

# Pediatric Cancers among Alaska Native People

Sarah H. Nash, PhD<sup>1</sup>, Garrett Zimpelman, BA<sup>1</sup>, Laura Schulz, MD<sup>2</sup>, and Matthew Hirschfeld, MD<sup>3</sup>

**Objective** To evaluate the descriptive epidemiology of pediatric cancers among Alaska Native people. **Study design** We used data from the Alaska Native Tumor Registry, a population-based registry capturing cancer information among Alaska Native people 1969-present. Specifically, we examined all cases of cancer diagnosed among individuals ages 0-19 years. Cases were classified according to the *International Classification of Childhood Cancers*, 3rd edition (ICCC-3). We estimated incidence and distribution of cases by ICCC-3 cancer site, comparing between the time periods 1969-1996 and 1997-2016. We assessed 12-month and 5-year cause-specific survival, and examined differences over the time period, adjusted for age, sex, and ICCC-3 site.

**Results** Incidence rates of pediatric cancers increased between 1969 and 1996 (n = 134) and 1997 and 2016 (n = 186) among Alaska Native people, from 139.8 in 1 000 000 (95% CI, 116.99-165.7) to 197.54 in 1 000 000 (95% CI, 170.1-228.1). Distribution of ICCC-3 sites differed between time periods (*P* < .0001). Finally, cancer survival was high; the 12-month survival probability from all ICCC-3 sites combined was 0.88 (95% CI, 0.84-0.92) and the 5-year survival probability was 0.76 (95% CI, 0.70-0.81) for 1969-2016. After adjusting for age, sex, and ICCC-3 site, we observed a 57% decrease in the risk of death when comparing Alaska Native pediatric cancer cases diagnosed in 1997-2016 with those diagnosed in 1969-1996.

**Conclusions** This information will be of value for our understanding of pediatric cancers among Indigenous peoples of the US, and will also be informative for clinicians providing care to this population. (*J Pediatr 2020;227:288-94*).

ancer is the leading cause of disease-related death in children nationwide, ranking only behind motor vehicle crash and firearm-related injury, and accounting for 9.1% of child and adolescent deaths nationwide. Mortality rates are higher for American Indian and Alaska Native children and adolescents compared with their US white counterparts, and exhibit regional variation, with the highest rates observed among Alaska Native children living in Alaska.<sup>2</sup> Furthermore, although the leading causes of death are similar among US white and American Indian and Alaska Native children and adolescents, data specific to Alaska Native children and adolescents living in Alaska show slight differences. 1,2 Cancer is not among the ten leading causes of death for Alaska Native children aged 0-14 years, but is the fifth leading cause of death for Alaska Native individuals aged 15-24 years, behind suicide, unintentional injury, homicide, and heart disease. Differences in pediatric cancer incidence rates also exist. Rates are lower among all American Indian and Alaska Native children and adolescents nationwide compared with all other racial groups in the US; however, only 1 report has compared cancer incidence rates between Alaska Native people in Alaska and other ethnic groups. 4-6 This report, published almost 20 years ago, indicated that rates among Alaska Native children were actually similar to those observed among white children in the US, and higher than those observed among American Indian and Alaska Native children living in New Mexico. This information agrees with what we know about variations in site-specific cancer incidence rates among American Indian and Alaska Native adults nationwide; for example, rates of gastric, lung, and colorectal cancers are known to be higher among Alaska Native people than their American Indian and Alaska Native counterparts in the contiguous 48 states.<sup>7-9</sup>

This study examines childhood and adolescent cancers among American Indian and Alaska Native people living in Alaska. We used data from the Alaska Native Tumor Registry (ANTR), a population-

based central cancer registry that records cancer information for American Indian and Alaska Native people living in Alaska. The previous report of cancer among Alaska Native children and adolescents, which also used data from the ANTR, reported on cases diagnosed between 1969 and 1996; therefore, this report focuses primarily on cases diagnosed during the most recent 20-year period (1997-2016). However, we also present data from 1969-1996 for comparison. We present specific information on cancer frequency, incidence, and survival. We anticipate that these findings will be of interest to clinicians

ANTR Alaska Native Tumor Registry

Epstein-Barr virus

ICCC-3 International Classification of Childhood Cancers, 3rd edition

Surveillance, Epidemiology, and End Results

From the <sup>1</sup>Alaska Native Epidemiology Center, Community Health Services, Alaska Native Tribal Health Consortium; <sup>2</sup>Alaska Pediatric Oncology; and <sup>3</sup>Alaska Native Medical Center, Anchorage, AK.

