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The Risk of Preterm Birth Among Women with a History of Leukemia or Lymphoma

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Abstract

Objective: Leukemia and lymphoma are top cancers affecting children, adolescents and young adults with high five-year survival rates. Late-effects of these cancers are a concern in reproductive-age patients, including pregnancy outcomes such as preterm birth. Our study aimed to evaluate whether diagnosis of leukemia or lymphoma prior to pregnancy was associated with preterm birth (<37 weeks gestation).

Methods: We conducted a cross-sectional study using a population-based dataset from California with linked birth certificates to hospital discharge records and an Iowa-based sample that linked birth certificates to Surveillance, Epidemiology, and End Results (SEER) cancer registry data.

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Preterm birth was defined using birth certificates. We ascertained history of leukemia and lymphoma using discharge diagnosis data in California and SEER registry in Iowa.

Results: Prevalence of preterm birth in California and Iowa was 14.6% and 12.0%, respectively, in women with a history of leukemia/lymphoma compared to 7.8% and 8.2%, respectively, in women without a cancer history. After adjusting for maternal age, race, education, smoking, and plurality, Women with history of leukemia/lymphoma were at an increased risk of having a preterm birth in California (odds ratio (OR) 1.89; 95% confidence interval (CI) 1.56–2.28) and Iowa (OR 1.61; 95% CI 1.10–2.37) compared to those with no cancer history.

Conclusion: In both California and Iowa, women with a history of leukemia or lymphoma were at increased risk for preterm birth. This suggests the importance of counselling with a history of leukemia/lymphoma prior to pregnancy and increased monitoring of women during pregnancy.

Keywords

preterm birth; leukemia; lymphoma; gestational age; premature

INTRODUCTION

Leukemias and lymphomas, which are among the most frequent cancers affecting children, adolescents and young adults, are highly curable with five-year survival approximately 80% for most types (1). Once young people reach reproductive age, they are often concerned about the negative impact of their prior cancer on their reproductive health including infertility or adverse pregnancy outcomes such as preterm birth.

Preterm birth (PTB) is defined as having a baby born too early, specifically <37 weeks gestation. According to the World Health Organization, there are approximately 15 million babies every year who are born preterm, which is more than 1 in 10 babies (2). In the United States in 2018 alone, approximately 1 in every 10 newborns was born preterm; 2018 was the fourth straight year that the rate increased (3). There are 1.1 million deaths due to preterm birth globally and it continues to be one of the single greatest contributors to infant mortality in the US and to disability-adjusted life years worldwide (4, 5). Identifying women at higher risk for preterm birth is important to inform research that aims to improve pregnancy outcomes in women with pre-existing conditions.

There have been several studies of the effects of childhood, adolescent and young adult leukemia/lymphoma on pregnancy outcomes (6–14). The majority of these studies were retrospective cohort studies with less than 500 individuals with leukemia and lymphoma. The studies with more than 500 individuals used self-reported outcomes and/or compared outcomes to control groups that included individuals with another cancer-type (7, 12, 14). Prior studies have yielded mixed results with some showing an increased risk of preterm birth among those with a history of leukemia/lymphoma (7–10) while others showed no significant risk (6, 8, 11–14).

We evaluated the relationship using birth-certificate-based measures of preterm birth linked with cancer information for two different large population-based US samples. Our primary

objective was to evaluate the relationship of diagnosis of leukemia or lymphoma prior to pregnancy with preterm birth.

METHODS

Data Source, Linkages, and Study Population

We had access to two retrospective administrative data sources, which included women who gave birth from two different geographical areas: the State of California and the State of Iowa. From the State of California, we conducted secondary data analysis on an existing birth certificate-linked dataset with mother and infant hospital discharge information from one year prior to birth (mother only) to one year post-delivery (mother and infant) for births that occurred in California from 2007 to 2012. We have used this dataset for previous studies of preterm birth (15, 16). This dataset is maintained by the California Office of Statewide Health Planning and Development (OSHPD). In Iowa, we developed a new dataset by linking Iowa birth certificates with Surveillance, Epidemiology, and End Results (SEER) cancer registry data covering the State of Iowa. Eligible participants included women who were Iowa residents age 44 or under at the time of a leukemia or lymphoma diagnosis between 1973 and 2018, linked to the first Iowa birth certificate after their cancer diagnosis date. Up to two randomly selected unexposed births were selected by matching on birth month and birth year to each Iowa exposed infant. The unexposed infant had to have a mother who was an Iowa resident and 18 years of age or older at delivery.

