

PREVALENCE OF PRESCRIPTION PSYCHOACTIVE MEDICATION USE IN ADOLESCENT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

Authors: Yin Ting Cheung^{1*} PhD; Wei Liu² PhD; Tara M. Brinkman³ PhD; Deokumar Srivastava² PhD; Wendy M. Leisenring⁴ PhD; Rebecca M. Howell⁵ PhD; Nicole J. Ullrich⁶ MD, PhD; Karen M. Lommel⁷ DO, MHA, MS; Pim Brouwers⁸ PhD; Todd M. Gibson³ PhD; Leslie L. Robison³ PhD; Gregory Armstrong³ MD; Kevin R. Krull³ PhD

1. School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong
2. Department of Biostatistics, St. Jude Children's Research Hospital, USA
3. Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, USA
4. Clinical Statistics, Clinical Research Division, Fred Hutchinson Cancer Research Center, USA
5. Department of Radiation Physics, Division of Radiation Oncology, The University of Texas MD Anderson Cancer Center, USA
6. Neuro-Oncology, Boston Children's Hospital, USA
7. Department of Psychiatry, University of Kentucky College of Medicine, USA
8. National Institute of Mental Health (NIH), U.S. Department of Health and Human Services, USA

*Presenting and Corresponding author:

Yin Ting Cheung

Rm 801, 8/F.,

Lo Kwee-Seong Integrated Biomedical Sciences Building, Area 39

The Chinese University of Hong Kong

Shatin, N.T., Hong Kong

Email: yinting.cheung@cuhk.edu.hk

Introduction

Long-term survivors of childhood cancer are at-risk for developing physical, emotional, and cognitive late effects which may be managed pharmacologically. The prevalence of psychoactive medication use in adolescent survivors is unknown.

Objectives

To compare the prevalence of psychoactive medication use in adolescent survivors, against adolescent siblings, and identify treatment, clinical and behavioral predictors of medication use.

Methods

Participants included 5665 adolescent (≤ 18 years old) survivors of childhood cancer from the CCSS and 921 sibling controls (Table 1). Parent-reports of psychoactive medication use and behavioral functioning (Behavior Problems Inventory) were analyzed. Multivariable logistic regression was performed to compare odds ratios (OR) of risk factors for psychoactive medication use, adjusted for age, sex and race.

Results

Survivors were significantly more likely to report psychoactive medication use than non-cancer siblings (18% vs 6%, $P < 0.001$; Table 2). Survivors of CNS tumors or those treated with higher doses of cranial radiation were more likely to use psychoactive medication (Table 3). Cancer-related pain was strongly associated with non-opioid (OR [95% CI] 5.29 [2.52–11.1]) and opioid (OR [95% CI] 4.83 [2.71–8.63]) analgesic use. Use of stimulants, antidepressants and analgesics was more prevalent in survivors with decreased attention, antisocial behavior and emotional distress (Table 3), as well as those who received special education services (OR [95% CI] 2.39 [2.12–2.70]).

Conclusions

Use of psychoactive medication was more prevalent among adolescent survivors, and is associated with pain and more significant behavior problems. Future research should examine the impact of psychoactive medication use during adolescence on health-related quality of life and functional attainment during adulthood.

Table 1: Clinical Characteristics and Demographics of Adolescent Survivors and Non-cancer Siblings

	Survivors N=5665	Siblings N=921
	n (%)	n (%)
Sex		
Male	3047 (53.8)	488 (53.0)
Female	2618 (46.2)	433 (47.0)
Race[^]		
White/non-Hispanic	4533 (81.6%)	763 (86.2%)
Others	1020 (18.4%)	122 (13.8%)
Age at assessment* (years)	14.9 (2.4)	14.5 (2.9)
Household Income[^]		
< \$60,000	3311 (64.8)	508 (60.5)
≥\$60,000	1995 (35.2)	364 (39.5)
Diagnosis		
Leukemia	2276 (40.2)	
CNS tumor	906 (16.0)	
Lymphoma	290 (5.1)	
Wilms' tumor	838 (14.8)	
Neuroblastoma	930 (16.4)	
Soft Tissue Sarcoma	425 (7.5)	
Age at Diagnosis* (years)	3.1 (2.3)	
Chemotherapy[^]		
None	857 (16.3%)	
Intravenous methotrexate	1025 (18.2%)	
Intrathecal methotrexate	1854 (33.8%)	
Corticosteroids	2020 (53.1)	
Cranial Radiation (maximum prescribed dose)		
None	3447 (75.7)	
<20 Gy	780 (17.1)	
20-29 Gy	299 (6.6)	
≥ 30 Gy	29 (0.6)	

*mean (standard deviation)

[^]numbers do not add up to the total N due to missing data

Table 2: Comparison of Psychoactive Medication Use in Adolescent Survivors and Non-cancer Siblings

	Survivors N=5665	Siblings N=921	Comparison [#]	
	n (%)	n (%)	Odds Ratio (95% CI)	<i>P</i>
Use of psychoactive medication (any class)	1037 (18.3)	61 (6.6)	2.7 (2.1 – 3.6)	<0.001
Medication class*:				
Antidepressants	184 (3.2)	13 (1.4)	2.7 (1.4 – 4.9)	0.002
Anxiolytics/sedatives/hypnotics	73 (1.3)	1 (0.1)	--	--
Anticonvulsants	345 (6.1)	8 (0.9)	7.3 (3.2 – 16.5)	<0.001
Non-opioid analgesics	142 (2.5)	8 (0.9)	2.4 (1.2 – 4.8)	0.017
Opioids	322 (5.7)	16 (1.7)	2.1 (1.3 – 3.6)	0.0035
Muscle relaxants	23 (0.4)	2 (0.2)	--	--
Neuroleptics	52 (0.9)	5 (0.5)	--	--
Stimulants	223 (3.9)	21 (2.3)	2.8 (1.6 – 4.9)	0.0002

* Drugs were grouped based on the American Hospital Formulary Service Classification

Models are adjusted for age, sex and race

-- Comparisons were not conducted for these medication classes due to limited sample size within the sibling group.

