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

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## ABSTRACT

**Background:** Positive health-related behaviours are essential for the future wellbeing of childhood cancer survivors, though relatively few maintain healthy behaviours into adulthood.

**Methods:** Neurocognitive function and emotional distress were examined in 6,440 adult survivors from the Childhood Cancer Survivor Study, and used to predict rates of expected health-related behaviours. Covariates included cancer diagnosis, age, sex, body mass index, insurance status, income and antidepressant medication use, and multivariable models were constructed adjusting for these factors.

**Findings:** In multivariable regression models, survivors with neurocognitive problems in task efficiency (RR = 0.77, 95% CI = 0.72–0.84) were less likely to meet the Centers for Disease Control guidelines for weekly physical activity. Survivors with neurocognitive impairment were more likely to engage in general survivor care (RR = 1.20, 95% CI = 1.10–1.30), and less likely to engage in dental care (RR = 0.92, 95% CI = 0.88–0.97). Obese survivors were less likely to report receiving a bone density exam (RR = 0.67, 95% CI = 0.54–0.82), a mammogram (RR = 0.71, 95% CI = 0.57–0.89), and a skin exam (RR = 0.78, 95% CI = 0.68–0.89). Survivors reporting somatisation, i.e. vague physical symptoms associated with anxiety, were more likely to report receiving echocardiograms (RR = 1.53, 95% CI = 1.32–1.77).

**Interpretation:** These results support the link between neurocognitive and emotional problems and health-related behaviours in adult survivors of childhood cancer. Monitoring neurocognitive and emotional outcomes may help to identify survivors at risk for poor adherence to prescribed health behaviours and health screening exams.

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## 1. Introduction

Improvements in therapeutic protocols for childhood cancer have resulted in a large number of long-term adult survivors.<sup>1</sup> Ageing survivors are at increased risk for subsequent chronic illness and second malignant neoplasms.<sup>2,3</sup> Adherence to recommended health behaviours and health screening guidelines is important for reducing this risk and detecting secondary complications. However, relatively low rates of survivors report completion of recommended health screening.<sup>4</sup>

Neurocognitive and emotional functioning are important consideration when examining health behaviours in cancer survivors. Neurocognitive impairment, particularly problems with memory and executive function, may limit an individual's ability to adhere to treatment specific to their medical condition. Impaired memory and/or executive functions have been associated with poor health behaviour in healthy adult, adults with psychiatric problems and adults with chronic illness.<sup>5–9</sup> In adults living with HIV, those with neurocognitive impairment are 2.5 times more likely to demonstrate non-adherence to treatment.<sup>7,8</sup> Patients at risk for cardiovascular disease demonstrate significantly lower medication adherence rates if they have neurocognitive impairment.<sup>9</sup> Symptoms of emotional problems are also associated with lower engagement in healthy behaviours,<sup>10–12</sup> and use of antidepressant medication is a potential risk factor for obesity.<sup>13</sup>

Less than optimal healthcare utilisation is associated with neurocognitive and emotional functioning in a variety of populations. In a nationally representative community sample of 6,651 elderly individuals, reduced neurocognitive functioning was identified as a significant barrier to accessing outpatient healthcare services.<sup>14</sup> Conversely, increased emotional distress is associated with increased healthcare utilisation.<sup>15,16</sup> In a study of over 40,000 patients recruited by the Department of Veterans Affairs, non-psychiatric healthcare utilisation was increased in patients reporting symptoms of depression.<sup>15</sup> Similarly, data from the National Health Survey suggest increased symptoms of depression and anxiety is associated with increased primary care utilisation.<sup>16</sup>

Although neurocognitive impairment may limit an individual's ability to adhere to treatment recommendations, and to access appropriate healthcare, emotional distress may stimulate attempts to access care of any type. The aim of the current study was to examine the association between neurocognitive and emotional functioning and health-related behaviours amongst adult survivors of childhood cancer. We hypothesised that patients with neurocognitive dysfunction would be less likely to meet CDC guidelines for weekly physical exercise or to engage in regular sun protection, and less likely to participate in medical screening for cardiovascular disease and second malignant neoplasms. We also hypothesised that patients with emotional distress would be less likely to engage in physical exercise or regular sun protection, but would display increased visits for late effects likely to be associated with their previous cancer diagnosis.