S.N., G.Z., and the Alaska Native Tumor Registry are supported by the National Cancer Institute (NCI) Surveillance, Epidemiology and End Results Program, NCI contract number HHSN26120130010I, Task Order HHSN26100005. M.H. is supported as a co-investigator by 2 grants, Diet and the CPT1A Arctic Variant: Impact on the Health of Alaska Native Children (NIH/NICHD R01HD089951-02) and the Clinical Sites for the IDeA States Pediatric Clinical Trials Network (NIH 1UG1HD090875-01). The funders had no role in the study design; collection, analysis or interpretation of data; the writing of the report; the decision to publish these data. The authors declare no conflicts of interest.

0022-3476/\$ - see front matter. © 2020 Elsevier Inc. All rights reserved https://doi.org/10.1016/j.jpeds.2020.07.036

**EBV** 

**SEER** 

interested in childhood and adolescent cancers, particularly among Indigenous populations, as well as individuals with a broader interest in cancer among American Indian and Alaska Native people.

## Methods

Data indicate that 147 752 American Indian and Alaska Native people reside in Alaska, including 56 827 people aged under 18 years (individuals reporting American Indian and Alaska Native identity alone, or in combination with another racial identity). 10 American Indian and Alaska Native people comprise 19.5% of the Alaskan population, and almost 90% of American Indian and Alaska Native people living in Alaska identify as Alaska Native; therefore, hereafter we will refer to all American Indian and Alaska Native people resident in Alaska as "Alaska Native people." 11 Healthcare for Alaska Native people is provided by more than 20 regional tribal health organizations, and the Alaska Native Tribal Health Consortium, a tribal health organization that provides statewide medical subspecialty and surgical services for all Alaska Native people. There is one tribally managed tertiary healthcare facility in the state, located in Anchorage: the Alaska Native Medical Center. However, almost all pediatric cancer care in Alaska is provided at other Anchorage-based, nontribal clinics and hospitals to consolidate services and provide the highest quality care for the relatively small number of pediatric cancer cases that occur in Alaska. Unusual or challenging cancer cases may be treated out of state, usually by facilities in Seattle, Washington, or Portland, Oregon.

#### **Data Sources**

Cancer data were collected by the ANTR, a population-based central cancer registry that records information on American Indian and Alaska Native people who meet eligibility requirements for Indian Health Service benefits, who have been diagnosed with cancer in Alaska since 1969, and who resided in Alaska at the time of diagnosis. The ANTR has been collecting cancer information according to the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program standards since its inception and has been a full member of the SEER Program since 1999. According to ANTR standard case-finding practices, cases were ascertained through a variety of sources, including hospital discharge diagnoses for tribal and nontribal health facilities in Alaska; tumor registry and pathology files of the Alaska Native Medical Center and other in-state healthcare facilities; linkage to the Alaska Cancer Registry and the Washington State Cancer Registry; and death certificates (<1% cases were registered solely on the basis of information from a death certificate). Mortality data were obtained from the Centers for Disease Control and Prevention's National Center for Health Statistics; additional death clearance procedures to determine vital status and cause of death included linkage with the Social Security Administration, and Centers for Medicare and Medicaid, as well as reviewing Alaska death certificate information in collaboration with the Alaska Cancer Registry. Information on treatment occurring outside of Alaska was obtained through linkage with other population-based cancer registries. For the purposes of this analysis, we report on cancers diagnosed between January 1, 1969, and December 31, 2016, with our primary focus on cases diagnosed in the last 20 years (1997-2016). Patient characteristics collected by the tumor registry and reviewed in this study include age at diagnosis and sex. Clinical characteristics included histologic subtype, laterality, and cancer stage (SEER Historic Stage A: local vs regional vs distant/un-known).<sup>12</sup>

#### Case Definition

Cases were restricted to those diagnosed among children (aged 0-14 years) and adolescents (aged 15-19 years). Cases included only primary malignant neoplasms, and were classified into 12 major groups using the *International Classification of Childhood Cancer*, 3rd edition (ICCC-3). <sup>13</sup>

