $p<.05$). Approximately 54% of the sample demonstrated evidence of cardiac complications. Neuroimaging abnormalities (e.g., cerebral volume loss and white matter leukoencephalopathy) were significantly associated with measures of processing speed ($p<.01$) and fine motor speed ($p<.01$). HL survivors demonstrate increased rates of brain impairment, reflected through neurocognitive assessment and neuroimaging studies. Given the sample size, these findings should be interpreted with caution, but do support the need for larger studies in this population.

21. NEUROPSYCHOLOGICAL DEFICITS IN A PEDIATRIC CANCER SURVIVOR CLINIC: IMPLICATIONS FOR SCREENING OF ATTENTION AND EXECUTIVE FUNCTIONING Katherine S Spencer, MA; Laura A Greve, PsyD; Lillian R Meacham, MD; Ann C Mertens, PhD; Karen Wasilewski-Masker, MD, MSc. *Emory School of Medicine, Aflac Cancer Center at Children's Healthcare of Atlanta, Atlanta, GA, USA*

Background: Identification of neuropsychological (NP) impairment in pediatric cancer survivors is important due to the potential negative impact on academic, psychological, and vocational functioning. We describe specific NP complications detected in a cancer survivor program (CSP) with comprehensive NP testing.

Methods: The first 519 patients seen in the Aflac CSP (excluding brain tumor patients) were assessed for NP problems. A previous analysis revealed 216 (41.6%) of these 519 patients evidenced broadly defined NP problems. 81 (37.5%) patients received a comprehensive NP battery. NP testing results and treatment variables were abstracted from the medical records.

Results: The 81 patients were 55.6% male and 66% Caucasian. Cancer diagnoses included leukemia (72.8%), lymphoma (11.1%), sarcomas (9.9%), neuroblastoma (4.9%), and renal tumors (1.2%). Children were diagnosed at a mean age of 4.1 years (range 0–12 years) and NP evaluations were at a mean age of 10.6 years (range 3–17 years). Treatment exposures with known NP effects in the 81 patients included high-dose methotrexate (6.2%), high-dose cytarabine (3.7%), intrathecal therapy (IT; 77.8%), total body irradiation (TBI; 35.8%), and cranial radiation (24.7%). Patients often received more than one treatment with NP effects. NP testing revealed the

following deficits: academic achievement (63%), attention (59%), executive functioning (48%), visual-spatial (40.7%), memory (35.8%), reading/writing (34.6%), math (32.1%), fine motor (32.1%), sensorimotor (17.3%), speech/language (17.3%), processing speed (16%), and intellectual functioning (13.6%). In univariate analysis, the only significant association was between executive function deficits and TBI exposure (OR 3.35, p< .05).

Conclusions: The high frequency of attention and executive functioning deficits is noteworthy, due to risk of resultant educational, vocational, and financial problems. The significant association between TBI exposure and NP functioning is consistent with the literature. With the availability of interventions including cognitive rehabilitation, behavioral modification, and psychopharmacological treatments, early identification of attention and executive functioning may enhance survivor outcomes.

22. LEARNING DIFFICULTIES OF CHILDREN AND YOUNG ADULTS FOLLOWING CANCER TREATMENT Diane Puccetti MD; Jens Eichoff, PhD; Stephanie Farrell, PhD; Kristin Millin, MD; Teresa Pellino, PhD, RN; Amy Plumb, MD; Peggy Possin, RN; Gary Williams, MD; Joel Wish, PhD. *American Family Children's Hospital, University of Wisconsin Hospital and Clinics, Madison, WI, US; Department of Pediatrics, University of Wisconsin, Madison, WI, USA; Colorado State University, Department of Statistics, Fort Collins, CO, USA*

Background: The purposes of the study were twofold: 1) to identify the prevalence of learning difficulties endorsed by parents/caretakers of children (aged 6 to 17 years) and by young adults (aged 18 to 25 years) who have been treated for childhood cancer at our cancer center and 2) to compare the incidence of endorsed learning difficulties of children/young adults who have been treated for childhood cancer to a control group of children/young adults who have not had treatment for childhood cancer.

Methods: Two groups were recruited: one who had cancer treatment and a control group who did not have cancer treatment and had no chronic medical illness. Control patients were matched by age and gender to the characteristics of the cancer group. A letter of information, consent, and survey were sent to parents of patients age 6 to 17 years and to patients age 18 and over. A medical record audit was done for the cancer group to determine what cancer treatments were received.

Results and conclusions: Surveys were returned from 312 subjects, 159 from the cancer group and 153 from the control group. Seventy-nine percent of the cancer group was above the threshold score for learning difficulties compared to 61% of the control group. A factor analysis was performed and revealed 6 subscales. The cancer group had higher scores than the control group on four of the subscales: learning skills, verbal skills, attention, and school/solving. Scores were similar for the activity and energy subscales. As in previous studies, our population of cancer survivors has a high incidence of learning difficulties. Implications for clinical screening and support will be discussed.

23. MOTOR PERFORMANCE FOLLOWING CHEMOTHERAPY FOR CHILDHOOD CANCER A. Hartman, PhD; C. van den Bos, MD, PhD; N. van Dartel; T. Stijnen, PhD; R. Pieters, MD, PhD. *Department of Pediatric Oncology/Hematology, Erasmus MC Sophia Children's Hospital, Rotterdam, The Netherlands; Academic Medical Center/Emma Children's Hospital, Amsterdam The Netherlands; Physiotherapy Practice, Bennekom, The Netherlands; Department of Medical Statistics and Bioinformatics, Leiden University Medical Center Leiden, The Netherlands*

Objectives: The aim of the study was to determine the extent of long-term motor problems and writing difficulties in children with acute lymphoblastic leukaemia (ALL), Wilms' tumor (WT), B non-Hodgkin lymphoma (B-NHL) and malignant mesenchymal tumors (MMT) and to investigate whether these were related to the use of vincristine.

Methods: In 127 children who completed vincristine containing chemotherapy at least one year earlier, aged 4–12 years, motor performance was measured with the Movement Assessment Battery for Children (movement-ABC). Handwriting of survivors and matched controls was assessed with the Concise Assessment Scale for Children's Handwriting. Muscle strength was measured with a hand-held dynamometer and passive ankle dorsiflexion with a goniometer; results were compared to healthy controls.

Results: The movement-ABC scores of the total group were significantly lower than age-related norm values ($p<0.001$). There were no differences in scores between children with ALL, WT, B-NHL and MMT, or between children who had received low (0–20 mg/m^2) intermediate (20–40 mg/m^2) or high (>40 mg/m^2) cumulative doses of vincristine. No significant difference in writing speed or in quality of writing scores was found. Strength was reduced in ankle dorsiflexors bilaterally ($p<0.001$), wrist dorsiflexors on the non-dominant side ($p< 0.001$) and pinch grip bilaterally ($p=0.01$). Passive ankle dorsiflexion was significantly reduced bilaterally ($p<0.01$). Movement-ABC percentile score was affected by pinch grip strength on the non-dominant ($p<0.004$), and dominant side ($p=0.024$) but not by strength of other muscle groups or by passive ankle dorsiflexion.

Conclusions: Motor performance was impaired in all patient groups, but was not related to cumulative vincristine dose. No long-term problems in speed or quality of writing were found. Peripheral muscle strength and passive ankle dorsiflexion were reduced. However, neither decreased muscle strength nor reduced ankle dorsiflexion could completely explain the reduction in scores on the movement-ABC.

24. CEREBROVASCULAR HEMODYNAMICS IN PEDIATRIC BRAIN TUMOR (BT) SURVIVORS RECEIVING DONEPEZIL S.M. Castellino; J.A. Toozel; K. McMullen; B. Hildebrand, S.K. Parsons, C. Tegeler. *Wake Forest University Health Sciences, Departments of Pediatrics, Public Health Sciences, Radiation Oncology and Neurology, Winston-Salem, NC, USA; Tufts University School of Medicine and Tufts Medical Center, Boston, MA, USA; New Health Sciences Inc (NHSi), Bethesda, MD, USA*

Background: Pediatric brain tumor (BT) survivors who received radiation therapy are at risk for progressive neurocognitive dysfunction and late cerebrovascular events. Although demyelination and reduced white matter volume has been associated with neurocognitive dysfunction, less is known about the role of cerebrovascular hemodynamics in late sequelae in this population. We explored the application of transcranial doppler (TCD) with Hemodynamic Vascular Analysis (HVA™, NHSi) in a childhood BT population enrolled on a pilot trial of the acetylcholinesterase inhibitor, donepezil.

Methods: TCD/HVA™ was performed concurrent with a battery of neuropsychological evaluations at baseline, week 12 and 24 on drug, and following washout in pediatric BT survivors. HVA™ employs a relationship of vectors to estimate flow index (velocity/resistance), pressure index (log of force of flow/resistance), and compliance index (log of force of flow/velocity) in 18 cerebrovascular segments of the circle of Willis. Mixed model analysis was used to evaluate cerebrovascular index changes on and off donepezil therapy.

Results: Donepezil was initiated in 12 children (median age 12.3 yrs) at a median of 5.8 years (range 2–15.2) following cranial radiation for a primary BT. The majority of participants were survivors of medulloblastoma (n=8); the median cumulative radiation dose was 55.8 Gy (range 50.5–60). Although baseline intelligence quotient, estimated by the Peabody Picture Vocabulary Test, was 87.5 (range 61–117), all participants reported some neurocognitive impairment. Significant changes were noted on HVA™ in the posterior circulation. Donepezil treatment was associated with a significant decrease in the flow index (p=0.03), and an increase in the compliance index (p=0.05) in the posterior circulating artery. The pressure index in the basilar artery was significantly elevated in at week 24 on drug (p=0.005).

Conclusions: TCD/HVA™ is a feasible tool, and may be a novel biomarker in assessing radiation vasculopathy and pharmacologic interventions targeted to such in long term survivors.

25. ANNUAL INCREASE IN BODY MASS INDEX IN ADULT CHILDHOOD CANCER SURVIVORS IS ASSOCIATED WITH ADMINISTERED TREATMENT C.A.J. Brouwer MD, PhD; J.M. Vonk, PhD; W.V. Dolsma, MD, PhD; N. Zwart, Bc; W.J.E. Tissing, MD, PhD; H.L. Hooimeijer, MD; J.A. Gietema, MD, PhD; A. Postma, MD, PhD. *Department of Pediatrics, Division of Pediatric Oncology; Departments of Epidemiology, Radiation Oncology, and Medical Oncology, University Medical Center Groningen and University of Groningen, The Netherlands*

Background: To evaluate body mass index (BMI) and annual BMI increase in 377 adult childhood cancer survivors (CCS) after treatment with anthracyclines, platinum, and/or radiotherapy.

Methods: BMI (weight/height^2) was calculated consecutively from diagnosis until final height (FH). BMI <18.5 kg/m^2 was considered underweight, BMI ≥25 kg/m^2 overweight, BMI ≥30 kg/m^2 obesity. The prevalence of underweight and overweight/obesity at FH was compared with age-matched controls. The association between BMI at FH and treatment was assessed by multivariate logistic regression. Additionally the annual BMI increase during follow-up after treatment was assessed by multilevel analysis. Analyses were adjusted for age and underweight/overweight at diagnosis and age at FH.

Results: The prevalence of overweight at FH did not differ between CCS and controls, while underweight was more prevalent in CCS (14% vs. 4%, p<0.001). Overweight at FH was associated with cranial/craniospinal radiotherapy (CRT) (OR 2.23, 95% CI 1.17–4.26) and underweight at FH with anthracyclines >300 mg/m^2 (OR 2.84, 95% CI 1.33–6.06). In the CCS, annual BMI increase was +0.47 (0.34–0.60) kg/m^2/year. In CCS with CRT ≥30 Gy, annual BMI increase was greater compared with those with less or no CRT (+0.15 (0.04-0.25) kg/m^2/year, p=0.008). A higher cumulative anthracycline dose was associated with a smaller annual BMI increase [-0.03 (-0.05–-0.0005)] kg/m^2/year per 100 mg/m^2, p=0.046).

Conclusions: In a selected population of adult CCS, a greater annual BMI increase is observed in those who received high-dose CRT resulting in a higher prevalence of overweight at FH in CRT-treated survivors. A smaller annual BMI increase is associated with cumulative dose of anthracyclines, resulting in more underweight at FH in anthracycline-treated survivors.

26. TIME COURSE OF WEIGHT CHANGE IN SURVIVORS OF CHILDHOOD CANCERS Maheen Hassan, Lilibeth Torno, MD. *University of California, Irvine, Irvine, CA, USA; Children's Hospital of Orange County (CHOC), Orange, CA, USA*

Background: To evaluate the prevalence of abnormal weight in a cohort of pediatric cancer survivors, identify in which time frame changes in weight occur, and identify contributing clinical and treatment variables.

Methods: The charts of 255 cancer survivors from the Long-Term Follow-up Clinic at CHOC Cancer Institute were reviewed. The heights and weights of these patients were recorded at diagnosis, end of treatment and most recent follow up appointment. Patients were placed in weight categories based on their Basal Metabolic Index (BMI) if over the age of 20 or BMI percentile if younger.

Results: Survivors of ALL were more likely to be overweight or obese (OR=2.4; 95% CI 1.3 to 4.5 for females and OR 1.7; 95% CI 1.0 to 2.9 for males). Survivors at increased risk for being obese were female survivors of germ cell tumors (OR 5.1; 95% CI 1.04 to 25.4), female survivors of other leukemias (OR 4.1; 95% CI 1.1 to 15.3), and male survivors of brain tumors (OR 3.3; 95% CI 1.4 to 7.6). Young age at diagnosis (<10 years) among males and overweight/obesity at diagnosis were significant predictors of overweight/obesity at last assessment.

Survivors of ALL had a significantly higher mean BMI percentile at the end of therapy than at diagnosis. Alternatively, female survivors of germ cell tumors and male survivors of brain tumors had a significant increase in BMI percentile between end of treatment and follow up visit regardless of cranial irradiation.

Conclusion: Patients with ALL had an increased risk of being obese at follow up and showed early weight gain, between diagnosis and end of treatment. Close monitoring during treatment may allow early intervention. Females with germ cell tumors and males with brain tumors were also at increased risk for obesity though their weight gain occurred after treatment ended. Age at cancer diagnosis and BMI weight category at diagnosis were significant influences, while radiation, chemotherapy and BMT were not.

27. BODY MASS INDEX (BMI) CHANGES OVER THE COURSE OF TREATMENT OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)
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Background: Obesity is reported in excess among survivors of pediatric ALL. This study examines the trajectory of body mass index (BMI) over the course of therapy to identify optimal timing for a preventive intervention.

Methods: In a retrospective cohort study of all patients (ages 1–21 years) treated for ALL at Vanderbilt Children's Hospital between 2000–2008 (n=188), prevalence, severity, and risk factors for obesity were assessed along the treatment continuum.

Results and conclusions: At the start of therapy, 36% of patients were overweight (>85th percentile) and 19% were obese (>95th percentile). BMI increased from induction to consolidation with return to baseline by the start of delayed intensification. This was followed by a steady increase in median BMI over the early part of maintenance therapy, which persisted to the end of therapy. At maintenance course 8, 54% were overweight and 29% were obese, while at end of therapy, 49% were overweight and 21% were obese. A mixed effect model was used to assess risk factors for increased BMI during maintenance. BMI z-score increased by 0.079 for every 100 days in maintenance ($p<0.001$); increased baseline BMI z-score was also a predictor for increased BMI z-score ($p<0.001$). Earlier age at diagnosis ($p=0.03$) and treatment with cranial radiotherapy ($p=0.007$) were predictors of lower BMI z-score. Total glucocorticoid dose, sex, and need for supplemental feeds were not significant predictors. In a subgroup analysis (n = 143), average parental BMI did not predict increased BMI during maintenance therapy, but correlated with patient's BMI at induction (Spearman $\rho=0.31$ $p=0.005$). The maintenance phase of therapy may be an ideal time for a preventive intervention to limit increases in BMI and associated potential adverse long term health effects.

28. BODY MASS INDEX IN ADULT SURVIVORS OF CHILDHOOD CANCER COMPARED TO THE GENERAL POPULATION– A REPORT FROM THE SWISS CHILDHOOD CANCER SURVIVOR STUDY
Corina S. Rüegg, MSc; Gisela Michel, PhD; Nicolas X. von der Weid, MD; Cornelia E. Rebholz, MSc; Michael Paulussen, MD; Pierluigi Brazzola, MD; Marie-Pierre F. Strippoli, MSc; Claudia E. Kuehni, MD, MSc. For the Swiss Pediatric Oncology Group (SPOG). *Institute of Social- and Preventive Medicine (ISPM), University of Bern, Switzerland; Pediatric Hematology/Oncology Unit, Children's University Hospital, University of Lausanne, Switzerland; Paediatric Oncology/Haematology, University Children's Hospital Basel (UKBB), Switzerland; Ospedale Regionale di Bellinzona e Valli, Bellinzona, Switzerland*

Background: We assessed whether body mass index (BMI) and risk factors for overweight differed between childhood cancer survivors and the general population.

Methods: In the Swiss Childhood Cancer Survivor Study (SCCSS) a detailed questionnaire was sent in 2008 to all adult survivors (≥20 years) registered in the Swiss Childhood Cancer Registry (SCCR), diagnosed 1976–2003 at an age of <16 years. BMI was calculated from self reported height and weight and categorized as underweight (<18 kg/m^2), normal (18–24.9), overweight (25–29.9) and obese (≥30 kg/m^2). We compared BMI of survivors with age and sex standardized data from representative controls (Swiss Health Survey 2007). Differences in predictors of overweight (BMI≥25) between survivors and controls were assessed in a logistic regression model including interaction terms.

Results: The sample included 1026 survivors and 5533 controls (response rates 75% and 66% respectively). Among cancer survivors, 3.7% (n=38) were underweight, 68.1% (699) normal, 21.5% (221) overweight and 6.6% (68) obese. Age and sex standardized proportions for the normal population were 2.8% (n=155), 73.2% (4048), 19.4% (1072) and 4.7% (258) respectively (p=0.003).

Risk factors for overweight in the combined model were: being survivor (OR=1.8, $p<0.001$), male sex (OR=2.8, $p<0.001$), age ≥30 (OR=1.6, $p<0.001$), medium (OR=1.5, $p<0.001$) and low (OR=2.2, $p<0.001$) education, being married (OR=1.5, $p<0.001$), no daily

walking (OR=1.3, p<0.001) and no sports (OR=1.3, p<0.001). No association was found with nationality and with having children. Gender differences were more pronounced in controls (p for interaction =0.013), while other risk factors had comparable effects in both groups.

Conclusions: Childhood cancer survivors in Switzerland had an increased risk of being underweight, overweight or obese compared to the general population, despite comparable socio-demographic risk factors. Further research should identify causes for the excess risk with the goal of developing prevention strategies.

