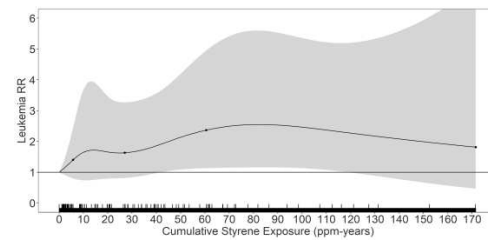


S1a. Butadiene, trimmed ppm-years



S1b. Styrene, trimmed ppm-years

Figure S1. Restricted cubic splines for trimmed butadiene ppm-years and leukemia (S1a) and trimmed styrene ppm-years and leukemia (S1b). Models used trimmed data (excludes all unexposed person-time and all person-time with ppm-years above the 95th percentile of the exposure distribution of leukemia decedents, at 1,144 ppm-years for butadiene and at 171 ppm-years for styrene). Rugs just above the X-axis of each figure depict the frequency of all observations (lower rug) and leukemias (upper rug) at corresponding monomer exposure values. Circles indicate cutpoints for quartiles 2, 3 and 4 and for the 95th percentile.

Table S1 Cross-tabulation of cases of each outcome by quartiles of butadiene and styrene ppm-years						
	Butadiene ppm-years		Styrene ppm-years			
<i>All leukemia</i>	0	>0-< 5.76	5.76-< 27.00	27.00-< 60.53	60.53-1203.21	Total
0	23	3	2	1	0	29
>0-< 34.00	0	17	6	3	0	26
34.00-< 121.28	0	7	10	7	2	26
121.28-< 363.64	0	0	8	10	7	25
363.64-7741.41	0	0	1	7	18	26
Total	23	27	27	28	27	132
<i>Lymphoid leukemia</i>	0	>0-< 8.52	8.52-< 27.21	27.21-< 69.29	69.29-1203.21	Total
0	10	1	2	0	0	13
>0-< 44.73	0	5	3	1	0	9
44.73-< 213.43	0	4	4	2	0	10
213.43-< 376.31	0	0	2	3	5	10
376.31-7741.41	0	0	0	4	6	10
Total	10	10	11	10	11	52
<i>Myeloid leukemia</i>	0	>0-< 5.21	5.21-< 20.71	20.71-< 48.25	48.25-340.52	Total
0	11	2	0	0	1	14
>0-< 25.20	0	7	5	1	0	13
25.20-< 70.05	0	5	4	5	0	14
70.05-< 230.08	0	0	5	5	3	13
230.08-2009.71	0	0	0	3	10	13
Total	11	14	14	14	14	67
<i>AML*</i>	0	>0-< 5.21	5.21-< 19.73	19.73-< 34.00	34.00-340.52	Total
0	6	2	0	0	1	9
>0-< 19.14	0	4	4	0	0	8
19.14-< 59.19	0	1	3	3	1	8
59.19-< 185.63	0	1	1	4	2	8
185.63-2009.71	0	0	1	2	5	8
Total	6	8	9	9	9	41
<i>NHL</i>	0	>0-< 5.97	5.97-< 23.61	23.61-< 59.67	59.67-231.34	Total
0	24	5	4	0	1	34
>0-<17.94	0	11	5	2	1	19
17.94-< 117.22	0	3	9	7	0	19
117.22-< 334.83	0	0	4	9	6	19
334.83-1495.51	0	2	0	3	14	19
Total	24	21	22	21	22	110
<i>Multiple myeloma</i>	0	>0-< 2.80	2.80-< 14.67	14.67-< 77.99	77.99-839.61	Total
0	16	2	1	0	1	20
>0-< 31.42	0	7	3	0	0	10
31.42-< 107.78	0	0	6	4	0	10
107.78-< 386.04	1	1	1	5	2	10
386.04-2397.73	0	0	0	2	8	10
Total	17	10	11	11	11	60

Table S1 Cross-tabulation of cases of each outcome by quartiles of butadiene and styrene ppm-years

Butadiene ppm-years	Styrene ppm-years					Total
	0	>0–< 4.63	4.63–< 20.74	20.74–< 61.70	61.70–1203.21	
<i>B-cell malignancy</i>	0					
0	49	7	7	0	2	65
>0–< 27.04	0	23	8	5	1	37
27.04–< 124.38	0	8	18	11	0	37
124.38–< 370.89	1	0	5	17	14	37
370.89–7741.41	0	3	2	8	24	37
Total	50	41	40	41	41	213

*Abbreviations: AML, acute myeloid leukemia; NHL, non-Hodgkin lymphoma.

