

CCSS 2012 Investigator Meeting Psychology Working Group

Kevin R. Krull, PhD

- Manuscripts
 - Recently published / in press
 - Under review / drafted
- Approved concepts in progress
- New concepts in development
- Future priorities

Manuscripts Recently Published

J Natl Cancer Inst 2010; 102: 881-893

JNCI JOURNAL OF THE NATIONAL CANCER INSTITUTE

Neurocognitive Functioning in Adult Survivors of Childhood Non-Central Nervous System Cancers

Nina S. Kadan-Lottick, Lonnie K. Zeltzer, Qi Liu, Yutaka Yasui, Leah Ellenberg, Gerard Gioia, Leslie L. Robison, Kevin R. Krull

Summary

- Survivors < 6 years at diagnosis more likely to report attention, memory and emotional regulation problems
- Females more likely to report attention and memory problems
- CRT dose associated with neurocognitive problems

Region-specific radiotherapy and neuropsychological outcomes in adult survivors of childhood CNS malignancies

Gregory T. Armstrong, Neelam Jain, Wei Liu, Thomas E. Merchant, Marilyn Stovall, Deo Kumar Srivastava, James G. Gurney, Roger J. Packer, Leslie L. Robison, and Kevin R. Krull

Summary

- Dose response effect of radiation to temporal brain regions and memory impairment:
 - OR = 1.95 with CRT ≥ 30 to < 50 Gy
 - OR = 2.34 with CRT ≥ 50 Gy



Neurocognitive functioning and health-related behaviours in adult survivors of childhood cancer: A report from the Childhood Cancer Survivor Study



Kevin R. Krull ^{a,*}, Robert D. Annett ^b, Zhenyu Pan ^c, Kirsten K. Ness ^a, Paul C. Nathan
Deo Kumar Srivastava ^c, Marilyn Stovall ^e, Leslie L. Robison ^a, Melissa M. Hudson ^{a,f}

Summary

- Survivors with attention problems less likely to meet CDC guidelines for physical activity
- Those with organization problems less likely to receive dental care
- Obese survivors less likely to receive bone density exam and mammogram

Pediatr Blood Cancer. 2011 Dec 15;57(7):1197-203.

Pediatr Blood Cancer

Predictors of Independent Living Status in Adult Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study

Alicia Kunin-Batson, PhD,^{1*} Nina Kadan-Lottick, MD, MSPH,² Liang Zhu, PhD,³ Cheryl Cox, PhD,³
Veronica Bordes-Edgar, PhD,¹ Deo Kumar Srivastava, PhD,³ Lonnie Zeltzer, MD,⁴ Leslie L. Robison, PhD,³ and
Kevin R. Krull, PhD³

Summary

- CNS tumor survivors 7.5 times less likely to live independently
- Survivors with attention problems 70% less likely to live independently

Post-Traumatic Stress Disorder

Pediatrics 2010;125:e1124

PEDIATRICS[®]
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Prevalence and Predictors of Posttraumatic Stress Disorder in Adult Survivors of Childhood Cancer

Margaret L. Stuber, Kathleen A. Meeske, Kevin R. Krull, Wendy Leisenring, Kayla Stratton, Anne E. Kazak, Marc Huber, Bradley Zebrack, Sebastian H. Uijtdehaage, Ann C. Mertens, Leslie L. Robison and Lonnie K. Zeltzer

Summary

- 4.2 fold increased risk of PTSD in survivors vs. siblings
- Increased risk associated with treatment intensity, lower income, lower education, unemployment



PAIN® 152 (2011) 2616–2624

PAIN®

www.elsevier.com/locate/pain

Pain in long-term adult survivors of childhood cancers and their siblings: A report from the Childhood Cancer Survivor Study

Qian Lu^{a,*}, Kevin R. Krull^b, Wendy Leisenring^c, Jason E. Owen^d, Toana Kawashima^c, Jennie C.I. Tsao^e,
Bradley Zebrack^f, Ann Mertens^g, Gregory T. Armstrong^b, Marilyn Stovall^h, Leslie L. Robison^b,
Lonnie K. Zeltzer^e

Summary

- Survivors have two fold increased risk for migraine and headaches, and four fold increased risk for other pain
- Increased risk of pain associated with younger age at diagnosis, female gender, unemployment

Psycho-Oncology

Psycho-Oncology **20**: 1259–1268 (2011)

Psychological outcomes of siblings of cancer survivors: a report from the Childhood Cancer Survivor Study

David Buchbinder^{1*}, Jacqueline Casillas², Kevin R. Krull³, Pam Goodman⁴, Wendy Leisenring⁴, Christopher Recklitis⁵, Melissa A. Alderfer⁶, Leslie L. Robison³, Gregory T. Armstrong³, Alicia Kunin-Batson⁷, Margaret Stuber² and Lonnie K. Zeltzer²