29. A CROSS-SECTIONAL STUDY OF OVERWEIGHT IN PEDIATRIC SURVIVORS OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) Erin Love, RD; Jane Schneiderman, MSc; Sylvia Lee, BSc; Mary Barron, MSc, RD; Elena Tsangaris; Stacey L. Urbach, MD, MPH; Patricia Staneland, RN, BScN; Mark L. Greenberg, MB, ChB; Paul C. Nathan MD, MSc. *Department of Clinical Dietetics; Department of Physiology and Experimental Medicine; Divisions of Hematology/Oncology and Endocrinology, Department of Pediatrics, The Hospital for Sick Children, Toronto, ON, Canada*

Background: Survivors of childhood ALL are at increased risk for obesity which can lead to long-term morbidity. This cross-sectional study examined the relationship between body mass index (BMI; kg/m^2) and demographic and lifestyle factors in a cohort of ALL survivors followed in the late effects clinic at The Hospital for Sick Children.

Description: We enrolled consecutive survivors of ALL (>2 years off therapy) who attended the clinic over a one year period. BMI at diagnosis and end-therapy were extracted from hospital charts, and current BMI was measured. Survivors were classified as overweight/obese (BMI for age ≥85%ile) or normal/underweight (BMI for age <85%ile). We assessed the relationship between current BMI and caloric intake (two 24-hour food recalls), physical activity (Habitual Activity Estimation Scale questionnaire), and sedentary behavior (2004 Canadian Community Health Survey).

Results: 102/157 (65%) eligible survivors consented to enrollment. Median age was 14.3 years (range 8.4–18.6) and median time from end of treatment 7.4 years (range 2.5–13.1). 8/102 patients (8%) received cranial radiation. The proportion of overweight/obese patients was 21%, 45%, and 35% at diagnosis, end-therapy, and current assessment respectively. Gender, age at diagnosis, time since therapy, socioeconomic status, and being overweight/obese at diagnosis were not significantly associated with being overweight/obese at current assessment. The two groups reported similar levels of physical activity and sedentary behavior. The overweight/obese group reported consuming less calories (delta 373kcal, p=0.017), fat (delta 17g, p=0.04), and carbohydrates (delta 45g, p=0.02).

Conclusion: Many children with ALL gain weight during therapy and fail to return to normal weight after treatment concludes. Current lifestyle factors do not appear to explain the difference between normal and overweight survivors, although underreporting of dietary intake by overweight/obese survivors may have occurred. Clinicians should focus on ways to minimize weight gain during therapy rather than waiting for treatment to conclude.

30. ADIPOSITY IN BRAZILIAN SURVIVORS OF CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA: A WELL-KNOWN EVENT REVISITED Adriana Aparecida Siviero-Miachon, MD; Maria Lucia de Martino Lee, MD; Monica dos Santos Cypriano, MD; Solange Andreoni, PhD; Bruno Geloneze, MD, PhD; Henrique Manoel Lederman, MD, PhD; Gil Guerra-Junior, MD, PhD; Angela Maria Spinola-Castro, MD, PhD. *Division of Pediatric Endocrinology, Department of Pediatrics, Federal University of Sao Paulo–UNIFESP/EPM, Brazil; Pediatric Oncology Institute–IOP/GRAACC, Department of Pediatrics, UNIFESP/EPM, Brazil; Division of Biostatistics, Department of Preventive Medicine, UNIFESP/EPM, Brazil; Division of Endocrinology, Laboratory of Investigation on Metabolism and Diabetes–LIMED, Department of Medicine, Faculty of Medical Sciences, University of Campinas–UNICAMP, Brazil; Division of Pediatric Endocrinology, Department of Pediatrics, Faculty of Medical Sciences, UNICAMP, Brazil*

Purpose: To analyse the effect of sex and cranial irradiation on adiposity in Brazilian survivors of childhood Acute Lymphocytic Leukemia.

Methods: Fifty six survivors, both sexes, off treatment, divided into irradiated (n=25/56; 44,6%), and nonirradiated (n=31/56; 55,4%) groups, transversally evaluated according to adiposity indexes (body mass index, circumferences, body composition, fat distribution, and leptin) to determine the effect of sex and cranial irradiation on these variables (linear regression analysis model).

Results: Age at evaluation was 18,6±2,5 years, 8,5±3,5 years after therapy withdrawal. Neither sex nor irradiation influenced body mass index z-score. Twenty-one out of 56 (37,5%) subjects showed an increase in waist-to-height ratio, and there was a trend toward elevation in irradiated group (p=0,06). Female sex and irradiation showed a positive effect on total body fat. Two out of 56 (3,6%) patients were considered obese, regarding body mass index z-score, while 20/56 (35,7%) subjects, according to total body fat, predominantly in irradiated group (p=0,02). Irradiation also showed a positive effect on abdominal fat (total, visceral, and subcutaneous) (p<0,01). Patients presented with hyperleptinemia (51,8%), mainly in males (p<0,01). Relative leptin levels (adjusted by fat mass index and total adipose tissue) were increased in nonirradiated males (interaction of sex and irradiation). Nevertheless, there was no correlation between leptin and other adiposity indexes.

Conclusions: Adolescent and young adult survivors of Acute Lymphocytic Leukemia, 8,5±3,5 years after therapy withdrawal, were not considered obese, according to body mass index. On the other hand, they showed centripetal fat deposition (concerning waist-to-height ratio), increased total body fat and abdominal distribution, every index related to cranial radiotherapy. Leptin profile and altered fat compartment possibly indicate a disease of adipose tissue, role of cranial irradiation, even though other mechanisms, including ethnics and genetics, have to be further studied in this population.

31. ADVERSE OUTCOMES IN UNDERWEIGHT CHILD AND ADOLESCENT SURVIVORS OF CANCER AND RECIPIENTS OF HEMATOPOIETIC STEM CELL TRANSPLANTS Jamie Dargart, MD; Kimberley Dilley, MD, MPH. *Children's Memorial Hospital, Northwestern University, Chicago, IL, USA*

Background: Childhood cancer survivors are more likely to be underweight compared to their siblings and the general population. Underweight survivors are more likely to experience adverse health outcomes.

Methods: Patients eligible for retrospective medical record review were seen in a single institution long-term survivor clinic. Recent weight and height measurements were used to determine weight status according to CDC guidelines. Non-underweight controls were matched to underweight cases based on diagnosis category and age at diagnosis, then gender and race/ethnicity, when possible. McNemar test or paired Student's t-test was used for comparisons, as appropriate.

Results: 33 case-control pairs were identified. The most common diagnosis was acute lymphoblastic leukemia, followed by Wilms tumor, neuroblastoma, and rhabdomyosarcoma. The average length of follow up was 11.52 years for cases and 10.57 years for controls. The number of pairs mismatched for diagnosis, gender, race/ethnicity, treatment, or time to follow up was not significant. Adverse outcomes by category are shown in the following table:

Adverse Outcome	Cases n = 33 (%)	Controls n = 33 (%)	McNemar p value
Auditory/Ear	5 (15.2)	4 (12.1)	1.000
Cardiac	7 (21.2)	3 (9.1)	0.344
Dental	4 (12.1)	3 (9.1)	1.000
Dermatologic	6 (18.2)	4 (12.1)	0.687
Endocrine	16 (48.5)	10 (30.3)	0.180
Gonadal failure	8 (24.2)	4 (12.1)	0.289
Gonadal failure (n = 12)			
Female-female pairs	2 (6.1)	2 (6.1)	1.000
Gonadal failure (n = 19)			
Male-male pairs	6 (18.2)	1 (3.0)	0.063
Growth hormone deficiency	9 (27.3)	4 (12.1)	0.227
Hypothyroidism	5 (15.2)	3 (9.1)	0.727
Gastrointestinal/Hepatic	6 (18.2)	3 (9.1)	0.508
Hematologic/Splenic	2 (6.1)	2 (6.1)	1.000
Metabolic	1 (3.0)	5 (15.2)	0.125
Musculoskeletal	11 (33.3)	6 (18.2)	0.227
Neurocognitive	10 (30.3)	12 (36.4)	0.727
Neurologic	2 (6.1)	2 (6.1)	1.000
Ocular/Visual	7 (21.2)	10 (30.3)	0.508
Pulmonary/Upper respiratory	8 (24.2)	3 (9.1)	0.125
Renal/Genitourinary	4 (12.1)	3 (9.1)	1.000
Secondary malignancy	2 (6.1)	0 (0.0)	NS
Any adverse outcome	30 (90.9)	26 (78.8)	0.344
Any grade 3–4 adverse outcome	15 (45.5)	7 (21.2)	0.057

Conclusion: Most case and control subjects experienced adverse outcomes within 10 years, with a trend toward an increased prevalence of adverse outcomes among underweight survivors.

32. BODY MASS INDEX (BMI) PREDICTS MORTALITY AND CHRONIC GVHD AFTER PEDIATRIC ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (HCT) FOR HEMATOLOGIC MALIGNANCIES Paul A. Hoffmeister, MPH; Barry E. Storer, PhD; Ann E. Woolfrey, MD; Paul A. Carpenter, MD; Jean E. Sanders, MD; and K. Scott Baker, MD, MS. *Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; Department of Pediatrics, University of Washington Medical School, Seattle, WA, USA*

Background: Although obesity may adversely affect various health outcomes, the effect of pre-transplantation body mass index (BMI) on transplant outcomes has not been studied in pediatric patients.

Methods: We analyzed the impact of BMI on transplant outcomes in 184 patients aged 2–18 years who underwent HCT for hematologic malignancies from 1999-2008. Patients were divided into 4 groups based on age-and-gender-adjusted BMI percentiles. Patients in the <25th, 26–75th, 76–95th, >95th percentile BMI groups were classified as below normal weight, normal weight, at risk for overweight, and overweight respectively. Cox proportional hazards regression models for survival, relapse, non-relapse mortality (NRM), acute graft-versus-host-disease (AGVHD), and chronic GVHD (CGVHD) were performed using BMI groups as the main effect and the normal BMI (26-75th percentile) as the baseline comparison. Models were adjusted for race (white vs. non-white), risk of relapse (high vs. low), donor type (related vs. unrelated), HLA match (yes vs. no), regimen (TBI vs. non-TBI), and diagnosis (ALL, AML, CML, MDS/JMML). Fifty-six patients relapsed and 85 developed CGVHD. Seventy patients died, 44 of relapse and 26 of other causes. Below normal weight children had elevated risks of death (HR 6.4, p<0.0001), relapse (HR 5.6, p=0.0007), and NRM (HR 11.5, p=0.0006). Overweight children had elevated risks of death (HR 2.3, p=0.02), NRM (HR 3.6, p=0.04), and CGVHD (HR 2.1, p=0.02). BMI was not associated with AGVHD. CGVHD was seen in 69% of overweight compared to 49% of non-overweight (≤95th) children. Among non-relapse deaths, AGVHD related deaths (13% vs. 1%, p=0.001) and CGVHD related deaths (12% vs. 5%, p=0.22) were higher in overweight than non-overweight children.

Conclusion: Below normal weight and overweight children with hematologic malignancies have a higher risk of poor outcomes after HCT and more attention should be given to nutritional status and weight prior to HCT.

33. DIETARY PATTERNS AND ADHERENCE TO NUTRITIONAL GUIDELINES AMONG PEDIATRIC SURVIVORS OF ACUTE LYMPHOBLASTIC LEUKEMIA Eric J. Chow, MD MPH; Jill H. Simmons, MD; Catherine Pihoker, MD; Claire Wharton, BS; K. Scott Baker, MD, MS; Debra L. Friedman, MD, MS. *Department of Pediatrics, Seattle Children's Hospital, Seattle, WA, USA; Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; Department of Pediatrics, Vanderbilt University School of Medicine and the Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, TN, USA; Cancer Control and Prevention Program, Vanderbilt-Ingram Cancer Center, Nashville, TN, USA*

Background: Pediatric survivors of acute lymphoblastic leukemia (ALL) are at increased risk of obesity. In addition to treatment exposures such as cranial radiotherapy and glucocorticoids, factors such as diet and physical activity may also influence weight gain. The goal of this study was to determine if dietary differences exist between normal and overweight/obese survivors and between survivors and siblings.

Methods: In this prospective cross-sectional pilot study (2007–2009), validated food frequency and physical activity questionnaires were administered to ALL survivors diagnosed 1990–2008 and a subset of healthy siblings.

Results: Data on 112 survivors and 27 siblings (both groups, median age 14 years; range 5–21) found similar levels of overweight (18.5% vs. 16.1%) and obesity (18.5% vs. 24.1%; p=0.87) and physical activity (median score distribution, p=0.69) between the 2 groups. After adjusting for current age and sex, the proportions of survivors and siblings who met recommended nutritional guidelines also were similar: <30% calories from fat (30.4% vs. 25.9%); <300 mg/day cholesterol (73.2% vs. 66.6%); <25% calories from added sugars (98.2% vs. 96.3%); recommended levels of fruit (10.7–23.2% vs. 14.8-18.5% depending on measurement scale), vegetable (51.8-56.3% vs. 59.3-64.0% depending on measurement scale), and fiber (7.1% vs. 11.1%). Dietary characteristics and physical activity levels also were not significantly different among normal weight, overweight, and obese survivors, even after adjustment for sex, current age, elapsed time since diagnosis, prior cranial radiotherapy, and growth hormone status.

Conclusions: Contemporary pediatric survivors of ALL and siblings manifest high rates of overweight and obesity. Reviews of dietary patterns suggest potential areas of improvement, including reducing dietary fat and increasing fruit, vegetable, and fiber intake. However, given similarities in dietary characteristics and physical activity levels across weight categories, other factors such as genetics, pre-diagnosis weight, and select treatment exposures may be more important in influencing post-therapy weight status.

34. ASSOCIATION OF ANTIDEPRESSANT USE AND OBESITY AMONG CHILDHOOD CANCER SURVIVOR STUDY (CCSS) PARTICIPANTS Daniel M. Green, MD; Liang Zhu, PhD; Marilyn Stovall, PhD; Vikki G. Nolan, PhD; Kirsten K. Ness, PhD; Sarah S. Donaldson, MD; Cheryl L. Cox, PhD; Kevin Oeffinger, MD; Lillian R. Meacham, MD; Charles A. Sklar, MD; Kevin R. Krull, PhD; Gregory T. Armstrong, MD, MSCE; Leslie L. Robison, PhD. *St. Jude Children's Research Hospital, Memphis, TN, USA; University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; Stanford University Medical Center, Stanford, CA, USA; Memorial Sloan Kettering Cancer Center, New York, NY, USA; Children's Healthcare of Atlanta, Atlanta, GA, USA*

Background: Several agents used for the treatment of psychiatric disorders, including paroxetine (Paxil), risperidone (Risperdal) and valproate (Depakote) are associated with weight gain in the general population.

Methods: We evaluated these exposures as well as demographic, lifestyle, and treatment factors that could be associated with obesity (body mass index (BMI) ≥30 kg/m^2) among 9284 adult (>18 years of age) CCSS survivors and 2861 adults within the CCSS sibling cohort (Sibs).

Results: Adjusted for sex, race/ethnicity and age, neither overweight nor obesity was more prevalent among CCSS survivors than among Sibs (p=0.23). In multivariable analyses restricted to the CCSS survivors, the relative risk (RR) of obesity (adjusted for age, sex, race/ethnicity) was higher among those who received cranial radiation (CRT) doses of 2000–3000 cGy (RR, 1.42, 95% CI, 1.19 to 1.69, p<0.01), and among those who received paroxetine during the preceding two years (RR, 1.58, 95% CI, 1.19 to 2.09, p<0.01); risks were lower among those who met Centers for Disease Control guidelines for vigorous physical activity (RR, 0.75, 95% CI, 0.65 to 0.86, p<0.01) or reported leisure time physical activity during the previous month (RR, 0.87, 95% CI, 0.76 to 1.00, p=0.04). Scores on the Brief Symptom Inventory depression, anxiety and somatic distress scores ≥63 were not associated with an increased RR for obesity in the multivariable model.

Conclusion: These preliminary data suggest that antidepressant use may contribute to obesity in adult CCSS participants. This observation requires confirmation in a longitudinal study of BMI change in relation to the timing of psychiatric drug initiation and discontinuation.

35. ALTERED ADIPOCYTOKINE SECRETION AND DEGREE OF INSULIN RESISTANCE (IR) WITH ADIPOSITY IN SURVIVORS OF BONE MARROW TRANSPLANTATION (BMT) WITH TOTAL BODY IRRADIATION (TBI) IN CHILDHOOD

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Background: To explore the relationship between IR, adiposity and adipocytokines in survivors of childhood BMT with TBI, known to have increased adiposity and an adverse metabolic profile.

Methods: 42 survivors of childhood BMT(23M), 19 non-BMT(12M) subjects having growth investigations had the following: 1. Body composition:auxology, DEXA; 2. GH status (ITT); 3. Fasting glucose, insulin, leptin, adiponectin, IL-6; 4. HOMAR calculated to assess IR.

Results: The groups were well matched for age, gender and pubertal stage. Assessments were either before(N=10) or during(n=25) GH treatment in BMT survivors. Median(range) age at and time since BMT were 7.7(2–16.7) and 7.9(0.4–18.1)yrs respectively.

	BMT	Non-BMT	P-value
Percentage body fat	32.4(11.9)	25.0(12.6)	0.033
Percentage truncal fat	33.1(13.5)	22.2(14.5)	0.006
Waist/hip ratio(WHR)	0.91(0.05)	0.94(0.06)	0.051
Growth hormone deficiency (GHD)	35	10	
Untreated GHD	10	10	
Insulin(μIU/ml)	10.4(0.05–68.3)	6.0(1.8–25.8)	0.01
Leptin(pg/ml)	13729(807–104932)	2943(200–74447)	0.002
Adiponectin(ng/ml)	5095(992–17544)	7962(2692–18565)	0.009
Leptin/adiponectin ratio(pg/ng)	2.69(0.11–48.4)	0.37(0.01–12.91)	0.000
IL-6(pg/ml)	0.33(0.05–20.3)	0.95(0.05–38.9)	0.085
HOMAR(μIU/ml*mmol/l)	2.3(0.05–18.3)	1.3(0.4–6.3)	0.016

Laboratory data were log-transformed and expressed as geometric mean(range) and compared by unpaired t-tests if normally distributed or Mann Whitney-U test if not (IL-6 data). Auxology data were expressed as mean(SD).

Adiposity, leptin and HOMAR were significantly increased in BMT survivors. HOMAR and leptin were highly correlated with %body fat, truncal body fat and WHR (r=0.461–0.743, p=0.000-0.002 respectively). Covariate analysis indicated an independent effect of BMT on IR (p=0.001) and leptin levels (p=0.000) after adjusting for body fat, independently of GH status or gender. Adiponectin was lower in the BMT group but did not correlate with % body fat.

Conclusions: We demonstrate not only significantly increased leptin, leptin/adiponectin ratio, HOMAR, and reduced adiponectin, but a difference in their relationship with adiposity in BMT survivors. BMT with TBI is associated with an altered pattern of adipocytokine levels and insulin resistance. This may be due to irradiation of fat and muscle during TBI.

