Original Article

Adult Leukemia Survival Trends in the United States by Subtype: A Population-Based Registry Study of 370,994 Patients Diagnosed During 1995-2009

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BACKGROUND: The lifetime risk of developing leukemia in the United States is 1.5%. There are challenges in the estimation of population-based survival using registry data because treatments and prognosis vary greatly by subtype. The objective of the current study was to determine leukemia survival estimates in the United States from 1995 to 2009 according to subtype, sex, geographical area, and race. **METHODS:** Five-year net survival was estimated using data for 370,994 patients from 43 registries in 37 states and in 6 metropolitan areas, covering approximately 81% of the adult (15-99 years) US population. Leukemia was categorized according to principal subtype (chronic lymphocytic leukemia, acute myeloid leukemia, and acute lymphocytic leukemia), and subcategorized in accordance with the HAEMACARE protocol. We analyzed age-standardized 5-year net survival by calendar period (1995-1999, 2000-2004, and 2005-2009), leukemia subtype, sex, race, and US state. **RESULTS:** The age-standardized 5-year net survival estimates increased from 45.0% for patients diagnosed during 1995-1999 to 49.0% for those diagnosed during 2000-2004 and 52.0% for those diagnosed during 2005-2009. For patients diagnosed during 2005-2009, 5-year survival was 18.2% (95% confidence interval [95% CI], 17.8%-18.6%) for acute myeloid leukemia, 44.0% (95% CI, 43.2%-44.8%) for acute lymphocytic leukemia, and 77.3% (95% CI, 76.9%-77.7%) for chronic lymphocytic leukemia. For nearly all leukemia subtypes, survival declined in successive age groups above 45 to 54 years. Men were found to have slightly lower survival than women; however, this discrepancy was noted to have fallen in successive calendar periods. Net survival was substantially higher in white than black patients in all calendar periods. There were large differences in survival noted between states and metropolitan areas. **CONCLUSIONS:** Survival from leukemia in US adults improved during 1995-2009. Some geographical differences in survival may be related to access to care. We found disparities in survival by sex and between black and white patients. ***Cancer* 2018;124:3856-3867**. © *2018 American Cancer Society*.

KEYWORDS: cancer, cancer registries, leukemia, National Program of Cancer Registries, population-based survival, Surveillance, Epidemiology, and End Results (SEER), United States.

INTRODUCTION

The age-standardized incidence rate of all leukemias combined in adults in the United States is 6.9 per 100,000 population per year, with a lifetime risk of developing leukemia of 1.5%.[1] Survival among adults with leukemia has been improving over the last 30 years, with 5-year survival rising from 33% in 1975 to 59% in 2005.[1] As with many cancers,

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Additional supporting information may be found online in the Supporting Information section at the end of the article.

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the absolute number of leukemia cases is expected to increase over the coming years, primarily due to the ageing population.[2]

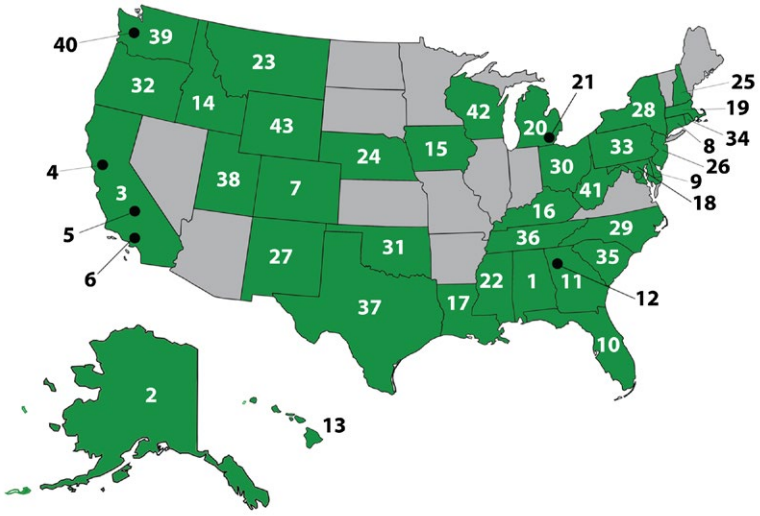
Survival estimates from population-based cancer registries typically are lower than those of clinical trials because eligibility criteria for trial participants often include restrictions based on age or comorbidities.[3] Population-based cancer registries in the United States receive federal support from the National Cancer Institute's Surveillance, Epidemiology, and End Results program[1]; the Centers for Disease Control and Prevention's National Program of Cancer Registries[4]; or both. These programs collect data including sex, race, tumor behavior, basis of diagnosis, age at diagnosis, and date of death or last known follow-up on all new cancer cases. These data are used to provide information regarding incidence, survival, prevalence, and mortality. This information is crucial to inform policymakers implementing cancer prevention and control strategies.[5]

Leukemias are categorized by the lineage of the cell affected (myeloid vs. lymphoid) and the rapidity of disease progression (acute vs. chronic). Within each category, the malignant cell may originate from different stages of maturation, taking on unique morphological, cytogenetic, and clinical characteristics. As many leukemias are too rare to power robust survival estimates, a consensus grouping of hematological malignancies was formed as part of the European Cancer Registry–based HAEMACARE project on hematologic malignancies.[6] This grouping is based on the World Health Organization classification of Tumours of the Haematopoietic and Lymphoid Tissues.[7]

The CONCORD-2 study established global surveillance of cancer survival in 2015, including data from 279 registries in 67 countries for 25.7 million patients diagnosed during 1995-2009. This included survival estimates for all adult patients with leukemia combined (873,588 patients worldwide), along with 9 other malignancies.[2] As part of a systematic analysis, this project focuses on US adults diagnosed with acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), and chronic lymphocytic leukemia (CLL) during the periods 1995-1999, 2000-2004, and 2005-2009 and presents survival by leukemia subtype, sex, race, and US state or metropolitan area.

MATERIALS AND METHODS

Data for 393,805 adult patients (those aged 15-99 years) diagnosed with leukemia between January 1995 and



1-Alabama*, 2-Alaska*, 3-California†*, *4-Greater Bay Area, 5-Greater California, 6-Los Angeles,* **7-Colorado*,** 8-Connecticut†, **9-Delaware*, 10-Florida*, 11-Georgia†*,** *12-Atlanta,* 13-Hawaii†, **14-Idaho*,** 15-Iowa†, **16-Kentucky†*, 17-Louisiana†*, 18-Maryland*, 19-Massachusetts*, 20-Michigan†*,** *21-Detroit,* **22-Mississippi*, 23-Montana*, 24-Nebraska*, 25-New Hampshire*, 26-New Jersey†*,** 27-New Mexico†, **28-New York*, 29-North Carolina*, 30-Ohio*, 31-Oklahoma*, 32-Oregon*, 33-Pennsylvania*, 34-Rhode Island*, 35-South Carolina*, 36-Tennessee*, 37-Texas*,** 38-Utah†, **39-Washington†*,** *40-Seattle,* **41-West Virginia*, 42-Wisconsin*, 43-Wyoming***

Figure 1. Participating registries in the analysis of leukemia survival trends in the United States, 1995-2009. †Surveillance, Epidemiology, and End Results registries; *National Program of Cancer Registries (bold); Metropolitan registries (italics).