Summary

- Psychological distress reported by 3.8% siblings, vs. 10% expected

Psycho-Oncology

Psycho-Oncology **20**: 1259–1268 (2011)

Perceived positive impact of cancer among long-term survivors of childhood cancer: a report from the childhood cancer survivor study

Brad J. Zebrack^{1*}, Margaret L. Stuber², Kathleen A. Meeske³, Sean Phipps⁴, Kevin R. Krull⁵, Qi Liu⁶, Yutaka Yasui⁶, Carla Parry⁷, Rachel Hamilton⁸, Leslie L. Robison⁹ and Lonnie K. Zeltzer¹⁰

Summary

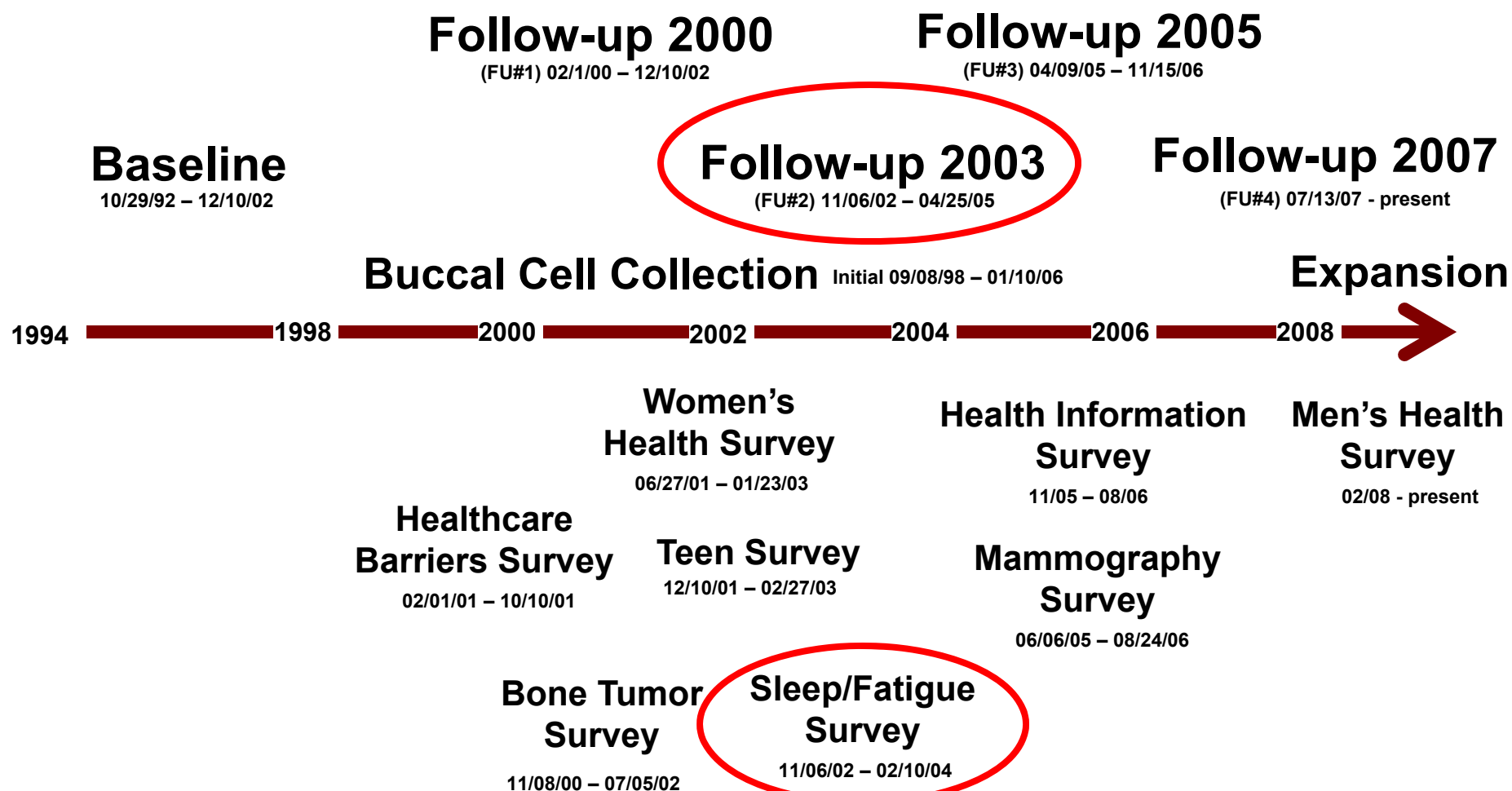
- Survivors more likely to report positive impact, with effect sizes ranging from 0.22 (Relating to Others) to 0.37 (Personal Strength)