36. EVALUATION OF CARBOHYDRATE METABOLISM AFTER ONCOLOGICAL TREATMENT IN CHILDREN WITH BRAIN TUMORS: PRELIMINARY REPORT dr Maja Okonska; dr n.med. Dorota Birkholz; dr Beata Sztangierska; dr n.med. Maria Korpal-Szczyrska; dr Hanna Magnuszewska; dr.hab.n.med. Elzbieta Drozynska. *Department of Paediatrics, Hematology, Oncology and Endocrinology, Medical University of Gdansk, Gdansk, Poland*

Background: To evaluate carbohydrate metabolism in patients after oncological treatment of brain tumor depending on the way of treatment and localization of the tumor.

Methods: 39 patients aged 3.9–17.67 yrs at examination time after oncological treatment of brain tumors were included. Remission time ranged 0.1–8.33 yrs. Three groups were identified: I (16 pts), tumors localized in hypopituitary region (HPR), 14/16 treated by surgery and 2/16 by surgery and radiotherapy (mean 35Gy), aged 11.15 yrs, 13/16 Tanner I; II (14 pts), tumors outside HPR, treated by surgery, chemo- and radiotherapy (mean 35Gy), aged 13.68 yrs, 2/14 Tanner I; III (9 pts), tumors localized outside HPR treated only by surgery, aged 10.06 yrs, 4/9 Tanner I. BMI-SDS was calculated. Fasting glucose and insulin levels were assessed and in OGTT. Fasting T-cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, HbA1c were measured. HOMA-IR and Matsuda and de Fronzo index were calculated.

Results: BMI-SDS was increased in gr.I (3,4SD);in gr.II and III was normal (0.62 and 1.,03 respectively). Diabetes diagnosed in 1 pt of gr.I, impaired fasting glucose in 1 pt of gr.III; there were no impaired glucose tolerance. Fasting insulin was elevated in 5/16 of gr.I and in 1/14 of gr.II. Insulin in 1st hour of OGTT was increased in 5/16 of gr.I, 4/14 of gr.II and in 2/9 of gr.III. Insulin in 2nd hour of OGTT was elevated in 5/16 of gr.I, 6/14 of gr.II and 3/9 of gr.III. T-cholesterol and LDL-cholesterol was increased in gr.II, but HDL-cholesterol was decreased and triglycerides was in upper limit in gr.I. HbA1c was normal in all groups. HOMA-IR was increased in 16/16 of gr.I, 14/14 of gr.II and 4/9 of gr.III. Matsuda and de Fronzo index was abnormal in 7/16 of gr.I, 5/14 of gr.II, and 2/9 of gr.III.

Conclusion: These results confirms that after oncological treatment of brain tumor disorders of carbohydrate metabolism appears, generally insulin resistance, especially if tumor was localized in HPR or radiotherapy was applied.

37. OVERWEIGHT AND HEALTH RELATED QUALITY OF LIFE AMONG ADULT SURVIVORS OF CHILDHOOD CANCER—A REPORT FROM THE SWISS CHILDHOOD CANCER SURVIVOR STUDY Corina S. Rüegg, MSc; Nicolas X. von der Weid, MD; Michael Paulussen, MD; Pierluigi Brazzola, MD; Stefan Essig; Cornelia E. Rebholz, MSc; Marie-Pierre F. Strippoli, MSc; Gisela Michel, PhD; Claudia E. Kuehni, MD, MSc. *Institute of Social- and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland; Pediatric Hematology/Oncology Unit, Children's University Hospital, University of Lausanne, Lausanne, Switzerland; Paediatric Oncology/Haematology, University Children's Hospital Basel (UKBB), Basel, Switzerland; Ospedale Regionale di Bellinzona e Valli, Bellinzona, Switzerland*

Background: We investigated whether overweight in adult childhood cancer survivors was associated with a reduction in health related quality of life (HRQOL).

Methods: In the Swiss Childhood Cancer Survivor Study (SCCSS) a detailed questionnaire was sent in 2008 to all adult survivors (≥20 years) registered in the Swiss Childhood Cancer Registry (SCCR), diagnosed 1976–2003 at an age of <16 years. BMI was calculated from self reported height and weight and categorized as normal (<25 kg/m^2) or overweight (≥25). HRQOL was measured with the SF-36, which includes 4 scales of physical health (physical functioning, role-physical, bodily pain, general health) and 4 scales of mental health (vitality, social functioning, role-emotional, mental health). A T-score of 50 (SD 10) corresponds to the mean of healthy controls. We used multiple linear regression (overall and stratified for gender) to assess associations between overweight and HRQOL adjusting for age, being immigrant, education, treatment, diagnosis and time since diagnosis.

Results: The sample included 1026 survivors from the SCCSS (response rate 75%); 291 (28%) were overweight (34% of males, 21% of females). Overall, survivors reported a similar or better HRQOL than the norm population. However, overweight survivors, had lower scores for all 8 scales compared to survivors of normal weight, with significant differences for physical functioning (p=0.003), role-emotional (p=0.028), bodily pain (p=0.048) and general health (0.011). For all subscales, the association was stronger for women than for men (with interaction tests reaching statistical significance for general health (p=0.048) and bodily pain (p=0.063)).

Conclusions: Overweight in childhood cancer survivors was associated with lower HRQOL, particularly in women. Considering this, together with the well known increased risks for long-term morbidity and mortality, strategies for prevention or early intervention of overweight in childhood cancer survivors must be developed.

Funded by Cancer Research Switzerland and Wyeth Foundation

38. ASSOCIATION BETWEEN BODY MASS INDEX IN SURVIVORS OF CHILDHOOD CANCER AND PSYCHOLOGICAL DISTRESS G Michel, PhD; N.X. von der Weid, MD; C.E. Rebholz, MSc; C.S. Rueegg, MSc; E. Bergstraesser, MD; C.E. Kuehni, MD, MSc; for the Swiss Pediatric Oncology Group. *Institute of Social- and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland; Pediatric Hematology/Oncology Unit, Children's University Hospital, University of Lausanne, Lausanne, Switzerland; University Children's Hospital, Zurich, Switzerland*

Background: We explored whether BMI in Swiss childhood cancer survivors is associated with psychological distress.

Methods: In the Swiss Childhood Cancer Survivor Study a detailed questionnaire was sent to all adult survivors (≥20 years) registered in the Swiss Childhood Cancer Registry, diagnosed between 1976–2003 at age <16 years. BMI was calculated from self-reported height and weight (underweight: <18kg/m^2, normal: 18–24.9, overweight: 25–29.9, obese: ≥30). Psychological distress was assessed using the Brief Symptom Inventory and survivors were categorized into those with potentially significant distress, and those with no distress. We used multivariable logistic regressions to assess associations between BMI and psychological distress adjusting for demographic (age, sex, partnership, unemployment, immigration) and medical variables (diagnosis, treatment, age at diagnosis, time since diagnosis, self-reported late effects).

Results: The sample included 1012 survivors (response rate 75%). Among cancer survivors, 38 were underweight (3.7%), 691 normal (68.3%), 216 overweight (21.3%) and 67 obese (6.6%). Significant distress was reported by 22.9% of survivors with a normal weight, but by 36.7%, 26.4% and 37.3% of those being underweight, overweight and obese respectively. 17.8% of overweight men reported distress compared to 46.9% of overweight women (p=0.007). Underweight survivors reported significant distress primarily for: somatization (OR=3.6), depression (OR=2.3), obsessive-compulsive tendencies (OR=2.8), and interpersonal sensitivity (OR=2.6); overweight survivors for: somatization (OR=2.2), depression (OR=1.9), paranoid ideation (OR=1.8), and global severity index (OR=1.9); and obese survivors for: interpersonal sensitivity (OR=2.1), paranoid ideation (OR=2.6), psychotic tendencies (OR=2.0),and global severity index (OR=2.8) (all compared to survivors of normal weight and adjusted for demographic and medical variables).

Conclusions: One sixth of overweight male survivors but almost half of overweight female survivors reported psychological distress. Because weight and psychological distress mutually influence each other, addressing both during follow-up appointments might improve survivors' well-being in the long-term.

39. LONG-TERM MEDICAL AND PSYCHOSOCIAL LATE EFFECTS IN CHILDHOOD CANCER AND BONE MARROW TRANSPLANT SURVIVORS

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Background: Much has been learned about the late effects of treatment that many pediatric and BMT survivors face. Although research has shown that most survivors are resilient, there is a subgroup that struggles with life after treatment. This chart review study aimed to further investigate factors that are associated with long-term psychosocial problems in childhood cancer and BMT survivors seen in a survivorship clinic, using a quantitative and qualitative assessment approach. Preliminary results of this study were previously presented at two conferences (Bingen et al., 2004) using a smaller sample size. While the majority of survivors scored within normal limits on parent and self-report questionnaires evaluating emotional and behavioral functioning, the majority also reported one or more survivorship concerns during a psychosocial interview. For this study, 197 childhood cancer and BMT survivors were identified and data were collected from questionnaires, qualitative interviews and medical chart review.

The cohort consisted of 103 females and 94 males, between 2 and 34 years of age. The mean age at diagnosis was 6 years. On average, survivors were 9 years post diagnosis and 7 years post treatment completion. Leukemia accounted for 43.4% of initial diagnoses; and 30.6% were BMT survivors.

Similar to the original study, results indicated no significant difference between the BMT and No-BMT groups on psychological functioning. However, 62.5% of the BMT group reported cognitive/school functioning concerns during the interviews; as compared to 34.2% of the No-BMT group (p<.004). Survivors 10 or more years post-treatment (9.6%) and survivors 0–5 years post-treatment (2.6%) had more documented fatigue compared to survivors 6–9 years post-treatment (0%), which was unrelated to type of treatment, diagnosis or age. Identifying those survivors most at risk for long-term psychosocial problems and its impact on post treatment quality of life remains a challenge that needs further research.

40. THE RELATIONSHIP BETWEEN PSYCHOSOCIAL FUNCTIONING DURING AND AFTER CANCER TREATMENT AND TREATMENT SEVERITY IN CHILDHOOD CANCER SURVIVORS

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Background: In adult cancer survivors a relationship between severity of cancer treatment and psychosocial distress during and after treatment has been established. The objective of this study is to examine this relationship in childhood cancer survivors.

Methods: Childhood cancer survivors were recruited in a Cancer Survivor Clinic (n=141) and the parent (child currently <18) or the survivor (>18) completed a questionnaire asking about depression, anxiety, behavior problems, anger problems, and sleep problems

before, during, and after treatment, and currently. An overall composite score was generated from these questions. Treatment severity was rated using the Intensity of Treatment Rating Scale 2.0.

Results: The sample was comprised of 2% Brain Tumor survivors, 57% Leukemia/Lymphoma survivors, 39% non-CNS Solid Tumor survivors, and 3% survivors of non-malignant conditions. The average age of diagnosis was 4.2 (range 0.2-14) with treatment severity rated as 1 (6.2%), 2 (32.8%), 3 (35.9%) and 4 (25%). Participants reported at least one item of psychosocial distress before treatment (9.7%), during treatment (28.7%), after treatment (37.9%), and currently (35.0%). The relationship between psychosocial distress over time and treatment severity was examined. There was a significant effect of time ($F=6.24$, $df=3,106$, $p<.001$) and treatment severity was significant at a trend level ($F=2.933$, $df=1, 106$, $p<.09$) but did not interact with changes in psychosocial distress over time ($F=2.02$, $df=3,106$, $p=.111$).

	Before	During	After	Currently
Behavior problems	4%	4%	12%	13%
Depression	1%	7%	11%	8%
Anxiety	3%	17%	20%	17%
Anger	4%	12%	15%	15%
Sleep problems	4%	14%	13%	12%

Conclusions: Psychosocial distress did not decrease following the termination of cancer treatment suggesting a long-term need for psychologists in cancer survivor care.

41. EMPLOYMENT STATUS AND SOCIO-ECONOMIC CLASSIFICATON OF ADULT SURVIVORS OF CHILDHOOD CANCER IN BRITAIN: BRITISH CHILDHOOD CANCER SURVIVOR STUDY Emma R. Lancashire, PhD; David L. Winter, HNC; Clare Frobisher, PhD; Raoul C. Reulen, PhD; Adam Glaser, MD; Michael M. Hawkins, DPhil; on behalf of the British Childhood Cancer Survivor Study (BCCSS). *Centre for Childhood Cancer Survivor Studies, School of Health and Population Sciences, University of Birmingham, Edgbaston, Birmingham, UK; Regional Paediatric Oncology Unit, St James's University Hospital, Beckett Street, Leeds, UK*

Background: To investigate employment status and socio-economic classification of adult survivors of childhood cancer in Britain.

Methods: Five categories of employment status among 10257 survivors and two levels of socio-economic classification among 7361 survivors were compared with expected levels from the general population (n=15730 and 14022, respectively). In addition, factors within the survivor population associated with each of these outcomes were identified.

Results: Deficits among survivors overall compared to expected levels were observed for working full or part time, caring for home and family, and being classed as managerial/professional. An overall excess was observed in relation to being unable to work due to illness or disability. In relation to working full or part time, deficits were restricted to CNS tumour survivors (irradiated OR=0.34:99%CIs=0.28-0.41, not irradiated OR=0.64:99%CIs=0.49-0.82), excesses were observed for Hodgkin's disease, non Hodgkin's lymphoma and other neoplasms. In relation to being classed as managerial/professional, the deficits were restricted to cranially irradiated leukaemia survivors (OR=0.68:99%CI=0.56-0.82) and CNS neoplasm survivors (irradiated OR=0.41:99%CIs=0.32–0.52, not irradiated OR=0.59:99%CIs=0.45-0.78). Except for Hodgkin's disease, survivors of all other cancer types were more likely than expected to be unable to work due to illness or disability.

Factors associated with at least one aspect of employment status and socio-economic classification were: sex; age at questionnaire completion; radiotherapy treatment; cancer type; age at cancer diagnosis; diagnosis with epilepsy. Additional factors associated with employment status were diagnosis with a second primary tumour, one or more hearing problem, one or more visual problem, or a recurrence.

Conclusions: Groups of survivors, in particular CNS tumour and cranially irradiated leukaemia survivors, have been identified as being at risk of poorer outcomes in relation to employment status and socio-economic classification. However some groups were found to have better than expected outcomes. There are implications for the clinical follow-up of specific groups of survivors.

42. PROSPECTIVE REGISTRATION OF ENDOCRINE SEQUELAE AFTER BRAIN TUMOR TREATMENT WITHIN THE HIT-2000 STUDY R. Jung, MD; Th. Langer, MD; M. Paulides, MD; S. Rutkowski; MD, H.G. Dörr; MD. *Late Effects Surveillance System, Hospital for Children and Adolescents, Erlangen, Germany; HIT-2000 Trial Center, Hospital for Paediatric Haematology and Oncology, Hamburg, Germany*

Background: This study is a companion to the HIT-2000 treatment trial for brain tumours and aims at prospective registration of endocrinologic complications.

Methods: All relapse-free patients treated according to the HIT-2000 trial are eligible for prospective follow-up within this study. Until May 1, 2009, N=1136 patients had been enrolled. Of these, n=344 had to be excluded for death, relapse or other reasons. Therefore

the study population is comprised of n=792 patients (n=495 (63%) male, n=297 (37%) female). Median age at diagnosis was 7,3 years. Tumor diagnoses were 48% medulloblastoma, 40% anaplastic ependymoma and 12% other.

Results: Preliminary results show a significant reduction in body height-SDS already at 4 months after end of treatment. Despite acceleration of growth, the height difference is not made up for during our follow-up interval. Mean serum IGF-1 concentrations decline already during brain tumour treatment and drop below the 5th percentile at 4 months after end of treatment; they rise again until 24 months after treatment, however. Toxicity regarding the thyroid axis translates into a rise of mean serum TSH levels after treatment in comparison to values obtained before start of therapy as an expression of latent hypothyroidism but also secondary hypothyroidism with decline in fT4 values in some cases.

Conclusions: These data show that endocrine complications appear already during antineoplastic treatment for brain tumours. Therefore it is required to monitor endocrine parameters already during therapy to adequately register hormonal dysfunction in these patients.

43. FERTILITY OF MALE ADULT SURVIVORS OF CHILDHOOD CANCER Krista Tromp, BSc; Joyce J. Claessens, MD; Sebastiaan L. Knijnenburg, MSc; Helena J. van der Pal, MD; Flora E. van Leeuwen, MD, PhD; Huib N. Caron, MD, PhD; Catharina C. Beerendonk, MD, PhD; Leontien C. Kremer, MD, PhD. *Department of Obstetrics and Gynaecology, University Medical Center St Radboud, Nijmegen, The Netherlands; Departments of Clinical Informatics and Medical Oncology, Academic Medical Center, Amsterdam, The Netherlands; Department of Paediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands; Department of Epidemiology, The Netherlands Cancer Institute, Amsterdam, The Netherlands*

Background: To evaluate the long-term effects of childhood cancer treatment on the reproductive status of adult male five-year survivors and to evaluate the risk factors associated with disturbances in reproductive endocrinology.

Methods: The study cohort included 565 male adult 5-year survivors of childhood cancer treated in the Emma Children's Hospital/AMC in The Netherlands between 1966 and 2003. Data concerning patient and treatment characteristics, reproductive endocrine status (serum FSH, LH and testosterone levels) and pregnancy outcomes were collected. Possible risk factors were assessed by multivariate logistic regression.

Results: Data on reproductive endocrine status were available for 488 survivors (86.4%). The median age at diagnosis was 7.8. The prevalence of an elevated FSH and decreased testosterone were 33% and 12% respectively. Use of procarbazine, cyclophosphamide, vinca-alkaloids, other alkylating agents, pelvic/abdominal irradiation, total body irradiation and surgery of the testicular region were identified as treatment-related risk factors for elevated FSH levels. During the follow-up period (median 15.0 years), 120 conceptions in 73 survivors resulted in 103 life births.

Conclusion: One third of male five-year survivors of childhood cancer showed elevated FSH levels, which is associated with severe disturbances in spermatogenesis. Therefore interest in pre-treatment preservation of fertility is essential in this population.

44. CRANIAL IRRADIATION DOES NOT RESULT IN PITUITARY-GONADAL AXIS DYSFUNCTION IN VERY LONG-TERM MALE SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA N.J. van Casteren; R. Pieters; G.R. Dohle; M. van Baalen; S. Neggers, M.M. van den Heuvel-Eibrink. *Departments of Internal Medicine and Urology, Section of Andrology, Erasmus MC–University Medical Center Rotterdam, Rotterdam, The Netherlands; Department of Pediatric Oncology/Hematology, Erasmus MC–Sophia Children's Hospital, Rotterdam, The Netherlands*

Introduction: One of the risks of childhood cancer treatment is fertility impairment later in life. In the past a large proportion of children with acute lymphoblastic leukemia (ALL) has received cranial irradiation as part of their treatment. The aim of this study was to evaluate whether cranial irradiation negatively affects pituitary regulated gonadal function in male survivors of childhood ALL.

Methods: We examined gonadal function, including Inhibin B, LH, FSH, testosterone, and pituitary axis function by measuring TSH, Free-T4 and IGF-I levels in 89 long-term male survivors of childhood ALL after a median follow-up time of 19 years (range 7–34 years).