For both California and Iowa, we only included live births. In both states, we included both singletons and multiples, and births with gestation between 20 and 44 weeks and maternal age of <45 years. Additionally, where possible, we included only the first pregnancy of mothers during the study period and first pregnancy after diagnosis. This information was not complete for the California data. We also excluded women who did not have complete information for the primary outcome of preterm birth and had more than one type of cancer.

Study Variables

The primary outcome variable in this study was preterm birth. Preterm birth is defined as a gestational age at delivery less than 37 weeks. In both California and Iowa, data on gestational age was obtained from birth certificates. Women who had a gestational age at birth that was ≥37 weeks were categorized as having a term birth.

The primary exposure variable of this study was a diagnosis of leukemia or lymphoma prior to birth. For California, to identify women with a history of leukemia and lymphoma, we used the following ICD-9 codes: 201.x-202.x, 203.1x, 204.x-208.x, V10.6, and V10.7. There have been two validation studies for these ICD-9 codes including V10 history codes although not specifically for pregnancy discharge data (17, 18). The sensitivity ranged from 80% to 90% and positive predictive values from 63% to 76% (17, 18). In Iowa, we used the 3rd edition of the *International Classification of Diseases for* Oncology: C024, C098-C099, C111, C142, C379, C422, C770-C779, C420, C421, and C424. The comparison group were women without a prior history of cancer.

We used birth certificate data from both Iowa and California to capture important covariates including maternal age, maternal race, maternal education, smoking during pregnancy, prior live births, plurality, and gestational hypertension. Maternal race was defined as non-Hispanic White, Asian, Black, Hispanic, or Other race; maternal education was trichotomized by years of education of <12 years, 12 years, and >12 years; smoking during pregnancy was dichotomized as either yes or no; prior live birth was categorized as 0, 1, 2, and 3 or more; plurality was dichotomized as having singleton and twins or more; and gestational hypertension was defined as a new onset of hypertension during pregnancy and included preeclampsia and eclampsia with Iowa using birth certificate data and California using diagnoses codes of ICD-9 642.1–3, 642.4–642.7. Prior live births was defined as births that occurred prior to the diagnosis of cancer and/or those births that occurred prior to the study period. Overall, there was <5% missing from any one variable, except for prior live births, there was <13% missing in Iowa. Furthermore, Iowa's SEER registry data included information about cancer diagnosis and treatment.

The Iowa Cancer Registry data allowed us to capture the following covariates: age at leukemia/lymphoma diagnosis, time since diagnosis to birth (<3 years, 3–5 years, 6–8 years, and 9 or more years), cancer stage (local, regional, distant, or unstaged), cancer treatment (chemotherapy only, chemotherapy and radiation, radiation only, and neither chemotherapy nor radiation), hormone therapy (yes/no), immunotherapy (yes/no), chemotherapy (yes/no), and radiation (yes/no).

Statistical Analysis

For both California and Iowa, we used Chi-square tests and t-tests to compare descriptive characteristics for categorical variables and continuous variables, respectively. To assess the relationship between preterm birth and leukemia/lymphoma, we used logistic regression models for the California data, and conditional logistic regression models to account for matching in the Iowa data. We also adjusted for potential confounders in the multivariate analyses. Additionally, we evaluated gestational hypertension as a potential mediator in the relationship between preterm birth and leukemia/lymphoma.

With SEER data providing cancer treatment information in Iowa, we conducted an Iowa-only analysis to evaluate treatment effects. In both California and Iowa, we also conducted a sensitivity analysis to evaluate preterm birth among only singleton pregnancies. Additionally, among women with preterm births, we compared leukemia/lymphoma history for women with spontaneous preterm birth versus women with indicated preterm birth. We also assessed the relationship between preterm birth with each cancer, leukemia and lymphoma, separately (Supplementary Table A1). All analyses were conducted in SAS 9.4 (SAS Institute, Cary, NC). A p-value <0.05 was considered as statistically significant.

Methods and protocols for the study using California data were approved by the Committee for the Protection of Human Subjects within the Health and Human Services Agency of the State of California. De-identified data was provided to the researchers by the California Office of Statewide Health Planning and Development (Protocol # 12–09–0702) and determined not to qualify as human subjects research by the University of Iowa Institutional Review Board (IRB no.: 201602793). For Iowa data, the study was approved

by the University of Iowa Institutional Review Board. Data was approved for linkage by the Iowa Department of Public Health (RA 3873) and by the University of Iowa Institutional Review Board (IRB no: 201811805).