Table S2 Exposure-response analyses of butadiene and lymphohematopoietic cancers: number (N) of cases, adjusted rate ratio (RR) with 95% confidence interval (CI) by exposure quartile (Q), beta-coefficient (β) with 95% confidence interval (CI) and trend p-value for butadiene ppm-years, reduced models

Butadiene ppm-years, model*	All leukemias			Lymphoid leukemia			Myeloid leukemia		
	N	RR	95% CI (S,H) §	N	RR	95% CI (S,H) §	N	RR	95% CI (S,H) §
Unexposed	29	1.0	ref	13	1.0	ref	14	1.0	ref
Q1	26	1.05	0.60 to 1.84	9	0.71	0.29 to 1.73	13	1.16	0.53 to 2.54
Q2	26	1.36	0.76 to 2.43	10	0.84	0.34 to 2.09	14	1.95	0.88 to 4.33
Q3	25	1.62	0.89 to 2.96	10	2.70	1.08 to 6.76	13	1.47	0.64 to 3.35
Q4	26	2.52	1.39 to 4.58	10	1.97	0.79 to 4.94	13	1.72	0.74 to 4.00
β [95% CI], trend p-value, AIC†, all person-time‡	2.57x10 ⁻⁴ [(0.75 to 4.39) x10 ⁻⁴], p=0.006, AIC=2382 (R)			4.02x10 ⁻⁴ [(1.29 to 6.75) x10 ⁻⁴], p=0.004, AIC=931 (S,R,P,H)			1.08x10 ⁻⁴ [(-2.82 to 4.99) x10 ⁻⁴], p=0.586, AIC=1229 (S,P,H)		
β [95% CI], trend p-value, AIC, exposed person-time‡	2.41x10 ⁻⁴ [(0.63 to 4.18) x10 ⁻⁴], p=0.008, AIC=1781 (none)			4.91x10 ⁻⁴ [(1.51 to 8.31) x10 ⁻⁴], p=0.005, AIC=660 (S,R,P)¶			0.63x10 ⁻⁴ [(-3.50 to 4.76) x10 ⁻⁴], p=0.766, AIC=924 (none)**		
β [95% CI], trend p-value, AIC, exposed person-time ≤95 th percentile at 1,144 ppm-years‡	10.30x10 ⁻⁴ [(2.52 to 18.14) x10 ⁻⁴], p=0.010, AIC=1670 (R,P,H)			15.00x10 ⁻⁴ [(4.37 to 25.59) x10 ⁻⁴], p=0.006, AIC=616 (S)¶			-0.16x10 ⁻⁴ [(-14.68 to 14.37) x10 ⁻⁴], p=0.983, AIC=880 (A,Y,R,P,H)**		
	Non-Hodgkin lymphoma			Multiple myeloma			B-cell malignancy††		
	N	RR	95% CI (S,P,H) §	N	RR	95% CI (S,P,H) §	N	RR	95% CI (S,R,P,H) §
Unexposed	34	1.0	ref	20	1.0	ref	65	1.0	ref
Q1	19	0.91	0.51 to 1.64	10	0.60	0.27 to 1.33	37	0.76	0.50 to 1.17
Q2	19	0.57	0.31 to 1.05	10	0.70	0.31 to 1.61	37	0.70	0.45 to 1.08
Q3	19	0.93	0.50 to 1.72	10	0.67	0.29 to 1.57	37	0.95	0.60 to 1.48
Q4	19	1.29	0.69 to 2.40	10	1.17	0.51 to 2.73	37	1.38	0.88 to 2.18
β [95% CI], trend p-value, AIC, all person-time‡	0.25x10 ⁻⁴ [(-3.62 to 4.13) x10 ⁻⁴], p=0.898, AIC=1970 (P,H)			-0.82x10 ⁻⁴ [(-5.08 to 3.45) x10 ⁻⁴], p=0.707, AIC=1056 (A,Y,S,R,P,H)			1.17x10 ⁻⁴ [(-0.73 to 3.06) x10 ⁻⁴], p=0.228, AIC=3782 (S,R,P,H)		
β [95% CI], trend p-value, AIC, exposed person-time‡	1.55x10 ⁻⁴ [(-2.24 to 5.34) x10 ⁻⁴], p=0.424, AIC=1312 (P)			-0.34x10 ⁻⁴ [(-4.41 to 3.73) x10 ⁻⁴], p=0.869, AIC=664 (S,R,H)			1.96x10 ⁻⁴ [(-0.06 to 3.98) x10 ⁻⁴], p=0.058, AIC=2514 (S,R,P)		
β [95% CI], trend p-value, AIC, exposed person-time ≤95 th percentile at 1,083 ppm-years‡	14.10x10 ⁻⁴ [(5.09 to 23.02)x10 ⁻⁴], p=0.002, AIC=1281 (S,P,H)			6.13x10 ⁻⁴ [(-6.86 to 19.12) x10 ⁻⁴], p=0.355, AIC=631 (S,R,P)			11.00x10 ⁻⁴ [(4.45 to 17.62)x10 ⁻⁴], p=0.001, AIC=2379 (P,H)		

