

Psychology Working Group

A Report from the Childhood Cancer Survivor Study

Kevin R. Krull, PhD

CCSS
Childhood Cancer
Survivor Study



An NCI-funded Resource

Working Group Membership

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- Kevin Krull, PhD, Neuropsych, SJCRH
- Tara Brinkman, Psychology, SJCRH
- Pim Brouwers, Neuropsych, NIMH
- Austin Brown, PhD, Epidemiology, Baylor
- Lauren Daniel, Psychology, Rutgers
- Kim Edelstein, Neuropsych, Princess Margaret
- Jordan Gilleland, Psychology, Emory
- Kristy Hardy, Neuropsych, Children's National
- Bob Hayashi, Oncology, Washington U
- Allison King, Neuro-Oncology, Washington U
- Jin-shei Lai, Psychometrics, Northwestern
- Ellen van der Plas, Neuropsych, Iowa
- Emily Walling, Oncology, Michigan
- Elizabeth Wells, Neurology, Children's National

Working Group Progress

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- 13** Published/In Press Manuscripts (since Investigator Meeting, June 2017)
- 6** Currently Submitted Manuscripts
- 16** Analyses/Manuscripts in Process
 - 3 manuscripts drafted
 - 4 recently completed analyses
 - 6 analyses currently ongoing
 - 3 recently approved concepts awaiting analysts
- 11** Concepts in development

Manuscripts Drafted/Submitted

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- Yin Ting Cheung (Chinese University of Hong Kong); Psychoactive medication use in adolescent survivors of childhood cancer
- Rebecca Foster (Washington U); Psychosocial outcomes in adolescent survivors of Wilms tumor
- Kristin Stefanski (Cincinnati Children's Hospital); Psychological outcomes in pediatric AML survivors

Childhood Cancer Survivor Study

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Neurocognitive, Emotional and Quality of Life Outcomes in Pediatric Acute Myeloid Leukemia Survivors: A report from the Childhood Cancer Survivor Study

Kristen Stefanski, Julia S. Anixt, Pamela Goodman, Katherine Bowers, Wendy Leisenring,
K. Scott Baker, Karen Burns, Rebecca Howell, Stella Davies, Leslie Robinson,
Gregory Armstrong, Kevin Krull, Christopher Recklitis

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		AML-BMT (N=186)	AML-Chemo (N=303)	Siblings (N=3274)
Characteristic		Median (Range)	Median (Range)	Median (Range)
Age primary cancer diagnosis		8 (0-20)	7 (0-20)	
Age at evaluation		30 (17-48)	29 (16-49)	32 (9-58)
Variable	Categories	N (%)*	N (%)*	N (%)*
Sex	Male	84 (48.8%)	125(45.3%)	1489 (48.3%)
	Cranial Radiation Dose			
	Zero	75 (45.9%)	211(73.4%)	
	1-14.7 Gy	80 (45.5%)	6 (2%)	
	>14.7 Gy	15 (8.7%)	71 (24.6%)	
Methotrexate IT Dose (mg/m²)	0 (none)	122 (71.2%)	165 (61%)	
	1-71	39 (20.1%)	45 (16%)	
	>71	16 (8.7%)	66 (23%)	
Methotrexate IV/IM dose (mg/m²)	0 (none)	115 (67.9%)	250(88.4%)	
	1-75	36 (20.6%)	11 (4.3%)	
	>75	22 (11.5%)	25 (7.4%)	
Cytosine Arabinoside	Yes	175 (96.4%)	277(94.3%)	
Steroids	Yes	89 (52.4%)	105(37.7%)	

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Outcome	Groups	% Impaired	Relative Risk (95% CI)	P-value
CCSS Neurocognitive Questionnaire[†]				
Memory	Siblings	11.4	Ref	
	AML	24.6	2.1 (1.5, 3)	<0.001*
Organization	Siblings	16.2	Ref	
	AML	21.4	1.3 (1, 1.8)	0.065
Emotional Regulation	Siblings	8	Ref	
	AML	17.7	2.1 (1.4, 3)	<0.001*
Task Efficiency	Siblings	13.7	Ref	
	AML	25.5	1.8 (1.4, 2.5)	<0.001*
≥2 NCQ elevated subscales	Siblings	12.6	Ref	
	AML	25.8	2.0 (1.5, 2.8)	<0.001*