Results: Twenty-nine out of 89 male ALL survivors received cranial irradiation. Inhibin, FSH, LH, Testosterone, testicular volume as well as TSH and Free-T4 levels were not different in the cranial irradiated group as compared to the non-irradiated group (Table). In contrast, IGF-I levels were significantly lower in the cranial irradiated group. Survivors treated with total body irradiation or testicular irradiation had significantly decreased gonadal function based on hormone levels.

Conclusions: These data show that, in contrast to the negative influence on the growth hormone axis, cranial radiotherapy as part of ALL treatment does not have a deleterious long-term effect on the hypothalamic–pituitary-gonadal axis or pituitary-thyroid axis.

Table: Hormone levels according to treatment modality. The two patients treated with orbital irradiation and mediastinal irradiation are not shown. Normal range is given for each hormone. Values given as median and range. Z-scores are given as mean and standard deviation.

	Complete group	No radiotherapy	Cranial irradiation (med 25 Gy, range15–30)	P-value¥	Total body irradiation	P-value¥	Testicular irradiation	P-value¥
Number of patients	87	55	25		4		3	
Age at diagnosis (yrs)	5.0 (0–15)	6.0 (1–15)	4.2 (0.1–14)	0.02	4 (4–12)	0.70	5 (2–5)	0.27
Age at follow-up (yrs)	25 (18–40)	24 (18–34)	29 (23–40)	<0.0001	25 (22–35)	0.25	30 (21–33)	0.11
Follow-up time (yrs)	19 (7–34)	18 (7–24)	26 (16–34)	<0.0001	18 (15–31)	0.13	25 (16–31)	0.01
Inhibin-B (150–400 ng/l)	155 (0–393)	155.5 (67–392)[a]	177.0 (35–393)	0.85	15 (10–20)*	<0.0001	10 (0–10)	<0.0001
Testosterone (10.0–30.0 nmol/l)	16.2 (7.7–29.4)	16.6 (7.7–29.4)	16.4 (11.1–20.9)	0.21	12.2 (11.8–16.0)	0.09	11.9 (9.0–17.0)	0.14
SHBG(10–70 nmol/l)	28.9 (10.6–67.7)	26.2 (10.6–51.4)	31.6 (15.1–51.3)	0.03	22.8 (15.0–40.2)	0.80	47.8 (42.7–67.7)*	<0.0001
LH (1.5–8.0 U/l)	4.0 (0.1–18.9)	3.4 (0.1–8.1)	3.1 (1.3–5.3)	0.38	10.8 (7.7–13.9)*	<0.0001	13.9 (8.2–18.9)*	0.08
FSH (2.0–7.0 U/l)	4.0 (1.1–58.7)	3.4 (1.3–14.1)	4.3 (1.1–15.7)	0.14	23.7 (15.9–31.4)*	0.01	48.2 (42.8–58.7)*	0.01
Testicular volume (>15ml)	20 (2–25)	20.0 (13–25)	20.0 (10–25)	0.79	12.5 (4–13)*	0.02	2.5 (2–3)*	<0.0001
Free T4 (11–25 pmol/l)	14.8 (11.8–22.7)	15.1 (11.6–30.1)[b]	15.0 (11.8–22.7)[c]	0.69	12.5 (12.3–12.6)[#]	0.06	14.8[j]	0.79
TSH (0.4–4.3 mU/l)	1.3 (0.36–3.43)	1.14 (0.37–2.48)[d]	1.2 (0.46–2.76)[e]	0.42	1.9 (0.36–3.43)	0.19	0.79[j]	0.61
Height (cm)	178 (163–192)	182 (165–192)	175 (163–189)	0.006	169 (167–184)	0.035	170 (165–186)	0.13
Body Mass Index	24.1 (17.9–39.6)	23.9 (17.9–39.6)	25.4 (19.2–33.8)	0.04	19.5 (18–24.2)	0.06	20.7 (19.6–21.4)	0.13
IGF-I (15–47 nmol/l)	24.3 (6.5–54.2)	27.4 (13.1–54.2)h	17.3 (12.8–47.5)[i]	0.003	20.6 (11.5–32.3)	0.17	7.8 (6.5–23.0)	0.02
IGF-I (z-scores)	-0.49 (1.3)	-0.11 (1.1)	-0.82 (1.1)	0.02	-0.82 (1.3)	0.24	-2.2 (1.6)	0.01

¥p-values as compared to the non-irradiated group; [a]n=54, [b]n=10,c n=21, d n=11,e n=21,f n=1,g n=21,h n=38, i n=21, j n=1

45. REPRODUCTIVE OUTCOME IN YOUNG ADULT SURVIVORS OF CHILDHOOD CANCERS ATTENDING AFTER COMPLETION THERAPY (ACT) CLINIC

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Background: To assess the Reproductive outcome in young adult (Age>18 yrs) survivors of childhood cancers registered in After Completion of Therapy (ACT) Clinic between Feb. 1991 to Feb. 2009.

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

Results: 463/1076 (43%) survivors registered in ACT Clinic from Feb. 1991 to Feb. 2009 are young adults. Male: female ratio is 3:1 (346:117). 279/463 (60%) are survivors of hematological malignancies, 184/463 (40%) are survivors of solid tumors. 71/463 (15%) are married. 210/463 (45%) are unmarried and in 182/463 (40%) marital status is unknown. Further data was obtained from 49/71 married survivors who are following up regularly. 36/49 (74%) are males and 13/49 (26%) are females. 34/49 (69%) are survivors of hematological malignancies majority being Hodgkins disease and 15/49(31%) are survivors of solid tumors. Median age at diagnosis was 9 yrs (3–16 yrs).Median time since cessation of treatment is 19 yrs (8–35 yrs).Median duration of follow up in ACT Clinic is 14 yrs (0–18yrs). 22/49 (45%) married survivors have no children. 27/49(55%) have children (4 are expecting to have offspring).18/27 (67%) are males of which 1 has adopted child and 17 have children through assisted reproduction. 9/27 (33%)are female survivors and all have conceived normally.

Conclusion: Gonadal failure and infertility are important sequelae of previous exposure to chemotherapy and radiotherapy during treatment of childhood cancers. Male survivors are more at risk for infertility as compared to female survivors. Premarital counseling about fertility and assisted reproduction, although culturally sensitive issue forms an essential component of young adult survivor's follow-up.

46. MALE HEALTH AND PERCEPTIONS OF RISK FOR TESTICULAR/SEXUAL DYSFUNCTION: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background: Limited research has been conducted in the long-term implications of treatment for childhood cancer on sexual function among adult males.

Methods: We surveyed male subjects from the CCSS, a cohort of 5+ year survivors of childhood cancer diagnosed from 1970-86. Subjects were asked to complete a male health questionnaire (MHQ) with items on puberty and sexual development, fertility, testosterone and erectile dysfunction therapy and perceptions of risk of male health problems. Demographic information was ascertained from questionnaires and treatment data was abstracted from medical records. Gonadotoxic therapy was defined as treatment with alkylating agents or cranial, pelvic, testicular or total body radiation.

Results: 3016 survivors expressed interest in the MHQ and 1634 (54.2%) completed the questionnaire. Survivors were an average of 37.4 years of age (range 21–59), and 56.5% reported very good to excellent health. 90.3% of survivors had received gonadotoxic therapy. 152(9.5%) reported having ever received treatment with testosterone of whom 105 were currently on testosterone therapy, and 496 (54.7%) of those who tried to have children reported infertility. 92.9% of survivors reported being sexually active in the past year and 94 (5.8%) were treated for erectile dysfunction. Gonadotoxic therapy was associated with testosterone treatment (OR 10.4; 95% CI 2.2–186.1) and infertility (OR 4.6; 95% CI 2.6–8.2). The proportion of survivors who received gonadotoxic therapy but did not report their perceived risk to be slightly more or much more compared to peers was 35.3% for infertility, 58.5% for low testosterone and 68.3% for sexual dysfunction.

Conclusions: Survivors' perceptions of their risks do not accurately reflect their expected risk due to exposure. Education and screening related to testicular function should be a regular component of long-term follow-up care. Additional analyses of this population are underway to evaluate treatment-specific risks for testicular/sexual dysfunction.

47. FERTILITY PRESERVATION FOR PREPUBERTAL BOYS: SAFETY, ACCEPTABILITY AND EARLY TRANSLATIONAL RESULTS Jill P. Ginsberg, MD; Thomas F. Kolon, MD; Claire A. Carlson, BSN, RN; Kat Lin, MD; Wendy L. Hobbie, MSN, RN, CRNP; Elizabeth Wigo, BS; Xin Wu, PhD; Ralph L. Brinster, VMD, PhD. *Division of Oncology and Department of Urology, 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, University of Washington, Seattle, WA, USA; Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA, USA; Department of Animal Biology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA, USA*

Background: Gonadotoxicity is an unfortunate consequence of pediatric cancer treatment. Fertility preservation must be considered at time of diagnosis, when an opportunity exists to intervene before therapy-related gonadal damage occurs. Prepubertal males have no mature spermatozoa, posing a challenge for fertility preservation. Testicular tissue cryopreservation is a potential option but is still experimental. We report on a novel protocol that offers testicular cryopreservation to families of prepubertal boys with newly diagnosed malignancies. The aims were to determine the acceptability and safety of this procedure and to explore appropriate culture procedures for *in vitro* expansion of spermatogonial stem cells (SSCs).

Methods: Parents of prepubertal boys with diagnoses at highest risk for treatment-related gonadal damage were offered the option of testicular cryopreservation. Half of the biopsy was frozen for the subject's future use and the remainder used for research. Data on negative intraoperative and/or acute post-operative sequelae of testicular biopsies were assessed. Tissue designated for research was utilized for microarray analysis and SSC culture conditioning studies. In addition, animal transplantation studies were undertaken in an effort to optimize culture procedures.

Results and Conclusions: Since January 2008, 16 of 21 families (76%) consented to testicular cryopreservation, indicating the prospective acceptability of this option to parents of boys aged 3 months–14 years. In all cases, testicular biopsy caused no acute adverse effects. Early translational studies have demonstrated that genes known to be essential for mouse SSC self-renewal (e.g., Ret proto-oncogene; GDNF-family receptor α1; B-cell CLL/lymphoma 6, member B) were highly expressed in both prepubertal human spermatogonia and mouse gonocytes. Furthermore, when human prepubescent germ cells were transplanted into mouse testes, the cells preserved themselves by migrating to the "basement" membrane of the seminiferous tubule where they were maintained for months.

48. PSYCHOSEXUAL FUNCTIONING AMONG WOMEN IN THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS) Jennifer Ford, PhD; Toana Kawashima, MS; John Whitton, MS; Wendy Leisenring, ScD; Caroline Laverdière, MD; Marilyn Stovall, PhD; Lonnie Zeltzer, MD; Mary Randolph-Frye, PhD; Leslie Robison, PhD; Charles Sklar, MD. *Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Fred Hutchinson Cancer Research Center, Seattle, WA, USA; University of Montreal, Montreal, QC, Canada; The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; University of California, Los Angeles, Los Angeles, CA, USA; St. Jude Children's Research Hospital, Memphis, TN, USA*

Background: Data on psychosexual functioning among adult survivors of childhood cancer are quite limited. This study seeks to assess the impact of survivorship on psychosexual functioning and quality of life among young adult female survivors of childhood cancer who are participants in the CCSS.

Methods: We recruited female survivors who were at least 18 years of age and completed the Follow-up 1 CCSS study questionnaire. 2178 of 4643 eligible survivors (46.9% participation rate) and 410 of 1066 siblings (38.4% participation rate) completed the Women's Health Survey that included questions on sexual functioning, sexual self schema, psychological and physical symptoms, and quality of life. Participants were more likely to be older, married, more highly educated, diagnosed with cancer at older ages (survivors only), Caucasian (survivors only), and have ovarian failure (survivors only) compared to women who did not participate. Participants were approximately 30 years old (mean [Range] age in years: survivors=29.9 [18.0–51.0], siblings=32.1 [18.0–52.0]).

Results: In multivariable linear and logistic regression models controlling for age, marital status, education level, income and ethnicity, survivors reported significantly greater sexual difficulties, including significantly lower sexual arousal ($p < 0.001$), desire($p < 0.001$), interest($p<0.001$), and satisfaction($p=0.0092$) as compared to siblings (mean differences were between 0.23 and 0.31, cutoff of 0.2 indicative of clinical significance) and worse quality of life (defined as scoring ≤40 on subscales of the SF-36) on the domains of physical functioning(OR=0.39, p=0.0080) and general health perceptions(OR=0.41, $p<0.001$) compared to siblings. Additionally, the odds of survivors reporting anxiety/fears(OR=1.32, p=0.019) were significantly greater than for siblings.

Conclusions: Future analyses will examine differences in psychosexual functioning within our cohort of survivors associated with sociodemographics, diagnosis/treatment, ovarian functioning and/or hormone replacement variables.

Identification of the prevalence of and risk factors for psychosexual dysfunction are essential for the future development of targeted interventions for survivors who experience sexual dysfunction.

49. POSTPARTUM HEMORRHAGE IN FEMALE CHILDHOOD CANCER SURVIVORS PREVIOUSLY TREATED WITH ABDOMINAL RADIOTHERAPY

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Background: To describe pregnancy outcome in female childhood cancer survivors.

Methods: From a total cohort of 238 female survivors, 40 women were included. Data on pregnancy outcome were compared with data from a unique cohort of control subjects (n=9.031) retrieved from The Netherlands Perinatal Registry, a nationwide database of pregnancy outcome parameters of all births in The Netherlands between January 2000 and December 2005, registered by midwives, obstetricians and pediatricians. Data were matched for age at pregnancy, year and month of delivery and parity.

Results: At diagnosis, survivors were 6.9 years old (median; range 0.1–16.8 yrs) and at time of pregnancy, the median age was 29.7 years (range 21.4–36.8 yrs). The median time between stop of therapy and date of delivery was 20.2 years (range 6.9–32.5 yrs). Seventeen women had survived childhood acute lymphoblastic leukemia or non-Hodgkin lymphoma and 4 women had been treated for Hodgkin lymphoma. The remaining survivors had been treated for solid tumors (n=19). Most women were primigravida (n=28/40; 70%). Pregnancies were uneventful in survivors treated with chemotherapy only or surgery only. Survivors who previously received radiotherapy to the abdomen (n=6) delivered more preterm (mean gestational age in survivors = 34.9 weeks vs. 39.1 weeks in controls; P=0.001). Their offspring had normal birth weight after adjustment for gestational age (mean birth weight in offspring of survivors 2.503 g vs. 1.985 g; P=0.22). They also had more often postpartum hemorrhage than controls (33% in survivors vs. 5% in controls; $P<0.01$).

Conclusions: Childhood cancer survivors irradiated to the abdomen have an earlier delivery and more often postpartum haemorrhage. This stresses the need for close monitoring of the delivery, including inpatient perinatal care in this group of childhood cancer survivors.

50. POST-RADIOTHERAPY THYROID DYSFUNCTION IN LONG TERM SURVIVORS OF CHILDHOOD HODGKIN'S DISEASE: A PRACTICAL APPROACH TO MANAGEMENT IN DEVELOPING COUNTRIES

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Background: To assess the long term effect of radiation on thyroid function in survivors of childhood HD, registered in After Completion Therapy (ACT)Clinic between Feb. 1991 to Aug. 2009.

Method: HD Survivors who received RT to thyroid were evaluated with Thyroid Function Tests (TFT) and further categorized into three groups; (A) with normal TFTs, (B)TSH <4 fold above normal and (C)TSH >4 fold above normal. This latter group and those with progressively increasing TSH from Group B were treated with L-thyroxine. Those with thyromegaly underwent evaluation and treatment.

Results: 334/1073 (31%) of HD survivors (median age at diagnosis 8 yrs; R=1–19 yrs) were registered in ACT clinic. 173/334(52%) HD survivors received radiation to neck. TFTs were done in 164/173(95%); 68/164 (41%) were normal and 96/164 (59 %) were abnormal. 1/96(1%) had low TSH with clinical hyperthyroidism. Remaining 91/96 who are on regular follow up were divided into group B (75%; 68/91) and Group C (25%; 23/91). (Median RT dose= 30 Gy;R=16–47Gy). Median duration of follow-up after RT was 12 years (4–36

years). All Group C and 7/68 (10 %) from Group B who had progressive increase in TSH on follow up received L-thyroxin. Thyromegaly was seen in 16/164; 10%(10-diffuse and 6-nodular). 12/16 (75%) underwent FNAC; 7/12 (58%) had benign histology and 5/12 (42%) had doubtful histology. Throidectomy was done in all 5 (3-benign, 2-papillary CA).

Conclusion: Considerable debate has been generated over whether compensated hypothyroidism (raised TSH and normal T4) actually represents a mild yet significant form of hypothyroidism, or merely a biochemical abnormality. Our results indicate that Group C should be given replacement therapy, as this group tends to progress to overt hypothyroidism if left untreated. Those in Group B may be followed yearly, replacement therapy being reserved for a small group who show progressive increase in TSH value. Compliance with life long L-Thyroxine therapy, though cheap, is a major problem and default in therapy may lead to fluctuations in T4 levels adversely affecting the growth. This needs to be balanced against the risk of subsequent thyroid neoplasm.

51. PREVALENCE OF ADVANCED BONE AGE IN A COHORT OF PATIENTS WHO RECEIVED 13-CIS-RETINOIC ACID Wendy L. Hobbie, MSN, CRNP, FAAN; Claire A. Carlson, BSN, RN; Denise Gruccio, MSN, CRNP; Sogol Mostoufi-Moab, MD; Jill P. Ginsberg, MD. *Divisions of Oncology and Endocrinology, The Children's Hospital of Philadelphia, Philadelphia, PA, USA; University of Pennsylvania, School of Nursing, Philadelphia, PA, USA; Department of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA, USA*

Purpose: Autologous stem cell transplant is standard treatment for patients with high-risk neuroblastoma. In the last decade, 13-cis-retinoic acid (13-cis-RA) has been added to the treatment of this disease. In survivors of neuroblastoma, short stature is consistently observed and the etiology is multifactorial. Causes include growth hormone deficiency as well as poor growth of irradiated long bones. Within our survivorship population, we have observed that a number of patients also have advanced bone ages (one of the labeled side effects of 13-cis-RA). There is a paucity of data on the incidence of advanced bone age/ premature epiphyseal closure in neuroblatoma patients treated with 13-cis-RA.

Objectives: 1) Determine the prevalence of advanced bone age/ premature epiphyseal closure in patients with high risk neuroblastoma treated ±13-cis-RA. 2) Determine if treatment exposures (TBI alone, TBI plus 13-cis-RA or 13-cis-RA alone) impact the occurrence of advanced bone age.

Methods: Survivors diagnosed with high-risk neuroblastoma and treated with autologous stem cell transplant at CHOP between 1990 and 2005. 1) Alive and at least 5 years from diagnosis and 2 years from completion of all therapy. 2) Has been seen at least once in CHOP's Cancer Survivorship Program and had a bone age.