RESULTS

The descriptive characteristics of both the California cohort and the Iowa cohort can be seen in Table 1 and the flowcharts are shown in Figures 1 and 2. In California, a total of 1,024 women had a history of leukemia or lymphoma and 2,468,625 women had no history of cancer coded in the dataset. In Iowa, there was a total of 515 women with a history of leukemia or lymphoma and 1,009 unexposed selected with no history of cancer. In both states, women were mostly non-smokers and had singleton pregnancies. Women with a history of leukemia/lymphoma gave birth at an older age and had a higher education level than women without a history of cancer in both California and Iowa. The racial and ethnic distributions of the two samples were consistent with known demographic differences between the two states. In California, where there is more racial and ethnic diversity, particularly notable differences between women with and without a history of leukemia or lymphoma were that women with a history of leukemia or lymphoma were less likely to be Hispanic (34.5% vs 50.6%, respectively) or Asian (7.3% vs 12.3%).

The cancer and treatment characteristics from the Iowa SEER registry are shown in Table 2. As expected, due to differences in age-specific incidence patterns and treatment options for leukemia and lymphoma, those with a history of leukemia had a more distant history of their cancer (78.6% were diagnosed 9 or more years prior to pregnancy) compared with lymphoma patients (32.4% were diagnosed 9 or more years prior). Only 9.5% of leukemia patients were diagnosed within 3 years before pregnancy compared with 23.1% of those with prior lymphoma. Lymphoma patients were more likely to receive radiation or chemoradiation than leukemia patients who were most likely to receive chemotherapy only.

The prevalence of preterm birth in California among those without a history of cancer was 7.8%, compared to 14.6% in those with a history of leukemia/lymphoma (unadjusted odds ratio (OR) 2.03; 95% CI 1.71–2.42) (Table 3). The relationship between leukemia/lymphoma and preterm birth remained after adjusting for maternal age, race, education, smoking and plurality (OR: 1.89; 95% CI 1.56–2.28). In Iowa, the prevalence of preterm birth among women without a cancer history was 8.2%, compared to 12.0% in women with a history of leukemia/lymphoma (unadjusted OR 1.50; 95% CI 1.07–2.11) (Table 3) and this remained after adjusting for maternal age, race, education, smoking and plurality (OR: 1.61; 95% CI 1.10–2.37). There was no evidence of mediation through gestational hypertension as the odds ratio did not change in either Iowa (OR: 1.61 vs 1.56) or California (OR: 1.89 vs. 1.89) when this variable was added to the models (Table 3).

In analyses aimed at examining the potential increased risk associated with cancer treatments in Iowa (Table 4), sample sizes were small and estimates imprecise. Although no statistically significant differences in the odds of preterm birth by cancer treatment were observed, there was an indication that a history of radiation (14.8% had preterm birth) or chemo-radiation (16.9% had preterm birth) treatment was associated with greater adjusted

risk of preterm birth compared with treatment using chemotherapy alone (9.6% had preterm birth).

In our analyses evaluating the relationship between preterm birth and each of the cancer types separately in both California and Iowa (Supplementary Table S1), increased risk was seen with each cancer type, and especially with lymphoma. This indicates that results may have been driven by those with a history of lymphoma. However, leukemia had a smaller sample size, which led to imprecise estimates.

It has been shown that the risk for preterm birth is higher in multiples compared to singletons (19, 20). To address this, we conducted sensitivity analysis to assess the risk of preterm birth among women with a history of leukemia/lymphoma compared to women without a history of cancer using only singleton pregnancies. In both California and Iowa, the adjusted odds ratios did not appreciably change when restricted to only singletons (California: OR = 1.94 (95% CI 1.59–2.35); Iowa: OR = 1.77 (95% CI 1.19–2.64)). Additionally, we evaluated spontaneous and indicated preterm birth only among those with a preterm birth. In California, there was no significant difference in odds of a leukemia/lymphoma history between those with spontaneous preterm birth and those with indicated preterm birth (OR 0.81; 95% CI 0.52–1.26). In Iowa, due to inadequate sample size in sub-group analyses, we were not able to differentiate between spontaneous and indicated preterm birth as the model would not converge.

