[CANCER RESEARCH 40, 439–443, February 1980]
0008-5472/80/0040-0000$02.00

High Cancer Mortality Rates from Childhood Leukemia and Young Adult Hodgkin's Disease and Lymphoma in the New Jersey-New York-Philadelphia Metropolitan Corridor, 1950 to 1969[1]

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ABSTRACT

In comparison to the United States as a whole and to their total population age-adjusted rates, the New Jersey-New York-Philadelphia Metropolitan Region was found to have excessively high childhood leukemia and high young adult Hodgkin's disease and lymphoma cancer mortality rates in the period from 1950 to 1969.

INTRODUCTION

Leukemia, Hodgkin's disease, and lymphoma are systemic cancers. From 1950 to 1969, they accounted for about 9% of cancer mortalities in the United States. Their importance among children and young adults (age groups 0 to 34 yr) is far greater, since these 3 disease categories account for about one-half of the cancer deaths for persons less than 35 yr of age.

As part of a study of cancer mortality and risk factor patterns in the New Jersey-New York-Philadelphia Metropolitan Regions (3, 4), the authors sought to determine if the study area exhibited unusual childhood and young adult mortality patterns. The report that follows demonstrates that substantially elevated leukemia, Hodgkin's disease, and lymphoma mortality rates do exist.

MATERIALS AND METHODS

Data. The REG[3] contains 25 million people and 49 counties, including all of the State of New Jersey, the New York Metropolitan area, the Philadelphia Metropolitan area, and adjacent counties that have been sources of commuters to the cities and have been resettlement areas for the urban industrial counties (Chart 1). The REG was constructed to control for intraregional migration as much as possible.

Mortality counts for 1950 to 1969 were provided by the National Cancer Institute, conforming to the Sixth and Seventh Revisions of the ICD (7, 8). In order to be able to study age groups, the mortalities were initially aggregated into the following 17 age categories (yr): 0 to 4, 5 to 9, 10 to 14, 15 to 19, 20 to 24, 25 to 29, 30 to 34, 35 to 39, 40 to 44, 45 to 49, 50 to 54, 55 to 59, 60 to 64, 65 to 69, 70 to 74, 75 to 84, and greater than 84. Separate tabulations were obtained for white males and white females for the REG and RON.

Before reviewing the methods and results, it is important to set forth the limitations of the data. First, the REG is an approximation. A few more counties might have been added and others deleted. Until better migration data become available, however, approximations will be required.

Second, each of the mortality categories is an aggregate of specific diseases. Our leukemia category (ICD 204) includes a set of diseases which differ histologically, in incidence by age, and in probable etiology (2, 5, 6). Similarly, our lymphoma category (ICD's 200, 202, 205) includes lymphosarcoma and reticulosarcoma, other forms of lymphoma, and mycosis fungoides (7, 8). In short, we used the National Cancer Institute's grouping of the diseases (7, 8). Using aggregated diseases has probably, although not necessarily, understated the results.

Methods. The methodological approach was to compute and compare parallel cancer mortality rates for the REG and RON. The following rates and their specific purposes are summarized below.

1. Age-specific rates for the white male and female populations for each of the above 17 age groups of 5 years each were computed in order to make the finest possible comparisons between the REG and the RON. Ten-yr age group aggregates were also computed to broaden the population at risk base.

2. Age-adjusted rates for the total white male and female populations were prepared to obtain the most general perspective.

3. Age-adjusted rates for the white male and female populations 0 to 34 yr old were calculated in order to help substantiate the 5- and 10-yr rates while at the same time eliminate the influence of the middle-aged and elderly populations. Persons 35 yr and older accounted for 81% of the REG white population cancer mortalities attributed to leukemia, Hodgkin's disease, and lymphoma from 1950 to 1969. It should be noted that 0 to 34 yr was a compromise between those who suggested 20-yr age groups and those who suggested 0 to 44 or 0 to 54 yr.

Having computed separate but parallel rates for the REG and RON, 2 sets of statistics were computed. One was a simple age-specific rate index derived by dividing the REG rate by the RON rate and multiplying the result by 100. The RON and REG comparisons were made to eliminate the influence of the REG's population (about 10% of the nation's) on the national totals. A rate of 100 means that the rate of the area of interest is identical to the national rate. The age-specific rate indices also allowed us to calculate excess or deficits in mortality. For example, if the REG's white male leukemia 15- to 19-yr age group index is 112, we can calculate the number of excess

[1] The research was supported by the New Jersey Department of Environmental Protection and the United States Environmental Protection Agency (Grant EPA R805526010).