Cancer June 1, 2011

Fatigue, Vitality, Sleep, and Neurocognitive Functioning in Adult Survivors of Childhood Cancer A Report From the Childhood Cancer Survivor Study

Nancy R. Clanton, PhD¹; James L. Klosky, PhD¹; Chenghong Li, PhD²; Neelam Jain, PhD³; Deo Kumar Srivastava, PhD²;
Daniel Mulrooney, MD⁴; Lonnie Zeltzer, MD^{5,6,7}; Marilyn Stovall, PhD⁸; Leslie L. Robison, PhD³; and Kevin R. Krull, PhD³

CCSS Survey History



Participants (n=1,426)

	Mean (SD)	Range		
Age at Diagnosis	11.9 (5.6)	0-21		
Time Since Diagnosis	24.0 (4.7)	16.2- 34.3		
Current Age	35.9 (7.5)	19.2-53.4		
		Frequency	Percent	
Sex	Female	742	52.0	
Income	<20,000	135	9.5	
	20,000-39,999	250	17.5	
	≥40,000	919	64.5	

Primary Measures

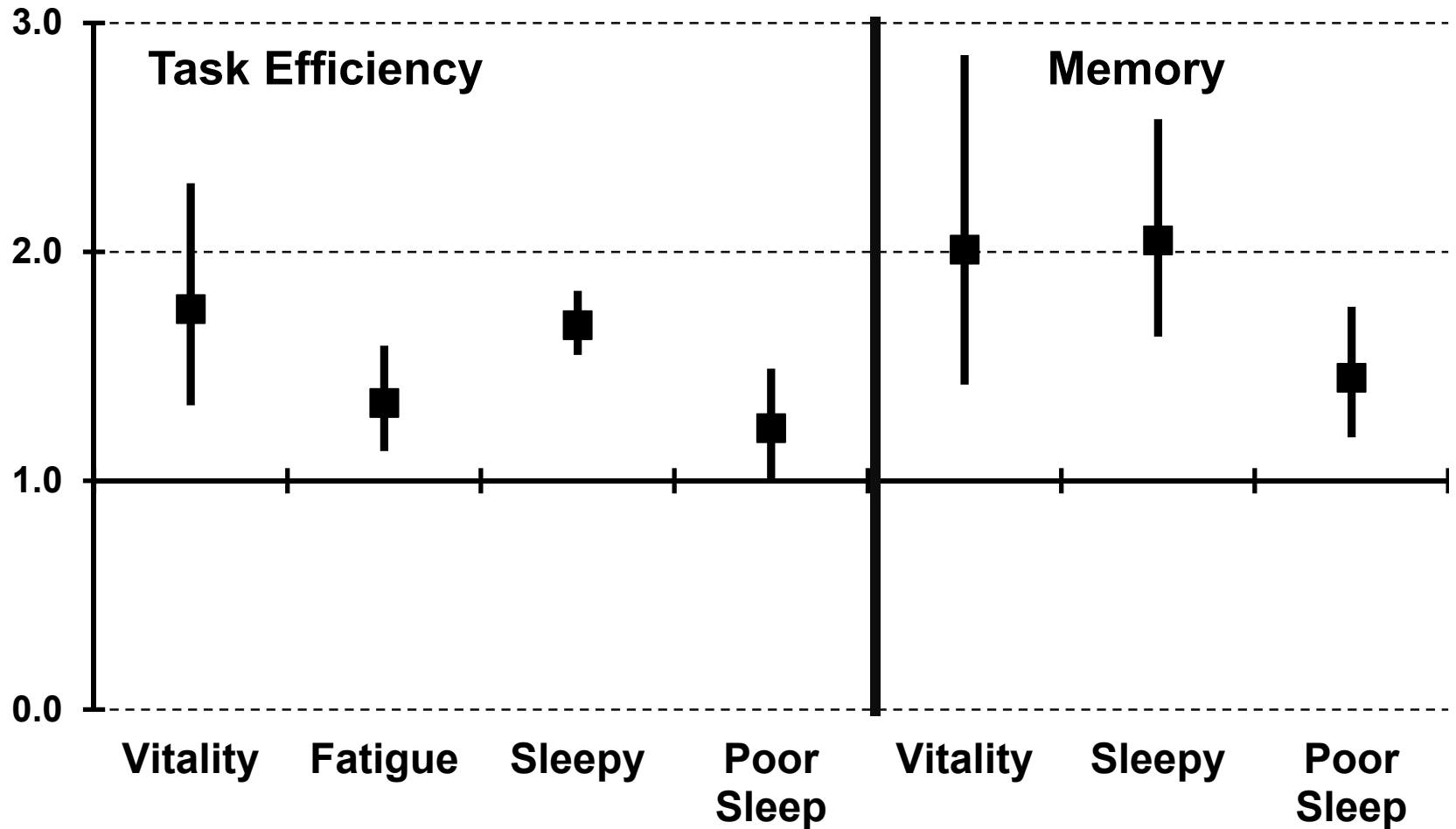
- Outcomes
 - CCSS Neurocognitive Questionnaire
 - Task Efficiency (attention and processing speed)
 - Memory (short and long-term memory)
 - Organization (executive functioning)
 - Emotional Regulation (inhibitory control)
- Predictors
 - Medical Outcomes Short Form-36, Vitality subscale
 - FACIT-Fatigue
 - Pittsburgh Sleep Quality Index
 - Epworth Sleepiness Scale

