

# Predictors of Poor Adherence to Follow-up Care in Survivors of Childhood Cancer

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In the United States, life expectancy of children given a diagnosis of cancer has dramatically improved. The overall 5-year survival rate of patients with childhood cancer has increased from 62% to 86% over the last 40 years.<sup>1</sup> Additionally, from 2011 to 2015, mortality declined by 1.5% annually in children with a cancer diagnosis.<sup>2</sup> Therefore, the population of childhood cancer survivors (CCSs) has grown in the United States, with the population estimated to be 420,000 individuals and expected to soon exceed 500,000 patients.<sup>3</sup>

Long-term comorbidities in CCS have been documented. The Childhood Cancer Survivor Study (CCSS) reported that adult CCSs were more likely to have long-term health complications than were their healthy siblings.<sup>4,5</sup> Toxicity from radiotherapy and chemotherapy may be a contributing factor to the increased likelihood of chronic disease in CCSs.<sup>6,7</sup>

Current guidelines from the Children's Oncology Group (COG) and the National Academy of Medicine call for CCS long-term follow-up and risk-based patient care. A recommendation to receive long-term follow-up visits once a year is given to almost all CCSs; however, the schedule may vary depending on characteristics of the patient, cancer type, and treatment.<sup>8</sup> The goal of CCS

continuous care is 3-fold: early identification and prompt treatment of late effects, ongoing surveillance of comorbidities, and monitoring of overall health status with healthy lifestyle promotion.

Despite these guidelines, CCSs' follow-up care continues to be suboptimal.<sup>9,10</sup> Predictive factors for the absence of follow-up include older age at diagnosis, absence of stem cell transplantation, treatment with surgery alone, and lack of insurance.<sup>11,12</sup> More research is needed to identify knowledge gaps and other factors contributing to suboptimal follow-up in CCSs. By identifying the contributory factors, local oncology centers can develop interventions to improve adherence to follow-up care, decrease the disease burden, and improve CCSs' quality of life.

## Methods

We reviewed our internal institutional database and identified CCSs diagnosed over 13 years. Inclusion criteria were 1) receipt of a diagnosis of a neoplasm at age 0 to 18 years and completion of any treatment (eg, supportive therapy, surgical resection, radiation therapy, or chemotherapy) from January 1, 2004,

to June 1, 2017; 2) no evidence of disease during the CCSs' last visit to our pediatric oncology/survivorship clinic; 3) treatment completion before June 1, 2017; and 4) loss to follow-up (ie, no

visits to our pediatric oncology/survivorship clinic) for more than 2 years after treatment completion. Exclusion criteria included death from any cause and active survivorship follow-up at our clinic. (In general, survivorship follow-up varied depending upon cancer type; it generally involved attending a scheduled appointment every 3 to 4 months during the first 2 to 3 years post treatment and then

once or twice a year.) We screened for deaths using health care system electronic medical records (EMRs), the Social Security Death Index, and free online obituary search engines.

Individuals who completed their treatment but without follow-up with our pediatric oncology team for more than 2 years (730 days) were identified as "CCS lost to follow-up," and these individuals comprised our target survey population. Current phone numbers were obtained from EMRs for all CCSs meeting inclusion criteria. CCSs were contacted over the telephone; 3 attempts were made for



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telephone contact on separate occasions timed 1 week apart. Verbal consent and survey responses were obtained from the CCS if individuals were aged at least 18 years at the time of the phone call or from a parent/guardian if they were younger than 18 years at the time of the phone call. A standardized script, consent, and survey questions were used, with individual responses recorded.

Basic demographic data were obtained through a chart review of EMRs. Data on the following variables were obtained for CCSs meeting inclusion criteria: current age, age at diagnosis, sex, race, cancer type, treatment modality, history of stem cell transplantation, date of the last visit, and health insurance at last visit (private or public). All aspects of the study were approved by our institutional review board.