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[3] The abbreviations used are: REG, study region; ICD, International Classification Of Diseases, Sixth and Seventh Revisions; RON, rest of nation.

Received June 14, 1979; accepted November 6, 1979.

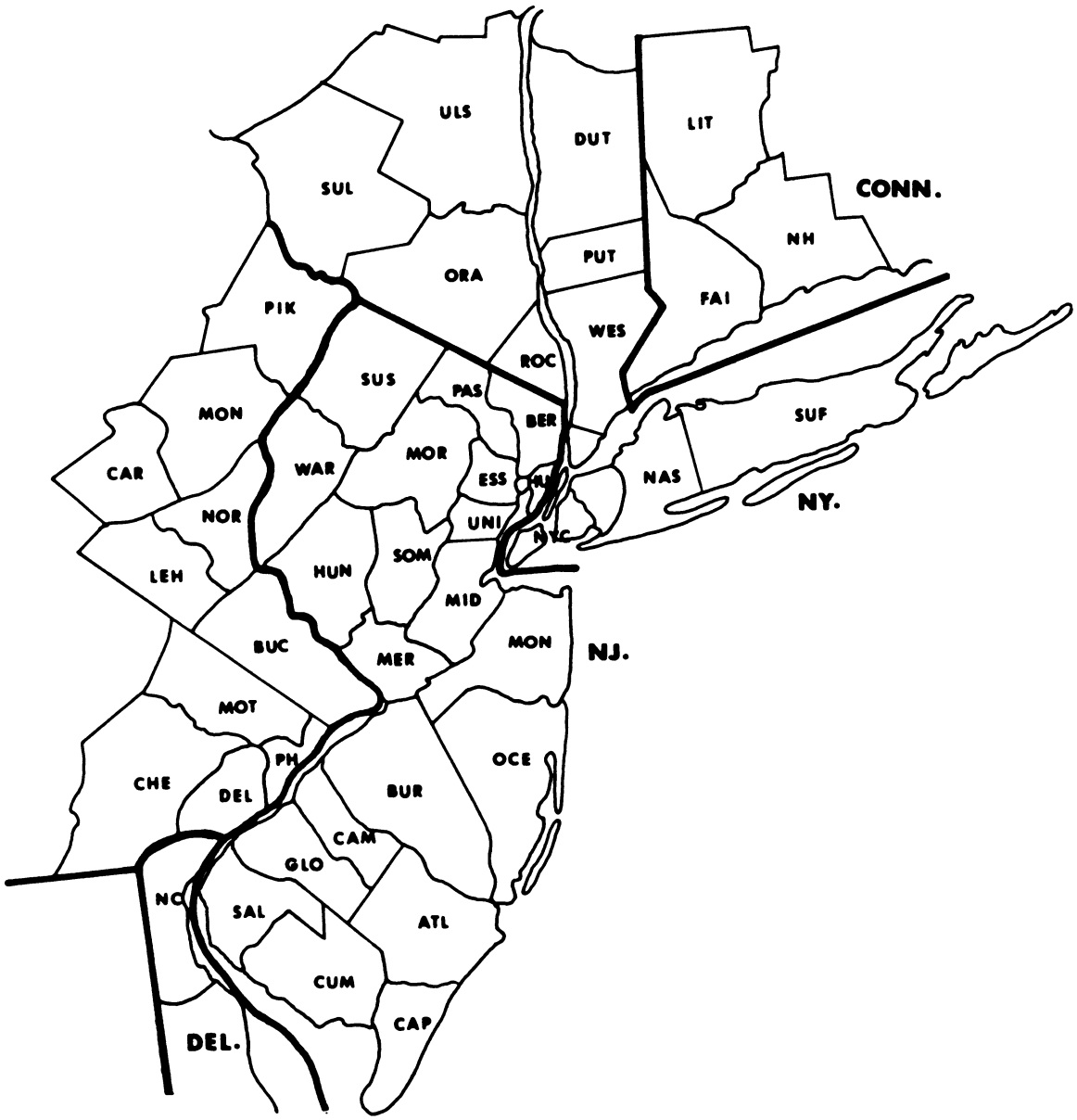

Chart 1. Forty-nine-county study area. Connecticut: FAI, Fairfield; LIT, Litchfield; NH, New Haven. Delaware: NC, New Castle. New Jersey: ATL, Atlantic; BER, Bergen; BUR, Burlington; CAM, Camden; CAP, Cape May; CUM, Cumberland; ESS, Essex; GLO, Gloucester; HU, Hudson; HUN, Hunterdon; MER, Mercer; MID, Middlesex; MON, Monmouth; MOR, Morris; OCE, Ocean; PAS, Passaic; SAL, Salem; SOM, Somerset; SUS, Sussex; UNI, Union; WAR, Warren. New York: DUT, Dutchess; NAS, Nassau; NYC, New York City; ORA, Orange; PUT, Putnam; ROC, Rockland; SUF, Suffolk; SUL, Sullivan; ULS, Ulster; WES, Westchester. Pennsylvania: BUC, Bucks; CAR, Carbon; CHE, Chester; DEL, Delaware; LEH, Lehigh; MON, Monroe; MOT, Montgomery; NOR, Northampton; PH, Philadelphia; PIK, Pike.

mortalities in the REG.

The second set of statistics began with the standard error of the age-specific death rates. Developed by Chiang (1), this frequently used statistic (7) allows us to prepare confidence limits for the age-specific rates and therefore to determine if the rates of the REG are significantly different from those of the RON. Specifically, variances and confidence limits for the REG and RON rates were calculated. When the confidence limits did not overlap, it was concluded that the rates of the REG and the RON were significantly different.

RESULTS

There is a clear and statistically significant excess of childhood leukemia, teenage and young adult Hodgkin's disease, and lymphoma in the REG (Table 1). The REG leukemia age-specific rate index peaks at ages 5 to 14 yr, about 15% higher than that of the RON, and then it gradually declines (Table 1). By ages 65 to 74 yr, the REG leukemia rates are at or below the average of the RON. The Hodgkin's and lymphoma rates suddenly rise to a peak at 15 to 24 yr between 20 and 88% higher than the RON rates and then again gradually drop off.