## **Statistical Analyses**

Differences in patient and clinical characteristics were assessed using the  $\chi^2$  test for categorical variables, or the Fisher exact test for comparisons that contained cell sizes of less than 5, and 1-way ANOVA for continuous variables. Cancer incidence rates were expressed as average annual rates, expressed per 1 000 000 population and age-adjusted to the US Census 2000 standard population using the direct method. Denominators for rate calculations were derived from population estimates from the US Bureau of the Census and National Center for Health Statistics for Alaska Native people (bridged estimates) and US white people, available from the National Cancer Institute's SEER Program. 11 Where comparisons are made with data from whites in the US, we used the SEER 13 Research Database, again available from the National Cancer Institute's SEER Program. 20-year limited duration prevalence counts were estimated using the SEER\*Stat Software (National Cancer Institute, Surveillance Research Program, Bethesda, Maryland). In accordance with prevailing standards, survival analyses were restricted to cases of known age, histologically confirmed and followed over time; cases that were identified solely on the basis of death certificates or autopsy reports were excluded from the survival analyses. 14 We use cause-specific survival analyses, because these methods are more appropriate for use in populations where generic life tables may not accurately represent the experience of the population (such as Indigenous peoples). Cause-specific survival is a method of assessing net survival, which provides information on the net effect of a cancer diagnosis in the absence of other causes of death. In a population-based setting, differences in net cancer survival reflect differences in survival owing to the cancer rather than competing causes of death.<sup>15</sup> Patients still alive on December 31, 2016, or who had died of other causes were censored from these analyses. We used Cox proportional

hazards models to examine the risk of death between time periods, adjusted for age and sex.

All statistical tests were 2-sided and were assessed at an alpha level of a *P* of less than .05. Statistics were generated using the SEER\*Stat Software version 8.3.5 (National Cancer Institute's Surveillance Research Program, Bethesda, Maryland) and SAS version 9.4 (SAS Institute Inc, Cary, North Carolina). Incidence rates and case counts are not provided where cell sizes were less than 10 to protect individuals' privacy and ensure the stability of the estimates presented. Institutional review board review was not required for this study, because it used publicly available surveillance data; tribal review and approval from the Alaska Native Tribal Health Consortium and Southcentral Foundation were obtained for publication of this study.

# **Results**

Over 47 years of surveillance, 320 cases of ICCC-3-classified cancer were diagnosed among Alaska Native people aged less than 20 years (**Table I**). More than one-half (58%) of these cases occurred in the most recent 20-year period (1997-2016). During this time period (1997-2016), pediatric cancers accounted for 2.5% of cancers among Alaska Native people (n = 186). Twenty-year limited prevalence estimates indicated 132 (95% CI, 110, 157) pediatric cancer survivors, split between 0-14 years at prevalence (58; 95% CI, 44-75), 15-19 years (32; 95% CI, 22, 45), and more than 20 years (42; 95% CI, 30-57).

**Table I** describes case counts and incidence rates for Alaska Native pediatric cancer cases, comparing the most recent 20-year period (1997-2016; hereafter "recent" time period), to the 1969-1996 (hereafter "earlier" time period; data

previously reported by Lanier et al, but presented here for comparison). Data are reported for all ages to maximize cell sizes. In the most recent time period, approximately three-quarters of Alaska Native pediatric cancer cases were diagnosed among children (0-14 years; n = 140 [75%]), with the remaining 25% of cases diagnosed among adolescents (15-19 years; n = 46). The most common cancer type among Alaska Native children was leukemia (38% in recent time period), followed by central nervous system malignancies (17%), and lymphomas (15%). Among Alaska Native adolescents, other malignant epithelial neoplasms and melanomas were the most common (30%), followed by leukemia and lymphomas, which were almost equally represented (18% and 20%, respectively).

We examined change in both ICC-3 site distribution and cancer incidence over time (Table I, Figure 1, and Figure 2). Although not the primary focus of the current analysis, Table II (available at www.jpeds.com) presents incidence compared with US white. Site distribution differed between children and adolescents (P < .001) in both time periods (Figure 1). We also observed significant differences in the distribution of sites between the earlier and recent time periods for both children (P = .037) and adolescents (P = .031). Specifically, hepatic tumors comprised a relatively large proportion of cancers in the earlier time period (13%), whereas these cancers were relatively uncommon in the recent time period (3%). Overall, the rate of childhood cancers among Alaska Native people aged less than 20 years during the recent time period was 197.5 (95% CI, 170.1-228.1) per 1 000 000 population; this was slightly higher than in the earlier time period (incidence rate, 139.8; 95% CI, 117.0-197.5 per 1 000 000 population). Changes in the 20-year average annual incidence rates varied by ICCC-3 site (Figure 2).