The statistical package SPSS Statistics 19 (IBM) was used to analyze data. Continuous variables were compared using *t*-test analysis; comparisons of categorical variables were performed using  $\chi^2$  tests or Fisher exact tests, as appropriate. Statistical significance was defined as  $P < .05$ .

## Results

In all, 276 participants were initially identified as CCSs during the study period. Participants were excluded if they had died due to any cause (41 patients), had been referred to another institution for care (8 patients), had completed treatment less than 2 years before (14 patients), had been in documented active follow-up at our oncology clinic (108 patients), or had no records of treatment (2 patients), leaving a total of 103 CCSs eligible for surveys and analysis.

The included sample was made up primarily of men (53%) and White individuals (96%). The mean age at diagnosis was 9.5 years (SD, 5.6 years). Mean time since diagnosis was 10.4 years (SD, 3.3 years), and the mean time from the last visit to start of study was 5.0 years (SD, 1.7 years). Leukemia/

**TABLE 1. Survey Responses**

Do you see a health care provider for your post cancer care?	n (%)
No	16 (53%)
Yes	14 (47%)
<b>For "yes"</b>	
<b>Type of health care provider</b>	
Primary care physician	4 (29)
Oncologist	8 (57)
Cancer survivorship clinic	0
Other	2 (14)
<b>For "no"</b>	
<b>Reported reasons for not seeing a health care provider</b>	
Transfer of care	1 (6)
Relocation to a new area/state	2 (13)
Change of primary oncologist	0
Lack of knowledge about cancer follow-up	11 (68)
Financial reasons (costs/co-pays)	0
Other	2 (13)
<b>Do you have health insurance?</b>	
No	0 (0%)
Yes	30 (100%)
<b>Which type of insurance?</b>	
Public	12 (40%)
Private	18 (60%)

lymphoma was the most common diagnosis (43%), followed by solid tumors (37%). Chemotherapy alone was the most frequent treatment modality (40%), followed by surgery (30%) and chemotherapy plus surgery (19%). All patients (100%) had health insurance at the time of diagnosis; 48% had public insurance (eg, Medicaid) and 52% had private insurance.

Of the 103 eligible CCSs who did not have documented follow-up within the previous 2 years, 30 answered survey questions via the telephone, with 2 additional participants declining to participate. We were unable to contact the remaining 71 individuals, either due to a change of primary phone number, no answer, or unavailability at the time of phone calls.

Survey responses are listed in **Table 1**. More than half the respondents (16 patients [53%]) did not report receiving cancer-related care with a health care provider as a survivor. Of the 14 participants reporting survivorship care, 8 CCSs (57%) reported receiving continued care from an oncologist; follow-up visits included 4 patients (29%) to a primary care physician, 1 patient (7%) to a neurologist, and 1 patient (7%) to a neurosurgeon. The most common reasons for not receiving follow-up care included lack of knowledge regarding cancer follow-up (11 patients [68%]), relocating to a new state (2 patients [13%]), transfer of care to a different oncologist (1 patient [6%]), and other reasons (2 patients [13%]). Financial reasons were not a reported determinant of poor follow-up.

Participants reporting no active follow-up had more years elapsed since the diagnosis (mean [SD], 11.5 years [3.5 years]) than did those who received follow-up survivorship care (mean [SD], 9.1 years [2.5 years];  $P = .046$ ; **Table 2**). Age, sex, and race had no association with follow-up status. All survey respondents reported having health insurance at the time of survey; however, more respondents in the active follow-up group than in the group reporting no follow-up had private insurance (71.4% vs 50%, respectively;  $P = .23$ ). Only 1 respondent received a stem cell transplant and reported being in follow-up.