NCQ by Fatigue / Sleep

		Task Efficiency	Memory	Organization	Emotional Regulation
	N	%impaired	%impaired	%impaired	%impaired
Fatigued					
Yes	197	53.3	37.1	24.4	39.6
No	1229	15.6	9.2	11.4	6.8
Poor Sleep					
Yes	248	40.7	29.4	23	28.2
No	1178	16.6	9.6	11.1	7.7
Sleepiness					
Yes	195	43.1	32.3	25.1	26.7
No	1231	17.3	10	11.3	8.9
Low Vitality					
Yes	567	33.2	22.8	19.8	22.6
No	859	12.7	6.6	8.8	3.8

Impairment = score \geq 90th %ile of age and sex matched sibling cohort

Attention and Memory Problems



Adjusted for age, sex, cranial radiation, and depression

Antioxidant enzyme polymorphisms and neuropsychological outcomes in medulloblastoma survivors: a report from the Childhood Cancer Survivor Study

Julienne Brackett, Kevin R. Krull, Michael E. Scheurer, Wei Liu, Deo Kumar Srivastava
Marilyn Stovall, Thomas E. Merchant, Roger J. Packer, Leslie L. Robison, M. Fatih Okcu

Summary

- 109 survivors of medulloblastoma vs. 143 siblings
- CCSS-NCQ and BSI-18
- Emotional distress associated GSTM1 deletions

J Clin Oncol. 2012 May 21

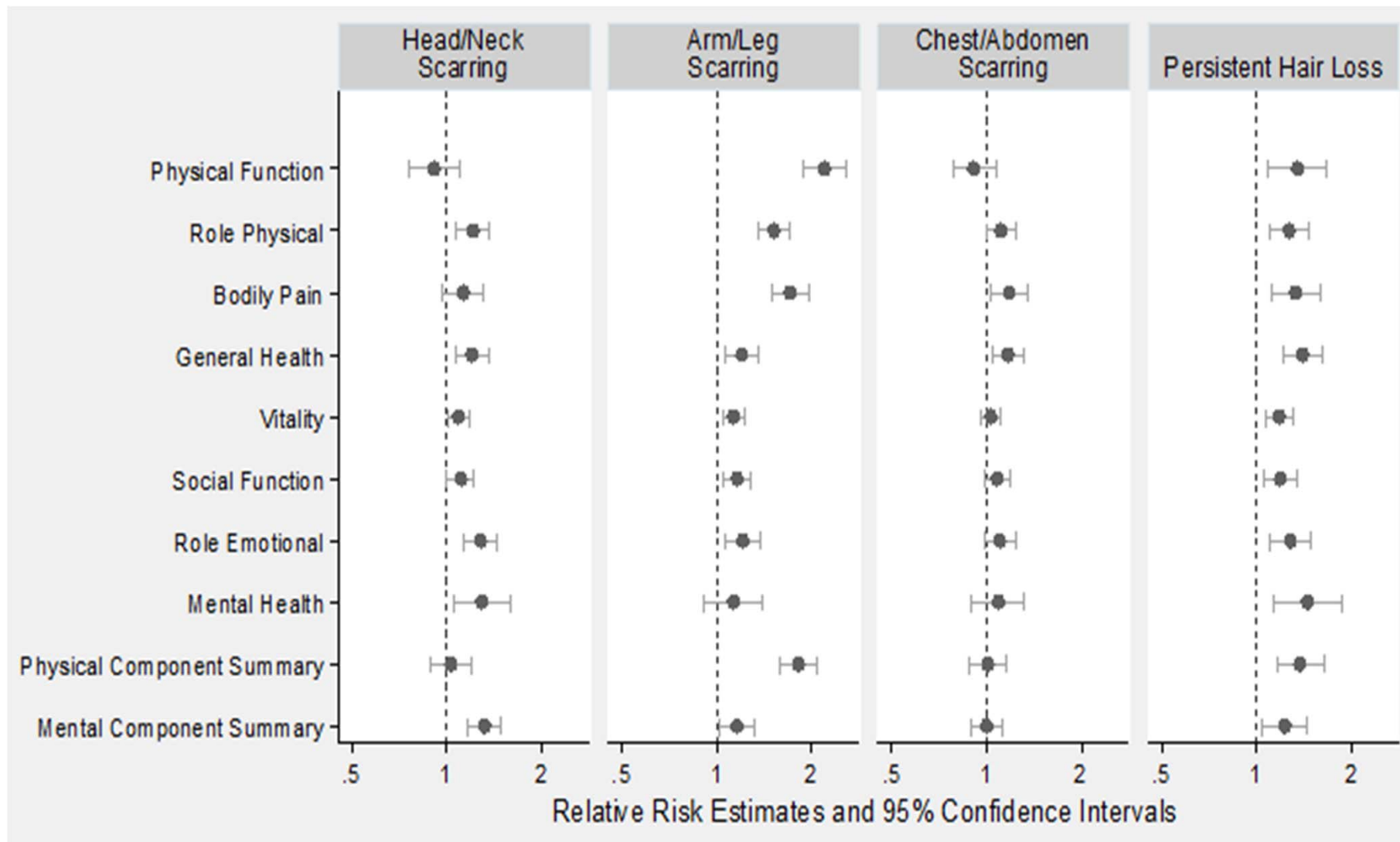
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Scarring, Disfigurement, and Quality of Life in Long-Term Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study