## 2. Methods

### 2.1. Participants

Participants were adult survivors from the Childhood Cancer Survivor Study (CCSS), a cohort study designed to evaluate the impact of childhood cancer and its treatment on long-term function and health.<sup>17–19</sup> Eligible participants were treated for one of eight cancer diagnoses at 26 institutions between 1970 and 1986 when <21 years of age. Human subjects committees at each institution approved the study protocol before participant enrolment. Participants provided informed consent for questionnaires and medical record abstraction. Cohort entry was limited to those individuals who survived for at least 5 years after their original diagnosis. Participants have completed multiple questionnaires since their original enrolment (full questionnaires are available at <http://ccss.stjude.org>). The study population available for the current analyses included 9308 survivors who completed the 2003 Follow-Up Survey (data freeze conducted in 2008). Exclusion criteria included paralysis or mental retardation, conditions potentially impacting outcomes independent of predictor variables (e.g. requiring significant others to regulate health-related behaviours). These conditions were identified through responses to items on the questionnaires, and 619 survivors met this exclusion. This resulted in 8689 eligible survivors, of which 6440 (74%) provided complete survey data.

### 2.2. Questionnaire and medical record abstraction

Primary outcomes included physical activity, sun protection, dental care, physician care and risk-based survivor health screening exams. Physical activity was measured in weekly minutes of moderate and vigorous activity, dichotomised according to whether or not the participant met national standards established by the Centers for Disease Control (CDC; i.e. 150 and 75 minutes of moderate or vigorous intensity activity weekly, respectively).<sup>20</sup> Sun protection was defined as reporting 'always' or 'often' wearing sunscreen or avoiding prolonged exposure. Dental care was defined as reporting at least one visit in the previous year. Physician care was categorised based on questions related to visits with a health care provider (physician or nurse) within the preceding 2 years. Questions asked whether the visit was related to the previous cancer, and whether the provider gave advice on risk reduction or discussed or ordered screening tests for cancer-related sequelae. Responses were categorised into one of four mutually exclusive groups: (1) no health care, (2) general healthcare (visits unrelated to previous cancer), (3) general survivor care (at least one visit related to previous cancer, but no advice on risk reduction and no screening tests discussed or ordered), and (4) risk-based survivor care (care that included advice on risk reduction, or discussion or ordering of screening tests for cancer-related sequelae).

Risk-based survivor health screening exams included echocardiogram, colonoscopy, bone density exam, mammogram, pap smear and skin exam. Adherence was defined as meeting recommended long-term follow-up guidelines for survivors of childhood, adolescent and young adult cancers

(see <http://www.survivorshipguidelines.org>), and meeting US Preventive Services Task Force recommendations for age-based health screening (see <http://www.uspreventiveservicestaskforce.org>). Only survivors at-risk, according to these guidelines, were included in the individual screening analyses, with risk defined according to individual characteristics and treatment exposures. Echocardiograms were expected for survivors who received radiation that potentially impacted the heart and/or anthracyclines, with the frequency of the expected exam dependent upon age and intensity of exposure. Colonoscopies were expected for survivors  $\geq 35$  years old treated with  $\geq 30$  Gy radiation that potentially impacted the gastrointestinal tract, or  $\geq 50$  years old for those without  $\geq 30$  Gy. Bone density exams were expected for survivors treated with corticosteroids or methotrexate. Mammograms were expected for female survivors treated with  $\geq 20$  Gy radiation to the breast who are  $\geq 25$  old or  $\geq 8$  years off therapy and for all female survivors  $\geq 42$  years old. Pap smear exams were expected for female survivors  $\geq 23$  years old. Skin exams were expected for survivors treated with radiation.