Table 3: Factors Associated with Psychoactive Medication Use in Survivors

	Medications (overall)	Anti-depressant	Anxiolytics/sedatives/hypnotics	Anti-convulsants	Non-opioid analgesics	Opioid analgesics	Stimulants
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Diagnosis							
Leukemia (reference)	1.0	1.0	1.0	1.0	1.0	1.0	1.0
CNS tumor	1.4 (1.2-1.6)	1.8 (1.1-2.8)	1.0 (0.5-2.0)	2.0 (1.5-2.7)	0.6 (0.3-1.1)	1.0 (0.7-1.4)	1.5 (1.0-2.3)
Others	1.1 (0.9-1.2)	1.9 (1.3-2.7)	0.6 (0.3-1.2)	1.0 (0.7-1.3)	0.9 (0.6-1.3)	0.9 (0.7-1.2)	1.4 (1.0-2.0)
Cranial Radiation Therapy							
None (reference)	1.0	1.0	1.0	1.0	1.0	1.0	1.0
<20 Gy	0.9 (0.8-1.2)	1.0 (0.6-1.8)	1.1 (0.4-2.7)	0.6 (0.4-1.0)	1.4 (0.8-2.5)	1.2 (0.8-1.8)	0.5 (0.3-0.8)
20-29 Gy	0.9 (0.6-1.2)	1.0 (0.4-2.4)	0.4 (0.1-2.7)	0.7 (0.4-1.3)	1.4 (0.6-3.2)	0.47 (0.2-1.3)	0.6 (0.3-1.3)
≥ 30 Gy	1.3 (1.1-1.5)	0.8 (0.4-1.3)	0.9 (0.4-2.2)	1.8 (1.4-2.4)	1.3 (0.7-2.5)	1.4 (0.9-2.2)	1.0 (0.6-1.6)
Clinical conditions							
Cancer-related pain	2.3 (1.7-3.1)	2.2 (1.0-5.0)	6.1 (2.0-19.1)	2.2 (1.2-4.1)	4.3 (2.2-8.4)	4.3 (5.6-7.2)	1.1 (0.4-3.4)
Epilepsy	3.6 (3.2-4.2)	1.8 (1.2-2.8)	5.6 (3.0-10.6)	34.4 (24.3-48.7)	1.4 (0.8-2.4)	1.2 (0.8-1.9)	1.8 (1.2-2.8)
Migraine/headaches	1.6 (1.4-1.8)	2.0 (1.5-2.8)	1.2 (0.6-2.4)	1.1 (0.9-1.5)	3.1 (2.1-4.6)	2.5 (1.8-3.5)	1.2 (0.8-1.7)
Behavioral factors*:							
Antisocial	1.8 (1.6-2.1)	2.7 (2.0- 3.8)	1.1 (0.5- 2.2)	1.2 (0.8- 1.7)	1.5 (0.9- 2.2)	1.6 (1.1- 2.2)	3.2 (2.4- 4.3)
Depression/Anxiety	2.2 (2.0-2.5)	5.3 (4.0- 7.1)	2.2 (1.2- 3.9)	1.4 (1.1- 1.9)	2.0 (1.4- 3.0)	1.8 (1.3- 2.4)	3.2 (2.5- 4.2)
Headstrong Behavior	2.0 (1.8-2.3)	3.9 (2.9- 5.2)	2.0 (1.2- 3.6)	1.3 (1.0- 1.8)	2.2 (1.5- 3.1)	1.7 (1.2- 2.1)	3.7 (2.9- 4.9)
Attention Deficit	2.8 (2.5-3.2)	4.8 (3.5- 6.5)	2.8 (1.6- 4.7)	3.2 (2.5- 4.2)	1.7 (1.2- 2.4)	1.5 (1.1- 2.0)	8.0 (6.0-10.7)
Peer Conflict/Social Withdrawal	2.2 (1.9-2.5)	4.2 (3.1- 5.6)	2.4 (1.4- 4.1)	2.3 (1.8- 2.9)	1.8 (1.2- 2.5)	1.5 (1.1- 2.0)	3.4 (2.6- 4.4)
Special education service	2.4 (2.1-2.7)	3.2 (2.4 – 4.4)	3.9 (2.3-6.6)	5.6 (4.3-7.3)	1.3 (0.9-1.9)	1.3 (1.1-1.7)	3.4 (2.6-4.6)

Models are adjusted for age, sex and race

* Risk associated with behavioral factors is for survivors meeting criteria of impairment (i.e., symptoms greater than 90th percentile of sibling group)