Karen E. Kinahan, Lisa K. Sharp, Kristy Seidel, Wendy Leisenring, Aarati Didwania, Mario E. Lacouture, Marilyn Stovall, Anand Haryana, Leslie L. Robison, and Kevin R. Krull

Scarring and Disfigurement



Manuscripts Recently Completed

Psychoactive Medication

Prevalence and Predictors of Prescription Psychoactive Medication Use in Adult Survivors of Childhood Cancer

Tara Brinkman, Nicole Ullrich, Nan Zhang, Daniel Green, Lonnie Zeltzer, Karen Lommel, Pim Brouwers, Kumar Srivastava, Neelam Jain, Leslie Robison, Kevin Krull

Summary

- Prevalence taken from from Baseline
- Follow-up surveys used to examine change and new onset
- Medications coded into categories based on American Hospital Formulary Service

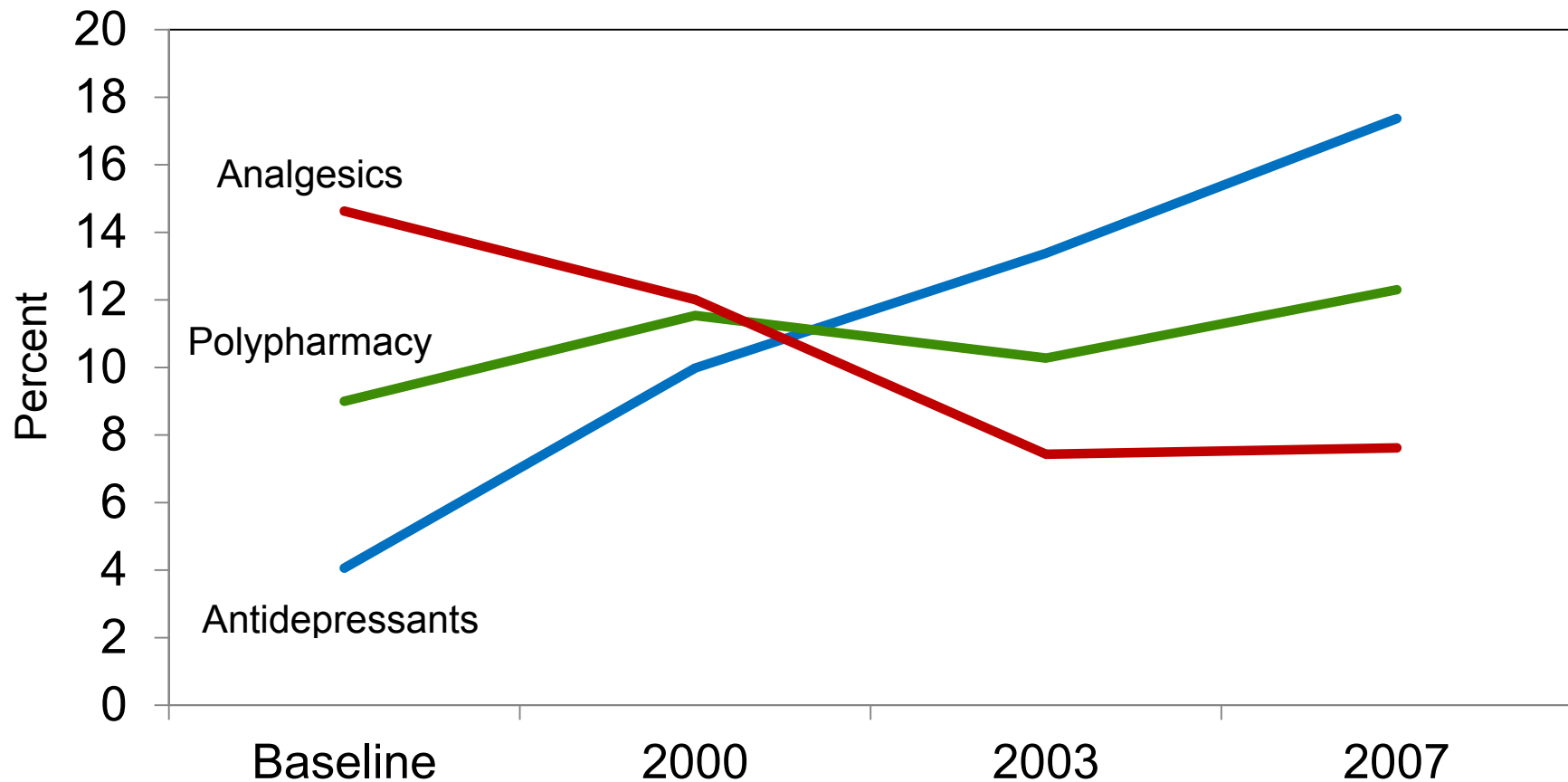
Psychoactive Medication

	Baseline Use	New Onset Use
Medication Class	OR(95%CI)	OR(95%CI)
Non-Opioid Analgesics	1.52(1.28-1.81)	1.27(1.05-1.54)
Opioids	1.36(1.15-1.62)	1.40(1.14-1.71)
Antidepressants	0.96(0.75-1.22)	1.10(0.96-1.25)
Anxiolytics/Sedatives/Hypnotics	1.64(1.17-2.28)	1.27(1.03-1.57)
Stimulants ^b	0.64(0.39-1.03)	1.30(0.88-1.93)
Neuroleptics ^b	1.20(0.70-2.07)	1.50(1.01-2.20)
Polypharmacy ^c	1.49(1.21-1.83)	1.40(1.20-1.64)

Adjusted for age, sex, race/ethnicity, household income, health insurance, stroke/seizure, pain, and psychological distress.

(Brinkman et al, Under Review)