Primary predictors of health behaviour and healthcare utilisation included measures of neurocognitive and emotional functioning. The CCSS Neurocognitive Questionnaire (CCSS-NCQ), a self-report measure, was recently validated in a large cohort of adult survivors of childhood cancer. Four primary factors were identified: Task Efficiency, Emotional Regulation, Organisation, and Memory.<sup>21</sup> The Emotional Regulation and Organisation factors are primarily measures of executive functions. The Task Efficiency and Memory factors include behaviours related to attention and memory abilities, respectively. The CCSS-NCQ was normed on a large cohort of siblings of cancer survivors.<sup>21</sup> The Brief Symptom Inventory – 18 (BSI) is a self-report measure of emotional distress, including specific indices of depression, anxiety and somatisation.<sup>22,23</sup> The standardisation manual provides norms from a nationally representative sample of community controls. The questions comprising both scales are available in the 2003 Follow-up Survey, the CCSS-NCQ comprises questions J1–J25 whilst the BSI-18 comprises questions G1–G18.

Covariates included cancer diagnosis (categorised into three groups – leukaemia, CNS tumours and others [including Hodgkin lymphoma, non-Hodgkin lymphoma, Wilms' tumour, neuroblastoma, soft tissue sarcoma and bone cancer]), current age, sex, body mass index (BMI), health insurance, household income and self-reported use of antidepressant medication. BMI was categorised as follows: underweight BMI  $< 18.5$ , normal weight BMI  $18.5$ – $24.9$ ; overweight BMI  $25$ – $29.9$ ; obese BMI  $\geq 30$ . For the physical activity outcome, reported activity at the time of entry into the CCSS study was used as a covariate.

### 2.3. Statistical analyses

Descriptive statistics were calculated for all predictors, outcomes and covariates. Neurocognitive and emotional functioning predictors were dichotomised according to whether survivors reported a level of symptoms considered to represent clinical impairment. For the CCSS-NCQ, clinical impairment was defined as a symptom level reported in  $\leq 10\%$  of a

sibling normative sample. For the BSI, clinical impairment was defined as a symptom level reported in  $\leq 10\%$  of the national standardisation sample. Backward selection to multiple variable modelling was performed for each of the outcomes discussed above using generalised linear regression models, assuming a binomial distribution and log link. In order to adjust for the multiple comparisons, a Bonferroni correction to alpha levels was applied. The least significant variables (i.e. largest  $p$ -value) were dropped one at a time until all the variables left in the model were significant at  $p < 0.004$ . Factors having more than two classes (e.g. diagnosis, BMI) were kept or removed based on the  $p$ -value of the Likelihood Ratio Test. Relative risks of predictors and covariates left in the final model for each outcome were calculated.

**Table 1 – Patient and treatment characteristics.**

	Mean	SD
Age (years)	32.0	7.6
	Number	Percent (%)
Sex		
Male	3,155	49.0
Female	3,285	51.0
BMI classification		
Underweight	489	7.6
Normal range	2,862	44.4
Overweight	1,862	28.9
Obese	1,227	19.1
Antidepressant use	955	14.8
Diagnosis		
Leukaemia	2,145	33.3
CNS tumours	660	10.3
Hodgkin lymphoma	872	13.5
Non-hodgkin lymphoma	505	7.8
Wilms tumour	646	10.0
Neuroblastoma	418	6.5
Soft tissue sarcoma	606	9.4
Bone cancer	588	9.1
Radiation site		
Brain	1765	27.4
Chest	1215	18.9
Neck	1026	15.9
Abdomen	1166	18.1
Spine	413	6.4
Pelvis	906	14.1
Limb	263	4.1
Total body	79	1.2
Chemotherapy		
Alkylator	3,125	48.5
Anthracycline	2,466	38.3
Epipodophyllotoxin	460	7.1
Antimetabolite (IV)	2,773	43.1
Antimetabolite (IT)	4,430	68.8
Corticosteroids	2,890	44.9

Note: BMI classifications were defined as follows: underweight = BMI  $< 18.5$ , normal weight = BMI  $18.5$ – $24.9$ ; overweight = BMI  $25$ – $29.9$ ; obese = BMI  $\geq 30$ . Radiation site and chemotherapy variables used to identify survivors recommended for specific health screening exams.