December 2009 were provided by 43 registries in 37 states and in 6 metropolitan areas that collectively cover approximately 81.0% of the US national population (Fig. 1). The variables in the data set included a unique identifier; sex; age at diagnosis; last known vital status; International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) morphology code; date of diagnosis; race (as self-defined by patients); and basis of diagnosis (morphological/cytological verification, clinical verification, and death certificate only). A total of 10,071 (2.6%) patient records did not meet the eligibility criteria and these patients were excluded. Reasons for exclusion comprised data that were incomplete, patients aged outside the age range of 15 to 99 years, and diagnoses of uncertain or benign behavior. Of records eligible for survival analysis, those with coding and classification errors, invalid dates or date sequences, or incongruence between age and morphology were also excluded. Each registry was issued 3 data quality reports (protocol adherence, exclusions, and editorial) and were invited to correct any inconsistencies identified. In all, 3.3% of patients diagnosed based on death certificate only or whose disease was detected at autopsy were excluded.

We categorized leukemias into 3 principal groups: acute myeloid leukemia (AML; 34.7%), acute lymphocytic leukemia (ALL; 14.0%), and chronic lymphocytic leukemia (CLL; 51.3%). Subtypes of leukemia then were subdivided further into HAEMACARE groups, which were defined by ICD-O-3 morphology codes 9670-9981 (Table 1).

We examined the distribution of age at diagnosis, sex, race, and data quality indicators such as the percentage of diagnoses with microscopic verification and patients lost to follow-up. Patients were grouped into 3 calendar periods of diagnosis: 1995-1999, 2000-2004, and 2005-2009. We used the 5 age groups set out in the International Cancer Survival Standard for age standardization: 15 to 44, 45 to 54, 55 to 64, 65 to 74, and 75 to 99 years.[8] Race was coded as "black," "white," and "other." The basis of diagnosis was coded as "morphologically verified" if there was cytological, histological, or microscopic evidence of verification.

Statistical Analysis

We estimated 5-year net survival with the estimator of Pohar-Perme et al,[9] implemented with the program *stns*[10] in Stata statistical software (version 14; StataCorp, College Station, Texas).[11] Net survival is the probability of surviving up to a given time since diagnosis after controlling for competing causes of death (background mortality). The cohort approach was used for the calendar periods 1995-1999 and 2000-2004 because at least 5 years of potential follow-up were available for all patients. The period approach was used for patients diagnosed between 2005 and 2009 in which 5 years of follow-up were not available for all patients. This approach provides a robust short-term prediction of the eventual cohort-based survival.[12]

To control for wide differences in background mortality, we used the life tables prepared for the CONCORD-2 study.[13] These contain all-cause mortality rates in the general population of each state or metropolitan area by single year of age, sex, and race, for each calendar year from 1995 to 2009. For patients with cancer whose race was coded as "other," we used the life tables for all races combined. Robust life tables for black patients were not available in 6 states in which the black population is small (Alaska, Hawaii, Idaho, Montana, New Hampshire, and Wyoming). In those 6 states, survival estimates for black patients are not presented separately.

Age-standardized net survival was estimated for each HAEMACARE group of malignancies, stratified by sex, race, and calendar period. When there were fewer than 10 patients in a given age group, the data were merged with the adjacent age group to create 2 age-specific estimates. When there were two or more age-specific estimates based on fewer than 10 patients, only unstandardized estimates are presented.

Approval for the CONCORD-2 data was obtained from the Ethics and Confidentiality Committee of the UK Health Research Authority (ECC 3-04(i)/2011) and the National Health Service Research Ethics Committee (11/LO/0331). Separate statutory and/or human subjects research approvals were obtained from each cancer registry.

RESULTS

A total of 370,994 patients were included in the analysis: 89.1% were white, 7.3% were black, and 3.6% were of other race. Men comprised 57.5% of the patients. The median age at the time of diagnosis was 69.3 years.

CLL was the most common leukemia for all age groups with the exception of those aged 15 to 44 years, for whom AML was more frequent (see Supporting Table 1). All leukemias were more common in males. For HAEMACARE groups, the sex disparity was smallest for acute myeloid leukemia (group 22), in which 54.0% of those diagnosed were men (Table 2). Burkitt lymphoma (10.8%) was most common among black patients, and acute (precursor cell) lymphoblastic leukemia was most common among other races (5.4%). The number of cases

TABLE 1. HAEMACARE grouping of leukemias with corresponding ICD-O-3 morphology codes

HAEMACARE Group	Description	ICD-O-3 Morphology Codes
Acute lymphocytic leukemia		
11	Burkitt	9687-Burkitt lymphoma, NOS 9826-Burkitt cell leukemia
15	Lymphoblastic lymphoma/acute (precursor cell) lymphoblastic leukemia	9727-Precursor cell lymphoblastic lymphoma, NOS 9728-Precursor B-cell lymphoblastic lymphoma 9729-Precursor T-cell lymphoblastic lymphoma 9835-Precursor cell lymphoblastic leukemia, NOS 9836-Precursor B-cell lymphoblastic leukemia 9837-Precursor T-cell lymphoblastic leukemia
20	Leukemia, NOS	9800-Leukemia, NOS 9801-Acute leukemia, NOS 9805-Acute biphenotypic leukemia
Acute myeloid leukemia		
21	Myeloid leukemia, NOS	9860-Myeloid leukemia, NOS
22	Acute myeloid leukemia	9840-Acute myeloid leukemia, M6 type 9861-Acute myeloid leukemia, NOS 9866-Acute promyelocytic leukemia (APML) 9867-Acute myelomonocytic leukemia 9870- Acute basophilic leukemia 9871-Acute myeloid leukemia with abnormal marrow eosinophils 9872-Acute myeloid leukemia minimal differentiation 9873-Acute myeloid leukemia, without maturation 9874-Acute myeloid leukemia with maturation 9891-Acute monocytic leukemia 9895-Acute myeloid leukemia, with multilineage dysplasia 9896-Acute myeloid leukemia, t(8,21) (q22,q22) 9897-Acute myeloid leukemia,11q23 abnormalities 9910-Acute megakaryoblastic leukemia 9920-Therapy-related acute myeloid leukemia, NOS 9930-Myeloid sarcoma 9931-Acute panmyelosis with myelofibrosis 9984-Refractory anemia with excess blasts in transformation [obs] 9987-Therapy-related myelodysplastic syndrome, NOS
Chronic lymphocytic leukemia		
6	Chronic lymphocytic leukemia/small lymphocytic lymphoma	9670-Malignant lymphoma, small B lymphocytic, NOS 9823-B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma
17	Mature B-cell leukemia	9833-Prolymphocytic leukemia, B-cell type
18	Mature B-cell leukemia, hairy cell	9940-Hairy cell leukemia
19	Lymphatic leukemia	9820-Lymphoid leukemia, NOS 9832-Prolymphocytic leukemia, NOS

Abbreviations: ICD-O-3, *International Classification of Diseases for Oncology, 3rd Edition*; NOS, not otherwise specified.