Psychoactive Medication



(Brinkman et al, Under Review)

Psychoactive Medication

Psychoactive Medication Use and Neurocognitive Function in Adult Survivors of Childhood Cancer

Tara Brinkman, Nan Zhang, Nicole Ullrich, Pim Brouwers,
Daniel Green, Kumar Srivastava, Lonnie Zeltzer, Marilyn Stovall,
Leslie Robison, Kevin Krull

Summary

- Controlling for CRT, pain, distress, and stroke/seizure in survivors:
 - Antidepressants associated with impaired task efficiency (OR=1.80), memory (OR=1.53) and emotional regulation (OR=2.06)

Symptomatic Stroke

Radiation, Atherosclerotic Risk Factors and Stroke Risk in Young Adult Survivors of Pediatric Cancer

Sabine Mueller, Heather Fullerton, Kayla Stratton,
Wendy Leisenring, Rita Weathers, Marilyn Stovall, Gregory
Armstrong, Robert Goldsby, Roger Packer, Charles Sklar,
Daniel Bowers, Leslie Robison, Kevin Krull

Examining Relations between Posttraumatic Growth and Posttraumatic Stress in Long-Term Survivors of Childhood Cancer

James Klosky, Sean Phipps, Toana Kawashima, Wendy Leisenring, Mary Randolph-Frye, Brad Zebrack, Margaret Stuber, Leslie Robison, Kevin Krull

Summary

- Survivors and siblings from 2003 Follow-up
- Correlations between post-traumatic stress symptoms and post-traumatic growth symptoms very small

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Approved Concepts in Progress