DISCUSSION

In two unique populations (Iowa and California) we found that there was a statistically significant increase in the odds of preterm birth among women with a prior history of leukemia or lymphoma compared to women without any prior history of cancer. Our findings are consistent with previous studies assessing the risk of preterm birth in women with a history leukemia/lymphoma (Supplementary Table S2). Although there was variability in outcome ascertainment between the studies, the findings were consistent in directionality and magnitude. The risk estimates for preterm birth in these other studies were consistent with ours and ranged from 1.50 to 2.60 for leukemia and 1.59 to 2.11 for lymphoma (6–10). Specifically, in a study by Haggar et al., the risk for preterm birth among leukemia patients was 1.72 (95% CI 1.18–2.41), and in another study by Anderson et al., there was an increased risk of 1.59 (95% CI 1.06–2.37) among Hodgkin lymphoma patients (8, 10). Although these studies assessed leukemia and lymphoma separately, they both found results of the same magnitude and direction as we did. There were, however, other studies that found no statistically significant relationship between preterm birth and leukemia/lymphoma with risks ranging from 0.4–1.54 (6, 8, 11–14). Some of these used self-reported outcome data from questionnaires, were conducted mostly outside of the United States, and included mostly women diagnosed between 15–39 years of age.

Possible explanations for the increase in preterm births among women with a history of leukemia or lymphoma include the late-effects of cancer treatment. Chemotherapy drugs such as platinum agents and anthracyclines can cause renal impairments and cardiotoxicities (21–24). The renal impairments can lead to hypertension and preterm birth (25, 26).

Additionally, obesity is a risk factor for preterm birth, and corticosteroids, which are medications used in the treatment for cancer that can cause obesity (27–29). The exact mechanism for corticosteroid and increases in body mass index are unknown, but a potential mechanism is that corticosteroids could cause changes in fat distribution and metabolism and increase gluconeogenesis (30, 31). Future studies, with carefully collected and longitudinal data on BMI before and during pregnancy, are needed to investigate these potential mechanisms leading to preterm birth in women with a history of leukemia or lymphoma.

Furthermore, radiotherapy, especially to the abdominopelvic region such as for some lymphoma patients, can potentially damage the vagina, uterus, and/or ovaries and thus lead to vaginal stenosis and fibrosis, uterine vasculature and musculature damage, and premature ovarian insufficiency (32–38). This damage can lead to adverse birth outcomes such as preterm birth (35, 36).

Potential limitations of our study include misclassification of cancer history, lack of details on cancer type and treatment characteristics in the California data, and insufficient power for separate analyses of spontaneous and medically indicated preterm birth. The California study used ICD-9 codes including V10 history codes from the birth discharge abstract (86% of patients) and any discharges in the year prior to birth (14% of patients) to determine our primary exposure of leukemia or lymphoma. This could have potentially led to misclassification of our exposure by missing leukemia/lymphoma history in some subjects. Also, since we did not have the cancer date of diagnosis in California, we could not distinguish between women who had a recent cancer diagnosis, including some who were actively being treated for leukemia/lymphoma during pregnancy, and women with a diagnosis longer before pregnancy. In Iowa, we also did not have the power to further stratify by different age groups and time intervals between diagnosis and childbirth. Additionally, in both California and Iowa we were unable to assess in-vitro fertilization, which is a known risk factor for preterm birth and a potential mediator of the relationship between cancer and preterm birth, given the observation that cancer patients are more likely to receive in-vitro fertilization. Also, another limitation was that in Iowa, we were only approved to match on birth month and year for obtaining our unexposed births and could not match on other important factors such as maternal and paternal age at childbirth. Finally, we did not have adequate statistical power to assess indicated versus spontaneous preterm birth. However, the damage to the uterus and vagina caused by cancer treatment and impairments such as uterine vasculature and musculature damage, uterine fibrosis and cervical shortening can potentially lead to either spontaneous or medically indicated preterm birth (32–40). Despite these limitations, our study yielded results similar to previously conducted studies and it should be noted that any missed cancer diagnoses in the control group would have led to a dampening of our risk estimates which further bolsters our findings.

The replication of findings in two large samples – the whole States of Iowa and California – is a strength of this study. The racial/ethnic diversity of the populations, one a primarily urban population and the other a mix of urban and rural, and the two distinct methods of measuring leukemia/lymphoma history, enhance generalizability of the findings. Additional strengths include use of birth certificate data for the outcome of preterm birth for both states,

which is an improvement on studies that relied on self-reported data. We were also able to ascertain complete information on cancer diagnoses and treatments from the Iowa SEER Cancer Registry.