Table I. Case counts and incidence rates (per 1 000 000 population) for pediatric cancers by ICCC-3 site classification among Alaska Native children, diagnosed 1969-2016, stratified by time period\*

	1969-2016 All ages (00-19 years)		1969-1996 All ages (00-19 years)		1997-2016 All ages (00-19 years)	
	Count	IR (95% CI)	Count	IR (95% CI)	Count	IR (95% CI)
All ICCC cancers	320	167.5 (149.6-186.9)	134	139.8 (117.0-165.7)	186	197.5 (170.1-228.1)
I Leukemias, myeloproliferative and myelodysplastic diseases	97	49.6 (40.2-60.5)	36	36.6 (25.6-50.8)	61	64.1 (49.0-82.3)
Acute lymphocytic leukemia	60	30.3 (23.1-39.0)	24	24.5 (15.6-36.5)	36	37.4 (26.2-51.8)
Acute myeloid leukemia	20	10.5 (6.4-16.2)	-	· <del>-</del>	14	14.9 (8.2-25.0)
ll Lymphomas and reticuloendothelial neoplasms Hodgkin lymphomas	44	23.2 (16.9-31.2)	14	14.8 (8.0-24.8)	30	32.3 (21.7-45.9)
Non-Hodgkin lymphomas (except Burkitt lymphoma)	17	9.2 (5.4-14.8)	-	_	13	14.1 (7.5-24.1)
III CNS and miscellaneous intracranial and intraspinal neoplasms	47	24.8 (18.2-33.0)	18	18.7 (11.0-29.5)	29	31.2 (20.9-44.8)
IV Neuroblastoma and other peripheral nervous cell tumors	-	-	-	_	-	_
V Retinoblastoma	10	4.9 (2.3-9.0)	-	_	-	_
VI Renal tumors	17	8.4 (4.9 -13.6)	_	-	-	-
VII Hepatic tumors	24	12.8 (8.2-19.0)	18	19.7 (11.7-31.1)	_	-
VIII Malignant bone tumors	12	6.4 (3.3-11.2)	-	· <del>-</del>	_	-
IX Soft tissue and other extraosseous sarcomas	23	12.3 (7.8-18.4)	-	_	15	16.2 (9.0-26.6)
X Germ cell and trophoblastic tumors and neoplasms of gonads	10	5.4 (2.6-9.9)	_	_		. ,
XI Other malignant epithelial neoplasms and melanomas	27	15.4 (10.1-22.3)	_	_	18	19.8 (11.8-31.3)
XII Other and unspecified malignant neoplasms	-	· – ′	-	-	-	` <b>-</b>

CNS, central nervous system; IR, incidence rate.

290 Nash et al

<sup>\*</sup>Data not given where case count <10.

December 2020 ORIGINAL ARTICLES

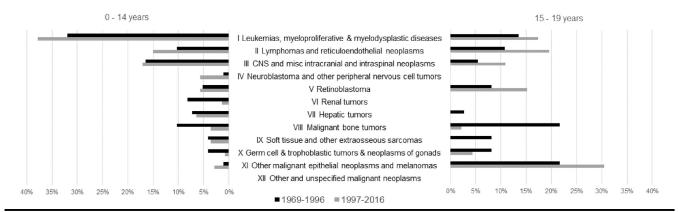
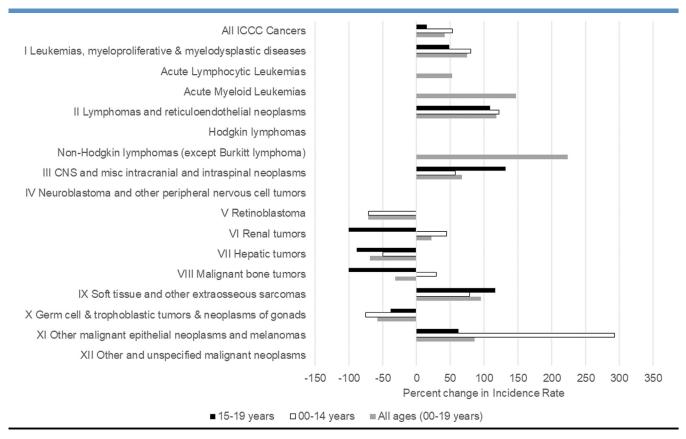


Figure 1. Distribution of pediatric cancer cases among ICCC-3 sites, by time period, stratified by age at diagnosis, among Alaska Native children, 1969-2016.

Unfortunately, owing to small case counts and wide CIs, we were unable to detect any significant differences by ICCC-3 site between time periods. However, we did observe decreases in the incidence of retinoblastoma, hepatic tumors, malignant bone tumors, and germ cell tumors. In contrast, we observed increases in the incidence of leukemia, lymphoma, central nervous system neoplasms, soft tissue and other extraosseous sarcomas, and other

malignant epithelial neoplasms and melanomas. Despite an overall increase in incidence rates for leukemia among adolescents (15-19 years), we did observe a decrease in the incidence of acute lymphocytic leukemia for this group.