Since the peaks in Table 1 are clearly manifested for both the male and female populations, it is hard to believe that they are random. Indeed, nearly all of the REG rates of particular concern (age groups 0 to 34 yr) were significantly different from their RON counterparts at the 0.05 and 0.01 level.

Given the fact that more than 25 million people live in the

Table 1

Comparison of REG and RON age-specific rates for leukemia, Hodgkin's disease, and lymphoma, 1950 to 1969

Age group (yr)	Leukemia (ICD 204) WM[a] Index[b]	p[c]	REG rates/ 100,000	WF Index	p	REG rates/ 100,000	Hodgkin's (ICD 201) WM Index	p	REG rates/ 100,000	WF Index	p	REG rates/ 100,000	Lymphoma (ICD 200, 202, 205) WM Index	p	REG rates/ 100,000	WF Index	p	REG rates/ 100,000
0–4	100		5.4	102		4.7	[d]		0.0	[d]		0.0	100		0.8	100		0.5
5–9	118	99	5.3	*123*	99	4.3	[d]		0.1	[d]		0.1	100		0.9	75		0.3
10–14	*119*	99	3.2	114	90	2.4	100		0.4	[d]		0.2	100		0.8	100		0.4
15–19	114	95	3.2	112	80	1.9	*188*	99	1.5	150	99	0.9	*130*	95	1.3	125	90	0.5
20–24	109	90	2.4	107		1.5	141	99	2.4	*173*	99	1.9	120	90	1.2	*150*	95	0.6
25–29	113	90	2.6	100		1.6	125	99	3.0	150	99	2.1	127	95	1.4	140	95	0.7
30–34	112	90	2.9	120	95	2.4	128	99	3.2	153	99	2.3	121	95	1.7	125	90	1.0
35–39	113	90	3.5	112	90	2.8	116	95	2.9	146	99	1.9	124	99	2.6	142	99	1.7
40–44	115	95	4.7	109	85	3.6	100		2.8	146	99	1.9	121	99	4.0	133	99	2.8
45–49	111	95	6.1	102		4.4	128	99	3.7	133	99	2.0	121	99	5.8	131	99	4.2
50–54	107	90	8.9	112	95	6.5	111	90	4.0	111	85	2.0	124	99	8.9	110	90	5.4
55–59	107	90	13.4	113	99	9.3	114	90	4.9	129	99	2.7	112	99	12.0	113	95	8.1
60–64	100		19.6	110	95	12.9	96		5.2	110	80	3.2	106	85	15.6	108	90	10.7
65–69	98		29.3	107	90	18.0	103		6.1	100		3.7	107	90	20.5	111	95	14.7
70–74	96		41.0	101		24.3	98		6.5	102		4.4	106	80	24.6	105		17.8
75–84	90		55.2	97		34.5	104		7.2	90		4.3	104		28.3	97		19.3
84+	87		63.8	90		36.6	58		3.2	91		4.0	95		22.5	92		15.6