Longitudinal Distress

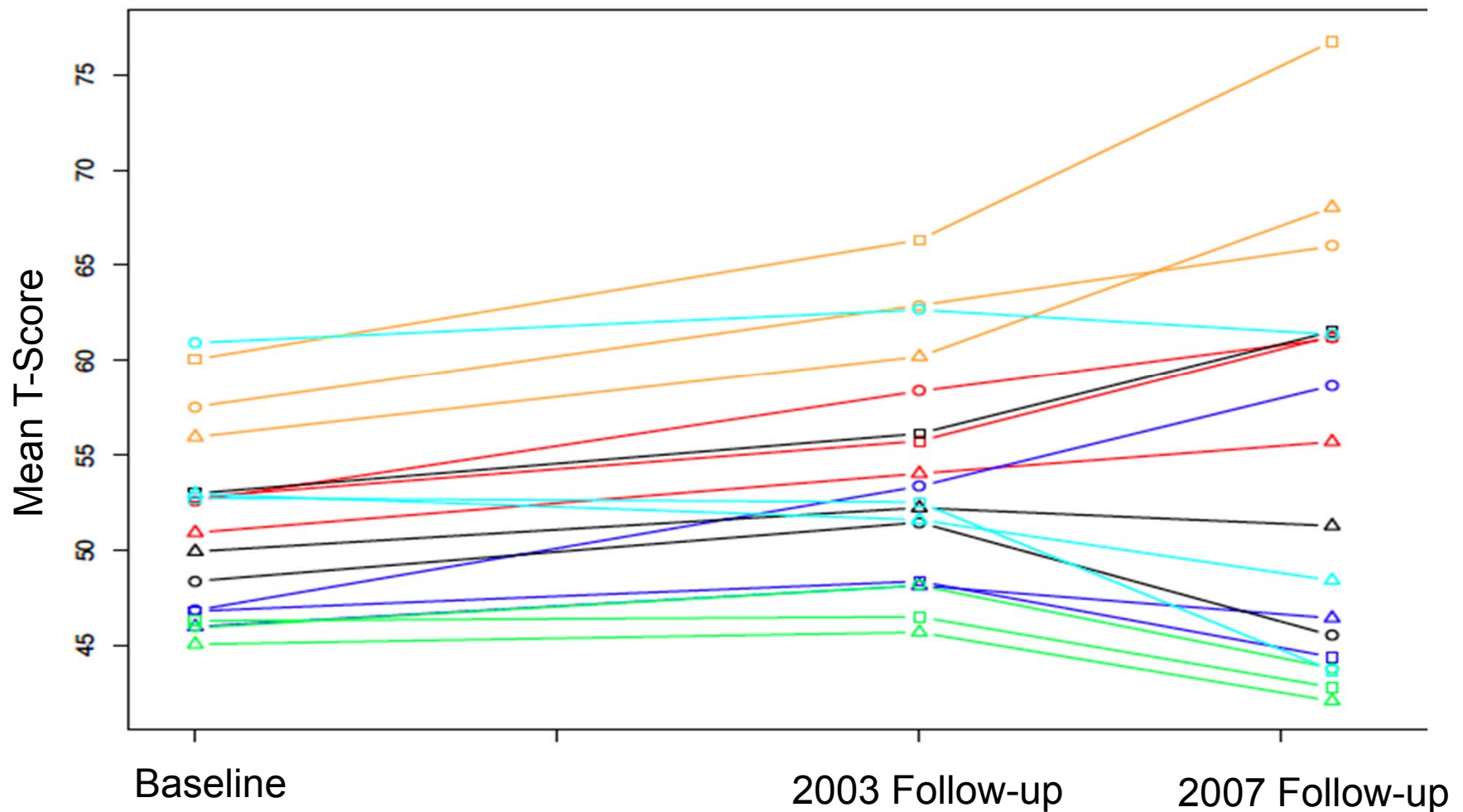
Longitudinal Patterns of Psychological Distress in Adult Survivors of Childhood Cancer

Tara Brinkman (St. Jude)

Aims:

- To characterize patterns of change in distress from Baseline through 2007
- To investigate patterns of change in suicidal ideation from Baseline through 2007.
- To identify disease, treatment and demographic characteristics related to patterns of psychological distress
- To examine the association between changes in psychological distress and social functioning (i.e. employment, marriage)

Longitudinal Patterns of Distress



(Brinkman, Williamsburg 2012)

Late Onset & Recurrent Suicide Ideation

	Survivors N=7,561		Siblings N=2,408			
	N	%	N	%	OR	95% CI
Baseline	475	6.3	101	4.3	1.8	1.4-2.2
2003	446	5.9	77	3.2	2.1	1.7-2.7
2007	396	5.2	63	2.6	1.8	1.4-2.4
Very Late Onset	564	8.0	98	4.1	2.2	1.5-3.1
Recurrent	235	3.1	35	1.5	2.0	1.6-2.4

Late Onset

- Poor physical health status (OR=2.0)
- Headaches (OR=1.5)
- Seizures (OR=2.3)
- Depressive Sx (OR=2.9)

(Brinkman, SLOP 2012)

Longitudinal Patterns of Late Effects in Adult Survivors of Childhood Brain Tumors

Thomas Hardie (Drexel/CHOP)

Aims

- To identify longitudinal patterns of psychosocial outcomes (education, employment, marriage and income) in adult survivors of CNS tumors
- To explore associations with disease and treatment factors
- To examine the associations with psychological/neuropsychological late effects

Adolescent Risk Factors

Predictors of Future Quality of Life in Adolescent Survivors of
Childhood Cancer

Vikki Nolan (U Memphis)

Aims

- To develop predictive models that identify recently diagnosed adolescent cancer patients that are at risk for poor mental and/or physical HRQOL

Developmental Disabilities

Mental Retardation and Learning Disability in Survivors of Childhood Cancer Diagnosed in Infancy