Results: Survivors who received TBI alone (n=8), all had normal bone ages. 23% of survivors who received TBI in combination with 13-cis-RA (n=17) had advanced bone age. 50% of survivors who did not receive TBI but did receive 13-cis-RA (n=8) had advanced bone age (4/8). 32% of neuroblastoma survivors who have received 13-cis-RA as part of their therapy have an advanced bone age.

Conclusions: Children treated with 13-cis-RA are at risk for advanced bone age that may dramatically impact the end adult height. Ongoing evaluation of this population is necessary to examine the effect of 13-cis-RA on end adult height.

52. LONG TERM HEALTH OUTCOMES AFTER TREATMENT FOR CANCER IN TEENAGE AND YOUNG ADULTHOOD Raoul C Reulen, PhD; Anjali Shah, PhD; Sarah Darby, PhD; Angela Edgar, MD; Richard Feltbower, PhD; Lorna Fern, MD; David Forman, PhD; Robert M Grant, MD; Diana Greenfield PhD; Tony Moran PhD; John A Radford, MD PhD; Peter Rose, MD; Helen Spoudeas, MD; Hamish Wallace, MD; Jeremy, Whelan MD; Michael M Hawkins, DPhil. *Centre for Childhood Cancer Survivor Studies, School of Health and Population Sciences, Public Health Building, University of Birmingham, Birmingham, UK; CRUK Cancer Survival Group, London School of Hygiene and Tropical Medicine, London, UK; Clinical Trial Service Unit & Epidemiological Studies Unit, University of Oxford, Oxford, UK; Royal Hospital for Sick Children, Departments of Paediatric Haematology & Oncology, Edinburgh, UK; Centre for Epidemiology and Biostatistics, Paediatric Epidemiology Group, University of Leeds, UK; University College Hospital, Department of Oncology, London, UK; National Cancer Intelligence Network, London, UK; St. Brycedale Surgery, Kirkcaldy, UK; Cancer Research Centre, Weston Park Hospital, Sheffield, UK; North West Cancer Intelligence Service, Centre for Cancer Epidemiology, Christie Hospital, Manchester, UK; Cancer Research UK Department of Medical Oncology, Christie Hospital, Manchester, UK; University of Oxford, Department of Primary Health Care, Oxford, UK*

Background: To identify subgroups of the almost 300,000 individuals diagnosed with cancer aged 15 to 39 years, in England and Wales, between 1971 and 2006 at substantially increased risk of particular fatal or nonfatal adverse health outcomes. A database will be established to investigate the observed and expected risks of: specific causes of death, specific types of subsequent primary cancer and specific types of non-cancer morbidity (including cardiovascular, pulmonary, urological, hepatic and endocrine conditions). Evidence for the cure of specific types of cancer would also be assessed.

Methods: Record linkages between the established database and the national death and cancer registries, the Hospital Episode Statistics (HES) for England, the Patient Episode Database for Wales (PEDW) in Wales, the General Practice Research Database (GPRD) and the Myocardial Ischaemia National Audit Project (MINAP) will be undertaken.

Results: From such linkages it will be possible to identify groups of patients (defined by type of cancer, age at diagnosis, calendar year of diagnosis, period of follow-up, attained age and sex) at a substantially increased risk of specific adverse health outcomes. These would be used as a basis for: (i) undertaking nested case-control studies, including the collection of detailed cancer treatment information, of such adverse health outcomes, and (ii) if the risks identified are of sufficient importance to the Department of Health then specific groups could be considered for recall to clinics for counselling, screening or other interventions.

Conclusions: This large population-based study will be the first comprehensive investigation of serious adverse health outcomes of cancer therapy relating exclusively to those diagnosed aged 15 to 39 years. It will provide a reliable evidence base available for developing survivorship programmes, educating clinicians and patients, and informing future clinical and epidemiological trials.

53. **THE FREQUENCY OF NEWLY DIAGNOSED HEALTH CONDITIONS DIAGNOSED 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 and Yale Cancer Center, New Haven, CT, USA*

Purpose: Specialty childhood cancer survivorship clinics have been established to screen for potential long-term therapy-related effects. However, the additional merit of health care delivered by a comprehensive survivor clinic, beyond usual medical care, is unknown. We sought to determine the frequency of newly identified cancer therapy-related late effects in childhood cancer survivors at their initial visit to Yale HEROS clinic (New Haven, CT).

Methods: This retrospective cohort study included patients diagnosed with cancer at an age <21 years who attended HEROS Clinic from 2/2002-6/2009 and who were within 3–10 years after diagnosis, a period in which most cancer patients receive regular medical follow-up. All HEROS attendees were screened according to the Children's Oncology Group Long-Term Follow-Up Guidelines in addition to an interview with a psychologist. The frequencies of previously known and newly discovered health conditions at the first HEROS clinic visit were ascertained and described.

Results: Sixty-nine patients were eligible for analysis (current age 6–32 years, 58% female). Sixty-one (88%) were in regular medical follow-up. Prior cancer diagnosis included leukemia (33%), lymphoma (17%), sarcoma (22%), brain tumors (7%), Wilms tumor (12%), neuroblastoma (3%) and other (6%). The table displays the frequency of previously known, newly-identified, and total chronic health conditions. The initial HEROS visit resulted in additional diagnoses in most categories reviewed. Newly identified hormonal abnormalities, cardiovascular disease, and osteoporosis were diagnosed in 14%, 14%, and 9% of patients, respectively. Psychological screening resulted in previously unrecognized mental health disease and neurocognitive impairment in 29% and 30% of patients, respectively. Rare pulmonary and no subsequent cancer conditions were discovered.

Conclusions: The HEROS clinic detected multiple therapy-related conditions that were previously unrecognized in childhood cancer survivors receiving regular medical care, supporting the importance of individualized screening at a specialty survivor clinic.

Table. Frequency of Treatment-Related Complications in Yale HEROS Survivor Clinic, Patients 3–10 Years Post Diagnosis

	Known before Specialty Clinic Visit	Newly Identified at Specialty Clinic Visit	Total
Hormonal abnormality	22% (15/69)	14% (10/69)	36% (25/69)
Mental Health Condition	26% (18/69)	29% (20/69)	55% (38/69)
Neurocognitive Impairment	26% (18/69)	30% (21/69)	57% (39/69)
Neurological Complication	22% (15/69)	12% (8/69)	33% (23/69)
Cardiovascular Disease	10% (7/69)	14% (10/69)	25% (17/69)
Osteoporosis	0% (0/69)	9% (6/69)	9% (6/69)
Pulmonary Disease	1% (1/69)	1% (1/69)	3% (2/69)
Subsequent Cancer	1% (1/69)	0% (0/69)	1% (1/69)

54. CHILDHOOD CANCER: DO FEMALES EXPERIENCE MORE ACUTE TOXICITIES THAN MALES? A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP Kathleen Meeske, PhD, RN; Lingyun Ji, MS; Anna Butturini, MD; David Freyer, DO; MS; Paul Gaynon, MD; Kathleen Ruccione, MPH, RN; Richard Sposto, PhD; Stuart Siegel, MD. *Childrens Hospital Los Angeles, Los Angeles, CA, USA*

Purpose: Drug dosing is based on a gender-independent estimate of body surface area. In childhood acute lymphoblastic leukemia (ALL), females have a consistently better event-free survival than males. However, long-term follow-up studies often find an increase in treatment-related late effects among female cancer survivors. The purpose of this study is to determine if females also experience

more acute toxicities than males during active treatment.

Methods: We reviewed data collected on the Children's Cancer Group (CCG) high-risk ALL study, CCG-1961. We studied 830 female and 1224 male patients enrolled between 1996 and 2002, ages 1–21 years. Linear and logistic regression were used to analyze differences in hospital days, length of treatment courses, incidence of grade 3 and 4 toxicities (CCG Toxicity Rating Scale) and reported supportive care use between males and females for the first four phases of treatment. Analyses were adjusted for age, race, treatment regimen, phase and body surface area.

Results: Females had significantly more hospital days than males (Δ=1.6, 1.3, 1.2 and 1.4 days, $p<0.001$, <0.01, <0.001 and <0.001, for Induction, Consolidation, Interim Maintenance and Delayed Intensification, respectively). Females had more grade 3 and 4 toxicities: nervous system (OR=1.6, $p<0.01$), gastro-intestinal (OR=1.6, $p<0.0001$), pancreas (OR=1.7, $p<0.0001$), and infections (OR=1.6, $p<0.001$). Risk of having therapy delayed more than a week due to treatment-related toxicities was significantly higher for females (OR=1.2, $p<0.02$). Females received more IV antibiotics (OR=1.2, $p<0.01$), IV antifungals (OR=1.7, $p<0.0001$), IV analgesics (OR=1.3, $p<0.05$), parenteral nutrition (OR=1.9, $p<0.0001$) and blood products (OR=1.8, $p<0.0001$).

Conclusions: Females treated on CCG-1961 experienced more acute toxicities than males. It appears that female pediatric cancer patients may be at higher risk of developing both acute and long-term complications. Sex-specific differences in outcomes may be due to factors such as differences in body composition, endogenous hormones and drug metabolism. Further study is needed to better understand the disparities in treatment-related toxicities found among male/female pediatric cancer patients.

55. PULMONARY COMPLICATIONS IN SURVIVORS OF CHILDHOOD CANCER: A LONG-TERM FOLLOW-UP STUDY Renée L. Mulder, MSc; Nienke N.M. Thönissen, MD; Heleen J.H. van der Pal, MD; Paul Bresser, MD, PhD; Caro C.E. Koning, MD, PhD; Huib N. Caron, MD, PhD; Leontien C.M. Kremer, MD, PhD. *Department of Pediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands; Departments of Pulmonology, Medical Oncology and Radiation Oncology, Academic Medical Center, Amsterdam, The Netherlands; Department of Medical Oncology, Academic Medical Center, Amsterdam, The Netherlands; Department of Radiation Oncology, Academic Medical Center, Amsterdam, The Netherlands*

Background: Survivors of childhood cancer treated with bleomycin, radiotherapy involving the lungs and/or surgery involving the lungs are at risk of developing pulmonary complications. Several studies have evaluated the prevalence and risk factors of pulmonary complications after treatment for childhood cancer. The reported prevalence of pulmonary complications varied across the studies. Most studies however had limited sample size, short follow-up duration and/or did not perform pulmonary function tests. To our knowledge, until now no studies have investigated the risk and risk factors of subclinical pulmonary complications in a large cohort of long-term survivors of childhood cancer.

Purpose: To evaluate the prevalence of subclinical pulmonary complications and to identify associated risk factors in a large cohort of childhood cancer survivors treated with potentially pulmotoxic therapy between 1966 and 1996 with a minimal follow-up of five years after diagnosis.

Methods: All children (<18 years) who were treated for a primary malignancy in the Emma Children's Hospital/Academic Medical Center between 1966 and 1996, who survived for at least five years after diagnosis and who were treated with potentially pulmotoxic therapies will be included in this study cohort. As outcome measurement three parameters of subclinical pulmonary function will be evaluated: vital capacity (VC), forced expiratory volume in 1 second (FEV1) and carbon monoxide diffusion capacity corrected for alveolar volume (TLCOcVA). Subclinical pulmonary complications will be graded according to the Common Terminology Criteria for Adverse Events.

Results: The results of this study will be presented at the conference.

Conclusions: This cohort study will evaluate the prevalence and associated risk factors of subclinical pulmonary complications in long-term survivors of childhood cancer.

56. PEDIATRIC CANCER SURVIVORS ARE AT HIGH RISK FOR CHRONIC KIDNEY DISEASE Jennifer G. Jetton, MD; M. Fatih Okcu, MD, MPH; Zoann E. Dreyer, MD; Rosalind Bryant, PhD, APRN-BC, PNP; Hilary Suzawa, MD; Stuart L. Goldstein, MD. *Renal Section/Pediatrics Hematology-Oncology Section/Pediatrics, Baylor College of Medicine, Houston, TX, USA*

Background: Few pediatric studies describe the long-term impact of cancer and its treatment on kidney function. Recent published data from our center suggest children are at risk for chronic kidney disease (CKD)/chronic kidney injury (CKI) following a single episode of acute kidney injury. Given the multiple kidney insults that can occur during cancer treatment, the pediatric cancer survivor cohort may thus be at high risk for developing CKD/CKI. Such insults include not only nephrotoxic chemotherapies, but also tumor lysis, aminoglycosides, and sepsis. We therefore conducted a prospective study of patients in Texas Children's Cancer Center Long-Term Survivor Clinic to determine their kidney outcomes. We hypothesized that these patients are at risk for CKD/CKI. Patients with kidney tumors,

neuroblastoma, and stem cell transplant were excluded. Outcomes were: est GFR (high or low) by Schwartz formula (age <18 yrs) or MDRD (age ≥18 yrs), hypertension (HTN), microalbuminuria (MAlb), proteinuria (Prot) and tubular dysfunction (Tub dys).

Methods: 150 pts (44% female) were enrolled from October 2008 to August 2009. Mean age at cancer diagnosis and visit were 5.3±3.8 yrs (range 0.01–19.7 yrs) and 15.1±5.2 yrs (range 5.7–34.5 yrs) respectively. Most common cancer diagnosis was pre-B ALL (n=84, 56%).

Table. Prevalence of Kidney Outcomes

HTN	↑ or ↓ GFR	Prot	MAlb	Tub dys
32 (21%)	78 (52%)	4 (3%)	7 (5%)	3 (2%)

HTN + GFR	HTN + Prot	HTN + MAlb	GFR + Prot	GFR + MAlb	GFR + Tub dys
14 (9%)	1 (0.6%)	1 (0.6%)	1 (0.6%)	3 (2%)	1 (0.6%)

Results and Conclusions: We observed a high prevalence (69%) of CKD/CKI in pediatric cancer survivors, suggesting these patients are at risk for long-term renal sequelae and warrant regular surveillance. Future analyses include determination of patient and treatment-related risk factors for CKD/CKI in order to develop a Kidney Risk Scoring system for early identification of high-risk patients.

57. GASTROINTESTINAL SYMPTOMS AND NON-MALIGNANT DISEASE IN IRRADIATED SURVIVORS OF HODGKIN'S LYMPHOMA

Tamara Chang, MD; Lisa Diller, MD; Lisa B Kenney MD. *University of Massachusetts Medical Center, Worcester, MA; Dana Farber Cancer Institute/Children's Hospital Boston, MA, USA*

Background: Irradiated Hodgkin's lymphoma (HL) survivors are vulnerable to gastro-intestinal (GI) disease although the prevalence and spectrum of presenting symptoms are unknown.

Methods: To determine the prevalence of non-malignant GI disease and associated GI symptoms in irradiated HL survivors diagnosed age < 25 years, we reviewed clinic notes of 157 survivors treated with radiation therapy seen in our pediatric survivor clinic between 1994 and 2009.

Results: The 157 survivors median age at diagnosis=15 yrs (range 3-25); median age at follow-up= 33 yrs (range 13-59); median follow-up time=18 yrs; and 59% were female. Overall, GI disease was documented in 56/157 survivors (36%), 12 survivors had more than one GI diagnosis. The most common diagnosis was gastro-esophageal reflux disease (GERD) n=36, followed by Barrett's esophagitis n=4, cholecystitis/cholelithiasis n=5, GI dysmotility n=3, hiatal hernia n=3, small bowel arterio-venous malformation n=3, recurrent small bowel obstruction n=3, benign colonic adenomas= 3, esophageal stricture/achalasia n=2, non-Barrett's esophagitis n=2, gastritis n=2, irritable bowel syndrome n=2, gastrinoma n=1, gastric polyps n=1, autoimmune pancreatitis n=1, and lactose intolerance n=1. At the time of clinic visit, common GI symptoms were a presenting complaint for 24/157 survivors. Symptoms included heartburn/reflux n=10, dysphagia n=6, non-specific abdominal pain n=4, dyspepsia n=2, diarrhea n=1, and early satiety n=1. Survivors treated with 30 Gy or more radiation were more likely to have GI disease compared to those treated with <30 Gy (OR=4.3, 95% CI 1.9-10.0). Multiple logistic regression is planned to assess the contribution of demographics, HD treatment, and lifestyle factors to GI symptoms and disease prevalence.

Conclusions: Irradiated HD survivors have a high prevalence of GI disease including both common and rare diagnoses. Survivors should be routinely questioned about GI symptoms, and diagnostic evaluation for unusual diagnoses associated with common symptoms should be considered.

58. HEALTHCARE UTILIZATION AMONG YOUNG ADULT CANCER SURVIVORS IN BRITISH COLUMBIA, CANADA

Mary L. McBride, MSc; Anne-Marie Broemeling, PhD; Karen Goddard, MD; Maria Lorenzi, MSc; Suli Ma, MSc; Lauren MacDonald, MSc; Sheila Pritchard, MD; Paul Rogers, MD; Sam Sheps, MD; John J Spinelli, PhD; Lijing Xie MHSc. *Cancer Control Research Program and Division of Radiation Oncology, British Columbia Cancer Agency, Vancouver, BC, Canada; Centre for Health Services and Policy Research and School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada; British Columbia Children's Hospital, Vancouver, BC, Canada*

Abstract: Cancer and its treatment can produce complications that may not become apparent until years later. How such complications effect demand for health services is not yet understood in young adult cancer survivors. The CAYACS (Childhood/Adolescent/Young Adult Cancer Survivors) Research Program has assembled a cohort of cancer patients surviving at least five years, diagnosed from 1970 and onwards under 25 years in British Columbia, Canada. The CAYACS program examines multidimensional survivorship issues, through linkage to population-based administrative datasets that contain outcome information. In this study, healthcare utilization, as measured through hospitalizations, health care practitioner (HCP) visits and physician-ordered outpatient services in a three year period, was explored among survivors diagnosed aged 20 to 24 years. A total of 497 survivors and a randomly selected comparison group (4790 individuals) frequency matched by age and gender comprise the study groups. Nearly all (98.8%) survivors had a visit to a HCP (excluding oncologists), compared to 70% of population controls (RR=1.94; 95% CI 1.27–1.53). A higher proportion of survivors

of lymphoma, central nervous system tumors, and bone tumors had at least one visit to an oncologist, compared to other diagnostic groups. Survivors demonstrated twice the odds of having any hospitalization (OR=2.1; 95% CI 1.68-2.62), an increase in physician-ordered outpatient services (RR=1.27; 95% CI 1.23–1.32) and mean cost associated with said services (OR=1.33; 95% CI 1.19–1.48). Survivors having an original leukemia diagnosis, receiving combined radiation and surgery, or living in rural areas showed a higher demand for physician-ordered outpatient services. Limited research exists on survivors of cancers diagnosed in young adulthood and CAYACS provides a comprehensive methodology to gather province-wide information on this unique cohort. The results of this study illustrate the importance of addressing young adult survivors' needs in the health care system.