TABLE 2. Distribution (%) of leukemias in the United States, by sex and by race: 1995-2009

HAEMACARE Group			Sex				Race					
			Male		Female		White		Black		Other	
		No.	No.	%	No.	%	No.	%	No.	%	No.	%
Acute lymphocytic leukemia		**51,958**	**30,519**	**58.7**	**21,439**	**41.3**	**44,974**	**86.6**	**4,556**	**8.8**	**2,428**	**4.7**
11	Burkitt	9,665	6,764	70.0	2,901	30.0	8,171	84.5	1,041	10.8	453	4.7
15	Lymphoblastic lymphoma/ acute (precursor cell) lympho-blastic leukemia	25,421	14,956	58.8	10,465	41.2	21,859	86.0	2,187	8.6	1,375	5.4
20	Leukemia, NOS	16,872	8,799	52.2	8,073	47.8	14,944	88.6	1,328	7.9	600	3.6
Acute myeloid leukemia		**128,626**	**69,488**	**54.0**	**59,138**	**46.0**	**113,280**	**88.1**	**10,136**	**7.9**	**5,210**	**4.1**
21	Myeloid leukemia, NOS	4,457	2,439	54.7	2,018	45.3	3,921	88.0	392	8.8	144	3.2
22	Acute myeloid leukemia	124,169	67,049	54.0	57,120	46.0	109,359	88.1	9,744	7.8	5,066	4.1
Chronic lymphocytic leukemia		**190,410**	**113,296**	**59.5**	**77,114**	**40.5**	**172,272**	**90.5**	**12,436**	**6.5**	**5,702**	**3.0**
6	Chronic lymphocytic leukemia/small lymphocytic lymphoma	176,918	103,587	58.6	73,331	41.4	159,873	90.4	11,831	6.7	5,214	2.9
17	Mature B-cell leukemia	474	301	63.5	173	36.5	431	90.9	29	6.1	14	3.0
18	Mature B-cell leukemia, hairy cell	9,556	7,375	77.2	2,181	22.8	8,887	93.0	305	3.2	364	3.8
19	Lymphatic leukemia	3,462	2,033	58.7	1,429	41.3	3,081	89.0	271	7.8	110	3.2
	Total	**370,994**	**213,303**	**57.5**	**157,691**	**42.5**	**330,526**	**89.1**	**27,128**	**7.3**	**13,340**	**3.6**

Abbreviations: NOS, not otherwise specified.

per state ranged from 649 cases (Alaska) to 47,886 cases (California). The majority of cases (90.9%) were morphologically verified, ranging from 83.4% (Maryland) to 99.3% (Florida) (see Supporting Table 2).

For the US overall, age-standardized 5-year net survival for all sexes, races, and subtypes combined increased from 45.0% (95% confidence interval [95% CI], 44.6%-45.4%) in 1995-1999 to 49.0% (95% CI, 48.7%-49.4%) in 2000-2004, to 52.0% (95% CI, 51.6%-52.3%) in 2005-2009. This represents an absolute increase in 5-year net survival of 4.0% between 1995-1999 and 2000-2004, and 3.0% between 2000-2004 and 2005-2009.

Survival declined in successive age groups from 45 to 54 years for nearly all leukemia subtypes (Table 3). Gains in survival were highest in the younger age groups. For patients with AML between 1995-1999 and 2005-2009, survival increased by 12.1% in those aged 45 to 54 years compared with 1.4% in the those aged 75 to 99 years.

Age-standardized 5-year net survival increased for all 3 principal leukemias (Table 4). The greatest gains were noted among patients with ALL (5.3% between 1995-1999 and 2000-2004 and 3.9% between 2000-2004 and 2005-2009). Among HAEMACARE groups, there were large gains for patients with Burkitt lymphoma (9.5% [95% CI, 5.3%-13.5%] between 1995-1999 and 2000-2004 and 4.9% [95% CI, 1.4%-8.4%] between 2000-2004 and 2005-2009).

For patients diagnosed during 2005-2009, 5-year survival was 18.2% (95% CI, 17.8%-18.6%) for AML, 44.0% (95% CI, 43.2%-44.8%) for ALL, and 77.3% (95% CI, 76.9%-77.7%) for CLL (Table 5). Males were found to have slightly lower survival than females throughout the 15 years between 1995 and 2009. This disparity fell in successive time periods (1.5% in 1995-1999, 1.1% in 2000-2004, and 0.7% in 2005-2009).

Net survival for white patients was substantially higher than that for black patients throughout the 15-year period, with the absolute difference noted to increase (8.3% in 1995-1999, 9.5% in 2000-2004, and 10.9% in 2005-2009) (Fig. 2). Survival was higher for white than for black patients for each of the 11 subtypes of leukemia, except for mature B-cell leukemia, for which the data were sparse (Table 5). The largest racial disparities were noted for Burkitt lymphoma (11.7% in 1995-1999, 14.9% in 2000-2004, and 16.1% in 2005-2009) and