Survey respondents varied in cancer type and treatment regimen given (Table 2). In cases of central nervous system (CNS) tumors, patients typically underwent tumor surgical resection, with 1 patient receiving radiation with surgery. In cases of leukemia and lymphoma, the most commonly used chemotherapeutic agents were alkylating agents and anthracyclines given in standard doses per COG standard treatment protocols. In cases of solid tumors (eg, hepatoblastoma, Wilms tumor, rhabdomyosarcoma), patients underwent surgical resection of the tumor followed by chemotherapy with alkylating agents. One patient with Ewing sarcoma required amputation of the involved extremity. No cancer type or treatment modality was associated with increased follow-up.

**Discussion**

In our surveyed CCSs, approximately half the respondents (16 patients [53%]) reported not seeing a health care provider for survivorship care. This follow-up rate, although suboptimal, is similar to that reported in a survivorship study performed at Texas Children’s Cancer Center (55%) and higher than results reported in several large, multi-institutional CCS studies.<sup>12-14</sup> In the Swiss CCS study, only 19% of respondents reported regular follow-up,<sup>13</sup> whereas

**TABLE 2. Survey Responses**

Do you see a health care provider for your post cancer care?			
	Yes n = 14	No n = 16	P value
<b>Gender</b>			
Male	6 (43%)	9 (56%)	.46
Female	8 (57%)	7 (44%)	0
<b>Race</b>			
Caucasian	14 (100%)	15 (94%)	1.00
Other	0 (0%)	1 (6%)	
<b>Age at diagnosis (years)</b>			
	8.6 ± 5.2	10.1 ± 5.7	.48
<b>Time between diagnosis and survey (years)</b>			
	9.1 ± 2.5	11.5 ± 3.5	.046
<b>Current type of insurance (from survey)</b>			
Public	4 (29%)	8 (50%)	.23
Private	10 (71%)	8 (50%)	
<b>Type of cancer</b>			
Liquid tumor	5 (36%)	5 (31%)	1.00
Solid tumor	4 (29%)	6 (38%)	
CNS tumor	5 (36%)	5 (31%)	
<b>Stem cell transplant status</b>			
Transplant	1 (7%)	0 (0%)	.47
No transplant	13 (93%)	16 (100%)	
<b>Type of treatment</b>			
Chemotherapy	4 (29%)	5 (31%)	.94
Chemotherapy plus stem cell transplant	1 (7%)	0 (0%)	
Chemotherapy plus surgery	3 (21%)	4 (25%)	
Surgery	6 (43%)	6 (38%)	
Surgery plus radiation	0 (0%)	1 (6%)	

CNS, central nervous system.

in the North American CCS study, only 31.5% of participants reported receiving survivorship care.<sup>14</sup> However, at St. Jude Children’s Research Hospital, only 15% of CCSs were classified as nonattenders.<sup>15</sup> At the Children’s Hospital of Philadelphia, approximately 25% of CCSs reported not receiving survivorship care within 5 years of diagnosis.<sup>16</sup> Both these institutions have a

high ranking for CCS support and have numerous interventions in place to promote continued survivorship care.

Regardless of the initial follow-up rates for care after cancer, attendance falls over time. One study conducted at the Roswell Park Cancer Institute in Buffalo, New York, reported that the follow-up rate noted 1 to 5 years post treatment was 91.2%, but this decreased

to 68.5% during years 6 to 10.<sup>17</sup> Similarly, in our study, longer lengths of time since the cancer diagnosis was associated with absent survivorship care.

Older age at diagnosis has been a predictor of poor clinic attendance in other large institutional studies.<sup>12,16,18</sup> Pediatric oncology patients who are diagnosed in the second decade of life usually transition to adult providers over time. In the absence of well-defined care transition plans, regular follow-up often ceases when patients leave pediatric care.<sup>19</sup> However, age at diagnosis did not associate with follow-up status in our study.