*Models used attained age as of each day of follow-up as the time scale. See supplemental Table S1 for outcome-specific ranges of butadiene ppm-years by quartile.

†AIC, Akaike information criterion.

‡Covariates for each model are listed: A, age at hire; Y, year of hire; R, race; S, sex; P, plant; H, ever hourly.

§Covariates for the analysis of RRs by monomer exposure quartile.

¶Restricted to ever hourly due to lack of events among never hourly.

**Restricted to men due to lack of events among women.

††B-cell malignancy included lymphoid leukemia, non-Hodgkin lymphoma and multiple myeloma.

Table S3 Exposure-response analyses of styrene ppm-years and lymphohematopoietic cancers: number (N) of cases, adjusted rate ratio (RR) with 95% confidence interval (CI) by exposure quartile (Q), beta-coefficient (β) with 95% confidence interval (CI) and trend p-value for styrene ppm-years, reduced models

Styrene ppm-years, model*	All leukemias			Lymphoid leukemia			Myeloid leukemia		
	N	RR	95% CI (S,R,P,H) [§]	N	RR	95% CI (S,R,H) [§]	N	RR	95% CI (S,P,H) [§]
Unexposed	23	1.0	ref	10	1.0	ref	11	1.0	ref
Q1	27	1.13	0.61 to 2.08	10	0.76	0.29 to 2.00	14	1.26	0.54 to 2.98
Q2	27	1.13	0.60 to 2.13	11	1.26	0.47 to 3.34	14	1.36	0.56 to 3.29
Q3	28	1.84	0.97 to 3.52	10	1.20	0.44 to 3.31	14	1.84	0.74 to 4.54
Q4	27	2.01	1.03 to 3.89	11	1.70	0.62 to 4.67	14	1.78	0.71 to 4.49
β [95% CI], trend p-value, AIC [†] , all person-time [‡]	1.05x10 ⁻³ [(-0.09 to 2.18) x10 ⁻³], p=0.070, AIC=2378 (H)			1.58x10 ⁻³ [(0.25 to 2.91) x10 ⁻³], p=0.020, AIC=926 (H)			-2.32x10 ⁻⁴ [(-31.29 to 26.66) x10 ⁻⁴], p=0.876, AIC=1223 (S,R,H)		
β [95% CI], trend p-value, AIC, exposed person-time [‡]	0.86x10 ⁻³ [(-0.34 to 2.05) x10 ⁻³], p=0.159, AIC=1901 (S,H)			1.12x10 ⁻³ [(-0.44 to 2.69) x10 ⁻³], p=0.160, AIC=718 (R) [¶]			-3.68x10 ⁻⁴ [(-33.31 to 25.96) x10 ⁻⁴], p=0.808, AIC=996 (H)		