### 3. Results

Demographics and treatment characteristics of the survivors are presented in Table 1. Table 2 presents the percent of survivors with impairment on the CCSS-NCQ and BSI, and the percent who reported engagement in assessed health behaviours and healthcare utilisation. Less than half of all survivors reported meeting CDC guidelines for weekly physical exercise. A similar small number reported engaging in use of sun protection strategies. Roughly 12% of survivors reported receiving no health care in the past two years and 58% reported receiving only general health care. Only 17% of survivors reported receiving risk-based survivor oriented care in the two years prior to the survey. Dental care was reported by 71.7% of survivors. 85.1% of survivors recommended to receive a pap smear exam reported receiving such an exam, whilst 41.1% of survivors recommended to receive a mammogram reported such an exam. Few survivors recommended to receive other specific screening exams reported receiving such exams.

Table 3 presents results of the multiple variable models predicting relative risk for engaging in appropriate physical activity and sun protection. As expected, survivors who fell into the obese BMI category were less likely to report meeting CDC physical activity guidelines (RR = 0.80, 95% CI = 0.74–0.87). However, those who fell in the underweight category were also less likely to report meeting such guidelines (RR = 0.74, 95% CI = 0.76–0.94). Controlling for reported physical activity at baseline and current BMI, survivors with impaired task efficiency were less likely to report meeting CDC guidelines for weekly physical activity (RR = 0.77, 95% CI = 0.72–0.84). Older survivors (RR = 1.01, 95% CI = 1.01–1.01) and those with a history of a CNS tumour (RR = 1.04, 95% CI = 1.01–1.07) were more likely to report engaging in sun protection.

The results of the multiple variable models for prediction of physician-based healthcare and dental care are presented in Table 4. It should be emphasised that the significant effects reported below are present whilst controlling for age, sex, health insurance status and household income. Survivors

**Table 2 – Classification rates for primary predictors (CCSS-NCQ and BSI), primary health behaviours and healthcare utilisation outcomes.**

	N	# Impaired*	% Impaired
<i>CCSS-neurocognitive questionnaire</i>			
Task efficiency	6,440	1,444	22.4
Emotional regulation	6,440	807	12.5
Organisation	6,440	805	12.5
Memory	6,440	886	13.8
<i>Brief symptom inventory</i>			
Anxiety	6,440	493	7.7
Depression	6,440	740	11.5
Somatisation	6,440	860	13.4
	# Recommended	# Reported	Percent
Exercise	6,440	3,059	47.5
<i>Sun protection/avoidance</i>			
Sunscreen	6,440	2,860	44.4
Protective clothing	6,440	1,145	17.8
Wearing hat	6,440	2,297	35.7
Limit exposure	6,440	2,282	35.4
Stay in shade	6,440	2,108	32.7
<i>Physician health care</i>			
No health care		754	11.7
General health care		3,734	58.0
General survivor care		858	13.3
Risk based, survivor care		1,093	17.0
Dental care	6,440	4,614	71.7
Health insurance	6,440	5,679	88.2
<i>Recommended screening exams</i>			
Echocardiogram	2,072	610	29.4
Colonoscopy	753	108	14.3
Bone density exam	2,578	568	22.0
Mammogram	765	314	41.1
Pap smear	2,661	2,264	85.1
Skin exam	3,618	1,202	33.2

Note: Impairment defined as level of symptoms that fall  $\leq 10\%$  of the standardisation sample. Exercise based on meeting weekly physical activity guidelines recommended by the CDC. Physician health care categories are non-overlapping, with survivors classified into the highest category they met. Recommended screenings were based on survivor characteristics and treatment exposures, and only survivors with those characteristics or exposures were used in calculating percentages.

with impaired task efficiency were more likely to report receiving general survivor care compared to no care (RR = 1.20, 95% CI = 1.10–1.30), whilst those with impaired organisation were less likely to report dental care (RR = 0.92, 95% CI = 0.88–0.97). Although anxiety and depression were not associated with healthcare utilisation or dental care, those survivors who reported use of antidepressant medication were more likely to report receiving risk-based healthcare (RR = 1.20, 95% CI = 1.13–1.28). Of note, those survivors who fell into the obese category were also less likely to report dental care (RR = 0.92, 95% CI = 0.88–0.96).