Overall, our study found that there was an increased risk of preterm birth among women with a history of leukemia or lymphoma in both Iowa and California. Though challenging, it would be beneficial for additional studies to be conducted based on data with verified pregnancy outcomes, cancer and its treatments, and further assessment of the risk of preterm birth in leukemia and lymphoma patients separately and with each subtype such as acute lymphoblastic leukemia and non-Hodgkin's lymphoma. Future studies also need to address how leukemia or lymphoma impact fertility decisions and fecundity. Our study supports the importance of early identification of pregnant women and newborns at risk for complications, which should then inform preventive interventions. Moreover, the ability to characterize and understand the contributors to adverse birth outcomes such as preterm birth and complications in newborns is important as it provides the potential for improved, tailored prenatal care as women can be provided more information on their risks, options, and opportunities to prepare for an early birth.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclosure of Interest

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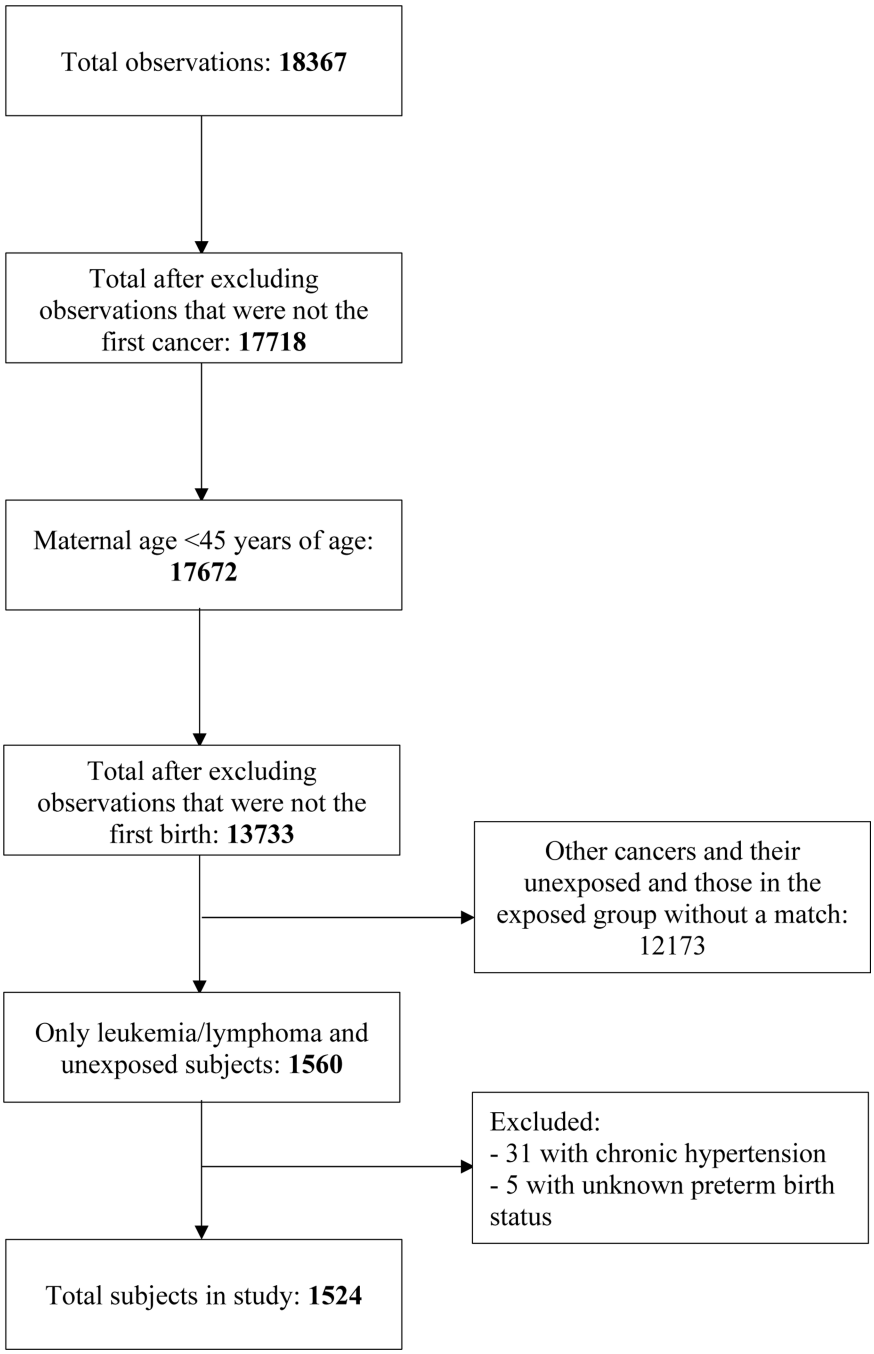