β [95% CI], trend p-value, AIC, exposed person-time \leq 95 th percentile at 171 ppm-years [‡]	3.98x10 ⁻³ [(-1.13 to 9.10) x10 ⁻³], p=0.127, AIC=1787 (S,R,H)			3.61x10 ⁻³ [(-4.31 to 11.54) x10 ⁻³], p=0.371, AIC=680 (S,R) [¶]			28.10x10 ⁻⁴ [(-47.58 to 103.76) x10 ⁻⁴], p=0.467, AIC=951 (S,H)		
	Non-Hodgkin lymphoma			Multiple myeloma			B-cell malignancy ^{††}		
	N	RR	95% CI (S,P,H) [§]	N	RR	95% CI (S,P,H) [§]	N	RR	95% CI (S,R,P,H) [§]
Unexposed	24	1.0	ref	17	1.0	ref	50	1.0	ref
Q1	21	0.83	0.43 to 1.57	10	0.93	0.41 to 2.13	41	0.91	0.58 to 1.42
Q2	22	1.03	0.53 to 2.00	11	0.61	0.27 to 1.39	40	0.84	0.52 to 1.34
Q3	21	1.11	0.56 to 2.20	11	0.44	0.19 to 1.02	41	0.87	0.54 to 1.40
Q4	22	1.50	0.76 to 2.96	11	0.93	0.38 to 2.25	41	1.20	0.73 to 1.95
β [95% CI], trend p-value, AIC, all person-time [‡]	-0.23x10 ⁻³ [(-2.54 to 2.07) x10 ⁻³], p=0.842, AIC=1970 (P,H)			0.15x10 ⁻³ [(-1.54 to 1.85) x10 ⁻³], p=0.858, AIC=1056 (A,Y,S,R,P,H)			5.68x10 ⁻⁴ [(-4.67 to 16.03) x10 ⁻⁴], p=0.282, AIC=3782 (S,R,P,H)		
β [95% CI], trend p-value, AIC, exposed person-time [‡]	-0.15x10 ⁻³ [(-2.52 to 2.22) x10 ⁻³], p=0.902, AIC=1501 (S,R,P)			0.31x10 ⁻³ [(-1.44 to 2.05) x10 ⁻³], p=0.731, AIC=730 (A,Y,S,R,P,H)			5.54x10 ⁻⁴ [(-5.08 to 16.16) x10 ⁻⁴], p=0.307, AIC=2806 (R,P,H)		
β [95% CI], trend p-value, AIC, exposed person-time \leq 95 th percentile at 213 ppm-years [‡]	4.20x10 ⁻³ [(-0.52 to 8.91) x10 ⁻³], p=0.081, AIC=1455 (S,P)			-1.57x10 ⁻³ [(-9.58 to 6.44) x10 ⁻³], p=0.700, AIC=640 (R,P,H)			17.10x10 ⁻⁴ [(-20.78 to 54.88) x10 ⁻⁴], p=0.377, AIC=2635 (S,R,P,H)		

*Models used attained age as of each day of follow-up as the time scale. See supplemental Table S1 for outcome-specific ranges of styrene ppm-years by quartile.

†AIC, Akaike information criterion.

‡Covariates for each model are listed: A, age at hire; Y, year of hire; R, race; S, sex; P, plant; H, ever hourly.

§Covariates for the analysis of RRs by monomer exposure quartile.

¶Restricted to ever hourly due to lack of events among never hourly.

††B-cell malignancies included lymphoid leukemia, non-Hodgkin lymphoma and multiple myeloma.

