Prescription Psychoactive Medication Use in Adolescent Survivors of Childhood Cancer and its Impact on Outcomes at Adulthood

A Report from the Childhood Cancer Survivor Study (CCSS)

Yin Ting Cheung¹, Wei Liu², Tara M. Brinkman², Deokumar Srivastava², Wendy M. Leisenring³, Rebecca M. Howell⁴, Nicole J. Ullrich⁵, Karen M. Lomme⁶, Pim Brouwers⁷, Todd M. Gibson², Leslie L. Robison², Gregory Armstrong², Kevin R. Krull²

1. School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong
2. St. Jude Children’s Research Hospital, USA
3. Fred Hutchinson Cancer Research Center, USA
4. The University of Texas MD Anderson Cancer Center, USA
5. Boston Children’s Hospital, USA
6. University of Kentucky College of Medicine, USA
7. National Institute of Mental Health, USA

Email: yinting.cheung@cuhk.edu.hk
## Faculty Disclosure

<table>
<thead>
<tr>
<th>Company Name</th>
<th>Honoraria/Expenses</th>
<th>Consulting/Advisory Board</th>
<th>Funded Research</th>
<th>Royalties/Patent</th>
<th>Stock Options</th>
<th>Ownership/Equity Position</th>
<th>Employee</th>
<th>Other (please specify)</th>
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X No, nothing to disclose

Yes, please specify:
Psychoactive Medication Use in Survivors

• Survivors of childhood cancer suffer from cancer- and treatment-related late effects:
  ➢ Sleep disturbances, fatigue, cognitive deficits and chronic pain \(^1,2\)

• Pharmacological treatments may be used to address these symptoms/conditions \(^3\)

• Psychoactive medications use early in life may impact long-term functional outcomes in adolescent survivors of childhood cancer

Objectives

• To evaluate the prevalence and factors associated with psychoactive medication use in adolescent survivors of childhood cancer

• To evaluate the associations between psychoactive medication use and survivors’ neurocognitive outcomes during adulthood
Childhood Cancer Survivor Study (CCSS)

- Funded by the National Cancer Institute (NCI) in 1994
- 31 contributing centers in the United States
- Retrospective cohort, diagnosed 1970 to 1999
- 5-year survivors and sibling controls
- Leukemia, Lymphoma, CNS Malignancies, Wilms Tumor, Neuroblastoma, Soft Tissue and Bone Sarcoma
- Detailed treatment data
- Wide range of patient-reported outcomes over multiple time-points
Diagnosed between 1970 to 1999

≥ 5 years

Baseline
(n=5665)

At adolescence: age ≤ 18 years
Age at baseline: 14.9 (2.4) years

- Psychoactive medication use
- Clinical and behavioral variables

Follow-up
(n=3193)

At adulthood: age > 18 years
Age at follow-up: 22.0 (2.5) years

Mean (SD)
7.6 (1.5) years
Psychoactive Medication Use (Adolescence)

• Proxy-reported at baseline
• **Prescription drugs** taken consistently for more than a month, or ≥30 days in one year during the previous 2 year period
• Classified based on the American Hospital Formulary Service Drug Information database (AHFS)

1. Antidepressants  
2. Anxiolytics/sedatives/hypnotics  
3. Anticonvulsants  
4. Non-opioid analgesics  
5. Opioids  
6. Muscle relaxants  
7. Neuroleptics  
8. Stimulants
Clinical and Behavioral Correlates (Adolescence)

- Neurologic variables:
  - Headache, bodily pain, and history of seizure
- Behavior Problem Index (BPI):
  - Depression/anxiety
  - Headstrong
  - Attention deficit
  - Peer conflict/social withdrawal
  - Antisocial
- Placement in learning disabled or special education program
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Tools</th>
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<tbody>
<tr>
<td>Neurocognitive function</td>
<td>CCSS- Neurocognitive Questionnaire</td>
</tr>
<tr>
<td></td>
<td>• Task efficiency</td>
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<tr>
<td></td>
<td>• Emotional regulation</td>
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<tr>
<td></td>
<td>• Organization</td>
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<td>• Memory</td>
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</tbody>
</table>
Statistical Analysis

• **Multivariable log-binomial models to:**
  • Compare psychoactive medication use between survivors and siblings at baseline
  • Identify clinical and treatment factors associated with psychoactive medication use
  • Evaluate association between psychoactive medication use and functional outcomes at adulthood