Figure 1.
Flowchart of Iowa dataset

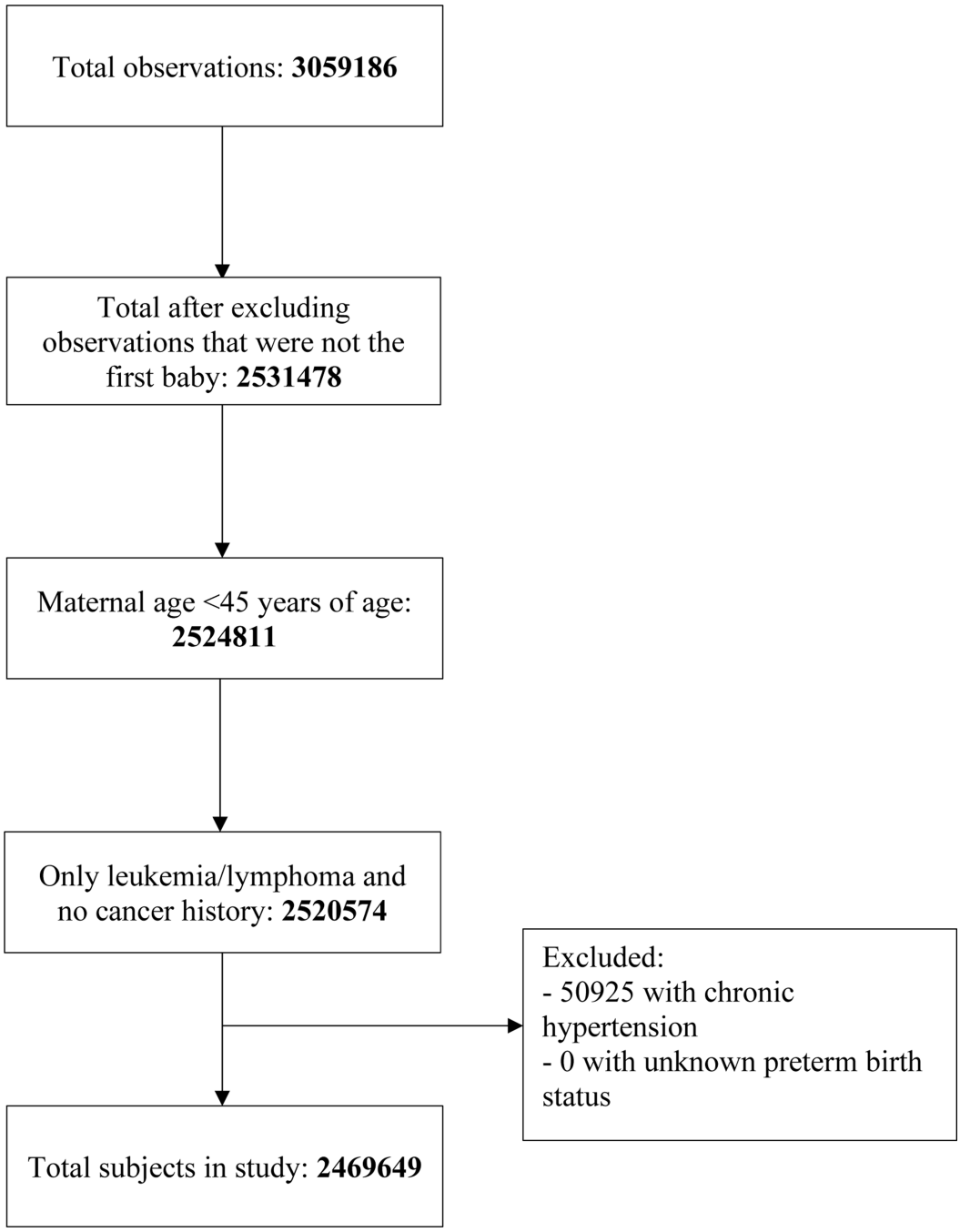

Figure 2.
Flowchart of California dataset

Table 1.

Descriptive characteristics by history of leukemia or lymphoma of California women who gave birth between 2007–2012 and Iowa women who gave birth between 1989–2018