59. A NATIONAL CANCER SURVIVORSHIP INITIATIVE FOR CHILDREN AND YOUNG PEOPLE Gill Levitt, MBBS; Patricia Morris; Judi Tapp; Faith Gibson, PhD; Adam Glaser, MBBS on behalf of the CYP workstream. *Great Ormond Street Hospital for Children NHS Trust, London, UK; NHS Improvement National Team; London South Bank University, London, UK; Yorkshire Regional Centre for Paediatric Oncology and Haematology, Leeds, UK*

Introduction: Within England and Wales a Cancer Reform Strategy was proposed to improve the care of patients with cancer. Pressure from patients, charities and health care professionals had placed the care and support of those living with or beyond cancer firmly on the national agenda. Through this the Department of Health established the National Cancer Survivorship Initiative (NCSI), a five year strategy to cover all aspects of living with and beyond cancer. With less than 1.5% of cancers occurring under the age of 30, the original focus was on adults. However, targeted lobbying identified the need for a specific focus on children and young people (CYP) within the NCSI.

Within the NSCI, the CYP workstream was formed with the aim of coordinating activities focused on improving the lives of children and young people treated for cancer through service improvement methodology.

Method: Health care professionals, researchers, service improvement leads, charity representatives, parents and survivors were asked to highlight the important issues. Paediatric oncology centres submitted expressions of interest in response to these issues.

Results: Nine clinical sites, 2 university based groups and 1 charity were commissioned to undertake this work covering:

- Different models of care from childhood through transition to adulthood
- Survivors care plans
- Assessment of risk stratification
- IT support
- Holistic needs of cancer survivors
- Patients lost to follow-up

With the help of service improvement leadership and funding (£1million) the sites will provide evidence of methods to improve quality of care and productivity in a cost effective way which will assist in commissioning of services.

Conclusion: Effective pressure on policy makers resulted in significant national investment to promote an agenda enabling improvement of survivors' experiences. Embedding aftercare within central national health policy will enhance equity of access and provision of care.

60. THE CURRENT STATUS OF FOLLOW-UP SERVICES FOR CHILDHOOD CANCER SURVIVORS: A REPORT FROM THE NEW ENGLAND CONSORTIUM Lisa B. Kenney, MD; Heather Bradeen, MD; Nina S. Kadan-Lottick, MD, MSPH; Lisa Diller, MD; Alan Homans, MD; Cindy L. Schwartz, MD. *Dana Farber Cancer Inst./Children's Hosp., Boston, MA, USA; Vermont Children's Hosp./FAHC, Burlington, VT, USA; Yale Cancer Center, New Haven, CT, USA; Hasbro Children's Hosp., Providence, RI, USA*

Background: National guidelines for follow-up care of childhood cancer survivors have been established. We hypothesize that institutions face common challenges in providing specialized services to meet the complex needs of survivors.

Methods: To describe pediatric survivor services available in a geographically and socio-economically diverse region of the US and to identify common challenges we surveyed all 12 academic institutions with pediatric oncology programs in the New England (NE) region.

Results: Participating sites diagnose a median of 34 (range 10–250) new pediatric cancers annually. The 12 institutions have 11 designated survivor clinics (1 has separate clinics for brain tumor and general oncology survivors; 2 integrate survivor care into acute oncology clinic). Survivor clinics meet weekly (n=5), monthly (n=5) or bi-monthly (n=1). Clinics are staffed by: pediatric oncologists (11/11); nurse practitioners (9/11); social workers/psychologists (9/11); RNs (5/11); primary care physicians (3/11); and sub-specialists (3/11). Most programs recommend annual follow-up for all survivors (7/11); however, point of entry into survivor programs is variable. Treatment summaries and care plans based on Children's Oncology Group guidelines are part of survivor care at each program. Almost all (10/11) refer to sub-specialists to manage late effects; most frequently endocrinology, cardiology, and neuropsychology. Only 4

programs identified a policy for transitioning survivors to adult care (2 to adult survivor programs, 2 to adult primary-care) and 4 reported this as a problem. Two clinics had no designated funding for survivor services; 8/11 receive institutional support; 5/11 philanthropic. Five institutions conduct research in survivorship (1 government-funded, 2 philanthropy-funded, 2 both).

Conclusions: Pediatric oncology services in the NE region are making progress toward meeting follow-up care goals for childhood cancer survivors. Funding for resource intense programs, transitioning care to adult clinical services, volume of subspecialty referral, and participation in research are common challenges that can potentially be addressed through regional collaboration.

61. COLLABORATIVE EFFORTS TO DEVELOP AND MAINTAIN A CHILDHOOD CANCER SURVIVOR COHORT: A REPORT FROM PROJECT REACH Christopher J. Recklitis, PhD MPH; Cheryl Medeiros-Nancarrow; Laura Fox; Anna Merport; Eric Zwemer; Sharon Bober, PhD; Robert Casey, PhD; Cori Liptak, PhD; Christine Chordas, MSN; Peter Manley, MD; Lisa Kenney MD, MPH; Lynda Vrooman, MD; Lisa Diller, MD. *Perini Family Survivors' Center, Dana-Farber Cancer Institute & Harvard Medical School, Boston, MA, USA*

Background: Enrolling adequate numbers of participants can be a challenge for survivorship researchers who may involuntarily compete for a small pool of survivors at a single institution. Consortia and cooperative groups can provide access to larger cohorts but may have limited opportunities to pilot new measures or interventions. To address these barriers, we developed Project REACH (**R**esearch **E**valuating **A**fter **C**ancer **H**ealth) to assemble a cohort of locally treated childhood cancer survivors who complete annual health surveys.

Methods: Previously planned survivorship studies were combined in a single research protocol which provides for ongoing subject contact. Investigators include psychologists, oncologists, and nurse practitioners, and study measures assess physical and emotional health outcomes including fatigue, pain, depression and sexual health. Shared resources include a single protocol, central database, and staff to recruit participants and manage data. Study arms allow tailoring of measures for distinct patient groups, with aims and measurements continually updated by protocol amendment. Regular mailings, participant incentives, and collection of in-depth contact information are used to maintain participation.

Results: Over 24 months, 435 eligible survivors were approached at a routine clinic visit, and 352 (81%) consented and completed a baseline survey. To date, 116 participants have completed the Year 2 survey, and only two have been lost to follow-up. Analysis of baseline data is underway. An ancillary survey of sun protection behaviors enrolled 220 (60%) of the 363 survivors contacted, and an intervention study to increase sun protection adherence is in-progress.

Conclusions: A collaborative study with centralized resources benefits survivorship researchers in a cancer center setting. Though the nature of a convenience cohort may limit generalizability, data from Project REACH support the development of multiple descriptive and intervention studies. Future aims including cohort expansion to include 800 survivors and 200 parents will be presented.

62. KNOWLEDGE AND RISK PERCEPTION OF LATE EFFECTS AMONG CHILDHOOD CANCER SURVIVORS BEFORE AND AFTER VISITING A CHILDHOOD CANCER SURVIVOR CLINIC Brooke O. Cherven, RN, MPH CPON; Sarah Brand, BS; Ann E. Mertens, PhD; Lillian R. Meacham, MD; Karen Wasilewski-Masker, MD, MSCR. *Aflac Cancer Center and Blood Disorders Service, Children's Healthcare of Atlanta, Atlanta, GA, USA; Emory University, Atlanta, GA, USA*

Background: Childhood cancer survivors are at risk for treatment-related medical problems and education about these risks is crucial to ensure appropriate surveillance and early intervention. In this study we explored survivors' baseline knowledge regarding late effects and measured change in knowledge after visiting a multi-disciplinary childhood cancer survivor clinic.

Methods: Participants over a recruitment period of one year completed a baseline questionnaire immediately before their first survivor clinic visit. During the visit survivors/parents received individualized education including a treatment summary, risk profile and surveillance plan using the Children's Oncology Group Long-term Follow-up Guidelines. A follow-up questionnaire (identical to the baseline) was distributed one month after the visit. Participants ≥16 years of age completed the questionnaires; the parent/guardian completed questionnaires for participants <16 years old. 66 participants completed the baseline survey and 35 completed the follow-up survey.

Results: An overall knowledge score of individual risk for secondary cancers, infertility, osteopenia, cataracts, neurocognitive, kidney, liver, lung, and cardiac problems improved for both parents and survivors. Parents correctly identified 67% of the late effects their child is at risk for at baseline which increased to 76% correct at follow-up ($p<.01$). The survivors' baseline knowledge score was 52% correct with 63% correct at follow-up ($p<.01$). The baseline survey identified knowledge gaps among survivors ≥16 years old regarding risk for infertility, secondary cancers and cardiac late effects. Of the survivors who reported being at risk for infertility, 11% were actually not at risk. 80% of survivors at risk for secondary malignancies, and 43% at risk for cardiac problems, did not identify themselves at risk.

Conclusion: Receiving individualized education during a survivor clinic visit increased participant knowledge regarding risk for late effects. Additional research is needed to further improve overall knowledge of late effects in this vulnerable population.

63. PSYCHOSOCIAL AND VOCATIONAL COUNSELING NEEDS IN CHILDHOOD CANCER SURVIVORS Shaini Joy, RN, OCN, MSN, FNP; Joann Ater, MD; Martha Askins, PhD; Rhonda Robert, PhD; Bartlett Moore, BA, MA, PhD; Sandra Medina, MS, LPC, LPA; Sujin Ann-Yi, MA, LMFT; Grace Yang, MEd, LPC. *Children's Cancer Hospital, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA*

Background: Advances in oncology have resulted in increasing number of individuals being successfully treated for childhood cancers. As their survival rates increase, so must pediatric oncology research on the long-term effects of disease and its treatment on quality of life and psychosocial adjustment.

Purpose: The purpose of this poster is to describe the current childhood cancer survivorship program at M.D. Anderson Children's Cancer Hospital that includes a psychosocial screening process and health-related quality of life assessment.

Method: A psychosocial screening interview was developed to identify individual psychosocial needs of long term survivors and to facilitate referrals to the following support services: social work, child and adolescent life, educational planning, career and vocational counseling, neuropsychology, psychology, and psychiatry. Caregivers and/or survivors voluntarily completed the interview prior to or on the day of follow-up. The caregivers and/or survivors were also requested to voluntarily complete the PedsQLTM 4.0 (Pediatric Quality of Life Inventory) Generic Core Version, Cancer Module, and Multidimensional Fatigue Scales on the day of the clinic visit to assess health-related quality of life.

Results: The interview data assists in identifying the most needed psychosocial services from the childhood cancer survivor's perspective. Specific referrals were made based on the support services requested by the survivors or caregivers.

Conclusion: Vocational/career counseling and neuropsychology evaluations were the most requested services by long-term survivors. Evaluation of the services requested and provided will help in implementing a comprehensive approach for the long term survivors of childhood cancers. Obstacles to accessing or following through with services are also included.

64. COMMUNICATION OF ADOLESCENTS WITH CANCER AND THEIR HEALTH CARE PROVIDERS DURING AN END OF ACTIVE TREATMENT MEDICAL APPOINTMENT Marilyn Stern, PhD; Jennifer Lamanna, MA; Claire Russell, BA; Laura Siminoff, PhD; Robyn Dillon, MSW; Kamar Godder, MD. *Departments of Psychology, Pediatrics, and Social and Behavioral Health and Division of Pediatric Hematology/Oncology, Virginia Commonwealth University, Richmond, VA, USA*

Background: A pilot study is currently being conducted to evaluate the quality and content of communication between adolescents with cancer (AWC) and their health care providers (HCP) during an end of active treatment visit (EACTV). Of specific interest is communication regarding post-treatment issues such as academics, careers, and long-term side effects.

Methods: An EACTV is audio-recorded for AWC (N=13), ages 10–21, who are within six months of ending active treatment. Parents and AWC also engage in a 'Recall and Reaction' session (also audio-recorded) to discuss perceptions of communication with the HCP team throughout treatment. Preliminary coding of the data from this pilot is currently underway using the Noldus Observer XT 7.0TM.

Results: Qualitative coding is currently underway to examine communication themes. Among the specific issues discussed are effects of treatment on academic performance, career interests, and higher education topics. The 'Recall and Reaction' session indicated that academic discussions mostly focus on homebound education or return to school issues, while career discussions center on future career plans.

Conclusion: The findings indicate the presence of a wide variety of academic and career issues being discussed between AWC and HCPs during the EACTV.

Research Implications: Further data collection and analysis are intended to guide the development of a communication intervention in which AWC are prompted to discuss academic and career-related issues at an EACTV. This intervention will assess how these discussions can be increased and to examine the effects of these discussions on academic and career-related outcomes.

Clinical Implications: Understanding the trends in academic-career communication during the EACTV is intended to enhance HCP/AWC communication and to ensure normative development in academic and career self-efficacy and planning for AWC.

65. THE TACTIC INITIATIVE: A MODEL OF SUCCESSFUL TRANSITIONING FROM PEDIATRIC ONCOLOGY TO INTERNAL MEDICINE Kerry M. Moss, MD; Brian S. Greffe, MD; Linda Overholser, MD; Jean S Kutner, MD, MSPH. *The Children's Hospital, Aurora, Colorado, USA; University of Colorado–Denver School of Medicine, Aurora, CO, USA*

Background: The TACTIC (Thriving After Cancer Treatment is Complete) initiative, a collaborative venture between pediatric oncology at The Children's Hospital and internal medicine at the University of Colorado, serves as a model of survivorship focused care with a unique emphasis on transitioning of patients into an adult primary care medical home.

Description: Currently there are over 270,000 long-term survivors of childhood cancer in the United States and recent identification of over 700 adult survivors of pediatric cancer within the Denver area alone. In an effort to recognize and address the late effects of childhood cancer therapy and the primary care needs of a now adult population, the TACTIC clinic was developed. Unlike many existing

childhood cancer survivorship clinics based in pediatric oncology clinics, the TACTIC clinic was established with an internal medicine focus allowing pediatric oncology to serve in a consultative role. The TACTIC clinic is held monthly housed in the Internal Medicine Department at the University of Colorado. During this multidisciplinary clinic each patient is evaluated by a pediatric oncologist, general internist, psychologist and cancer center nurse versed in survivorship. This assessment includes long term childhood cancer related follow-up, management of chronic health issues, general health maintenance and an assessment of the individual psychosocial needs of the patient. Patients are referred to a pool of educated and interested adult subspecialists on an as needed basis, further transitioning their services to within an adult care model.

Results and Conclusions: Serving over fifty long-term survivors in its first year of operation, the TACTIC initiative shows great promise as a successful model of transitioning, promoting a collaborative approach to long-term health, with a dual focus on past illness and future wellness. Preliminary feedback suggests high levels of patient satisfaction with the clinic experience and an increased commitment to their long-term health care plan.

66. ASSESSING THE UTILITY OF A TRANSITION PROGRAM: A SURVEY OF PARENT PARTICIPANTS Eileen C. Duffey-Lind, MSN, RN, CPNP; Laura Fox; Lisa Kenney, MD; Lynda M. Vrooman, MD; Christopher Recklitis, PhD; Lisa Diller, MD. *Dana-Farber Cancer Institute, Boston, MA, USA*

Background: An educational visit at the completion of therapy is offered to patients and families at our institution. The Transition Visit (TrV) includes: review of treatment, disease recurrence surveillance plan, discussion of potential late effects and receipt of a printed individualized "transition book" summarizing this information. The utility of the program has not been assessed.

Methods: We conducted a mailed survey of the 121 parent-participants in the program. Respondents reported their recollection of the TrV, their perception of the program, its timing, content and impact on well-being.

Results: Of 121 surveys, 49 were returned. The mean age of the patient at the time of TrV was 8.5 years (range 2–22 years), mean time from visit 2.1 years (range 1–3 years). 36/49 who returned the survey remembered the TrV. Almost all felt the visit was somewhat to very helpful (n=35). 6/36 reported that the visit was upsetting (n=3) or very upsetting (n=3). The book containing a treatment summary and follow-up plan was recalled by 34/36 (94%). Of the 33 who remembered the book, all reported it to be helpful, and 17/33 reported reduced anxiety associated with access to this written information. The "Late Effects" section of the book was reported to be the most frequently utilized section (30/33). 88% of respondents endorsed the timing of the TrV to be within 3 months of completion of therapy; 12/33 reported that psychosocial provider support at or after the TrV might have been helpful. Only 10/33 shared the book with their pediatrician.

Conclusions: A Transition Visit is helpful and may decrease anxiety for parents as their children enter into follow-up. At two years off-therapy, parents report accessing individualized information about late effects. Involvement of psychosocial professionals during the transition period might reduce anxiety, and communication with primary care providers needs improvement.

67. PROMOTING HEALTHY TRANSITIONS FOR CHILDREN COMING OFF ACTIVE CANCER TREATMENT Marilyn Stern, Ph.D; Suzanne Mazzeo, PhD; Jennifer Lamanna, MA; Matthew Bitsko, PhD; Claire Russell, BS., Robyn Dillon, MSW., Kamar Godder, MD. *Departments of Psychology and Pediatrics and Division of Hematology/Oncology, Virginia Commonwealth University, Richmond, VA, USA*

Pediatric cancer patients are at higher risk for obesity, diminished exercise capacity, hypertension and metabolic syndrome features related to cardiovascular disease (CVD) as adults than healthy children in the general population, Rates of overweight/obesity for pediatric ALL survivors are found to be over 40% five years after cancer treatment, with 21.2% classified as obese (body mass index, i.e., BMI >95%ile for age and gender) and 20% overweight (> .85 BMI <.95) (Chow et al., 2007). The possible mechanisms linking cancer and later CVD symptoms, including hypertension and obesity remain unclear. Treatment intensity and cranial radiation involvement have not been found to be important predictors of BMI or blood pressure change from end of treatment to five years into survivorship. In line with Siviero-Miachon et. al., 2008, we argue that parental perceptions and expectations about eating and exercise behaviors in these children may play an important role in the development or amelioration of the risk factors associated with these medical late effects among children and young adolescents who have been treated for cancer.

Given this background, we test the feasibility of an intervention addressing increasing rates of overweight/ obesity in childhood cancer survivors by focusing on parental perceptions and expectations. We have strong empirical support for the effectiveness of a parent-education intervention (NOURISH) for parents of both overweight/obese children and adolescents. We are piloting an adaptation of NOURISH and its potential use in working with parents of children between the ages of 5–12 treated for cancer. Two focus groups are set to be conducted. The first focus group assesses parental perceptions and concerns of their children's eating and weight-related behaviors. The second focus group focuses on topics as they pertain to children who have undergone treatment: 1) The risk factors for obesity; 2) parent feeding behaviors; and 3) parent and family dynamic shifts during the cancer experience. Implementation of the randomized control trial will begin soon after the pilot.

68. OUTCOMES OF AN INNOVATIVE EDUCATIONAL CONFERENCE SERIES FOR ADOLESCENT AND YOUNG ADULT SURVIVORS OF CHILDHOOD CANCER Constance Connor, LCSW; Holly DeLuca, MSN, PNP; Nancy Sacks, MS, RD, LDN; Karim Sadak, MD. Life with Cancer, Fairfax, VA, USA; Children's National Medical Center, Washington, DC, USA; Children's Hospital of Philadelphia, Philadelphia, PA, USA

Purpose: Late effects of treatment and adverse health consequences for adolescent and young adult survivors of childhood cancer have been well documented in both pediatric and adult literature. Knowledge that can improve the health of these survivors includes awareness of late effects of pediatric cancer and its treatment, long-term health implications of survivorship, and the importance of maintaining a healthy lifestyle. The literature also demonstrates that these educational topics are not popular with adolescent and young adult survivors, making dissemination of this important information to the target population challenging. We developed innovative interventions in an attempt to overcome this barrier.