[a] WM, white male; WF, white female.
[b] Computed by the formula: (REG/RON) × 100.
[c] Probability that REG rate is significantly higher than RON rate if probability exceeds 80%.
[d] Rate less than 0.3/100,000.

Table 2

Total and excess white population leukemia, Hodgkin's disease, and lymphoma mortalities in the region, in comparison to the RON in 1950 to 1969

Age group (yr)	A. Leukemia Male Total	Excess	Relative risk	Female Total	Excess	Relative risk	B. Hodgkin's disease Male Total	Excess	Relative risk	Female Total	Excess	Relative risk	C. Lymphoma Male Total	Excess	Relative risk	Female Total	Excess	Relative risk	Total of A, B, and C Total	Excess	Relative risk
0–34	3,911	382	1.11	2,967	296	1.11	1,384	348	1.34	1,038	358	1.53	1,175	144	1.14	607	82	1.16	11,082	1,610	1.17
35 or greater	13,525	−80	0.99	10,701	437	1.04	3,945	263	1.07	2,716	354	1.15	9,760	950	1.11	7,909	705	1.10	48,556	2,629	1.06
Total	17,436	302	1.02	13,668	733	1.06	5,329	611	1.13	3,754	712	1.23	10,935	1,094	1.11	8,516	787	1.10	59,638	4,239	1.08

REG, the number of excess mortalities is substantial (Table 2). Almost 60,000 white people died as a result of the 3 diseases during the 2 decades. Relative risk rates were calculated by applying the 5-yr age-specific rates of the RON to the REG and subtracting the difference between the RON and REG rates. The result is excess or deficit mortalities. Whereas the 0 to 34 yr age population accounts for 19% of the mortalities (more than 11,000), it is responsible for 38% (more than 1,600) of the excess deaths (Table 2, Column 21). Briefly summarizing, the REG has significantly higher childhood and young adult leukemia, Hodgkin's disease, and lymphoma mortalities than does the RON.

Have the relative differences between the REG and the RON increased during the recent past? In particular, we sought to determine if any of the 0 to 34-yr age group rates of the REG had increased substantially more rapidly than did their RON counterparts. When combined with the static analysis results, such a finding would imply a risk factor(s) worthy of special attention.

To provide an initial perspective, trends for the entire population were studied. Differences between the REG and the RON in leukemia and lymphoma have narrowed (Table 3). The REG and RON white male leukemia and white male and female lymphoma mortality rates increased from the 1950 to 1954 period to the 1965 to 1969 period; the RON rates increased more rapidly than did the REG rates. The REG white female leukemia rate decreased, while the RON rates increased. The result in all 4 cases is a narrowing of the gap between the REG and the RON.

There is no clear trend for Hodgkin's disease. The REG rates have increased, the RON rates show less change.

With the total-population, age-adjusted rates as a perspective, analysis of the 0 to 34-yr age group rates isolated the 15 to 24-yr age group as worthy of special attention. With respect to lymphoma, the REG rate for white females ages 15 to 24 yr increased 15% (Table 4, Column 18) between the 1950 to 1959 period to the 1960 to 1969 period, and the REG/RON ratio increased from 1.24 to 1.47 (Table 4, Columns 11 and 12). Hodgkin's disease exhibits an increasing REG excess relative to the RON among white males 15 to 34 yr old (Table 4, Columns 5 and 6). The REG white male, 15 to 24-yr rate increased 11%, an increase which widened the REG/RON gap.