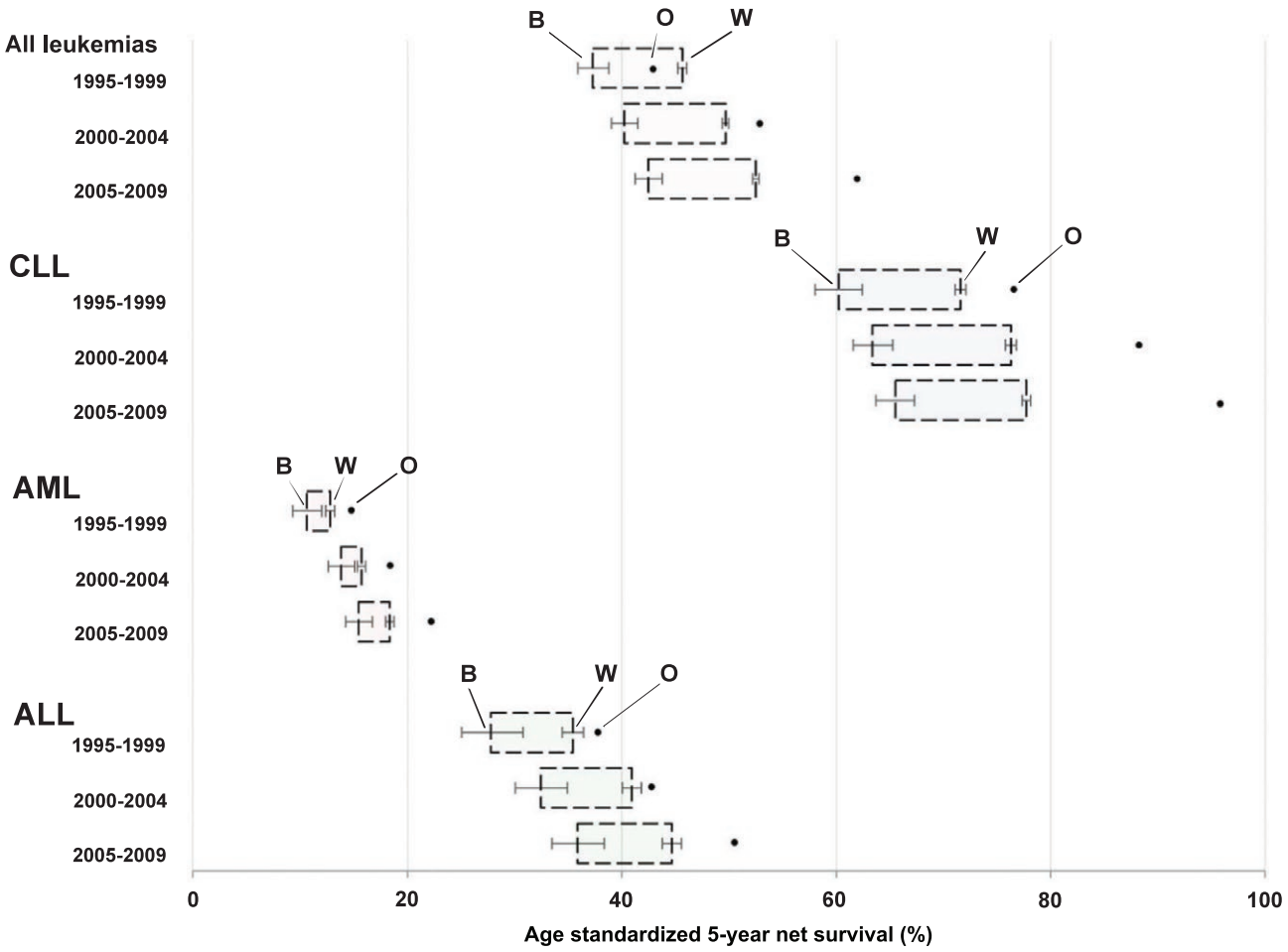


Figure 2. The absolute age-standardized 5-year net survival difference (shown as percentage) in principal groups between black (B), white (W), and other (O) races for leukemias in the United States, 1995-2009. The boxes represent the absolute difference between B and W races. Point estimates for B, W, and O races are shown on the x-axis. The 95% confidence intervals for W and B patients are shown by error bars. ALL indicates acute lymphocytic leukemia; AML, acute myeloid leukemia; CLL, chronic lymphocytic leukemia.

CLL/small lymphocytic leukemia (10.7% in 1995-1999, 12.8% in 2000-2004, and 12.3% in 2005-2009). For patients of "other" races, survival generally was higher than that for white patients; however, the estimates had wider 95% CIs. The range in survival estimates by registry also showed wide geographic disparity: from 40.9% in Mississippi to 56.5% in Seattle, Washington (Table 5). For patients with CLL, AML, and ALL, the racial difference in 5-year net survival was either constant or increasing (Fig. 2).

DISCUSSION

The current study reports data from 370,994 patients from 43 registries covering approximately 81.0% of the US population over a 15-year time period. Five-year net survival improved from 45.0% during 1995-1999 (95% CI, 44.6%-45.4%) to 49.0% during 2000-2004 (95% CI, 48.7%-49.4%) and 52.0% during 2005-2009 (95% CI, 51.6%-52.3%).

For patients diagnosed between 2005 and 2009, survival estimates were 44.0% for ALL, 18.2% for AML, and 77.3% for CLL. All 3 subtypes of leukemia showed improvements in survival, with gains in 5-year net survival of 9.2% for ALL, of 6.4% for CLL, and of 5.5% for AML from 1995-2009. The survival gains in ALL may be related to the use of the more intensive pediatric protocols in young adults,[14] and the use of tyrosine kinase inhibitors for patients with *BCR-ABL*–positive ALL.[15] Fludarabine-containing regimens were introduced as first-line treatment for patients with CLL in the 1990s, when these regimens were shown

TABLE 3. Age-specific net survival estimates by leukemia subtype (HAEMACARE group), United States: 1995-2009