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Outcome	Groups	% Impaired	Relative Risk* (95% CI)	P-value
CCSS Neurocognitive Questionnaire[†]				
Memory	Chemo	25.9	Ref	
	BMT	23.0	0.9 (0.6, 1.3)	0.50
Organization	Chemo	21.7	Ref	
	BMT	20.9	1.0 (0.6, 1.4)	0.82
Emotion Regulation	Chemo	19.4	Ref	
	BMT	15.2	0.8 (0.5, 1.3)	0.33
Task Completion	Chemo	25.8	Ref	
	BMT	25.2	1.0 (0.7, 1.4)	0.89
>=2 NCQ subscales	Chemo	26.9	Ref	
	BMT	24.4	0.9 (0.6, 1.3)	0.58

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Manuscripts Drafted/Submitted

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- Emily Crochet (Florida Institute of Technology); PTSS, health behaviors and health care utilization
- Kim Edelstein (Princess Margaret CC); Longitudinal associations between physical activity and neurocognitive outcomes
- Cindy Karlson (U Mississippi); Chronic pain and pain-related disability

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Pain, Chronic Pain, and Pain-Related Disability in Long-Term Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study

Cynthia Karlson, Nicole M. Alberts, Wei Liu, Tara M. Brinkman, Robert Annett,
Daniel Mulrooney, Fiona Schulte, Wendy M. Leisenring, Todd M. Gibson,
Rebecca Howell, Deokumar Srivastava, Kevin Oeffinger, Leslie L. Robison,
Gregory T. Armstrong, Lonnie K. Zeltzer, Kevin R. Krull

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	Survivor n (%)	Sibling n (%)	RR (95% CI)*
Chronic pain^b			
Yes	639 (9.1)	136 (6.5)	1.23 (1.02-1.49)
No	6407 (90.9)	1959 (93.5)	1.0
Pain-related disability^a			
Moderate	1061 (11.0)	267 (8.8)	1.28 (1.10-1.49)
Quite a bit/extreme	890 (9.2)	198 (6.5)	1.26 (1.06-1.51)
Not at all/a little bit	7691 (79.8)	2579 (84.7)	1.0
Worsened pain trajectory^b			
Worsened pain	597 (8.5)	149 (7.1)	1.21 (1.01-1.45)
Minimal pain	4916 (69.8)	1557 (74.3)	1.0
Worsened pain-related disability trajectory^b			
Worsened disability	516 (11.3)	116 (8.5)	1.33 (1.09-1.62)
Minimal disability	3227 (70.8)	1077 (78.8)	1.0

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Notes. CFI = 1.000;
RMSEA = 0.002.
Model adjusted for
age at diagnosis and
follow-up time.

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Manuscripts Drafted/Submitted

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- Stefanie Vuotto (College of Mount Saint Vincent); Psychological distress, functional dependence and neurologic morbidity
- Pete de Blank (Cincinnati Children's Hospital); The effect of NF1 status on late outcomes in adult survivors of childhood cancer
- Nina Kadan-Lottick (Yale U); Neurocognitive outcomes in survivors of osteosarcomas

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Neurocognitive Function in Adult Survivors of Osteosarcoma and Ewings Sarcoma: A

Report from the Childhood Cancer Survivor Study

Nina Kadan-Lottick, Mingjuan Wang, Daniel Zheng, Deokumar Srivastava, Wendy Leisenring,