Table 5 presents the results of the multiple variable models for prediction of recommended health screening exams. As discussed above, only survivors who are recommended to receive each exam were included in the respective analyses. In addition, these analyses again control for age, sex, health insurance status and household income. Contrary to expectations, survivors with memory impairment were nearly twice as likely to report receiving a colonoscopy (RR = 1.96, 95% CI = 1.33–2.89). Although symptoms of depression or general anxiety were not associated with health screening outcomes, those survivors reporting vague somatic complaints associated with anxiety were more likely to report receiving an echocardiogram (RR = 1.53, 95% CI = 1.32–1.77). In addition, the use of antidepressant medication was associated with an increased likelihood of receiving a bone density exam (RR = 1.41, 95% CI = 1.17–1.68). Of noted interest, survivors who met criteria for obesity were less likely to report receiving

a bone density exam (RR = 0.67, 95% CI = 0.54–0.82), a mammogram (RR = 0.71, 95% CI = 0.57–0.89) and a skin exam (RR = 0.78, 95% CI = 0.68–0.89).

#### 4. Discussion

Consistent with previous literature,<sup>24,25</sup> adult survivors of childhood cancer demonstrated low rates of engagement in protective health behaviours. Less than half of all survivors reported regular physical activity, and a similarly low percentage reported regular engagement in sun protection behaviours. Neurocognitive impairment, which was identified in over 20% of survivors, increased the risk of not engaging in these health behaviours. Survivors who reported problems with task efficiency were less likely to engage in regular physical activity, even when controlling for current BMI and prior history of physical activity. However, given the cross sectional nature of this study, it is unclear as to whether regular physical activity has a positive impact on these neurocognitive functions, or whether individuals with impairment in these neurocognitive functions have difficulty managing social circumstances in a manner to facilitate a regular exercise schedule. Certainly, good neurocognitive function can enhance one's ability to structure daily life events, and thereby enhance opportunities for healthy behaviours. Alternatively, regular exercise has been demonstrated to improve neurocognitive functions in elderly adults.<sup>26,27</sup>

**Table 3 – Relative risks for recommended physical activity and sun protection.**

	Physically active			Sun protection		
	RR	95% CI	p-Value	RR	95% CI	p-Value
Age	–	–	–	1.01	1.01–1.01	<0.0001
Sex						
Male (ref)	1.0			–	–	–
Female	<b>0.87</b>	<b>0.83–0.92</b>	<b>&lt;0.0001</b>	–	–	–
Active at baseline						
No (ref)	1.0			NA		
Yes	<b>1.36</b>	<b>1.29–1.44</b>	<b>&lt;0.0001</b>	NA		
BMI						
Normal range (ref)	1.0			–	–	–
Obese	<b>0.80</b>	<b>0.74–0.87</b>	<b>&lt;0.0001</b>	–	–	–
Overweight	0.95	0.90–1.00	0.05	–	–	–
Underweight	<b>0.84</b>	<b>0.76–0.94</b>	<b>0.002</b>	–	–	–
Diagnoses						
Other	–	–	–	1.0		
Leukaemia	–	–	–	0.99	0.97–1.02	0.60
CNS	–	–	–	<b>1.04</b>	<b>1.01–1.07</b>	<b>0.004</b>
Neurocognitive problems						
No problems (ref)	1.0			–	–	–
Task efficiency	<b>0.77</b>	<b>0.72–0.84</b>	<b>&lt;0.0001</b>	–	–	–
Organisation	0.89	0.81–0.98	0.02	–	–	–

Note: – Represents variables that did not remain in the model after the backward selection. Variables significant following Bonferroni adjustment for multiple comparisons are highlighted with bold font. Age used as a continuous variable (years). BMI classifications defined as: underweight = BMI <18.5, normal weight = BMI 18.5–24.9; overweight = BMI 25–29.9; obese = BMI ≥30. Other diagnosis category represents a combined group of Hodgkin Lymphoma, Non-Hodgkin Lymphoma, Wilm's tumour, Neuroblastoma, Soft tissue sarcoma, Bone cancer. Neurocognitive problems defined as a level of negative symptoms reported in ≤10% of standardisation samples.