Other large studies found that CCSs without insurance or those who were underinsured were less likely to attend follow-up cancer care.<sup>12,14,16,18-20</sup> In our study, all participants had health insurance at the time of their last office visit and at the time of survey. Insurance type (private vs public) had no association with follow-up. This finding was unexpected, since cancer survivors can have more difficulty in obtaining health insurance.<sup>21,22</sup> A survey study conducted 1 year after the enactment of the Patient Protection and Affordable Care Act found that CCSs had lower rates of employer-sponsored coverage, higher rates of Medicaid coverage, and greater difficulty in obtaining coverage than did their siblings.<sup>23</sup> In our survey subgroup, financial reasons were not reported as a reason for poor clinic attendance. This contrasts with other studies that reported higher education, employment status, and insurance status to be associated with increased follow-up rates.<sup>14,16,18,24</sup>

Previous work demonstrated that cancer type may be associated with follow-up adherence. This was not the case in our study. In contrast, both May et al and Barakat et al reported that CCSs with brain and other solid tumors were less likely to attend follow-up care.<sup>11,15</sup> CCSs with solid tumors were most likely to undergo tumor resection; they may consider themselves cured after the procedure.<sup>25</sup>

This may lead them to falsely believe that regularly scheduled follow-up is unnecessary.<sup>24-26</sup> However, after complete resection of solid tumors, especially brain tumors, the malignancy may recur.<sup>27</sup> Furthermore, CCSs with brain tumors who are treated with surgery have an increased incidence of various future adverse effects, including vision changes, neurocognitive problems, behavior issues, and endocrinopathies.<sup>28</sup> Focused survivorship care can help to identify and manage these complications.

Of 16 individuals who did not receive follow-up, 11 reported lack of knowledge as the main reason for their poor attendance to follow-up care. Similarly, Kadan et al reported that only 35% of participants acknowledged being at risk for long-term cancer-related adverse effects.<sup>29</sup> Some of our surveyed CCSs reported being cleared by their primary physician and being told that no follow-up was necessary. Whether the primary physicians counseled CCSs properly or there were perceived differences in the need for follow-up care is unknown. Primary care physicians may have limited knowledge about the long-term effects of childhood cancer treatments and may not be familiar with the complex care needed by these CCSs; thus, provider education regarding survivorship care may be required.<sup>30</sup>

In any case, CCSs, especially those treated for solid and CNS tumors, have a knowledge deficit regarding long-term risks related to their primary malignancy.<sup>17</sup> Further, primary care physicians may have knowledge gaps concerning surveillance guidelines set forth by the COG.<sup>31,32</sup> Efforts should be made to ensure that care is provided in consultation with an experienced oncologist, when possible. Physicians should know current survivorship guidelines and educate their CCSs at regular intervals, as adverse effects of cancer therapy may not be apparent until late adulthood.

Our cross-sectional survey conducted during the COVID-19 pandemic

(December 2019-June 2020) had a limitation—the response rate ( $\approx 30\%$ ) was lower than anticipated. As a result, the sample size was small, and comparisons may have been underpowered. Additionally, our patient population mostly was comprised of White individuals, and they reported having health insurance. As such, our results may not be generalizable to other patient populations that include different racial groups and insurance status distributions. The optimal way to locate, contact, and survey CCSs remains an area of potential research, as others have reported that response rates increased substantially after postal questionnaire administration.<sup>33</sup> We also cannot rule out sampling and nonresponse bias with voluntary subject participation. Also, almost all of our participants with no follow-up care requested contact information for our institution's pediatric cancer survivorship clinic; however, due to time constraints, we did not measure their return attendance to the clinic as survivors.

Multilevel targeted interventions to increase engagement in survivorship care among CCSs are needed; they include use of a cancer registry, contact with patients via their preferred method of appointment reminders, construction of a social support network for cancer survivors, and connection with community resources. Community level interventions targeted at increasing the education of primary care providers on guideline-based survivorship care would improve CCS health and quality of life.

## Conclusion

Follow-up care of CCSs is an understudied area, especially in West Virginia. Among the surveyed CCSs, knowledge deficits rather than financial reasons were the reported cause of the lack of follow-up care. Our findings can help oncology centers to develop future interventions targeted towards this patient population to promote guideline-driven, long-term survivorship follow-up care. ■

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