**Table III** describes the 1- and 5-year cause-specific survival for Alaska Native pediatric cancers, stratified by ICCC-3 site classification, for both time periods and all ages combined. Cause-specific survival probability from all cancers was



**Figure 2.** Change in incidence rate for childhood cancers, by age and ICCC-3 site, between time period (1969-1996 and 1997-2016). <sup>a</sup>Data are not given where cell case counts are less than 10. <sup>b</sup>Differences were calculated as percent change between earlier time period and recent time period, that is, positive change indicates rate was higher in the recent time period.

Table III. Cause-specific survival by ICCC-3 site for Alaska Native pediatric cancer cases diagnosed 1969-2016\*

ICCC-3 site	No. (deaths)N	/lonth	Survival s (95% CI)
I Leukemias, myeloproliferative and	92 (23)	12	(
myelodysplastic diseases		60	0.72 (0.61-0.81)
II Lymphomas and reticuloendothelial	43 (4)	12	(
neoplasms		60	0.90 (0.76-0.96)
III CNS and miscellaneous intracranial and	30 (10)	12	( /
intraspinal neoplasms		60	0.60 (0.38-0.76)
IV Neuroblastoma and other peripheral	_	12	-
nervous cell tumors		60	_
V Retinoblastoma	-	12	-
		60	_
VI Renal tumors	16 (2)	12	(
		60	0.94 (0.63-0.99)
VII Hepatic tumors	21 (8)	12	()
		60	0.74 (0.48-0.88)
VIII Malignant bone tumors	12 (7)	12	(
		60	0.50 (0.21-0.74)
IX Soft tissue and other extraosseous	22 (4)	12	(
sarcomas		60	0.80 (0.55-0.92)
X Germ cell and trophoblastic tumors and	_	12	-
neoplasms of gonads		60	_
XI Other malignant epithelial neoplasms	26 (9)	12	0.77 (0.56-0.89)
and melanomas		60	0.73 (0.52-0.86)
XII Other and unspecified malignant	-	12	-
neoplasms		60	-

<sup>\*</sup>Data not given where case count <10.

high: the 12-month survival probability was 0.88 (95% CI, 0.84, 0.92) and the 5-year survival probability was 0.76 (95% CI, 0.70, 0.81). Survival probability varied by ICCC-3 site. For many sites for which there were sufficient data to calculate survival, 12-month survival probability was greater than 90%; exceptions to this were malignant bone tumors, and other malignant epithelial neoplasms and melanomas. The 5-year survival probability was highest for lymphomas (0.90; 95% CI, 0.76-0.96) and renal tumors (0.94; 95% CI, 0.63-0.99), and lowest for malignant bone tumors (0.50; 95% CI, 0.21-0.74). Survival was higher in the recent period relative to the earlier period; a Kaplan-Meier plot is shown in Figure 3 (available at www.jpeds. com). In Cox proportional hazards models adjusted for age, sex, and ICCC-3 site, the risk of death was 57% lower in the recent period relative to the earlier period (hazard ratio, 0.53; 95% CI, 0.32-0.89).

# **Discussion**

Despite representing a small proportion of total cancer cases (2.5%) diagnosed among Alaska Native people of all ages, Alaska Native pediatric cancers are important to understand to ensure that the Alaska Tribal Health System and the associated nontribal health systems both within and outside of Alaska are providing the highest quality cancer care to Alaska Native children. We present the most recent epidemiologic data (1997-2016), and compare it with data published by Lanier et al (1969-1996) to understand whether and how

the epidemiology of pediatric cancers is changing in Alaska Native people. Our results indicate a significant increase in the incidence rate of all cancers between the 2 time periods, as well as an increase in incidence rates for several ICCC-3 cancer sites. Conversely, we observed a decrease in the risk of death between the 2 time periods, indicating that survival has improved. This pattern reflects trends observed at the national level, where increased incidence has been accompanied by decreased mortality and improved survival for many pediatric cancer sites. These findings will be informative for those involved in the provision of healthcare services and clinical care to Alaska Native people, as well as those interested in cancer among Indigenous populations.

In contrast to many other cancer sites examined in this study, we saw a substantial decrease in hepatic tumors between the 2 time periods. Lanier et al showed that Alaska Native children were at significantly greater risk of hepatocellular carcinoma relative to both white children in the US and American Indian and Alaska Native children in New Mexico.<sup>6</sup> All children in that study were hepatitis B antigen-positive, and the authors demonstrated a significant decrease in incidence of these tumors between cohorts born before and after the implementation of a statewide hepatitis B vaccination program began in 1982.<sup>6</sup> Our results confirm the continued success of this program for hepatic tumor prevention among Alaska Native children. This observation is paralleled by observations among Alaska Native adults, who have also seen a sharp decrease in hepatitis B-related cancers.16