Table S4 Exposure-response analyses of butadiene or styrene ppm-years and acute myeloid leukemia: number (N) of cases, adjusted rate ratio (RR) with 95% confidence interval (CI) by exposure quartile, beta-coefficient (β) with 95% confidence interval (CI) and trend p-value, reduced model

Model*	N	Butadiene		N	Styrene	
		RR	95% CI (S,P,H) [§]		RR	95% CI (R) [§]
Quartile†						
Unexposed	9	1.0	ref	6	1.0	ref
Q1	8	1.36	0.50 to 3.69	8	1.76	0.61 to 5.09
Q2	8	1.93	0.69 to 5.36	9	2.39	0.85 to 6.72
Q3	8	1.69	0.59 to 4.83	9	4.66	1.66 to 13.12
Q4	8	1.70	0.58 to 4.99	9	2.03	0.71 to 5.79
Trend:						
β [95% CI], trend p-value, AIC†, all person-time‡		-1.02×10^{-4} , [(-9.18 to 7.15) $\times 10^{-4}$], p=0.807, AIC=750 (R,P,H)			-6.10×10^{-4} [(-51.00 to 38.41) $\times 10^{-4}$], p=0.788, AIC=750 (R,P,H)	
β [95% CI], trend p-value, AIC, exposed person-time‡		-2.33×10^{-4} , [(-13.01 to 8.34) $\times 10^{-4}$], p=0.669, AIC=555 (P) [¶]			-1.12×10^{-3} [(-6.57 to 4.34) $\times 10^{-3}$], p=0.688, AIC=618 (S,P)	
β [95% CI], trend p-value, AIC, exposed person-time $\leq 95^{\text{th}}$ percentile at 1,144 ppm-years for butadiene and 171 for styrene‡		-1.39×10^{-3} [(-3.92 to 1.14) $\times 10^{-3}$], p=0.282, AIC=535 (P,H) [¶]			-3.01×10^{-3} [(-14.95 to 8.94) $\times 10^{-3}$], p=0.622, AIC=600 (R,P,H)	

*Models used attained age as of each day of follow-up as the time scale. See supplemental Table S1 for outcome-specific ranges of butadiene ppm-years by quartile.

†AIC, Akaike information criterion.

‡Covariates for each model are listed: A, age at hire; Y, year of hire; R, race; S, sex; P, plant; H, ever hourly.

§Covariates for the analysis of RRs by monomer exposure quartile.

¶Restricted to men due to lack of events among women.

Table S5 Adjusted* beta-coefficient (β) with 95% confidence interval (CI) and trend p-value for the relation between butadiene or styrene ppm-years, lagged 10 or 20 years, and lymphohematopoietic cancers (LHC), all person-time, reduced models