Marc Bornstein (NICHD)

Aims

- To examine cancer in infancy as a risk factor for cognitive development
- To examine the pattern of specific cognitive risk including mental retardation and learning/academic problems

Developmental Disabilities

- Mental retardation in 8,876 survivors vs. 2,520 siblings
 - Controlling for age, gender, and race, mental retardation in survivors vs. siblings OR = 9.1
 - Survivors diagnosed <10 years of age had increased risk when >35 Gy CRT
- Learning disability in 7,684 survivors vs. 2,231 siblings
 - Controlling for age, gender, and race, learning disability/special education in survivors vs. siblings OR = 2.6
 - Male survivors at greater risk for learning disability than females

Outcomes in AYA

Psychological and Neurocognitive outcomes in those diagnosed with cancer as adolescent and young adults in the CCSS

Pinki Prasad (LSU)

Aims

- To describe patterns of psychological and neurocognitive outcomes among survivors who were diagnosed as adolescents or young adults
- To determine changes in risk by age at diagnosis from prepubertal (age 10) to young adult status (age 18)

Adolescent Psychological Function

Physical Activity and Psychological Functioning Among Teenage Survivors of Childhood Cancers

Katie Devine (U. Rochester)

Aims:

- To examine associations between adolescent psychological functioning (self-esteem, emotional discomfort, psychosocial disorders), family involvement, home safety and health (diet and sedentary behavior) and
 - Physical activity
 - BMI

Impact of Chronic Disease on Neurocognitive and Psychosocial Functions

Kevin Krull (St. Jude)

Aims:

- To determine the association between chronic medical illness and neurocognitive function
- To determine the association between chronic medical illness and emotional distress
- To determine the association between chronic medical illness and symptoms of post-traumatic stress

Concepts in development AOI's Approved

SF-36 Measurement Invariance

Measurement invariance in health-related quality of life between young adult survivors of childhood cancer and their siblings

I-Chan Huang (U Florida)

Aims:

- To test differential item function (DIF) between survivors and siblings on each domain of the SF-36
- To test DIF between high and low perceived positive impact (or personal growth)
- To test DIF between short-term (< 25 years) and long-term survivors (≥ 25 years)

Psychosocial Factors and Fatigue

Psychosocial and physical factors influencing fatigue in survivors of childhood Hodgkin Lymphoma

Valerie Crabtree (St. Jude)

Aims:

- To investigate the association between pain, emotional distress, and physical functioning on levels of fatigue in survivors of childhood Hodgkin Lymphoma
- To investigate the influence of survivor demographics and treatment characteristics on these associations

Chronic Alcohol Consumption

Chronic alcohol consumption and neurocognitive function in adult survivors of childhood cancer

Tara Brinkman (St. Jude)

Aims:

- To examine the association between chronic alcohol consumption and neurocognitive function
- To examine the association between chronic alcohol consumption and psychological distress

Identifying Longitudinal Predictors of Quality of Life in Adolescent Survivors of Pediatric Cancer

Marilyn Stern (Virginia Commonwealth U)

Aims:

- To identify associations between child behavior at Baseline adolescent quality of life
 - Positive outcomes (satisfaction with health, achievement, resilience)
 - Negative outcomes (discomfort, risk, disorders)

Fatigue reported by childhood cancer survivors and its relationship to health outcomes

Jin-Shei Lai (Northwestern)

Aims:

- To link the FACIT Fatigue scale from CCSS to the PROMIS fatigue item bank to establish a cross-table between these two measurement tools
- To compare fatigue reported in CCSS to that reported by the US general population and adult cancer patients/survivors
- To examine associations between fatigue severity and demographic and treatment-related predictors

Health-Related Locus of Control

Health-Related Locus of Control in Childhood Cancer Survivors

Cara Kimberg (St. Jude)

Aims:

- To characterize the locus of control styles (internal, powerful others/external, chance external) demonstrated by childhood cancer survivors
- To examine the association between cancer treatment factors and locus of control styles
- To examine the impact of locus of control style on health behaviors and adherence to recommended healthcare utilization

Sensory-Motor Problems

Sensory-motor problems and associated functional outcomes in survivors of childhood central nervous system (CNS) tumors

Karin Walsh (Children's National Medical Center)

Aims:

- To examine the association between sensory impairments and later psychosocial function in survivors of childhood CNS tumors
- To examine the association between motor impairments and later psychosocial function in survivors of childhood CNS tumors

Psychology Group Priorities

- Aging and progression of symptoms over time
- Chronic health conditions and emotional and neurocognitive outcomes
- High-dose chemotherapy exposures in survivors from the expanded cohort
- Genetics moderators of emotional and neurocognitive outcomes
- Health and behavior interventions for neurocognitive, emotional and quality of life outcomes