Prognostic Factors, Survival Analyses and Risk of First and Second Primary Cancers on Burkitt Lymphoma/Leukemia: A Population-Based Study

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OBJECTIVES

To evaluate the population-based prognosis, survival, and risk factors associated with cancers that occur as first and second primary cancer (SPC) on Burkitt lymphoma/leukemia (BL/L).

METHODS

A retrospective cohort study using the Surveillance, Epidemiology, and End Results (SEER) Program (2008-2016) was performed. Descriptive statistical, Kaplan-Meier, time-dependent covariates Cox regression, and Poisson regression models analyses were conducted. Overall survival (OS) and disease-specific survival (DSS) were primary and secondary outcomes, respectively, reported with 95% confidence interval (CI) ($p < 0.05$ was statistically significant).

RESULTS

A total of 3,094 patients with BL/L were included (median, 45 years; IQR, 22-62). Estimated OS and DSS were 65.4 months (95% CI, 63.6-67.3) and 75.7 months (95% CI, 73.9-77.5), respectively. Lower OS and DSS ($p < 0.05$) were identified for older patients, black race, disease at advanced stage, patients with no chemotherapy/surgery, and patients who underwent radiotherapy (see Figure 1 and Table 1). Interrelated cancer risk demonstrated primary cancers as Hodgkin lymphoma (nodal) [RR, 7.6 (3.9-15.0; $p < 0.001$)], Kaposi sarcoma [34.0 (16.8-68.9; $p < 0.001$)], liver tumor [3.4 (1.2-9.3; $p = 0.020$)], trachea, mediastinum and other respiratory cancers [15.8 (2.2-113.9; $p = 0.006$)] behaving as risk factors for BL/L. On the other hand, BL/L behaved as a risk factor for the occurrence of SPCs as acute myeloid leukemia [4.6 (2.1-10.4; $p < 0.001$)], Hodgkin lymphoma (extranodal) [74.3 (10.0-549.8; $p < 0.001$)], and Kaposi sarcoma [35.1 (12.1-101.4; $p < 0.001$)]. However, BL/L acted as protective factor for breast cancer [0.1 (0.0-0.8; $p = 0.032$)] (see Figure 2).

CONCLUSIONS

Despite BL/L has a low incidence in the USA, the SEER Program enabled the identification of several cases, which allowed the conduction of survival and risk factors analyses. The results may assist the development of diagnostic and clinical recommendations for BL/L and guide the conduction of further studies on risk factors for hematological malignancies.