**Table 4 – Relative risks for the prediction of physician health care and dental care.**

	General healthcare			General survivor care			Risk based survivor care			Dental care		
	RR	95% CI	p	RR	95% CI	p	RR	95% CI	p	RR	95% CI	p
Age	–	–	–	–	–	–	–	–	–	<b>1.01</b>	<b>1.01–1.01</b>	<b>0.0002</b>
Sex												
Male (ref)	1.0			1.0			1.0			1.0		
Female	<b>1.14</b>	<b>1.11–1.71</b>	<b>&lt;0.0001</b>	<b>1.48</b>	<b>1.35–1.62</b>	<b>&lt;0.0001</b>	<b>1.35</b>	<b>1.25–1.46</b>	<b>&lt;0.0001</b>	<b>1.08</b>	<b>1.05–1.11</b>	<b>&lt;0.0001</b>
Insurance												
No (ref)	1.0			1.0			1.0			1.0		
Yes	<b>1.30</b>	<b>1.21–1.39</b>	<b>&lt;0.0001</b>	<b>2.24</b>	<b>1.82–2.75</b>	<b>&lt;0.0001</b>	<b>2.65</b>	<b>2.13–3.30</b>	<b>&lt;0.0001</b>	<b>1.57</b>	<b>1.43–1.72</b>	<b>&lt;0.0001</b>
Household income												
<20,000 (ref)	1.0			–	–	–	–	–	–	1.0		
≥20,000	<b>1.08</b>	<b>1.03–1.13</b>	<b>0.003</b>	–	–	–	–	–	–	<b>1.16</b>	<b>1.09–1.24</b>	<b>&lt;0.0001</b>
BMI												
Normal range (ref)	–	–	–	–	–	–	–	–	–	1.0		
Obese	–	–	–	–	–	–	–	–	–	<b>0.92</b>	<b>0.88–0.96</b>	<b>&lt;0.0001</b>
Overweight	–	–	–	–	–	–	–	–	–	0.99	0.96–1.03	0.59
Underweight	–	–	–	–	–	–	–	–	–	1.01	0.95–1.07	0.77
Diagnoses												
Other	–	–	–	–	–	–	–	–	–	1.0		
Leukaemia	–	–	–	–	–	–	–	–	–	0.98	0.95–1.00	0.07
CNS tumours	–	–	–	–	–	–	–	–	–	<b>1.06</b>	<b>1.03–1.09</b>	<b>&lt;0.0001</b>
Neurocognitive problems												
No problems (ref)	–	–	–	1.0						1.0		
Organisation	–	–	–	–	–	–	–	–	–	<b>0.92</b>	<b>0.88–0.97</b>	<b>0.002</b>
Task efficiency	–	–	–	<b>1.20</b>	<b>1.10–1.30</b>	<b>&lt;0.0001</b>	–	–	–	–	–	–
Antidepressant use												
No	–	–	–	–	–	–	1.0			–	–	–
Yes	–	–	–	–	–	–	<b>1.20</b>	<b>1.13–1.28</b>	<b>&lt;0.0001</b>	–	–	–

Note: – represents variables that did not remain in the model after the backward selection. Variables significant following Bonferroni adjustment for multiple comparisons are highlighted with bold font. Age used as a continuous variable (years). BMI classifications defined as: underweight = BMI <18.5, normal weight = BMI 18.5–24.9; overweight = BMI 25–29.9; obese = BMI ≥30. Other diagnosis category represents a combined group of Hodgkin Lymphoma, Non-Hodgkin Lymphoma, Wilm's tumour, Neuroblastoma, Soft tissue sarcoma, Bone cancer. Neurocognitive problems defined as a level of negative symptoms reported in ≤10% of standardisation samples.