		Age Group (Years)													
		15-44			45-54			55-64			65-74			75-99		
HAEMACARE group		NS	95%CI		NS	95%CI		NS	95%CI		NS	95%CI		NS	95%CI	
Acute lymphocytic leukemia																
11	Burkitt															
	1995-1999	**46.1**	42.8	49.4	**34.5**	29.0	39.9	**38.0**	31.3	44.7	**29.3**	23.3	35.3	**15.1**	9.4	20.9
	2000-2004	**58.3**	55.7	61.0	**36.9**	33.1	40.7	**42.3**	37.6	46.9	**34.6**	30.0	39.1	**24.6**	19.5	29.7
	2005-2009	**63.6**	61.2	66.0	**47.9**	44.1	51.7	**47.4**	43.1	51.7	**40.9**	36.0	45.9	**19.5**	15.3	23.7
15	Lymphoblastic lymphoma/acute (precursor cell) lymphoblastic leukemia															
	1995-1999	**46.0**	44.3	47.7	**25.5**	22.4	28.7	**18.4**	15.6	21.3	**12.3**	10.0	14.7	**8.0**	5.7	10.2
	2000-2004	**49.7**	48.2	51.2	**30.0**	27.2	32.7	**21.7**	19.1	24.2	**15.1**	12.7	17.6	**8.9**	6.7	11.2
	2005-2009	**52.7**	51.3	54.2	**32.1**	29.5	34.7	**25.6**	23.0	28.2	**18.0**	15.4	20.6	**10.7**	8.3	13.1
20	Leukemia, NOS															
	1995-1999	**40.8**	35.8	45.7	**28.1**	23.1	33.0	**22.4**	18.9	25.9	**13.6**	11.7	15.4	**8.0**	6.7	9.2
	2000-2004	**44.5**	39.9	49.1	**36.8**	31.4	42.3	**28.8**	24.9	32.7	**19.5**	17.0	22.0	**9.3**	7.9	10.6
	2005-2009	**52.8**	47.9	57.8	**44.2**	38.3	50.1	**33.5**	29.3	37.8	**26.7**	23.4	30.0	**10.9**	9.3	12.5
Acute myeloid leukemia																
21	Myeloid leukemia, NOS															
	1995-1999	**39.6**	31.4	47.8	**41.4**	30.7	52.2	**24.0**	17.3	30.8	**15.0**	10.7	19.4	**6.0**	3.1	9.0
	2000-2004	**56.0**	48.2	63.8	**43.1**	34.3	52.0	**34.3**	27.6	40.9	**20.6**	16.1	25.2	**12.6**	9.3	15.8
	2005-2009	**64.7**	57.6	71.8	**50.3**	41.6	58.9	**43.7**	36.4	51.1	**26.3**	21.0	31.6	**13.5**	10.1	16.9
22	Acute myeloid leukemia															
	1995-1999	**41.4**	40.1	42.8	**25.7**	24.2	27.2	**15.4**	14.3	16.4	**7.0**	6.4	7.5	**3.1**	2.6	3.5
	2000-2004	**45.9**	44.7	47.1	**32.8**	31.4	34.1	**18.9**	18.0	19.9	**9.3**	8.6	9.9	**3.6**	3.3	4.0
	2005-2009	**49.0**	47.8	50.2	**37.8**	36.5	39.2	**22.6**	21.6	23.6	**11.4**	10.7	12.1	**4.5**	4.0	4.9
Chronic lymphocytic leukemia																
6	Chronic lymphocytic leukemia/small lymphocytic lymphoma															
	1995-1999	**81.4**	79.4	83.4	**82.1**	80.9	83.3	**78.2**	77.2	79.2	**71.1**	70.2	72.0	**57.0**	55.7	58.3
	2000-2004	**86.2**	84.5	88.0	**86.2**	85.2	87.2	**83.2**	82.5	84.0	**76.2**	75.4	77.0	**61.1**	60.0	62.1
	2005-2009	**87.6**	85.9	89.3	**87.9**	87.1	88.8	**84.4**	83.6	85.1	**78.1**	77.3	78.9	**62.6**	61.6	63.7
17	Mature B-cell leukemia															
	1995-1999	**-**	-	-	**-**	-	-	**-**	-	-	**-**	-	-	**-**	-	-
	2000-2004	**-**	-	-	**45.7**	15.0	76.3	**46.4**	28.6	64.1	**45.0**	30.1	59.8	**29.7**	17.6	41.9
	2005-2009	**84.2**	56.7	100.0	**54.9**	32.3	77.4	**46.9**	30.6	63.1	**56.2**	41.8	70.5	**33.2**	20.8	45.6
18	Mature B-cell leukemia, hairy cell															
	1995-1999	**96.9**	95.1	98.8	**96.7**	94.9	98.6	**91.0**	87.8	94.3	**87.2**	83.0	91.4	**70.6**	62.6	78.7
	2000-2004	**98.0**	96.5	99.5	**97.4**	95.9	98.9	**97.1**	94.9	99.3	**94.0**	90.4	97.6	**71.8**	65.3	78.4
	2005-2009	**99.6**	98.6	100.0	**97.8**	96.3	99.3	**97.1**	95.0	99.2	**95.6**	92.1	99.1	**69.5**	63.2	75.7
19	Lymphatic leukemia															
	1995-1999	**61.1**	50.2	72.1	**53.7**	45.0	62.5	**53.8**	46.6	60.9	**44.8**	39.0	50.6	**30.9**	25.1	36.8
	2000-2004	**63.6**	52.5	74.7	**64.8**	55.2	74.4	**57.7**	49.7	65.8	**55.4**	48.5	62.2	**38.7**	32.4	45.0
	2005-2009	**69.5**	57.6	81.5	**69.1**	58.0	80.1	**65.9**	57.8	73.9	**64.9**	57.6	72.1	**43.7**	36.4	51.0
All leukemias																
	1995-1999	**50.3**	49.4	51.2	**55.5**	54.5	56.5	**53.4**	52.6	54.3	**44.8**	44.1	45.5	**32.8**	32.0	33.5
	2000-2004	**54.5**	53.7	55.3	**59.4**	58.6	60.2	**57.6**	56.9	58.3	**49.3**	48.7	50.0	**36.3**	35.6	36.9
	2005-2009	**57.6**	56.8	58.4	**62.8**	62.0	63.6	**60.6**	59.9	61.3	**53.0**	52.3	53.6	**38.2**	37.6	38.9

Abbreviations: 95% CI, 95% confidence interval; NOS, not otherwise specified; NS, net survival.

to have higher event-free survival than chlorambucil.[16] The introduction of rituximab likely also has improved survival.[17] Other than acute promyelocytic leukemia, anthracycline-based and cytarabine-based chemotherapy has been the mainstay of treatment for AML for many years. The more gradual survival gains observed in patients with AML are likely due to improvements in supportive care and stem cell transplantation.[18] In addition to treatment, better residual disease monitoring and refining of diagnostic techniques such as flow cytometry, polymerase chain reaction, and fluorescence in situ hybridization, resulting in better prognostic precision and more effective management strategies, have contributed to survival gains in patients with leukemia.[19]

For patients with AML, the modest survival gains over 15 years can be partially explained by minimal improvements (1.4%) among the elderly patients (75-99 years), for whom the disease burden is higher when compared with patients with ALL. Elderly patients often are less tolerant of cytotoxic treatment modalities due to frailty and comorbidities.[20] Moreover, the disease itself has a different cytogenetic and molecular profile in elderly patients, which may be explained by prior chemotherapy or radiotherapy for previous malignancies or hematological disorders such as myelodysplastic syndrome.[21]

Survival was consistently found to be higher for white than for black patients for nearly all subtypes of leukemia in all registries and throughout the 15 years between 1995 and 2009. For patients with ALL and AML, the racial difference in 5-year net survival is increasing. The gap in 5-year survival from acute leukemia between non-Hispanic white and African American or Hispanic patients was shown to increase between 1992 and 1996 and between 2002 and 2006.[22] This racial disparity is well established, and socioeconomic, cultural, and biological differences all have been put forward as contributors.[23] In the case of AML, it was noted that nonwhite ethnic groups were less likely to undergo matched unrelated hematopoietic stem cell transplantation due to lower donor availability.[24] Among patients with leukemia who were randomized to clinical trials, it was shown that racial disparities in survival disappear after controlling for prognostic factors and socioeconomic status.[25] In the clinical trial setting among patients with ovarian cancer, Abdel-Rahman et al showed that there was no socioeconomic inequality in survival outcomes (ie, when access to treatment is equal, these disparities disappear).[26] Reducing inequities in cancer care may go some way toward reducing this disparity.