Summary: Funded by the National Children's Cancer Society's *Beyond the Cure* program, we conducted a series of educational conferences and events for adolescent and young adult survivors and their parents over a four year period. Survivors were polled to assess learning needs and topics of interest. To encourage attendance at these "free" educational events we offered innovative incentives including college scholarships, free gym memberships, autographed books authored by conference presenters, free food, and other giveaways. The programs were geared toward increasing awareness of long-term effects, obtaining appropriate medical follow-up, and promoting a healthy lifestyle. Topics included overviews of late effects and contributing risk factors; fitness, nutrition and bone health; psychological implications of survivorship, sexuality and intimacy; fertility; stress reduction; and insurance, disability and employment. Survivors were provided with opportunities to participate in a variety of exercise classes (Zumba, kickboxing, yoga) and experience complimentary therapies (Reiki and massage). They were offered information at resource fairs and trialed web-based resources for survivors on the NCCS website.

Conclusions: Results of a consumer evaluation survey used to determine the impact of this educational conference series on adolescent and young adult survivors' awareness of late effects and changing health maintenance behaviors will be presented.

69. PREDICTORS OF ADHERENCE TO LONG TERM FOLLOW UP CARE IN CHILDHOOD CANCER SURVIVORS M. Fatih Okcu, MD, MPH; Leana May, MPH; Larry Laufman, EdD; Suzanne Holm, PhD; Kala Kamdar, MD, MPH; Lynette Harris, PhD; Toi Harris, MD; Cassi Provenzala, PA; Sule Unal, MD; Gulsah Oktay, MD; Rosalind Bryant, CNP, PhD; Zoann Dreyer, MD; Ernest Frugé, PhD. *Baylor College of Medicine, Texas Children's Cancer Center, Department of Pediatrics; Childhood Cancer Prevention and Epidemiology Center, Houston, TX, USA*

Introduction: Improvements in outcomes in pediatric cancer have been accompanied by significant sequela of the treatments, which sometimes emerge years after completion of therapy. It is recommended that patients be followed in late effects clinics for continued monitoring. However, many patients do not attend follow-up appointments. The reasons for this lack of adherence are as yet unknown. Understanding loss to follow-up patterns not only may decrease morbidity and mortality rates, but could also help develop institutional and national health policies aimed at improving pediatric cancer survival.

Objective: The purpose of this study was to identify patterns associated with adherence to post-cancer treatment follow-up in the Long-Term Survivor Clinic at Texas Children's Cancer Center (TCCC).

Methods: A retrospective chart review of all patients diagnosed and treated for a childhood cancer between 1998 and 2001 at TCCC (n=1177) was conducted. Medical records were reviewed and demographic, clinical, psychosocial, and socioeconomic characteristics were compared between the patients who continued to attend appointments and those who were lost to follow-up (defined as not attending the recommended next follow up appointment for more than 6 months). Frequencies and proportions for categorical variables were compared by Fisher's exact test and Chi-square analyses, and mean values for the continuous variables were compared by t-test or ANOVA. Logistic regression analyses were used for multivariable comparisons.

Results: Of the 1,177 charts identified, 488 survived their cancer and were not referred to another institution for follow up. Notably 258 (52.8%) of the patients were lost to follow-up. Those who continued in follow-up care were, on average, 1.6 years younger at diagnosis compared to the lost to follow-up group (5.9 years vs. 7.5 years, respectively, $p=0.001$). In univariate analyses the following patient characteristics were associated with a greater likelihood of being lost to follow-up with statistical significance ($p<0.05$): African American race, brain or solid tumor diagnosis, no stem cell transplantation, patients who underwent surgery, single-parent households, parents never married, live in an apartment, mobile home or a trailer at the end of treatment. In multivariable analyses, having a brain or solid tumor diagnoses and single parent household were independently associated with being lost to follow up.

Conclusion: We found a variety of patient characteristics associated with non-adherence to follow-up care including clinical and socioeconomic variables. These findings have been combined with other evidence (e.g., provider surveys, reviews of relevant literature) to form a comprehensive putative model of non-adherence to long term care including patient/family and provider/health-care system variables. Future research will refine and empirically test components of the model with the long term goal of designing intervention strategies to improve the both the quality of long term care and adherence for survivors of pediatric cancer.

70. CANCER SURVIVOR CLINIC ATTENDANCE: PATIENT CHARACTERISTICS Kristen M. Vangile, MPH, Sarah Brand, MA; Ann Mertens, PhD; Lillian Meacham, MD; Karen Wasilewski-Masker, MD, MSCR. *Cancer Center and Blood Disorders Service, Atlanta, GA, USA; Emory University, Atlanta, GA, USA*

Background: Childhood cancer survivors are at increased risk for late-effects for which they need survivor–focused care. At Children's Healthcare of Atlanta (CHOA) only 48% (433/909) of eligible patients participate in the Cancer Survivor Program (CSP). The objective of this study was to determine barriers to survivorship care.

Methods: Demographic information (age at diagnosis, gender, race, insurance status, zip code and diagnosis) was abstracted from the CHOA Tumor Registry and Cancer Survivor Database. Brain tumor patients, followed in a different clinic, were not included. Data were compared for 433 CSP patients (attended the CSP from 2003-2007) and 909 CSP-eligible patients (diagnosed from 1998-2002; alive in 2003). Insurance data were unavailable prior to 2001 for the CSP-eligible patients; therefore newly diagnosed patients from 2003-2007 were utilized as a comparison group to analyze insurance data.

Results: When compared to the CSP-eligible population, CSP patients were more likely to be younger at diagnosis (less that 13 years) (OR 3.53; 95% CI 3.14–3.92), diagnosed with a liquid versus solid tumor (OR 1.41, 95% CI 1.18–1.64), and non-Hispanic white compared with other races (OR 1.25, 95% CI 1.00–1.50). Geographic location inside versus outside the Metro Atlanta area was not a significant factor in CSP attendance. A shift in insurance coverage was evident between the newly diagnosed population (52% private) and the CSP patients (72% private). Those with private insurance were over twice as likely to attend the CSP (OR 2.44, 95% CI 2.20–2.68).

Conclusion: Low CSP attendance rates can be addressed by ensuring that all survivors are educated about the importance of survivorship-care upon completion of cancer therapy. Contact should be maintained with patients from the end of therapy through the first CSP visit. Attention should be directed to at-risk populations including those with solid tumors, older at diagnosis, and with Medicaid or no insurance.

71. HEALTH BEHAVIORS AND PREFERENCES OF CHILDHOOD CANCER SURVIVORS Joann L. Ater, MD; Raheem Paxton, PhD; Katie Bispeck; Cody Cruz; Angela Xu, MPH; Martha Askins PhD; Diana Urbauer, MS; Hoda Badr, PhD; Karen Basen-Engquist, PhD, MPH; Wendy Demark-Wahnefried, RD, PhD. *Divisions of Pediatrics, Behavioral Science, and Quantitative Sciences; University of Texas, M.D. Anderson Cancer Center, Houston, TX, USA; Mt. Sinai School of Medicine, NY, New York, USA*

To create health promotion interventions that have the potential for success, it is first important to examine the prevalence of health behavior practices among childhood cancer survivors and their family units to explore receptivity and preferences. We conducted a survey of dietary intake, physical activity, quality of life, and preferences for health topics, intervention strategy, and timing. Childhood cancer survivors currently between the age of 3 and 34 years who were diagnosed with CNS tumors (n=55), sarcomas (n=32), leukemia (n=55), or lymphoma (n=28) between 1992 and 2007; and were off treatment at least 6 months without progressive disease were eligible and participated. Of the 282 eligible patients, 170 (60.3% rate of participation) responded. Responders and non-responders did not differ significantly with respect to age, race, or age at diagnosis; however, responders were more likely female ($p<0.001$). The mean age of our sample was 17.8 years. Age stratified analyses (≤12 yrs, 13 to 17 yrs, 18+ yrs) revealed that only 51% perceived themselves as having very good or excellent health, with 18+ yr-olds lower at 39% ($p<.01$). Also fewer overweight/ obese than normal/ under weight survivors perceived their health to be excellent or very good (35% v. 61%; $p<0.01$). However, more overweight/ obese than normal weight survivors were interested in interventions for weight control (57% v. 32%; $p=0.0035$) and getting in shape (76% v. 50%; $p<0.005$). Over 18 year-olds were significantly more interested in preventing other problems (63%, $p<0.001$) compared to the others. The intervention strategy most favored by all age groups was computer-based when compared to clinic-based, camp-based, telephone, or mailed. Other results about diet and exercise behaviors and preferences will also be discussed. Based on this information, we are planning for a web-based diet and exercise intervention.

72. WHAT DO CHILDHOOD CANCER PARENT GROUPS AND SURVIVOR GROUPS EXPECT FROM HEALTH CARE PROVIDERS? A SURVEY OF PEDIATRIC ONCOLOGY HEALTH CARE PROVIDERS WITHIN PANCARE Edit Bardi MD, PhD; Gisela Michel, PhD; Nicolas X. von der Weid, MD; Julianne Byrne, PhD; Desiree Grabow, PhD; Leontien Kremer, MD; Eva Frey, MD; Claudia E. Kuehni, MD; Roderick Skinner, MD; Lars Hjorth, MD for the PANCARE network. *Ward of Hematology and Oncology, Department of Pediatrics, Markusovszky Teaching Hospital, Szombathely, Hungary; Institute of Social and Preventive Medicine, University of Bern, Switzerland. Pediatric Hematology-Oncology Unit, Centre Hospitalier Universitaire Vaudois, Service de Pédiatrie, Lausanne-CHUV, Switzerland; Boyne Research Institute, Duke House, Duke Street, Drogheda, Ireland; Long-term Surveillance at German Childhood Cancer Registry (GCCR) at the Institute for Medical Biostatistics, Epidemiology and Informatics (IMBEI), University of Mainz, Germany; Department Pediatric Oncology, Emma Childrens' Hospital/AMC, Amsterdam and Steering Group DCOG LATER project, Amsterdam, The Netherlands; Department of Pediatric Oncology and Hematology, St. Anna's Children's Hospital, Wien, Austria; Department of Paediatric and Adolescent Oncology, Royal Victoria Infirmary, Newcastle upon Tyne, UK; Division of Pediatric Oncology & Hematology, Children's Hospital, Lund, Sweden on behalf of all PanCare members*

Background: The PanCare (Pan-European Network for Care of Survivors after Childhood and Adolescent Cancer) Questionnaire Group wished to determine what Survivor Groups and Parent Groups expect from healthcare providers.

Methods: PanCare members completed one questionnaire each about Survivor and Parent Groups, responding on behalf of either their country (a "combined" response) or their center (allowing analysis of diversity within country).

Results: 32 PanCare members from 16 countries responded. Only 4 PanCare members stated that their country/unit had no Parent or Survivor Groups. Fifteen members had links with Parent Groups, 5 with Survivor Groups and 8 with combined Parent/Survivor Groups. The members knew the aims of and received support from these groups, but only 16 knew what Survivor/Parent Groups expected from health care providers. PanCare members stated that the aims of the Survivor/Parent Groups included 1) helping reintegration into normal life; 2) organizing meetings and camps for survivors and families, or weekends for parents; 3) facilitating contact between survivors and coordinating activities of different associations; 4) offering information about possible treatment-related late effects; 5) providing advocacy for improvements needed to achieve optimal health and psychosocial care for survivors. Some survivors provide financial/logistic support for meetings of health care profesionals. The responses reflected the fact that contacts with and access to support from Survivor/Parent Groups is not equal across Europe or within individual countries.

Conclusion: This survey has shown a large potential for collaboration between Survivor and Family Groups and healthcare teams, which could be intensified to give optimal support to the long-term needs of survivors and their families. This PanCare survey has provided valuable information about the expectations and needs of cancer survivors and their families across Europe and within individual countries.

73. PANCARE—A NEW NETWORK FOR CARE OF EUROPEAN CHILDHOOD CANCER SURVIVORS Lars Hjorth, Riccardo Haupt, Roderick Skinner, Desiree Grabow, Leontien Kremer, Florent de Vathaire, Mike Hawkins, Stanislaw Garwicz, Eva Frey, Julianne Byrne, Edit Bard, Claudia Kühni, Els Vandecruys, Maryna Krawczuk Rybak, Eva Widing, Catherine Rechnitze, Lorna Zadravec Zaletel, Tomas Kepak, Peter Mesar, Catalina Márquez Vega, Vilma Rutkauskaite, Ana Teixeira, Aimilia Tsirou, Leon H. Lau, Margit Serban, Arja Harila-Saari, Vesna Bogicevic, Ivajla Georgieva on behalf of all PanCare members *Epidemiology and Biostatistics Section, Scientific Directorate, Gaslini Children's Hospital, Genova, Italy; Department of Paediatric and Adolescent Oncology, Royal Victoria Infirmary, Newcastle upon Tyne, UK; German Childhood Cancer Registry (GCCR) at the Institute for Medical Biostatistics, Epidemiology and Informatics (IMBEI), University of Mainz, Germany; Department Paediatric Oncology, Emma Children's Hospital/AMC, Amsterdam, DCOG LATER project, The Netherlands; Unité 605 INSERM, Institut Gustave Roussy, Villejuif, France; Epidemiology, Centre for Childhood Cancer Survivor Studies, School of Health and Population Sciences, Public Health Building, University of Birmingham, Birmingham, USA; Division of Paediatric Oncology and Haematology, Children's Hospital, Lund, Sweden; Department of Paediatric Oncology and Haematology, St. Anna's Children's Hospital, Wien, Austria; Boyne Research Institute, Drogheda, Ireland; Department of Paediatric Oncology & Haematology, University of Debrecen, Hungary; Swiss Childhood Cancer Registry, Institute of Social and Preventive Medicine, University of Bern, Switzerland; Department of Paediatric Oncology & Haematology, University of Gent, Belgium; Department of Paediatric Oncology & Haematology, Medical University of Bialystok, Poland; Department of Paediatrics, Ullevaal University Hospital, Oslo, Norway ; Division of Paediatric Haematology and Oncology,Copenhagen University Hospital at Rigshospitalet, Copenhagen, Denmark; Institute of Oncology, University of Ljubljana, Slovenia; Department of Paediatric Oncology & Haematology, University Hospital of Brno, Czech Republic; Paediatric Oncology and Haematology Clinic of University Children´s Hospital, Banska Bystrica, Slovakia; University Children´s Hospital of Sevilla, Spain*

Department of Paediatric Oncology & Haematology, Vilnius University Children's Hospital, Lithuania; Instituto Português de Oncologia de Lisboa, Lisbon, Portugal; Greek Survivors' Association Kyttaro, Greece; Kids Cancer Care Foundation of Alberta, Canada; Spitalul Clinic de Urgenta pentru Copii, Louise Turcanu, Timisoara, Romania; Department of Paediatrics, University of Oulu, Oulu, Finland; Haematology and Oncology Department, Clinical Center Nis, Nis, Serbia; Bulgaria

Purpose: With over 300,000 childhood cancer survivors in Europe, a pan-European network has been created to address all aspects of childhood cancer survivorship.

Description: In March 2008 PanCare (Pan-European Network for Care of Survivors after Childhood and Adolescent Cancer) was founded in Lund, Sweden at a meeting attended by representatives from 14 European countries. PanCare's aims are to improve care for survivors by developing guidelines and providing education, perform collaborative research, and be a resource for research-based information concerning all late side-effects of cancer treatment. The long-term strategic aim of PanCare is to ensure that every European survivor of childhood and adolescent cancer receives optimal long-term care.

Results: Following four meetings (a fifth is planned for Paris in Spring 2010), PanCare has 141 members, representing 25 European countries plus Canada. Eighty members are Pediatric Oncologists, twenty-three Epidemiologists, twelve Survivors, four each represent Radiation Oncology and Psychology, three each Funding Bodies and Pediatric Endocrinology, whilst others represent Parents, Nurses, and other pediatric specialists. PanCare is currently working to develop research projects that will lead to evidence-based guidelines for long-term care of survivors. PanCare partnered SIOP-E in an EU proposal for a Network of Excellence in pediatric and adolescent oncology and also prepared a separate proposal for a Collaborative Project to predict long-term side effects of cancer therapy and ways to provide optimal care. Results from several PanCare questionnaires were presented at ESLCCC2009 in Edinburgh. A virtual cohort of

more than 80,000 childhood cancer survivors based in several population-based or institutional cancer registries will be the backbone for future etiological studies on late consequences of cancer therapies.

Conclusions: PanCare is a multidisciplinary pan-European network of professionals, survivors and their families. Data obtained through this network will be available also for international collaborative studies of rare complications impacting survivorship after childhood cancer.

74. LONG-TERM ADAPTATION PROBLEMS IN PEDIATRIC LEUKEMIA SURVIVORS: ROLE OF PSYCHOSOCIAL, GENETIC AND TREATMENT-RELATED FACTORS IN PREDICTING OUTCOME Sophie Marcoux, MSc; Maja Krajinovic, PhD; Albert Moghrabi, MD; Caroline Laverdièr, MD; Philippe Robaey, MD, PhD. *CHU Ste-Justine, Université de Montréal, Montréal, QC, Canada.; Centre hospitalier de Verdun, Montréal, QC, Canada*

Purpose of Study: Individualized predictive factors, such as age at diagnosis, do not yet allow a satisfying, effective prediction of neuropsychological sequels in pediatric cancer survivors. Researches have mainly focused on neurocognitive impact (e.g., IQ) and the literature on neurobehavioral outcomes is scarce. This study focused on quantifying prevalence of adaptation issues in this population, and risk factors associated.

Methods: Pediatric patients diagnosed with acute lymphoblastic leukemia (ALL) between 1993 and 1999 were invited to participate in a longitudinal study. This study aimed at identifying psychosocial, genetic and treatment-related factors likely to influence long-term adaptation problems in pediatric ALL survivors. Focus was on corticosteroids (CS) and polymorphisms in genes involved in their metabolism, since CS are well known to affect mood and behavior. Genetic polymorphisms involved in CS action were analyzed. Patient's parents fulfilled a questionnaire (CBCL) assessing child adaptation problems five times during the study. Linear multiple regression statistical modeling was used.

Results and Conclusions: Average global CBCL score 4 years post-diagnosis was in the normal range for the sample of patients; however, the proportion reaching clinical range was higher than expected (20,8% vs 15,9%). Results show that in addition to age at diagnosis, adaptation problems 3–4 years post-diagnosis can be predicted by measures of perceived familial well-being one year post-diagnosis (p=0,005). When also assessing a polymorphism in NF-kB1 gene (p=0,008) and the interaction between this polymorphism and the CS dose received during induction (p=0,035), the proportion of explained variance increases significantly (overall model: p=0,002). These data suggest that genetic as well as psychosocial factors should both be assessed when trying to optimize adaptation outcomes predictions in this population.