Monomer, Form of LHC (covariates)	ppm-years, lagged 10 years				ppm-years, lagged 20 years			
	β	95% CI	Trend p-value	AIC†	β	95% CI	Trend p-value	AIC
<i>Butadiene</i>								
All leukemia (Covariates)	2.55x10 ⁻⁴ (R)	(0.59 to 4.51)x10 ⁻⁴	0.011	2335	2.66x10 ⁻⁴ (S,R,P)	(0.05 to 5.26)x10 ⁻⁴	0.045	2116
Lymphoid leukemia (Covariates)	3.91x10 ⁻⁴ (S,R,P,H)	(1.00 to 6.82)x10 ⁻⁴	0.008	929	3.00x10 ⁻⁴ (S)	(-0.03 to 6.04)x10 ⁻⁴	0.052	861
Myeloid leukemia (Covariates)	1.13x10 ⁻⁴ (S, H)	(-3.02 to 5.28)x10 ⁻⁴	0.594	1176	2.17x10 ⁻⁴ (R,P,H)	(-2.69 to 7.03)x10 ⁻⁴	0.381	1057
AML§ (Covariates)	-0.69x10 ⁻⁴ (S,H)	(-9.06 to 7.68)x10 ⁻⁴	0.872	714	-0.14x10 ⁻⁴ (A, Y,S,R,P,H)	(-8.85 to 8.57)x10 ⁻⁴	0.975	641
NHL§ (Covariates)	1.00x10 ⁻⁵ (P, H)	(-42.51 to 44.51)x10 ⁻⁵	0.964	1966	-6.18x10 ⁻⁵ (A, Y,S,R,P,H)	(-67.04 to 54.67)x10 ⁻⁵	0.842	1876
Multiple myeloma (Covariates)	-7.54x10 ⁻⁵ (A, Y,S,R,P,H)	(-52.81 to 37.74)x10 ⁻⁵	0.744	1054	-8.97x10 ⁻⁵ (R, P, H)	(-62.51 to 44.57)x10 ⁻⁵	0.743	951
B-cell malignancy (Covariates)	1.13x10 ⁻⁴ (S,R,P,H)	(-0.94 to 3.20)x10 ⁻⁴	0.286	3775	0.67x10 ⁻⁴ (S,R,P,H)	(-2.00 to 3.33)x10 ⁻⁴	0.624	3513
<i>Styrene</i>								
All leukemia (Covariates)	1.02x10 ⁻³ (S,H)	(-0.24 to 2.28)x10 ⁻³	0.112	2328	0.97x10 ⁻³ (S,H)	(-0.63 to 2.57)x10 ⁻³	0.233	2114
Lymphoid leukemia (Covariates)	1.65x10 ⁻³ (H)	(0.19 to 3.10)x10 ⁻³	0.027	924	1.52x10 ⁻³ (S,R,P,H)	(-0.62 to 3.66)x10 ⁻³	0.163	865

Table S5 Adjusted* beta-coefficient (β) with 95% confidence interval (CI) and trend p-value for the relation between butadiene or styrene ppm-years, lagged 10 or 20 years, and lymphohematopoietic cancers (LHC), all person-time, reduced models

Monomer, Form of LHC (covariates)	ppm-years, lagged 10 years				ppm-years, lagged 20 years			
	β	95% CI	Trend p-value	AIC†	β	95% CI	Trend p-value	AIC
Myeloid leukemia (Covariates)	-4.20×10^{-4} (S,R)	$(-37.30 \text{ to } 28.90) \times 10^{-4}$	0.804	1176	-3.34×10^{-4} (S,P,H)	$(-44.92 \text{ to } 38.25) \times 10^{-4}$	0.875	1052
AML§ (Covariates)	-4.01×10^{-4} (S,H)	$(-47.21 \text{ to } 39.19) \times 10^{-4}$	0.856	714	-2.69×10^{-4} (A)	$(-51.28 \text{ to } 45.91) \times 10^{-4}$	0.914	633
NHL§ (Covariates)	-3.14×10^{-4} (P,H)	$(-28.65 \text{ to } 22.36) \times 10^{-4}$	0.809	1966	-7.18×10^{-4} (S)	$(-38.34 \text{ to } 23.97) \times 10^{-4}$	0.651	1868
Multiple myeloma (Covariates)	1.05×10^{-4} (A,Y,S,R,P,H)	$(-17.61 \text{ to } 19.70) \times 10^{-4}$	0.913	1054	-5.22×10^{-5} (A,Y,S,R,P,H)	$(-239.49 \text{ to } 229.05) \times 10^{-5}$	0.965	955
B-cell malignancy (Covariates)	5.39×10^{-4} (S,R,P,H)	$(-5.96 \text{ to } 16.74) \times 10^{-4}$	0.352	3775	3.06×10^{-4} (S,R,P,H)	$(-11.43 \text{ to } 17.55) \times 10^{-4}$	0.679	3513

*Cox regression analyses used time-dependent age as the time scale. Covariates for each model are listed in parentheses: A, age at hire; Y, year of hire; R, race; S, sex; P, plant; H, ever hourly.

†AIC, Akaike information criterion.

§Abbreviations: AML, acute myeloid leukemia; NHL, non-Hodgkin lymphoma.