Using data from population-based cancer registries minimizes the selection bias associated with variably defined catchment areas in hospital-based registries. Of the 393,805 patient records submitted from registries to the CONCORD study, only 2.6% were ineligible due to incomplete data, coding errors, or being outside the age range, or of benign behavior. Of the remaining records, 3.3% were registered solely from a death certificate or at autopsy, and were excluded because the date of diagnosis was unknown. The proportion of patients lost to follow-up was very low (0.8%). Net survival estimates for "other races" may be subjected to bias; these estimates are based on the background mortality of all races in the population because robust, state-specific life tables for individual racial groups were not available. As an example, Asian/Pacific Islander women in low unemployment areas have a life expectancy of up to 90 years[27] when compared with the population average of 80.7 years in the same areas. Net survival figures among this group of patients would be conservative due to the overestimation of background mortality by using life tables for all races combined. It is interesting to note that 5-year cause-specific survival for adults diagnosed with leukemia was 10.1% lower in Asian/Pacific Islanders than whites in 18 areas covered by the Surveillance Epidemiology and End Results program during 2008-2014, whereas the difference between the median age-standardized 5-year net survival estimates for leukemia in Asian and western populations in the CONCORD-3 study[28] became smaller during the period 2000-2014. This suggests that a large part of the difference in leukemia survival between whites and Asian/Pacific Islanders in the SEER program is likely to be attributable to better access to treatment, rather than race.

Innovations in leukemia treatment over the last 50 years are reflected in the survival gains presented in the current study, and are promoted through health policy and cancer control programs. The National Comprehensive Cancer Control Program (NCCCP), administered by the Centers for Disease Control and Prevention since 1998, funds all states, the District of Columbia, several tribes and tribal organizations, Puerto Rico, and several Pacific Island jurisdictions. Treatment and survival-specific initiatives described in NCCCP cancer plans include the strategic dissemination of information and educational resources among providers, the general public, and patients with hematologic cancer and their families and increased awareness regarding the nature of the disease, disparities that exist among minority and underserved populations, treatment options, availability of clinical trials, and

TABLE 4. Age-standardized 5-year net survival estimates for leukemias by calendar period, sex, and race

		Sex								Race								
		All			Male			Female			White			Black			Other		
HAEMACARE group		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI	
Acute lymphocytic leukemia																			
	1995-1999	**34.8**	33.8	35.7	**33.4**	32.3	34.6	**37.2**	35.6	38.8	**35.4**	34.4	36.5	**27.8**	25.1	30.7	**37.7**	33.8	42.1
	2000-2004	**40.1**	39.2	40.9	**40.0**	38.9	41.0	**40.3**	38.9	41.7	**40.9**	40.0	41.9	**32.5**	30.1	35.0	**42.8**	39.3	46.5
	2005-2009	**44.0**	43.2	44.8	**44.0**	43.0	45.0	**44.3**	42.9	45.7	**44.7**	43.8	45.6	**35.9**	33.5	38.4	**50.5**	47.2	54.1
11	Burkitt																		
	1995-1999	**39.4**	37.1	41.7	**37.8**	35.2	40.6	**45.1**	40.6	50.1	**40.6**	38.1	43.1	**28.9**	23.3	35.9	**39.3**	29.8	51.9
	2000-2004	**48.8**	47.1	50.7	**48.0**	45.9	50.2	**51.9**	48.5	55.6	**50.2**	48.3	52.3	**35.3**	30.8	40.3	**58.9**	51.7	67.0
	2005-2009	**53.7**	52.1	55.4	**52.9**	51.0	54.9	**56.2**	53.0	59.6	**55.9**	54.1	57.8	**39.8**	35.2	45.0	**55.9**	49.4	63.3
15	Lymphoblastic lymphoma/acute (precursor cell) lymphoblastic leukemia																		
	1995-1999	**34.0**	32.9	35.2	**33.1**	31.7	34.5	**35.6**	33.8	37.5	**34.7**	33.5	35.9	**26.2**	22.8	30.1	**36.5**	32.0	41.7
	2000-2004	**37.4**	36.4	38.4	**37.5**	36.2	38.8	**37.2**	35.6	39.0	**38.0**	36.9	39.1	**31.8**	28.7	35.3	**37.3**	33.2	41.9
	2005-2009	**40.3**	39.3	41.3	**40.6**	39.3	41.9	**40.1**	38.5	41.8	**40.8**	39.7	41.9	**32.7**	29.7	35.9	**45.0**	40.7	49.8
20	Leukemia, NOS																		
	1995-1999	**31.7**	28.8	34.9	**28.3**	24.4	32.7	**35.4**	31.3	40.2	**32.5**	29.2	36.2	**27.3**	21.3	34.9	**37.3**	27.0	51.5
	2000-2004	**36.2**	33.4	39.1	**34.2**	30.6	38.2	**38.7**	34.7	43.3	**37.9**	34.8	41.3	**28.6**	22.5	36.4	**32.2**	23.4	44.4
	2005-2009	**43.2**	40.3	46.4	**38.8**	34.9	43.2	**48.6**	44.3	53.3	**42.7**	39.4	46.3	**38.7**	31.3	48.0	**55.2**	44.1	69.1
Acute myeloid leukemia																			
	1995-1999	**12.7**	12.3	13.0	**11.7**	11.2	12.2	**13.9**	13.3	14.5	**12.8**	12.4	13.2	**10.6**	9.4	12.1	**14.8**	12.7	17.1
	2000-2004	**15.6**	15.3	16.0	**14.7**	14.3	15.2	**16.7**	16.2	17.3	**15.7**	15.4	16.1	**13.8**	12.6	15.1	**18.4**	16.6	20.4
	2005-2009	**18.2**	17.8	18.6	**17.3**	16.8	17.8	**19.3**	18.8	19.9	**18.4**	18.0	18.8	**15.5**	14.3	16.7	**22.2**	20.2	24.3
21	Myeloid leukemia, NOS																		
	1995-1999	**19.4**	16.9	22.2	**19.6**	16.4	23.4	**19.0**	15.5	23.2	**21.0**	18.3	24.1	**12.2**	7.3	20.4	**11.1**[a]	1.2[a]	21.0[a]
	2000-2004	**26.6**	24.2	29.3	**26.2**	23.1	29.8	**26.6**	23.0	30.7	**25.9**	23.3	28.7	**33.9**	26.3	43.6	**27.0**[a]	13.0[a]	41.0[a]
	2005-2009	**32.2**	29.5	35.0	**30.9**	27.6	34.6	**33.8**	29.8	38.4	**31.5**	28.7	34.6	**37.4**	29.0	48.3	**40.3**[a]	24.7[a]	56.0[a]
22	Acute myeloid leukemia																		
	1995-1999	**12.4**	12.1	12.8	**11.4**	11.0	11.9	**13.7**	13.1	14.3	**12.5**	12.1	12.9	**10.6**	9.3	12.1	**14.9**	12.9	17.3
	2000-2004	**15.2**	14.9	15.6	**14.3**	13.9	14.8	**16.4**	15.9	16.9	**15.4**	15.0	15.8	**12.9**	11.8	14.2	**18.3**	16.5	20.3
	2005-2009	**17.8**	17.4	18.1	**16.9**	16.4	17.4	**18.9**	18.3	19.5	**17.9**	17.5	18.3	**14.7**	13.5	16.0	**21.8**	19.9	24.0

TABLE 4. (*Continued*)