The increase in non-Hodgkin lymphoma observed between the 2 time periods could be related to an increase in Epstein-Barr virus (EBV) prevalence in the Alaska Native population. EBV is an infectious agent linked to increased risk of developing non-Hodgkin's lymphoma, and has also been shown to have a potential role in the development of adult nasopharyngeal cancers, which are observed at 17 times higher rates among Alaska Native people than whites in the US. 17-20 Although there is some evidence from the 1980s to suggest a high prevalence of EBV infection among Alaska Native children, further research is necessary to understand EBV prevalence over time among Alaska Native children, and whether EBV may be linked to the increased incidence of non-Hodgkin lymphoma observed herein.<sup>6</sup> Other risk factors for non-Hodgkin lymphoma in children include immunodeficiency (including immunodeficiency syndromes, infection with HIV, and organ transplantation), radiation exposure, and possibly a family history of this disease.<sup>21</sup>

Improvements in pediatric cancer survival nationally are thought to be linked to improvements in treatment as well as supportive care. The landscape of pediatric cancer care in Alaska has changed since cancer surveillance begun in 1969, with the development of local pediatric cancer resources and treatment. In 2005, the first pediatric oncology clinic opened in Alaska, giving Alaska Native children an option to remain in-state for most of their cancer care. Outcomes for these children have improved (Figure 3) and, by remaining closer to home for therapy, disruptions to family

292 Nash et al

December 2020 ORIGINAL ARTICLES

and patient satisfaction are minimized, relative to when all children had to leave the state for oncology services (MH, LS, personal communication, 2020). For some harder to treat, or rare, cancers that are best treated in a large pediatric oncology facility, families may still need to travel out of state, usually to Washington or Oregon. It is unknown to what degree increased in-state healthcare access directly contributed to increased survival observed between the 2 time periods; however, we know from patient surveys studies with Indigenous and non-Indigenous peoples that both individuals and families prefer to receive their care closer to home. 22-24 Furthermore, access to culturally appropriate, high-quality healthcare is known to improve cancer outcomes.<sup>25</sup> It is critical that Alaska Native children and their families continue to receive access to the highest quality cancer care and supportive services in Alaska for their continued health and well-being.

In considering access to cancer care services for Alaska Native children and adolescents, our results also support the need to consider ongoing follow-up care for cancer survivors. The number of pediatric survivors is increasing nationally, with an estimated 379 112 survivors alive in the US as of January 1, 2010.<sup>5</sup> Although we estimate that the number of pediatric cancer survivors among Alaska Native people is small, owing to the size of the Alaska Native population and the rarity of these cancers, this growing group is likely to have unique healthcare and cancer surveillance needs. 26,27 It is also critical to understand the needs of these individuals so that Tribal Health Organizations can ensure that these needs are being met. Yet, studies indicate that there is a dearth of childhood cancer survivorship research conducted among minority populations, not just Alaska Native people. We know of no published studies that examine the needs of Alaska Native cancer survivors, whether the cancer was diagnosed when the individual was a child or an adult.

The primary strength of this study was the use of highquality population-based data from the ANTR, an National Cancer Institute-supported SEER registry. In particular, the long history of cancer surveillance by this registry (almost 50 years), enabled us to examine trends in pediatric cancers over a long period of time. This was necessary, in part owing to the small size of this population, and the resulting low case counts for pediatric cancers. The small sample size provided a challenge to examining trends, particularly in specific age, sex, or cancer site strata, and cautious interpretation of these data may be warranted. Yet, this does not diminish the importance of this work; several researchers have noted the importance of small population cancer research.<sup>28,29</sup> It is possible that data collected by the ANTR on pediatric cancer cases were incomplete. This may have occurred, for example, if an individual was diagnosed and treated out of state. Although the ANTR has long conducted routine linkages with both in- and out-of-state partners to ensure complete case ascertainment and follow-up, we know that racial misclassification is higher outside of Alaska, and in urban, non-Indian Health Service (IHS) Purchased/Referred care delivery counties (such as those where Alaska Native people might typically seek treatment).<sup>30</sup> Therefore, there is a possibility that a small number of cases may not have been captured in the registry. Finally, it is possible that the quality of cancer registration may have changed over time, which could impact the interpretation of these data. However, we note that the ANTR has followed the SEER Program standards since its inception in 1974; therefore, we do not perceive there to have been any systematic shifts in registration procedures that are likely to have greatly impacted these results.

We were able to demonstrate that, although the incidence of pediatric cancers is increasing in this population, survival has also improved markedly. These results support the need for ongoing provision of specialist pediatric oncology services in Alaska for Alaska Native people, as well as to understand the unique healthcare and support service needs of Alaska Native pediatric cancer survivors as they age. We anticipate that these results will be of interest to those who provide clinical care services to Alaska Native children, as well as those with an interest in pediatric cancers, and indigenous health issues.