An additional finding consistent with the existing literature on adult survivors of childhood cancer is the low rate of health care utilisation in this cohort.<sup>4</sup> Only 30% of the cohort reported receiving survivor focused care (either general or risk-based), whilst nearly 12% reported receiving no health care at all. Although the overall rate of health care mirrors the rate of health insurance coverage, other factors are predictive of utilisation even when controlling for insurance coverage and household income. Survivors who report organisational problems were less likely to receive dental care.

Neurocognitive and emotionally-related factors were also associated with increased health care utilisation. These findings were present even when controlling for insurance status and household income. Survivors with impaired task efficiency were 20% more likely to report receiving general survivor care. This increased survivor care may result from the recognition that neurocognitive symptoms are a relatively common late effect of cancer therapy. Such symptoms may, in fact, be brought to light during the course of general survivor care, and patients who recognise these symptoms may be more likely to seek out care related to their general survivorship status. Alternatively, neurocognitive symptoms may co-occur with other late effects of central nervous system

targeted therapies (e.g. endocrinopathies) that cause survivors to seek survivor focused care. Such an association may also explain why survivors reporting memory problems were more likely to report receiving a colonoscopy. Somatisation is a condition associated with emotionally exaggerated experiences of physical symptoms, and can impact behaviour independent of other emotional symptoms.<sup>28</sup> Thus, it is not surprising to find this symptom pattern predictive of increased engagement in adherence to recommendations for an echocardiogram. Survivors who reported use of anti-depressant medication were also more likely to receive risk-based survivor care. Obviously, patients treated with antidepressants are more likely to already be connected to health care providers who monitor their medication prescription.

An unexpected finding in this study was the strong and pervasive risk associated with obesity. Not only were those survivors in the obese category at greater risk for not meeting recommended levels of physical exercise, they were also less likely to report receiving proper dental care, as well as receiving recommended bone density, mammogram and skin exams. This pattern of behaviour and lack of adherence to recommended medical examination, combined with the obese status, places these individuals at particularly high risk

Table 5 – Relative risks for recommended health screening exams.

	Echocardiogram			Colonoscopy			Bone density exam			Mammogram			Pap smear			Skin exam		
	RR	95% CI	p	RR	95% CI	p	RR	95% CI	p	RR	95% CI	p	RR	95% CI	p	RR	95% CI	p
Age	1.02	1.01–1.03	<0.0001	1.07	1.04–1.09	<0.0001				1.06	1.04–1.07	<0.0001				1.02	1.02–1.03	<0.0001
Insurance																		
No (ref)	1.0												1.0					
Yes	<b>2.13</b>	<b>1.49–3.06</b>	<0.0001	–	–	–	–	–	–	–	–	–	<b>1.15</b>	<b>1.06–1.25</b>	<b>0.001</b>	–	–	–
Household income																		
<20,000 (ref)	–	–	–	–	–	–	–	–	–	–	–	–	1.0			1.0		
≥20,000	–	–	–	–	–	–	–	–	–	–	–	–	<b>1.12</b>	<b>1.04–1.20</b>	<b>0.002</b>	<b>1.47</b>	<b>1.21–1.79</b>	<0.0001
BMI																		
Normal Range (ref)							1.0			1.0			–	–	–	1.0		
Obese	–	–	–	–	–	–	<b>0.67</b>	<b>0.54–0.82</b>	<0.0001	<b>0.71</b>	<b>0.57–0.89</b>	<b>0.003</b>	–	–	–	0.78	0.68–0.89	0.0002
Overweight	–	–	–	–	–	–	<b>0.75</b>	<b>0.63–0.90</b>	<b>0.002</b>	0.80	0.66–0.97	0.03	–	–	–	0.85	0.76–0.95	0.004
Underweight	–	–	–	–	–	–	<b>1.12</b>	<b>0.87–1.43</b>	<b>0.39</b>	0.86	0.65–1.15	0.31	–	–	–	1.06	0.91–1.25	0.45
Neurocognitive problems																		
No Problems (ref)				1.0														
Memory	–	–	–	<b>1.96</b>	<b>1.33–2.89</b>	<0.0001	–	–	–	–	–	–	–	–	–	–	–	–
Emotional problems																		
No Problems (ref)	1.0			–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Somatisation	<b>1.53</b>	<b>1.32–1.77</b>	<0.0001	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Antidepressant use																		
No							1.0									–	–	–
Yes	–	–	–	–	–	–	<b>1.41</b>	<b>1.17–1.68</b>	<b>0.0002</b>	–	–	–	–	–	–	–	–	–