Adjusting for covariates (sex, age at evaluation, treatment variables, health insurance status, and household income at baseline)
<table>
<thead>
<tr>
<th>Study Population Characteristics</th>
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<tbody>
<tr>
<td><strong>Survivors (N=5665)</strong></td>
</tr>
<tr>
<td>Age at cancer diagnosis (years)</td>
</tr>
<tr>
<td>Age at baseline evaluation (years)</td>
</tr>
<tr>
<td>Sex (male)</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
</tr>
<tr>
<td>Leukemia</td>
</tr>
<tr>
<td>CNS Tumor</td>
</tr>
<tr>
<td>Neuroblastoma</td>
</tr>
<tr>
<td>Wilms tumor</td>
</tr>
<tr>
<td>Soft tissue sarcoma/ Osteosarcoma</td>
</tr>
<tr>
<td>Hodgkin Disease/Non-Hodgkin Lymphoma</td>
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</tbody>
</table>
## Survivors vs Siblings

<table>
<thead>
<tr>
<th>Medication Type</th>
<th>Survivors</th>
<th>Siblings</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any psychoactive medication use</td>
<td>1037 (18.3%)</td>
<td>61 (6.6%)</td>
<td>2.7 (2.1 - 3.6)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>184 (3.2%)</td>
<td>13 (1.4%)</td>
<td>2.7 (1.4 - 4.9)</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>345 (6.1%)</td>
<td>8 (0.9%)</td>
<td>7.3 (3.2 – 16.5)</td>
</tr>
<tr>
<td>Non-opioid analgesics</td>
<td>142 (2.5%)</td>
<td>8 (0.9%)</td>
<td>2.4 (1.2 - 4.8)</td>
</tr>
<tr>
<td>Opioids</td>
<td>322 (5.7%)</td>
<td>16 (1.7%)</td>
<td>2.1 (1.3 – 3.6)</td>
</tr>
<tr>
<td>Stimulants</td>
<td>223 (3.9%)</td>
<td>21 (2.3%)</td>
<td>2.8 (1.6 – 4.9)</td>
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</tbody>
</table>

Odds Ratio (adjusted for sex, age and race)
## Factors Associated with Overall Medication Use

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>OR</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>CNS tumor (vs leukemia)</td>
<td>1.36</td>
<td>1.2 - 1.6</td>
</tr>
<tr>
<td>Others (vs leukemia)</td>
<td>1.05</td>
<td>0.9 - 1.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Seizures</th>
<th>OR</th>
<th>95% CI</th>
</tr>
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<tbody>
<tr>
<td>Yes (vs none)</td>
<td>3.62</td>
<td>3.2 - 4.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Headache/migraine</th>
<th>OR</th>
<th>95% CI</th>
</tr>
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<tbody>
<tr>
<td>Yes (vs none)</td>
<td>1.48</td>
<td>1.3 - 1.7</td>
</tr>
<tr>
<td>Mild (vs none)</td>
<td>1.38</td>
<td>1.1 - 1.7</td>
</tr>
<tr>
<td>Moderate (vs none)</td>
<td>1.92</td>
<td>1.6 - 2.4</td>
</tr>
<tr>
<td>Severe (vs none)</td>
<td>2.31</td>
<td>1.7 - 3.1</td>
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<table>
<thead>
<tr>
<th>Bodily pain</th>
<th>OR</th>
<th>95% CI</th>
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<tr>
<td>CRT &lt;20 Gy (vs none)</td>
<td>0.95</td>
<td>0.8 - 1.2</td>
</tr>
<tr>
<td>CRT 20 - 35 Gy (vs none)</td>
<td>0.88</td>
<td>0.6 - 1.2</td>
</tr>
<tr>
<td>CRT &gt;35 Gy (vs none)</td>
<td>1.28</td>
<td>1.1 - 1.5</td>
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</table>
Psychoactive medication use at adolescence is associated with parent-reported behavior problems and placement in special education.

Adjusted for age, sex, race, treatment variables and household income
Psychoactive medication use during adolescence was associated with neurocognitive problems at adulthood.

Adjusted for age, sex, race, treatment variables and household income.
Limitations

• Relied exclusively on proxy-reported psychoactive medication use

• Temporal relationship between onset of medication use and functional outcomes cannot be established
Summary and Implications

• Higher rates of psychoactive medication use in subgroups of adolescent survivors
  • Closer monitoring of adverse cognitive effects and functional impairments

• Psychoactive medication use during adolescence associated with long-term functional impairments
  • Non-pharmacological interventions to address distress and behavioral symptoms
The Childhood Cancer Survivor Study is an NCI-funded resource (U24 CA55727) to promote and facilitate research among long-term survivors of cancer diagnosed during childhood and adolescence.

Investigators interested in potential use of this resource are encouraged to visit:

http://ccss.stjude.org
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