	CALIFORNIA				IOWA			
Variable*	**Total (N=2,469,649)**	**Leukemia/ Lymphoma+ (N=1024)**	**No Cancer (N=2,468,625)**	**P-value**	**Total (N=1524)**	**Leukemia/ Lymphoma+ (N=515)**	**No Cancer (N=1009)**	**P-value**
Preterm Birth				<0.001				0.016
Preterm birth (<37 weeks)	192524 (7.8%)	150 (14.6%)	192374 (7.8%)		145 (9.5%)	62 (12.0%)	83 (8.2%)	
No preterm birth (37weeks or more)	2277125 (92.2%)	874 (85.4%)	2276251 (92.2%)		1379 (90.5%)	453 (88.0%)	926 (91.8%)	
Maternal Age at Birth				<0.001				0.002
<20	245360 (9.9%)	75 (7.3%)	245285 (9.9%)		92 (6.0%)	34 (6.6%)	58 (5.7%)	
20–24	530999 (21.5%)	177 (17.3%)	530822 (21.5%)		359 (23.6%)	92 (17.9%)	267 (26.5%)	
25–29	659507 (26.7%)	262 (25.6%)	659245 (26.7%)		505 (33.1%)	167 (32.4%)	338 (33.5%)	
30–34	608744 (24.6%)	281 (27.4%)	608463 (24.6%)		400 (26.2%)	157 (30.5%)	243 (24.1%)	
35–39	340692 (13.8%)	178 (17.4%)	340514 (13.8%)		138 (9.1%)	52 (10.1%)	86 (8.5%)	
40–44	84347 (3.4%)	51 (5.0%)	84296 (3.4%)		30 (2.0%)	13 (2.5%)	17 (1.7%)	
Maternal Age (Continuous)				<0.001				0.003
mean and std	28.1 (6.3)	29.2 (6.2)	28.1 (6.3)		27.8 (5.4)	28.3 (5.4)	27.5 (5.3)	
median and IQR	28.0 (23.0, 33.0)	29.0 (25.0, 34.0)	28.0 (23.0, 33.0)		28.0 (24.0, 32.0)	28.0 (25.0, 32.0)	27.0 (23.0, 31.0)	
min and max	(13.0, 44.0)	(13.0, 44.0)	(13.0, 44.0)		(16.0, 43.0)	(16.0, 43.0)	(18.0, 43.0)	
Maternal Race/Ethnicity				<0.001				<0.001
Asian	304811 (12.3%)	75 (7.3%)	304736 (12.3%)		^	^	^	
Black	124112 (5.0%)	53 (5.2%)	124059 (5.0%)		55 (3.6%)	13 (2.5%)	42 (4.2%)	
Hispanic	1249865 (50.6%)	353 (34.5%)	1249512 (50.6%)		70 (4.6%)	9 (1.7%)	61 (6.0%)	
Other race	179609 (7.3%)	97 (9.5%)	179512 (7.3%)		48 (3.2%)	8 (1.6%)	40 (4.0%)	
Non-Hispanic White	611252 (24.8%)	446 (43.6%)	610806 (24.7%)		1351 (88.6%)	485 (94.2%)	866 (85.8%)	

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	CALIFORNIA				IOWA			
Variable*	**Total (N=2,469,649)**	**Leukemia/ Lymphoma+ (N=1024)**	**No Cancer (N=2,468,625)**	**P-value**	**Total (N=1524)**	**Leukemia/ Lymphoma+ (N=515)**	**No Cancer (N=1009)**	**P-value**
Smoking History During Pregnancy				0.016				0.006
No smoking	2360594 (95.6%)	963 (94.0%)	2359631 (95.6%)		1298 (85.2%)	455 (88.3%)	843 (83.5%)	
Smoked during pregnancy	109055 (4.4%)	61 (6.0%)	108994 (4.4%)		215 (14.1%)	55 (10.7%)	160 (15.9%)	
Prior Live Births				<0.001				<0.001
0	1157853 (46.9%)	555 (54.2%)	1157298 (46.9%)		433 (28.4%)	195 (37.9%)	238 (23.6%)	
1	669706 (27.1%)	267 (26.1%)	669439 (27.1%)		495 (32.5%)	155 (30.1%)	340 (33.7%)	
2	382400 (15.5%)	123 (12.0%)	382277 (15.5%)		257 (16.9%)	60 (11.7%)	197 (19.5%)	
3 or more	258159 (10.5%)	79 (7.7%)	258080 (10.5%)		151 (9.9%)	32 (6.2%)	119 (11.8%)	
Maternal Education				<0.001				<0.001
<12 years	636044 (25.8%)	135 (13.2%)	635909 (25.8%)		132 (8.7%)	29 (5.6%)	103 (10.2%)	
12 years	625588 (25.3%)	215 (21.0%)	625373 (25.3%)		369 (24.2%)	101 (19.6%)	268 (26.6%)	
>12 years	1113706 (45.1%)	628 (61.3%)	1113078 (45.1%)		1013 (66.5%)	383 (74.4%)	630 (62.4%)	
Plurality				<0.001				0.178
Singleton	2425843 (98.2%)	988 (96.5%)	2424855 (98.2%)		1479 (97.0%)	504 (97.9%)	975 (96.6%)	
Twins and more	43806 (1.8%)	36 (3.5%)	43770 (1.8%)		45 (3.0%)	11 (2.1%)	34 (3.4%)	

*The data source for gestational hypertension was from hospital discharge diagnoses for California and from birth certificate for Iowa. All other variables from both states came from birth certificates.