ACKNOWLEDGEMENTS

Figure 1. Kaplan-Meier graphs for some significant variables of overall survival.
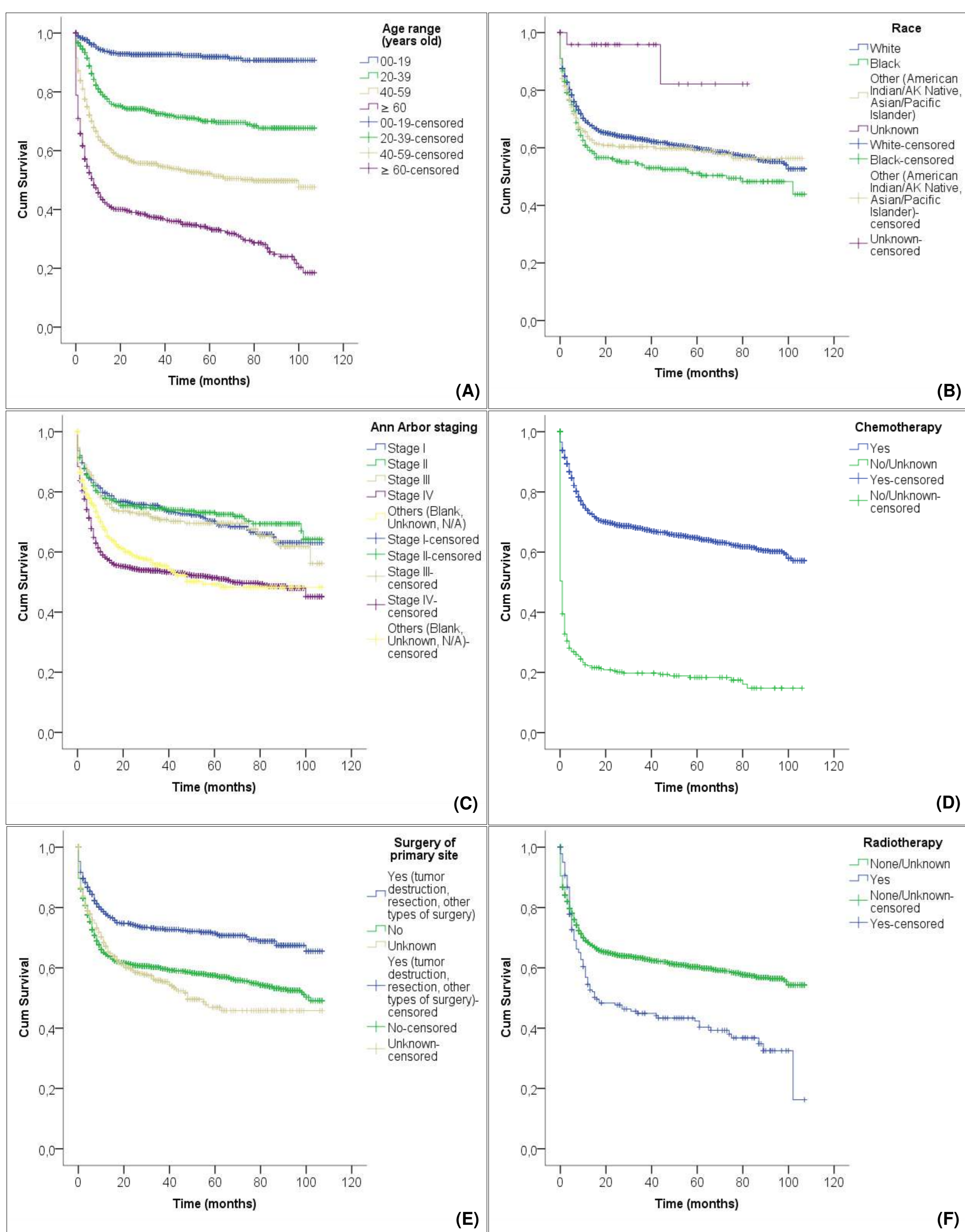
(A) Age range. (B) Race. (C) Ann Arbor staging. (D) Chemotherapy. (E) Surgery of primary site. (F) Radiotherapy. All variables were significant (p-value < 0.05) for all three statistical tests: Breslow (Generalized Wilcoxon), Tarone-Ware and Log Rank (Mantel-Cox).

Table 1. Multivariate analysis by time-dependent covariate Cox regression model for some significant variables in both overall and disease-specific survival.

Characteristics	Overall survival			Disease-specific survival		
	HR	95% CI	p-value*	HR	95% CI	p-value*
Age range (years old)						
00-19	1.0	-	-	1.0	-	-
20-39	3.5	2.5-4.8	< 0.001	3.8	2.7-5.6	< 0.001
40-59	6.1	4.5-8.4	< 0.001	7.3	5.1-10.6	< 0.001
≥ 60	10.4	7.5-14.4	< 0.001	10.1	6.8-14.9	< 0.001
Race						
White	1.0	-	-	1.0	-	-
Black	1.6	1.3-1.9	< 0.001	1.6	1.3-2.0	< 0.001
Other[a]	1.1	0.9-1.3	0.605	1.2	0.9-1.5	0.204
Unknown	0.2	0.1-0.8	0.023	0.3	0.1-1.1	0.059
Ann Arbor staging[b]						
Stage I	1.0	-	-	1.0	-	-
Stage II	1.1	0.8-1.4	0.651	1.2	0.8-1.6	0.343
Stage III	1.2	0.9-1.6	0.177	1.3	0.9-1.8	0.175
Stage IV	1.8	1.5-2.2	< 0.001	2.1	1.6-2.7	< 0.001
Others (Blank, Unknown, N/A)	1.5	1.1-1.9	0.005	1.6	1.1-2.2	0.006
Chemotherapy						
Yes	1.0	-	-	1.0	-	-
No/Unknown	4.0	3.5-4.6	< 0.001	3.8	3.2-4.5	< 0.001
Radiotherapy[c]						
Yes	1.0	-	-	1.0	-	-
No/Unknown	0.7	0.6-0.9	**0.001**	0.7	0.5-0.9	**0.002**
Surgery of primary site[c]						
Yes (tumor destruction, resection, other types of surgery)	1.0	-	-	1.0	-	-
No	1.4	1.2-1.6	< 0.001	1.3	1.1-1.6	**0.011**
Unknown	3.4	0.9-13.2	0.082	4.6	1.1-19.0	0.034