Todd Gibson, Kirsten K. Ness, Michael Bishop, Sheri Spunt, M. Fatih Okcu,

Leslie L. Robison, Gregory T. Armstrong, Kevin Krull

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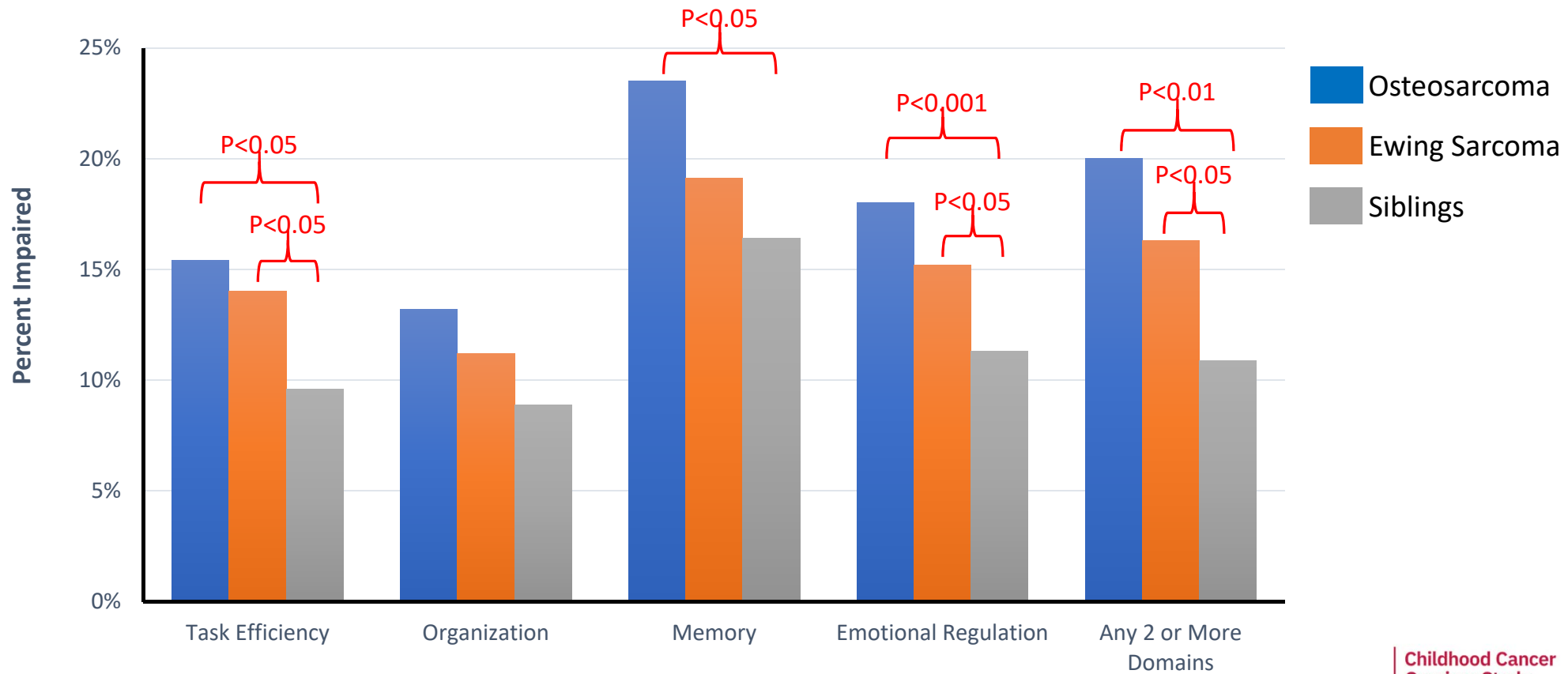
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		Osteosarcoma (N=604)	Ewings Sarcoma (N=356)	Siblings (N=697)
		median (min, max)	median (min, max)	median (min, max)
Age at evaluation (years)		37.0 (22.0, 51.0)	35.0 (18.0, 50.0)	32.0 (17.0, 54.0)
		n (%)	n (%)	n (%)
Female Sex		328 (54.3)	183 (51.4)	400 (57.4)
Age at diagnosis (years)	0-4.99	7 (1.2)	23 (6.5)	
	5.0-9.99	74 (12.3)	91 (25.6)	
	10.0-14.99	252 (41.7)	137 (38.5)	
	≥ 15.0	271 (44.9)	105 (29.5)	
Anthracycline	< 300 mg/m ²	198 (37.4)	105 (32.3)	
	≥ 300 mg/m ²	331 (62.6)	220 (67.7)	
Chronic conditions ≥ grade 2	0-1	376 (62.3)	275 (77.2)	667 (95.7)
	2 or more	228 (37.7)	81 (22.8)	30 (4.3)
		median (min, max)	median (min, max)	
Cumulative Methotrexate (G/m²)		84.7 (0.01, 497.4)	0.25 (0.052, 3.3)	

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Analyses Recently Completed

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- Caroline Hesko (U Chicago); Neurocognitive outcomes in adult survivors of neuroblastoma
- Caleb Nannes (Duke); Mental health outcomes in survivors of ALL treated with chemotherapy only
- Lisa Bashore (Cook Children's Hospital); Special education services and educational attainment in long-term survivors
- Ellen van der Plas (Iowa U); Neurocognitive outcomes in survivors of ALL treated with chemotherapy only

Analyses Ongoing

CCSS

- Jennifer Yeh (Boston Children's); Trends in utility-based health-related quality of life
- David Buchbinder (Children's Hospital OC); Psychological outcomes in siblings of childhood cancer survivors
- Ameera Fayad (U Buffalo); Loneliness in young adult survivors of childhood cancer
- Tara Brinkman (St. Jude); Temporal changes in radiation and neurocognitive and psychosocial outcomes in survivors of pediatric brain tumors
- Fiona Schulte (U Calgary); Longitudinal health-related quality of life
- Michael Scheurer (Baylor); Genetic susceptibility to neurocognitive impairment

Concepts Recently Approved

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- Neel Bhatt (St. Jude); Temporal changes in employment outcomes
- Satomi Sato (Ochanomizu University – Japan); Neurocognitive functioning, emotional and quality of life in Asian/Pacific Islander survivors
- AnnaLynn Williams (St. Jude); Psychosocial and neurocognitive outcomes in survivors of Hodgkin Lymphoma