Submitted for publication Apr 14, 2020; last revision received Jun 24, 2020; accepted Jul 9, 2020.

Reprint requests: Sarah H. Nash, PhD, 3900 Ambassador Drive, Anchorage, AK 99508. E-mail: shnash@anthc.org

## **Data Statement**

Data sharing statement available at www.jpeds.com.

## References

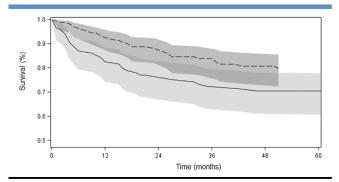
- Cunningham RM, Walton MA, Carter PM. The major causes of death in children and adolescents in the United States. N Engl J Med 2018;379: 2468-75.
- Wong CA, Gachupin FC, Holman RC, MacDorman MF, Cheek JE, Holve S, et al. American Indian and Alaska Native infant and pediatric mortality, United States, 1999-2009. Am J Public Health 2014;104: S320-8.
- Blake I, Holck P, Provost EM. Alaska Native mortality update: 2009-2013. Anchorage (AK). Alaska Native Epidemiology Center; 2016.
- Li J, Thompson TD, Miller JW, Pollack LA, Stewart SL. Cancer incidence among children and adolescents in the United States, 2001-2003. Pediatrics 2008:121:e1470-7.
- 5. Ward E, DeSantis C, Robbins A, Kohler B, Jemal A. Childhood and adolescent cancer statistics, 2014. CA Cancer J Clin 2014;64:83-103.
- Lanier AP, Holck P, Ehrsam Day G, Key C. Childhood cancer among Alaska Natives. Pediatrics 2003;112:e396.
- 7. White MC, Espey DK, Swan J, Wiggins CL, Eheman C, Kaur JS. Disparities in cancer mortality and incidence among American Indians and Alaska Natives in the United States. Am J Public Health 2014;104: S377-87.
- 8. Wiggins CL, Espey DK, Wingo PA, Kaur JS, Wilson RT, Swan J, et al. Cancer among American Indians and Alaska Natives in the United States, 1999-2004. Cancer 2008;113:1142-52.
- 9. Wiggins CL, Perdue DG, Henderson JA, Bruce MG, Lanier AP, Kelley JJ, et al. Gastric cancer among American Indians and Alaska Natives in the United States, 1999-2004. Cancer 2008;113:1225-33.
- Alaska Department of Labor and Workforce Development. Alaska population by age, sex, race (alone or in combination) and Hispanic origin.

- 2015. http://live.laborstats.alaska.gov/pop/index.cfm. Accessed March 23, 2017.
- 11. U.S Census Bureau. 2010 Census summary file 1. 2010. https://factfinder/census.gov. Accessed June 24, 2020.
- Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457-81.
- 13. Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International classification of childhood cancer. Cancer 2005;103:1457-67.
- Howlader N, Ries LA, Mariotto AB, Reichman ME, Ruhl J, Cronin KA. Improved estimates of cancer-specific survival rates from population-based data. J Natl Cancer Inst 2010;102:1584-98.
- Mariotto AB, Noone AM, Howlader N, Cho H, Keel GE, Garshell J, et al. Cancer survival: an overview of measures, uses, and interpretation. J Natl Cancer Inst Monogr 2014;2014:145-86.
- 16. Connelly M, Bruce MG, Bulkow L, Snowball M, McMahon BJ. The changing epidemiology and aetiology of hepatocellular carcinoma from 1969 through 2013 in Alaska Native people. Liver Int 2016;36: 1829-35.
- 17. Engels EA. Infectious agents as causes of non-Hodgkin lymphoma. Cancer Epidemiol Prev Biomark 2007;16:401-4.
- 18. Lanier A, Bender T, Talbot M, Wilmeth S, Tschopp C, Henle W, et al. Nasopharyngeal carcinoma in Alaskan Eskimos, Indians, and Aleuts: a review of cases and study of Epstein-Barr virus, HLA, and environmental risk factors. Cancer 1980;46:2100-6.
- 19. Raab-Traub N, Flynn K, Pagano J, Pearson G, Huang A, Levine P, et al. The differentiated form of nasopharyngeal carcinoma contains Epstein-Barr virus DNA. Int J Cancer 1987;39:25-9.
- Carmack A, Schade TL, Sallison I, Provost EM, Kelly JJ. Cancer in Alaska Native People: 1969-2013, the 45 year report. Anchorage (AK): Alaska