75. ROMANTIC RELATIONSHIPS OF EMERGING ADULT SURVIVORS OF CHILDHOOD CANCER: A QUALITATIVE STUDY Amanda L. Thompson, PhD; Kristin A. Long, MS; Anna L. Marsland, PhD, RN. *Children's National Medical Center, Washington DC, USA; University of Pittsburgh, Pittsburgh, PA, USA*

Background: To investigate emerging adult survivors' perceptions of their romantic partner relationships

Methods: Participants were recruited from a larger quantitative study of romantic relationships of emerging adult survivors of childhood cancer and comparison peers (Thompson, Marsland, Marshal, & Tersak, 2009). Semi-structured qualitative interviews were conducted with 18 female survivors, aged 19–25 (M = 21.6); age of diagnosis ranged from 2 to 15 yrs (M = 7.4). Participants answered a series of focused, open-ended questions about the nature of their past and present romantic relationships. All interviews were digitally recorded and transcribed verbatim. The principal investigator and a graduate-level research assistant independently coded the transcripts for content (as described by Auerbach and Silverstein, 2003). Themes were extracted and grouped according to similarity in content. Theoretical saturation was achieved after 14 interviews, and the final four interviews verified preliminary findings.

Results and Conclusions: Major themes that emerged from the data included: a) perceptions of increased maturity and feeling 'different' from peers and potential partners, b) challenges related to self-disclosure of emotions and cancer history, c) issues of body image and physical self-consciousness that interfere with partner intimacy, and d) worry regarding fertility, pregnancy, and health of future children. Concerns about the development and maintenance of romantic relationships were common among emerging adult survivors of childhood cancer. Findings support the importance of qualitative work, as existing quantitative measures of social quality of life may fail to capture issues salient to this population. Health-care providers should routinely assess developmentally significant issues like love/romance that are important markers of identity formation and ultimately impact long-term quality of life. Future research should utilize qualitative findings to generate testable hypotheses, incorporate the perspective of collateral reporters (i.e., romantic partners), and include observations of interactions between survivors and their partners.

76. COMPARISON OF HEALTH OF MOTHERS WHO ARE CAREGIVERS FOR YOUNG ADULT SURVIVORS OF CHILDHOOD BRAIN TUMORS WITH WOMEN IN THE GENERAL POPULATION Wendy L. Hobbie, MSN, CRNP, FAAN; Maureen Reilly, BSN, RN; Jill P. Ginsberg, MD. *The Children's Hospital of Philadelphia, Philadelphia, PA, USA; Widener University, Chester, PA, USA; University of Pennsylvania School of Nursing, Philadelphia, PA, USA*

Aim: Survivors of childhood brain tumors often have significant cognitive and physical late effects that require ongoing emotional, financial, and caregiving support from their families. Mothers most often fulfill the role of primary caregiver. However, to date no studies have examined the health status of these primary caregivers. Therefore, the purpose of this study was to compare the health of mothers who are caregivers for adolescent and young adult survivors of childhood brain tumors still living at home with the health of women in the general population.

Methods: Telephone interviews were conducted in this cross sectional study using structured questionnaires with a sample of 109 caregivers. Self report measures of the caregiver's health (SF-36) were administered and compared to scores for age matched women in the general population.

Results: The mean age of the caregivers is 51.68 years (SD=5.56). The mean age of their children is 21.12 years (SD=4.42) and their mean survival time is 13.29 yrs. (SD=5.96). A pattern of significant differences was identified regarding the caregivers' physical ($t_{(1,109)}$=-56.99, p < 0001) and mental health (p<0.001) as well as their role functioning secondary to physical issues ($t_{(1,109)}$=-75.6 1,p<0.001) and emotional issues ($t_{(1,109)}$=-13.66, p<0.001).

Conclusions: Although the results achieved significance, continued research with larger sample sizes over time is needed in order to verify these results as well as to test their possible association with survivor's functional outcomes.

77. LATE EFFECTS OF HAEMATOPOIETIC STEM CELL TRANSPLANTATION CONDITIONED WITH TOTAL BODY IRRADIATION Karen Johnston, Cecelia Oswald, Toby Trahair, Kristen Neville, Tracey O'Brien, Richard J Cohn. C*entre for Children's Cancer and Blood Disorders, Sydney Children's Hospital (SCH), Randwick and the School of Women's and Children's Health, University of New South Wales, Australia*

Background: We describe the late effects in survivors of HSCT conditioned with TBI in a single centre cohort.

Patients and Methods: 214 patients have received TBI as part of conditioning for HSCT at SCH between 1979 and 2007. 123 patients survived at least 2 years after transplantation (range 25 months–369 months). 13 patients died from progressive disease, 4 from treatment related complications (1 metabolic syndrome, 1 AIDS, 2 from 2nd malignancy) and 1 suicide. 4 patients died more than 10 years after transplantation. 21 patients referred from overseas or interstate were excluded, as were 2 patients lost to follow-up, leaving 82 eligible patients. Mean age at time of TBI was 8.8 years (range, 21 months–20 years) and mean age at time of study 21.5 years (range, 2–45).

Results: Patients who received TBI as part of their conditioning regimen were more likely to attend follow-up clinic or keep contact with their treating institution than non-TBI treated patients. All patients have at least 2 health issues related to TBI and many have up to 6. Common late effects include growth and pubertal failure, infertility, hearing impairment, orthopaedic complications, renal impairment, cataracts and thyroid abnormalities. TBI emerged as an independent risk factor for the development of hyperinsulinemia, impaired glucose tolerance and diabetes mellitus. The risk of late effects increased with time from exposure to TBI.

Conclusions: Whilst it is acknowledged that TBI is an effective ablative therapy, consideration of the long term cost to health is required. The burden of late effects after treatment with TBI is high and suggests the need for reconsideration of HSCT protocols. Children who are treated with TBI need to be followed regularly and continuously or transitioned to a well informed adult care provider, as the risk of multiple morbidities increases with time since exposure.

78. UTILIZATION OF PRESCRIPTION DRUGS AMONG SURVIVORS OF CHILDHOOD AND YOUNG ADULT CANCER IN BRITISH COLUMBIA CANADA Mary L. McBride, MSc; Suli Ma, MSc; Ken Bassett, MD; Colin Dormuth, ScD; Karen Goddard, MD; Maria Lorenzi, MSc; Lauren MacDonald, MSc; Lynne Nakashima, PharmD; Paul Rogers, MD; Sam Sheps, MD, MSc; John J. Spinelli, PhD; Jim M. Wright, MD, PhD. *Cancer Control Research Program, Systemic Therapy Program and Division of Radiation Oncology, British Columbia Cancer Agency, Vancouver, BC, Canada; Departments of Ophthalmology and Visual Sciences, and Anesthesiology, Pharmacology and Therapeutics, and School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada; Division of Hematology/Oncology, BC Children's Hospital, Vancouver, BC, Canada*

Abstract: Cancer patients can be affected by cancer and its treatment, and have ongoing needs for health care. The CAYACS (Childhood/Adolescent/Young Adult Cancer Survivors) Research Program has assembled a cohort of cancer patients diagnosed under 25 years of age from 1970 to 1996 in British Columbia, Canada, surviving at least five years from diagnosis. In this study, prescription drug utilization was explored using an administrative database. There were 1252 survivors diagnosed aged 0 to 14 years, 503 survivors diagnosed aged 15 to 19 years, and 932 survivors diagnosed aged 20 to 24 years. Prescriptions were evaluated from January 1, 2002 to December 31, 2004. In that period, 79.4%, 81.5% and 83.5% of survivors diagnosed at 0 to 14, 15 to 19, and 20 to 24 years respectively had at least one prescription. Central nervous system (CNS) tumour survivors, with mean total prescriptions 23.9, 24.0 and 30.5 in the three diagnosis age groups, had more prescriptions than leukemia survivors (mean 12.0, 15.1, and 13.1, in the respective age groups). Female survivors with mean total prescriptions 18.3, 24.6 and 22.5 in the three age groups had more prescriptions than male survivors

(mean total prescriptions 11.3, 11.2 and 16.9 respectively). The most common types of drugs prescribed were anti-infectives and CNS agents. Among survivors diagnosed under age 15 years, 59.9% were prescribed anti-infectives and 37.3% were prescribed CNS agents. For those diagnosed between age 15 and 19 years, 61.2% were prescribed anti-infectives and 54.1% were prescribed CNS agents. Corresponding percentages for those diagnosed age 20 years and above were 61.2% for anti-infectives and 52.9% for CNS agents. The results of this study will quantify demand for prescription drugs among survivors, identify subgroups of survivors with increased prescription drug needs, and types of drugs used, thus providing information on long term utilization in this group.

79. PHYSICIAN PREFERENCES AND KNOWLEDGE GAPS REGARDING THE CARE OF CHILDHOOD CANCER SURVIVORS: A SURVEY OF ASCO ONCOLOGISTS TO Henderson, MD, MPH; Mackenzie Kigin, BA; FJ Hlubocky, MA; KE Wroblewski, MS; CK Daugherty, MD. *Departments of Pediatrics, Medicine and Health Studies University of Chicago, Chicago, IL, USA*

Purpose: Outside of the pediatric oncology specialty, little is known about physicians' attitudes and knowledge regarding the health care needs and long term follow-up care (LTFU) of childhood cancer survivors (CCS). We sought to obtain adult cancer physicians' self-reported attitudes and knowledge regarding this population.

Methods: Following a pre-notification letter, surveys including a $5 gift card were mailed to 1,249 U.S. medical oncologists from the ASCO membership directory in November 2009. A second mailing to non-responders is planned.

Results: In response to the first mailing, 346 surveys have been returned (28% response rate). Respondents' median age is 53 years (range: 33–79); 80% men; 30% practice in an academic medical center; 16% in a cancer center; 51% in private practice. Respondents practiced a median of 20 years (range: 1–41) and see a median of 60 patients/week (range: 0–700). When describing comfort levels in caring for CCS (1=very uncomfortable; 7=very comfortable), respondents were most comfortable with survivors > 30 years (mean ± SD 6.2±1.3), less comfortable with those >18 years and <30 years (mean 5.7±1.4), and least comfortable with CCS ≤ 18 years (mean 3.6±2.0). In response to a vignette of a 26 year old female treated with mantle radiation at 16 years, based on available guidelines, 45% of respondents did not appropriately recommend yearly breast cancer surveillance; 84% did not appropriately recommend cardiac surveillance; and 55% did not appropriately recommend yearly thyroid screening. Only 4% of respondents answered all three questions in accordance with available guidelines, and those respondents were more likely to be familiar with the guidelines ($p<0.05$) and have received training in LTFU of CCS ($p=0.02$).

Conclusion: Medical oncologists express a range of preferences with regard to LTFU of childhood cancer survivors. Many appear unfamiliar with LTFU surveillance guidelines.

80. THE NECESSITY TO ESTABLISH A COMPETENT HELP DESK FOR FORMER CHILDHOOD CANCER PATIENTS D. Grabow, C Lacher, P Kaatsch. *German Childhood Cancer Registry (GCCR) at the Institute for Medical Biostatistics, Epidemiology and Informatics (IMBEI), University of Mainz, Germany*

Purpose: To investigate the subjective need of information reported by former childhood cancer patients being asked for their health status in a timely interval of one or more years in a cohort of long-term survivors, which has been built up at German Childhood Cancer Registry (GCCR).

Summary: In 2009, we contacted 10,349 former patients diagnosed with cancer in 1980-2004 from whom we had the latest information one or more years ago. Those who completed a short questionnaire about their health status had the possibility to add further comments to the questionnaire. We report on the analyses of comments and questions indicated by former patients.

Results: From 9,697 we reached (652 unknown addresses need further address research first), death was reported in 74 (<1%) patients, 27 (<1%) denied to answer the questionnaire, and up to now 6,378 (65.8%) answered a 2-page questionnaire about their health status. Under those who answered, 181 (2.8%) added comments and questions to the "further comments"-category while completing the questionnaire. In total, information of 181 former patients referred to 247 comments and questions.

We revealed questions mainly asked in four global categories: questions related to long-term surveillance (39.2%), general questions, or remarks about the work of GCCR (27.5%), aetiology related, or disease specific questions (23.5%), and personal offers to help or requests for help (8.8%; 1.1% of questions were not further specified). In detail the greatest interest among the long-term-surveillance category is in late effects (23.5%), fertility (9.7%; possibly linked to a study conducted in 2008), and follow-up care (6.0%).

Conclusion: This analysis shows a potential information need of former childhood cancer patients in many different categories. The next step would be to nominate experts in the field for each category as corresponding partner to establish a competent helpdesk for former patients.

81. DEVELOPMENT OF A COMPUTERIZED CLINIC MANAGEMENT SYSTEM TO FACILITATE STANDARDIZED FOLLOW-UP OF CHILDHOOD CANCER SURVIVORS Wendy Landier RN, MSN CPNP; Liton Francisco, BS; Karla Wilson, RN, MSN, FNP-C; Saro Armenian, DO, MPH; Samuel Phang, BA; Smita Bhatia, MD, MPH. *Department of Population Sciences, City of Hope, Duarte, CA, USA*

Background: Childhood cancer survivors are at high risk for treatment-associated chronic health conditions, necessitating exposure-related, risk-based monitoring for life. Organizing and delivering appropriate care is a complex process requiring clinical evaluation, screening, and health education tailored to the survivor's age, gender, diagnosis, therapeutic exposures, and time from exposures. Accurate and appropriate care can be extremely time-consuming, and is susceptible to errors due to the complexity. We have developed a computerized Clinic Management System that optimizes tailored healthcare delivery and facilitates data collection.

Methods: A Microsoft Access™ database was developed to facilitate clinic management functions, including patient recruitment and consenting, data entry, generation of treatment summaries (therapeutic exposures), determination of exposure-related potential late effects and recommended screening per Children's Oncology Group (COG) Long-Term Follow-Up (LTFU) Guidelines, and generation of customized patient education materials.

Results: Since its implementation, the Clinic Management System has been used to successfully facilitate care and data collection for 726 clinic visits within City of Hope's Childhood Cancer Survivorship Program. A computerized algorithm links therapeutic exposures to relevant COG LTFU Guidelines, and initiates automated generation of tailored screening recommendations and individualized health education summaries. The tailored screening recommendations serve as a platform for generating customized follow-up letters and recording of test results in the research database. Use of modular libraries within the database allows generation of patient education materials and follow-up letters in English and Spanish. Future plans include integration of the system with the web-based version of the COG LTFU Guidelines (Passport *for* Care[SM]).

Conclusions: Implementation of a computerized clinic management system to facilitate tailored survivorship care delivery and data collection is feasible, and has the potential to increase the accuracy and improve the efficiency of exposure-specific evaluation and screening for childhood cancer survivors.

82. A WEB-BASED CANCER SURVIVOR CARE PLAN FOR CHILDHOOD CANCER SURVIVORS AND FAMILY DOCTORS. R Blaauwbroek, K van der Meer, WJE Tissing, A Postma. *Departments of Pediatric Oncology and General Practice, University Medical Center Groningen, University of Groningen, The Netherlands*

Introduction: Increasing knowledge of late effects in childhood cancer survivors resulted in many paediatric cancer centres starting dedicated long-term follow-up clinics (LTFU). This tertiary care follow-up is not always appropriate especially not when survivors grow into adulthood.

To facilitate family doctor- driven follow-up for adult CCS and to empower adult CCS we designed a web-based cancer survivor care plan. This plan provides individualized patient data on disease, treatment and complications, which are extracted from the local database of the LTFU clinic as well as guidelines for screening of late effects. Survivors are informed about their individual health risk and about life-style recommendations. Family doctors have access to the individualized guidelines of their patients necessary for the screening of late effects. Results of the screening are entered in the local database for valuation by the tertiary care unit.

Methods: We designed a pilot study and invited adult CCS, off-treatment ≥5 years, with no mental disability and not attending any kind of follow-up program. Participants were advised to see their family doctor for assessment of late effects. Participating CCS and their family doctors had access to the web-based cancer survivor care plan, which was also provided on paper.

Main endpoints were numbers of participants, satisfaction ratings and compliance of family doctors with the recommended guidelines.

Preliminary Results: The eligibility criteria were fulfilled by 106 CCS. 86 of them agreed to participate, 3 family doctors refused, 9 CCS refused, 10 CCS could not be traced. All participating CCS highly approved the get-at-ability of their personal online health record.

Satisfaction ratings and compliance of family doctors will be evaluated shortly.

Discussion: 90% of traced CCS and nearly all of their family doctors agreed to participate. Online personal health records seem to meet CCS' needs and wishes.

83. HEAD-TO-HEAD COMPARISONS OF QUALITY OF LIFE INSTRUMENTS FOR YOUNG ADULT SURVIVORS OF CHILDHOOD AND ADOLESCENT CANCER I-Chan Huang, PhD; Gwendolyn Quinn, PhD; Merry-Jennifer Markham, MD; Elizabeth Shenkman, PhD; Patricia Shearer, MD, MS. *Institute for Child Health Policy and Department of Epidemiology and Health Policy Research, College of Medicine, University of Florida, Gainesville, FL, USA; Division of Health Outcomes and Behavior, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; Cancer Survivor Program (CSP) of the UF Shands Cancer Center and Department of Pediatrics, College of Medicine, University of Florida, Gainesville, FL, USA*

Background: Although several health-related quality of life (HRQOL) instruments exist for adult cancer survivors, little attention has been paid to identify appropriate instruments for young adult survivors of childhood and adolescent cancer (YASCAC). We aim to make head-to-head comparisons of 3 HRQOL instruments for YASCAC.

Methods: We collected data via telephone interviews between 05/01/2009 and 09/30/2009 from 141 YASCAC who were off therapy at least 2 years without cancer and enrolled in the CSP and/or the UF Tumor Registry. Each subject reported his/her late effects (yes/no) and HRQOL. HRQOL was measured using the Quality of Life in Adult Cancer Survivor (QLACS), Quality of Life-Cancer Survivor (QOL-CS), and SF-36. We used Cronbach's alpha coefficient to estimate reliability. We estimated Pearson's correlation coefficients to examine convergent/discriminant validity. We hypothesized homogenous domains (e.g., physical functioning and pain) among 3 instruments would be strongly correlated with each other compared to heterogeneous domains (e.g., physical vs. psychological functioning). We used effect sizes to evaluate late effect known-groups validity which is the extent to which HRQOL scores differ by late effects (yes/no).

Results: Cronbach's alpha coefficients were acceptable (>0.7) for all domains. Physical domains of the QLACS (e.g., pain) were strongly correlated with the SF-36's physical component summary (PCS), but weakly with mental component summary (MCS). Mental domains of the QLACS (e.g., negative feelings) were strongly correlated with MCS, but weakly with PCS. However, both physical and mental domains of the QOL-CS were strongly correlated with MCS compared to with PCS, suggesting poor convergent/discriminant validity. Effect sizes suggest greater discrimination (>0.5) by the QOL-CS and SF-36 for late effect known-groups compared to the QLACS.

Conclusion: The 3 HRQOL instruments are not superior to each other. We suggest using item response theory to select high quality items from different instruments to measure HRQOL for YASCAC more meaningfully.

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