Note: All junior investigators, 1st experience in CCSS

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Concepts Under Development

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- Cognitive and behavioral problems in adolescent CNS tumor survivors (Alicia Kunin-Batson)
- Cognitive aging in long-term survivors (Nick Phillips)
- Impact of genetic/congenital conditions on psychosocial/neurocognitive outcomes (Lisa Jacola)
- Impact of vision/hearing loss on psychosocial/neurocognitive outcomes (Pinky Prasad)
- Childhood surgery and post-traumatic stress disorder (Arin Madenci)
- Neighborhood socioeconomic/environmental disadvantage and psychosocial outcomes (Jinbing Bai)
- Longitudinal changes in functional independence in survivors of CNS tumors (Tara Brinkman)
- Childhood surgery and chronic pain (Arin Madenci)
- Latent patterns of psychosomatic symptoms (Rachel Tillery)
- Genetic determinants of PTSD (Christopher Recklitis)

Ancillary Studies

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Symptom progress and adverse health outcomes in adult survivors of childhood cancer; I-Chan Huang / Kevin Krull (MPIs); St. Jude Children's Research Hospital; R21CA202210 12/01/2015 – 11/30/2018.

Specific Aims:

- To profile individual symptom domains and clusters across 3 time points.
- To identify risk factors for symptom cluster changes.
- To investigate the prognostic value of individual symptom domains and symptom clusters for the development of chronic conditions and all-cause mortality in adult survivors of childhood cancers.

Ancillary Studies

CCSS

- Symptom prevalence increases over the trajectory of cancer survivorship
 - Risk factors of longitudinal symptom burden: female sex, smoking, cranial radiation therapy
- Higher longitudinal burden increases risks of CHCs, esp., neuropathy and severe/life-threatening conditions
 - Physical and pain symptoms at baseline are more strongly associated with CHCs compared to fatigue, depression, and anxiety

Ancillary Studies

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Daily and chronic experiences of pain in adult survivors of childhood cancer; Nicole Alberts (PI); St. Jude Children's Research Hospital; CCSS CDA and SJCRH CCDF 03/01/2018 – 02/28/2019.

- *Exploring Aspects of Survivors' Experience of Pain (EASE)* study on Eureka App.
- Aims to characterize prevalence, nature, and factors associated with chronic pain.
- Completed usability testing and opened up to recruitment last Fall.
- CCSS Career Development Award in support of this project.
- *EASE Breathe Study*, feasibility of a wearable device (Spire) designed to measure respiration, supported by St. Jude Comprehensive Cancer Center Developmental Funds Award.

Ancillary Studies

CCSS

eHealth intervention for late effects of childhood cancer; Tara Brinkman / Kevin Krull (MPIs);
St. Jude Children's Research Hospital; R01CA239689 07/01/2019 - 06/30/2024

Specific Aims:

- To examine the efficacy of an eHealth intervention for improving symptoms of insomnia among adult survivors of childhood cancer.
- To determine whether treatment of insomnia will improve neurocognitive function in adult survivors of childhood cancer with both insomnia and neurocognitive impairment.
- To explore the mediating effects of improved neurocognitive function, emotional distress, and cardiovascular health on the association between insomnia symptoms and quality of life.

Current Top Priorities

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- Recruit additional junior members to Working Group
- Submit 7 drafted/recently completed manuscripts
- Complete 9 ongoing/approved analyses
- Complete 10 concepts in development
- Finish analyses on Symptom ancillary study
- Complete data collection on Ease ancillary study
- Initiate recruitment on Sleep ancillary study

Future Top Priorities

CCSS

- Sleep and fatigue
 - Follow-up 6 sleep/fatigue survey on entire cohort
 - mHealth assessment to further characterize sleep/fatigue difficulties, along with antecedents and consequences
- Neurocognitive and psychosocial outcomes associated with aging
 - Phenotypes
 - Health, behavior and genetic predictors

Discussion: Opportunities and Threats

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- Threats or Challenges:

- Self-report assessment of neurocognitive outcomes in aging cohort
- Self-report assessment of sleep disorders
- Emphasis on longitudinal data over expanded scope (+/-)

- Opportunities:

- Expanded scope of mental health disorders (FU 7 social connections)
- Significant other / caregiver data (FU 7 query)
- mHealth assessment of neurocognitive function
- mHealth assessment of sleep

Immediate Opportunities for Investigators

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- Active participation in monthly Working Group discussions
- 10 concepts in development
 - Potential co-investigator roles
 - Lead investigator role on stalled concepts
- Sleep fatigue data in FU 6 to be released soon
- Ancillary studies