- Native Epidemiology Center, Alaska Native Tribal Health Consortium; 2015.
- Allen CEKK, Bollard CM, Gross TG. Malignant non-Hodgkin lymphomas in children. In: Pizzo PA, ed. Principles and practice of pediatric oncology. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2016.
- Fitch MI, Gray RE, McGowan T, Brunskill I, Steggles S, Sellick S, et al. Travelling for radiation cancer treatment: patient perspectives. Psychooncology 2003;12:664-74.
- 23. Nostedt MC, McKay AM, Hochman DJ, Wirtzfeld DA, Yaffe CS, Yip B, et al. The location of surgical care for rural patients with rectal cancer: patterns of treatment and patient perspectives. Can J Surg 2014;57:398.
- 24. Shalowitz DI, Nivasch E, Burger RA, Schapira MM. Are patients willing to travel for better ovarian cancer care? Gynecol Oncol 2018;148:42-8.
- **25.** Surbone A. Cultural aspects of communication in cancer care. Support Care Cancer 2008;16:235-40.
- Aziz NM, Oeffinger KC, Brooks S, Turoff AJ. Comprehensive long-term follow-up programs for pediatric cancer survivors. Cancer 2006;107: 841-8
- American Academy of Pediatrics Section on Hematology/Oncology Children's Oncology Group. Long-term follow-up care for pediatric cancer survivors. Pediatrics 2009;123:906-15.
- **28.** Srinivasan S, Moser RP, Willis G, Riley W, Alexander M, Berrigan D, et al. Small is essential: importance of subpopulation research in cancer control. Am J Public Health 2015;105:S371-3.
- 29. Etz KE, Arroyo JA. Small sample research: considerations beyond statistical power. Prev Sci 2015;16:1033-6.
- Espey DK, Wiggins CL, Jim MA, Miller BA, Johnson CJ, Becker TM. Methods for improving cancer surveillance data in American Indian and Alaska Native populations. Cancer 2008;113:1120-30.

294 Nash et al

December 2020 ORIGINAL ARTICLES



**Figure 3.** Survival probabilities among Alaska Native pediatric cancer cases (all sites, age <20 years); by period of diagnoses: 1969-1996 (solid line), 1997-2016 (dashed line) (shadings show 95% Cls).

Table II. Case counts and 25-year average annual incidence rates (per 1 000 000 population) for pediatric cancers by ICCC-3 site classification among Alaska Native and white children in the US, diagnosed 1992-2016\*

	All ages (00-19 years)		US White All ages (00-19 years)		
	Count	IR (95% CI)	Count	IR (95% CI)	
All ICCC-3 cancers	206	178.1 (154.5-204.2)	36628	180.5 (178.6-182.3)	
I Leukemias, myeloproliferative and myelodysplastic diseases	69	58.3 (45.4-73.9)	10008	48.9 (48-49.9)	
Acute lymphocytic leukemia	47	39.2 (28.8-52.2)	7836	38.3 (37.4-39.1)	
Acute myeloid leukemias	16	13.9 (7.9-22.6)	1648	8.1 (7.7-8.5)	
II Lymphomas and reticuloendothelial neoplasms	24	21 (13.5-31.3)	5113	25.6 (24.9-26.3)	
Hodgkin lymphomas	-	_	2605	13.1 (12.6-13.6)	
Non-Hodgkin lymphomas (except Burkitt lymphoma)	10	9 (4.3-16.5)	1774	8.9 (8.4-9.3)	
III CNS and miscellaneous intracranial and intraspinal neoplasms	30	26.2 (17.7-37.4)	6260	30.8 (30.1-31.6)	
IV Neuroblastoma and other peripheral nervous cell tumors	-	-	1734	8.2 (7.9-8.6)	
V Retinoblastoma	_	_	692	3.3 (3.0-3.5)	
VI Renal tumors	11	9.2 (4.6-16.5)	1355	6.5 (6.2-6.9)	
VII Hepatic tumors	12	10.3 (5.3-18.0)	498	2.4 (2.2-2.6)	
VIII Malignant bone tumors			1870	9.4 (9.0-9.8)	
IX Soft tissue and other extraosseous sarcomas	17	15.1 (8.8-24.2)	2414	11.9 (11.5-12.4)	
X Germ cell and trophoblastic tumors and neoplasms of gonads	-	-	2671	13.3 (12.8-13.8)	
XI Other malignant epithelial neoplasms and melanomas	19	17.7 (10.6-27.5)	3900	19.6 (19.0-20.2)	
XII Other and unspecified malignant neoplasms	-	-	113	0.6 (0.5-0.7)	

 $\it CNS$ , central nervous system;  $\it IR$ , incidence rate. \*Data not given where case count <10.