CI, confidence interval; HR, hazard ratio; N/A, not applicable.
*p-value from the Enter statistic test. [a]American Indian/AK Native, Asian/Pacific Islander. [b]Cases diagnosed until 2015. [c]Variable regrouped according to the similarities and number of events in each one of groups.
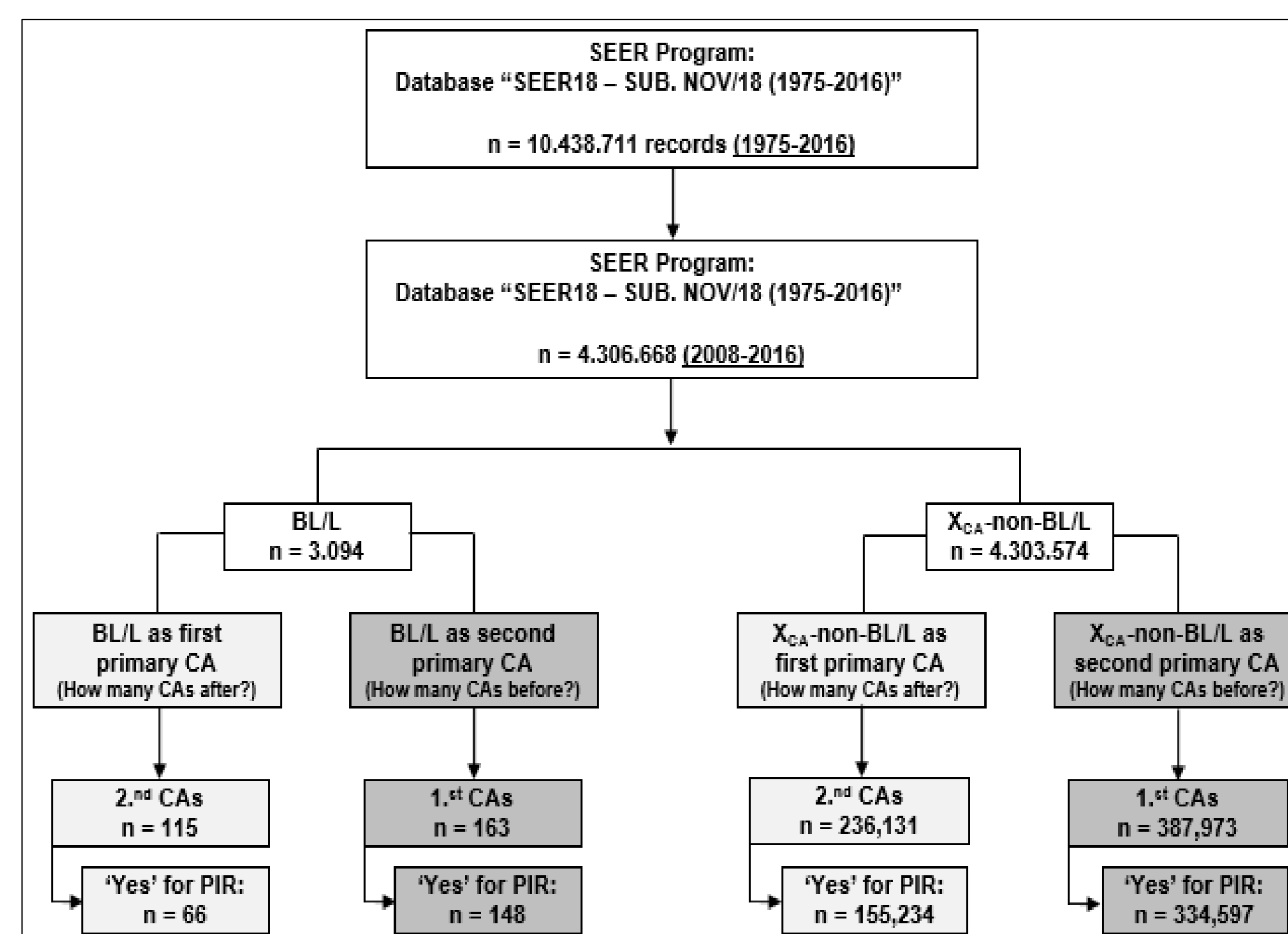
Figure 2. Data collection flowchart for risk analysis.

BL/L, Burkitt lymphoma/leukemia; CA, cancer; PIR, primary cancer by international rules; SEER, Surveillance, Epidemiology, and End Results; X_{CA}-non-BL/L, any cancer other than Burkitt lymphoma/leukemia.