		Sex								Race								
		All			Male			Female			White			Black			Other		
		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI	
Chronic lymphocytic leukemia																		
	1995-1999	**70.9**	70.4	71.5	**68.7**	68.0	69.5	**74.0**	73.3	74.8	**71.6**	71.0	72.1	**60.2**	58.1	62.5	**76.6**	72.8	80.6
	2000-2004	**75.6**	75.2	76.1	**73.3**	72.7	73.9	**79.1**	78.5	79.8	**76.3**	75.8	76.8	**63.4**	61.5	65.2	**88.3**	85.5	91.0
	2005-2009	**77.3**	76.9	77.7	**74.9**	74.3	75.5	**80.8**	80.2	81.4	**77.7**	77.3	78.2	**65.5**	63.7	67.3	**95.8**	93.4	98.3
6	Chronic lymphocytic leukemia/small lymphocytic lymphoma																	
	1995-1999	**70.7**	70.1	71.2	**68.1**	67.3	68.9	**74.3**	73.5	75.1	**71.3**	70.8	71.9	**60.6**	58.4	62.9	**76.1**	72.1	80.4
	2000-2004	**75.3**	74.9	75.8	**72.6**	72.0	73.2	**79.2**	78.6	79.9	**76.0**	75.5	76.5	**63.2**	61.3	65.1	**88.2**	85.4	91.1
	2005-2009	**76.9**	76.5	77.3	**74.2**	73.6	74.8	**80.8**	80.1	81.4	**77.4**	76.9	77.8	**65.1**	63.3	67.0	**95.5**	93.0	98.1
17	Mature B-cell leukemia																	
	1995-1999	**-**	-	-	**-**	-	-	**-**	-	-	**-**	-	-	**-**	-	-	**-**	-	-
	2000-2004	**37.8**	30.7	46.5	**36.4**[a]	26.1[a]	46.7[a]	**42.8**[a]	28.6[a]	57.1[a]	**36.3**[a]	27.7[a]	45.0[a]	**51.9**[a]	20.9[a]	82.8[a]	**-**	-	-
	2005-2009	**49.2**	42.3	57.2	**47.0**	39.4	56.2	**45.6**	35.3	58.9	**46.5**	39.3	55.2	**60.3**	40.6	89.4	**90.9**[a]	49.9[a]	100.0[a]
18	Mature B-cell leukemia, hairy cell																	
	1995-1999	**85.1**	82.4	87.9	**86.1**	82.7	89.6	**81.6**	76.9	86.5	**85.1**	82.4	88.0	**70.7**	55.5	90.1	**87.9**	75.8	100.0
	2000-2004	**89.0**	86.8	91.2	**89.1**	86.4	91.9	**87.5**	83.6	91.5	**89.1**	86.9	91.5	**76.8**	66.8	88.3	**87.8**	77.3	99.6
	2005-2009	**88.9**	86.8	91.1	**88.9**	86.3	91.6	**88.5**	84.8	92.3	**88.6**	86.4	90.8	**86.2**	75.0	99.0	**100.0**	93.5	100.0
19	Lymphatic leukemia																	
	1995-1999	**40.3**	39.3	41.3	**40.6**	39.3	41.9	**40.1**	38.5	41.8	**40.8**	39.7	41.9	**34.4**	25.3	46.7	**55.4**[a]	37.0[a]	73.7[a]
	2000-2004	**45.1**	42.0	48.4	**42.2**	38.5	46.4	**48.9**	44.0	54.5	**45.6**	42.4	49.1	**45.6**	35.2	59.0	**69.4**[a]	50.3[a]	88.4[a]
	2005-2009	**52.8**	49.4	56.5	**48.0**	43.5	53.0	**60.0**	55.0	65.3	**52.8**	49.2	56.7	**48.0**	33.1	62.9	**88.0**[a]	69.3[a]	100.0[a]
All leukemias																		
	1995-1999	**45.0**	44.6	45.4	**44.3**	43.8	44.8	**45.8**	45.2	46.3	**45.6**	45.3	46.0	**37.3**	35.9	38.7	**42.9**	40.6	45.4
	2000-2004	**49.0**	48.7	49.4	**48.5**	48.1	48.9	**49.6**	49.1	50.1	**49.7**	49.3	50.0	**40.2**	39.0	41.5	**52.9**	50.9	54.8
	2005-2009	**52.0**	51.6	52.3	**51.6**	51.2	52.1	**52.3**	51.8	52.8	**52.5**	52.1	52.8	**42.5**	41.3	43.7	**62.0**	60.1	63.8

Abbreviations: 95% CI, 95% confidence interval; NOS, not otherwise specified; NS, net survival.

[a]Unstandardized estimates.

TABLE 5. Age-standardized 5-year net survival estimates by registry, stratified by race: 1995-2009