Table 3

Comparison of REG and RON total population, age-adjusted rates for leukemia, Hodgkin's disease, and lymphoma, 1950 to 1954, 1955 to 1959, 1960 to 1964, and 1965 to 1969

	REG/RON × 100					
	Leukemia (ICD 204)		Hodgkin's (ICD 201)		Lymphoma (ICD 200, 202, 205)	
Time period	WM[a]	WF	WM	WF	WM	WF
1950–1954	109	112	115	123	121	116
1955–1959	104	107	108	134	112	112
1960–1964	101	106	109	122	108	112
1965–1969	95	102	121	125	106	105
$\frac{\text{REG 1965–1969}}{\text{REG 1950–1954}} \times 100$	102	95	105	106	129	134
$\frac{\text{RON 1965–1969}}{\text{RON 1950–1954}} \times 100$	117	105	99	105	147	148

[a] WM, white male; WF, white female.

Table 4

Comparison of trends in the REG and RON age-specific rates for leukemia, Hodgkin's disease, and lymphoma, 1950 to 1959 and 1960 to 1969

	Index computed by (REG/RON) × 100												REG 1960–1969 / REG 1950–1959 × 100					
	Leukemia (ICD 204)				Hodgkin's (ICD 201)				Lymphoma (ICD 200, 202, 205)				Leukemia		Hodgkin's		Lymphoma	
	WM[a]		WF		WM		WF		WM		WF							
Age group (yr)	50–59 (1)	60–69 (2)	50–59 (3)	60–69 (4)	50–59 (5)	60–69 (6)	50–59 (7)	60–69 (8)	50–59 (9)	60–69 (10)	50–59 (11)	60–69 (12)	WM (13)	WF (14)	WM (15)	WF (16)	WM (17)	WF (18)
0–4	105	96	96	109	*b*	*b*	*b*	*b*	94	107	92	100	77	88	*b*	*b*	94	78
5–14	126	114	119	118	*b*	*b*	*b*	*b*	103	97	94	107	95	103	*b*	*b*	99	97
15–24	121	107	108	111	145	154	183	150	143	120	124	147	97	100	111	100	91	115
25–34	113	112	106	108	123	127	159	147	128	128	117	148	90	86	100	95	107	96
Age-adjusted total population	106	98	109	104	111	115	128	123	116	107	114	109	102	97	103	99	117	123

[a] WM, white male; WF, white female.
[b] Rate less than 0.3/100,000.

With the exception of white females ages 5 to 14 yr, the REG leukemia rates did not increase. The decrease was sufficiently great to reduce the difference between the REG and RON white male rates. The differences between the REG and RON white female rates increased in 3 of the 4 cases (Table 4, Columns 3 and 4). However, when combined with the absolute decrease within the REG, white female leukemia seems less interesting than Hodgkin's disease and lymphoma among the 15 to 24-yr age group for follow-up studies.

DISCUSSION

Why did the New Jersey-New York-Philadelphia axis have excessive rates? Could the recently identified Rutherford cluster of childhood and young adult leukemia, Hodgkin's, and lymphoma rates be related to the more general regional pattern of relatively high childhood and young adult mortality rates described above? Likewise, could this general regional finding be directly related to Vianna's findings of excess Hodgkin's cases in Nassau and Suffolk Counties and other areas in New York State (9, 10)?

Several steps are planned in an effort to answer these questions: (*a*) county rates have been prepared and are being studied. (*b*) a finer breakdown of the 3 diseases will be obtained to determine if, as expected, only a few specific types are responsible for the excess; (*c*) more recent mortality data (1970 to 1975) have been obtained to determine if the relatively high rates of the REG have changed over time; (*d*) correlations between the age-specific rates and 71 risk factors gathered by our research team (3, 4) will be made at the county scale in order to try to derive risk factor clues. The risk factors include measures of social class, ethnicity, industrial location, air quality, traffic density, and other factors that the literature suggests may be associated with the presence of these diseases. These will be evaluated using weighted and unweighted regression and correlation analyses to seek risk factor clues and counties for case-control studies in the region; (*e*) similar analyses are planned on the 25 most populous metropolitan regions in the United States to determine if the New Jersey-New York-Philadelphia axis is unique in its excess of childhood leukemia and young adult Hodgkin's disease and lymphoma cancer mortality. Overall, the findings of this first study clearly suggest the need for further analyses.

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Cancer Res 1980;40:439-443.