+California: 324 Leukemia, 700 Lymphoma; Iowa: 126 Leukemia, 389 Lymphoma

^Maternal Race/Ethnicity: In Iowa, Asian was grouped with “Other race” due to <6 cell count

Table 2.

Cancer and treatment characteristics of Iowa study sample who were diagnosed between 1973–2018 by cancer type

Variable	Description	Data Source*	Leukemia (N=126)~	Lymphoma (N=389)~
Cancer Stage	Local	ICR		56 (14.4%)
	Regional			139 (35.7%)
	Distant		126 (100.0%)	80 (20.6%)
	Unstaged			114 (29.3%)
Age At Cancer Diagnosis	<5	ICR	37 (29.4%)	–
	5–9		36 (28.6%)	11 (2.8%)
	10–14		22 (17.5%)	36 (9.3%)
	15–19		11 (8.7%)	79 (20.3%)
	20–24		9 (7.1%)	129 (33.2%)
	25–29		7 (5.6%)	81 (20.8%)
	30–44		S	53 (13.6%)
Hormone Treatment	None	ICR	22 (17.5%)	239 (61.4%)
	Yes		104 (82.5%)	150 (38.6%)
Immune Treatment	None	ICR	118 (93.7%)	376 (96.7%)
	Yes		8 (6.3%)	13 (3.3%)
Time From Diagnosis To Delivery	<3 years	CALCULATED FROM ICR AND BC	12 (9.5%)	90 (23.1%)
	3–5 years		8 (6.3%)	99 (25.4%)
	6–8 years		7 (5.6%)	74 (19.0%)
	9+ years		99 (78.6%)	126 (32.4%)
Chemotherapy	No	ICR	S	86 (22.1%)
	Yes		123 (97.6%)	303 (77.9%)
Radiation Treatment	No	ICR	92 (73.0%)	182 (46.8%)
	Yes		34 (27.0%)	207 (53.2%)
Cancer Treatment Breakdown+	Chemotherapy only	GROUPED FROM ICR	89 (70.6%)	161 (41.4%)
	Both Chemotherapy and Radiation		34 (27.0%)	142 (36.5%)
	Radiation only		S	65 (16.7%)
	Neither Radiation nor Chemotherapy		S	21 (5.4%)

*Data source: ICR- Iowa Cancer Registry

+A total of 93 women received surgery, typically coded as lymph node surgery

~S = suppressed cells (<6 cell count)

Table 3.

Risk of preterm birth among women <45 years of age with leukemia/lymphoma who gave birth, by state

	California		Iowa	
	N	**With preterm birth**	**N**	**With preterm birth**
Leukemia/Lymphoma, N (%)	1,024	150 (14.6%)	515	62 (12.0%)
No Cancer, N (%)	2,468,625	192,374 (7.8%)	1,009	83 (8.2%)
Unadjusted model, OR (95% CI)		2.03 (1.71, 2.42) *		1.50 (1.07, 2.11) *
Model 1: adjusted for age, race, education, plurality, smoking OR (95% CI)		1.89 (1.56, 2.28) *		1.61 (1.10, 2.37) *
Model 2: adjusted for covariates in Model 1 plus gestational hypertension (OR (95%CI)		1.89 (1.56, 2.29) *		1.56 (1.05, 2.30) *

* $p<0.05$

Table 4.

Risk of preterm birth among Iowa women <45 years of age with leukemia/lymphoma who gave birth between 1989–2018 by cancer treatment

			Unadjusted model	Adjusted model*
Cancer Treatment+	**Total**	**With preterm birth, N (%)~**	**OR (95% Confidence Interval (CI))**	**OR (95% Confidence Interval (CI))**
Chemotherapy only	250	24 (9.6%)	Ref	Ref
Both Chemotherapy and radiation	176	26 (14.8%)	1.63 (0.90, 2.95)	1.72 (0.89, 3.33)
Radiation only	65	11 (16.9%)	1.92 (0.89, 4.16)	1.62 (0.66, 3.96)
Neither Radiation nor Chemotherapy	24	S	0.41 (0.05, 3.17)	0.33 (0.04, 2.77)

*Adjusted for time from diagnosis to delivery, diagnosis age, and cancer stage

+A total of 93 women received surgery, typically coded as lymph node surgery

~S = suppressed cells (<6 cell count)