	All Races			White			Black			Other		
Registry	NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI	
Alabama	**45.9**	44.2	47.6	**47.0**	45.2	48.9	**37.1**	33.3	41.3	**91.7**	78.7	100.0
Alaska	**50.8**	46.0	56.0	**54.2**	49.2	59.7	**-**	-	-	**21.9**	13.5	35.6
California	**45.3**	44.7	45.9	**45.9**	45.3	46.5	**38.7**	36.2	41.4	**44.5**	42.5	46.7
Greater Bay Area[a]	**48.4**	47.1	49.8	**50.4**	48.9	51.9	**41.8**	36.7	47.7	**38.9**	35.4	42.7
Greater California[a]	**44.1**	43.3	44.9	**44.2**	43.4	45.0	**38.9**	34.4	43.9	**47.2**	43.7	51.1
Los Angeles[a]	**45.5**	44.4	46.7	**46.4**	45.2	47.7	**36.9**	33.4	40.7	**46.6**	43.0	50.4
Colorado	**50.8**	49.3	52.5	**50.1**	48.5	51.8	**38.2**	29.0	50.5	**83.6**	75.3	92.8
Connecticut	**50.9**	49.3	52.5	**51.4**	49.7	53.0	**40.6**	33.8	48.7	**72.2**	59.8	87.1
Delaware	**44.5**	41.2	48.2	**45.2**	41.7	49.1	**36.5**	28.5	46.8	**66.8**[b]	42.5[b]	91.1[b]
Florida	**50.5**	49.8	51.2	**51.2**	50.5	51.9	**40.6**	38.0	43.5	**55.1**	49.2	61.7
Georgia	**47.9**	46.4	49.5	**49.2**	47.5	50.9	**43.4**	40.0	47.1	**45.7**	35.3	59.0
Atlanta[a]	**48.0**	45.7	50.4	**50.5**	47.9	53.2	**41.1**	36.5	46.3	**27.9**	19.6	39.7
Hawaii	**43.8**	40.8	47.0	**57.6**	52.5	63.1	**-**	-	-	**34.9**	31.5	38.8
Idaho	**50.8**	48.2	53.6	**51.2**	48.6	53.9	**-**	-	-	**29.2**[b]	10.1[b]	48.2[b]
Iowa	**52.9**	51.3	54.5	**52.8**	51.3	54.4	**35.0**[b]	17.9[b]	52.1[b]	**86.3**[b]	72.9[b]	99.7[b]
Kentucky	**49.3**	47.8	50.8	**49.5**	47.9	51.1	**41.4**	34.9	49.1	**79.3**[b]	67.1[b]	91.7[b]
Louisiana	**45.1**	43.6	46.6	**47.1**	45.4	48.8	**37.3**	34.0	40.9	**56.7**[b]	40.3[b]	73.2[b]
Maryland	**41.3**	39.7	43.0	**42.0**	40.3	43.9	**36.2**	32.4	40.5	**63.2**	53.8	74.3
Massachusetts	**49.9**	48.7	51.2	**49.6**	48.3	50.9	**45.4**	38.7	53.3	**76.8**	68.4	86.3
Michigan	**47.6**	46.7	48.5	**47.7**	46.8	48.7	**39.3**	36.3	42.5	**75.5**	68.3	83.4
Detroit[a]	**47.8**	46.4	49.3	**49.1**	47.5	50.8	**40.0**	36.6	43.8	**69.0**	58.1	82.0
Mississippi	**40.9**	37.5	44.6	**41.8**	38.1	45.9	**38.7**	31.8	47.1	**31.3**	34.8	59.2
Montana	**49.8**	46.7	53.1	**49.5**	46.4	52.9	**-**	-	-	**58.2**	45.7	74.0
Nebraska	**51.3**	49.2	53.6	**50.9**	48.8	53.2	**36.4**[b]	21.1[b]	51.7[b]	**81.8**[b]	70.6[b]	93.0[b]
New Hampshire	**55.4**	52.7	58.2	**55.2**	52.6	58.1	**-**	-	-	**60.7**[b]	39.5[b]	81.9[b]
New Jersey	**49.9**	48.9	50.9	**50.8**	49.7	51.8	**36.6**	33.1	40.4	**64.2**	57.0	72.2
New Mexico	**52.5**	50.1	55.0	**53.3**	50.9	55.8	**40.7**[b]	24.2[b]	57.3[b]	**27.5**	19.2	39.5
New York	**48.8**	48.1	49.5	**49.9**	49.1	50.6	**38.6**	36.3	41.0	**52.3**	47.7	57.5
North Carolina	**48.5**	47.3	49.7	**49.4**	48.1	50.7	**43.4**	40.0	47.0	**53.1**	44.2	63.8
Ohio	**47.0**	45.7	48.2	**47.2**	45.9	48.5	**41.0**	36.7	45.9	**61.6**	53.0	71.5
Oklahoma	**42.3**	40.6	44.1	**42.6**	40.8	44.5	**28.1**	21.6	36.4	**47.5**	40.3	56.0
Oregon	**48.8**	47.1	50.6	**48.3**	46.6	50.1	**43.8**	31.3	61.2	**63.6**	54.6	74.1
Pennsylvania	**48.1**	47.3	48.9	**48.2**	47.4	49.1	**40.2**	36.8	43.8	**66.9**	61.3	73.0
Rhode Island	**48.4**	45.4	51.5	**48.9**	45.9	52.1	**17.4**	9.0	33.4	**54.3**[b]	28.8[b]	79.9[b]
South Carolina	**46.9**	45.3	48.6	**48.7**	46.8	50.6	**37.9**	34.3	41.8	**70.3**	57.7	85.7
Tennessee	**47.5**	45.2	49.8	**48.3**	45.9	50.7	**35.5**	29.6	42.6	**52.9**	37.3	75.0
Texas	**50.4**	49.6	51.1	**50.5**	49.8	51.3	**44.0**	41.3	46.8	**70.8**	65.5	76.5
Utah	**50.9**	48.5	53.4	**51.0**	48.6	53.6	**41.4**[b]	11.3[b]	71.6[b]	**45.8**[b]	31.0[b]	60.5[b]
Washington	**55.4**	54.2	56.7	**55.6**	54.3	56.9	**49.9**	39.5	63.0	**54.8**	48.9	61.4
Seattle[a]	**56.5**	55.0	58.1	**57.4**	55.8	58.9	**51.6**	40.3	66.2	**42.2**	35.9	49.5
West Virginia	**46.0**	43.9	48.3	**45.8**	43.7	48.1	**49.6**[b]	35.5[b]	63.7[b]	**71.2**[b]	33.7[b]	100.0[b]
Wisconsin	**53.2**	51.9	54.4	**53.3**	52.1	54.6	**49.1**	41.3	58.4	**49.2**	40.6	59.6
Wyoming	**53.5**	49.1	58.3	**53.2**	48.7	58.0	**-**	-	-	**-**	-	-
Total	**47.5**	47.3	47.7	**47.8**	47.5	48.0	**40.8**	40.1	41.6	**54.7**	53.6	55.8

Abbreviations: 95% CI, 95% confidence interval; NS, net survival.
[a]Metropolitan registries.
[b]Unstandardized estimates.

support services for survivors. The continuance of these efforts is in part dependent on sustainable partnerships that can facilitate more effective community-clinical linkages and changes to ensure access to quality patient care among all patients. Future NCCCP efforts in these areas that specifically target black men and women with leukemia may help to alleviate the racial differences in survival.

Further highlighted in the current study is the issue of classification when making population-based survival comparisons in patients with leukemia. Rare leukemias within a group undoubtedly have an impact on survival, especially if they are more prevalent in certain populations. HAEMACARE[6] and INTERLymph[29] are 2 projects that address this issue. The real challenge to producing subtype-specific estimates in population-based studies is that the data usually are sparse and estimates are imprecise.

CONCLUSIONS

Survival from leukemia in the United States has improved between 1995 and 2009, increasing in each successive 5-year period. The results of the current study have identified major differences between disease subtype, sex,

and race, with the relative gains in survival mirroring the treatment milestones that have been achieved for each subtype. Although the survival gap between sexes appears to be converging, the racial gap has not. This could have many causes, but addressing the sociopolitical, economic, and cultural constraints that create barriers to treatment, trial enrolment, and donor availability will be required to reduce inequities in access to quality cancer care.

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Chris Bailey: Conceptualization, writing–original draft, and formal analysis. **Lisa C. Richardson**: Writing–review and editing and project administration. **Claudia Allemani**: Conceptualization, writing–review and editing, project administration, and funding acquisition. **Audrey Bonaventure**: Data validation and writing–review and editing. **Rhea Harewood**: Data validation, writing, and formal analysis. **Angela R. Moore**: Project administration and writing–review and editing. **Sherri L. Stewart**: Project administration and writing–review and editing. **Hannah K. Weir**: Writing–review and editing, project administration, and funding acquisition. **Michel P. Coleman**: Conceptualization, writing–review and editing, visualization, project administration, and funding acquisition.

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