Note: – Represents variables that did not remain in the model after the backward selection. Variables significant following Bonferroni adjustment for multiple comparisons are highlighted with bold font. Age used as a continuous variable (years). BMI classifications defined as: underweight = BMI <18.5, normal weight = BMI 18.5–24.9; overweight = BMI 25–29.9; obese = BMI ≥30. Neurocognitive and emotional problems defined as a level of negative symptoms reported in ≤10% of standardisation samples.

for future undetected chronic disease. The psychology literature identifies obesity as being associated with depression and social withdrawal,<sup>29,30</sup> which may account for these general maladaptive behaviour patterns. Such a pattern may warrant a multipronged approach to preventive interventions, including social engagement, behavioural therapy and psychopharmacology, when necessary.

There are several limitations inherent in this study. First, neurocognitive impairment and emotional symptoms were assessed through survivor self-report. Given the long-term status of the survivor cohort, some survivors may not be aware of the presence of limited neurocognitive functioning and, as such, the association with health behaviours and health care utilisation may have been underestimated. Still, self-report questionnaires are a reliable and valid procedure for the identification of neurocognitive and emotional functioning, and the specific measures used in this study have been validated in cancer survivor cohorts. A related limitation extends to the self-report nature of data collected on health behaviours and health care utilisation. Self-report of such behaviours is not inherently problematic, however, report by individuals who may truly have neurocognitive problems may be (e.g. survivors with memory problems being asked to recall health care utilisation practices). Although this may account for the increased likelihood of reporting colonoscopy in patients with memory problems, most associations with neurocognitive impairment were focused on task efficiency and organisation problems and, thus, the potential impact of this limitation appears small. An additional limitation is the lack of information on the knowledge of long-term follow-up guidelines on the part of the survivors or their primary care physicians. This information was not available, though its impact on adherence would certainly be worthy of future research efforts.

In summary, the findings of the current study demonstrate an association between neurocognitive and emotional functioning and engagement in health behaviours and health care utilisation. Survivors who develop neurocognitive impairment, regardless of the reason for the impairment, are at increased risk for reduced physical activity and are more likely to receive general survivor care. Survivors with symptoms of emotional dysfunction, as evidenced by either current symptoms or use of antidepressant medication, are at more likely to receive risk-based survivor care, echocardiograms, and bone density exams. Perhaps the more pervasive predictive variable is current BMI, which is associated with increased risk for non-adherence to multiple health-related behaviours.

The results of this study warrant recommendations for future investigations and health care practices. The demonstrated association between task efficiency and reduced physical activity should be explored in a prospective therapeutic trial. Since more physical activity is associated with less neurocognitive impairment in our model, perhaps interventions aimed at increased exercise can improve neurocognitive skills in those survivors with impairment, similar to what has been demonstrated in the literature on ageing adults. The association between emotional functioning and health care utilisation also warrants consideration. Increased emotional problems were related to enhanced health care utilisation. This pattern reinforces the importance of assess-

ing and intervening for emotional status in long term survivors of childhood cancer. Such monitoring is not only important for improving general quality of life, but may help to identify survivors at risk for poor adherence to prescribed health behaviours and health screening exams.

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## Conflict of interest statement

None declared.

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Dr. Krull had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. He will provide access to data used for this manuscript upon written request.

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