Adult Leukemia and Proximity-Based Surrogates for Exposure to Pilgrim Plant's Nuclear Emissions

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ABSTRACT. Possible associations between adult leukemia incidence and proximity-based surrogate measures of potential for exposure to radioactive emissions from the Pilgrim nuclear power plant in Plymouth, Massachusetts, were investigated. Included in this study were 105 nonchronic lymphocytic leukemia cases, diagnosed between 1978 and 1986 at age 13 y or older, that occurred in 22 towns near Pilgrim; population controls numbered 208. Residence within 4 mi (6.4 km) of Pilgrim during "high-emissions" years was related to case-control status (adjusted odds ratio [OR] = 3.88, 95% confidence interval [95% CI] = 0.81–10.64). A high "exposure" score (i.e., a value that accounted for downwind time) was also related to case-control status (OR = 3.46, 95% CI = 1.50–7.96). Some statistically significant dose-response trends were found. Cautious interpretation of associations is warranted in light of the low levels of reported emissions.

CITIZEN concern about potential health effects of living near nuclear facilities, as well as reports of elevated cancer rates near such plants, have served to instigate epidemiologic research. Results of early ecological analyses^{1–14} were mixed; positive findings originated mainly from the United Kingdom, where attention was focused on childhood leukemia occurrence near fuel-reprocessing plants (i.e., Sellafield [England] and Dounreay [Scotland]).

A second wave of investigations was sparked by Gardner et al., 15 who, in a case-control study, observed that a father's preconception radiation dose was related to leukemia occurrence in children born near Sellafield. The resulting controversial causal hypothesis did not appear to explain excess childhood leukemia near other nuclear plants in Great Britain. 16,17 Also, no association was found between father's preconception radiation exposure and childhood leukemia in regions of Ontario that were located near operating nuclear facilities. 18

In the United States, data were analyzed by Jablon et al.,19 who matched counties containing nuclear facilities to counties lacking such plants, and they failed to demonstrate a general increase in cancer mortality in U.S. counties that housed or were near nuclear-powered electric plants. Furthermore, Hatch et al.20 found no relationship between adult leukemia or all childhood cancers and either routine or accident emissions from the Three Mile Island plant; only weak evidence was found that linked emissions to childhood leukemia. Muirhead,21 however, who noted the study's low statistical power and susceptibility to misclassification from unaccounted-for migration, found the results predictable and called for analytical incidence studies of nuclear-plant neighbors who apparently had experienced elevated risks.

In this article, we present the results of the Southeastern Massachusetts Health Study²² (SMHS). The SMHS was a case-control study, which was conducted by the Massachusetts Department of Public Health (MDPH) at the state legislature's request on behalf of concerned citizens. The study was designed to test the hypothesis that leukemia incidence between 1978 and 1986 near the Pilgrim nuclear power plant in Plymouth, Massachusetts, was related to residential proximity to the plant and to other proximity-based surrogate measures of potential for exposure to the plant's radioactive emissions. Given the need to collect different information for young children (whose parents' exposures would be of interest) versus older individuals, interview data to date have been collected only for subjects who were over age 12 y at the time of diagnosis. The results reported here pertain only to this case series.

Descriptive analyses, in which Massachusetts Cancer Registry (MCR) data for the 1982–1984 period were used, had shown that adult leukemia incidence was elevated for Plymouth and for four towns to its north.²³ Nonetheless, comparisons of leukemia rates among

towns grouped on the basis of proximity alone had failed to reveal any evidence of a relationship.²⁴

Material and Method

Eligible cases included all persons who, during the period between 1978 and 1986, were residing in any 1 of 22 southeastern Massachusetts towns during the time they were diagnosed with leukemia (other than the chronic lymphocytic cell type). All towns were in Plymouth County; however, towns were included only if their populations were entirely or mostly contained within a circle of radius equal to 22.5 mi (36 km), centered on Pilgrim (Fig. 1). Four qualifying towns in Barnstable County (i.e., on Cape Cod) were excluded because they were included in a cancer study that was conducted concurrently with the SMHS.

Cases diagnosed before 1982 were determined from

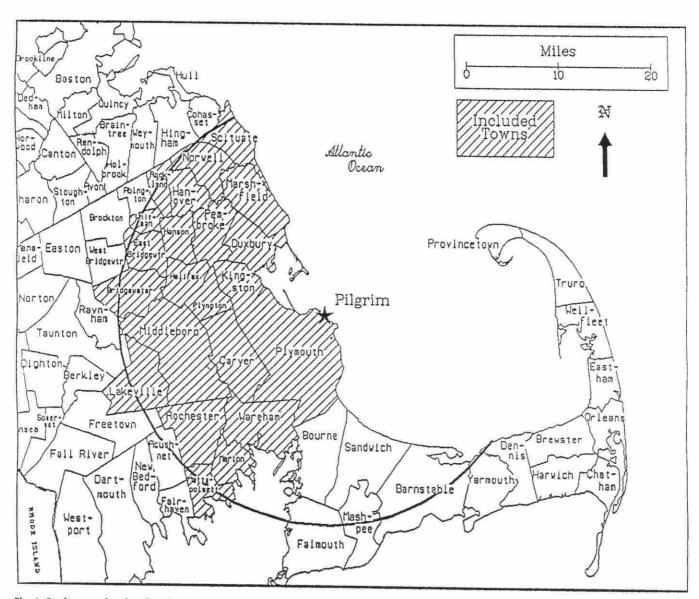


Fig. 1. Study area, showing the Pilgrim plant and the included/excluded towns within a 22.5-mi (36-km) radius.

tumor registrars or record keepers at 25 area hospitals that had ever reported leukemia cases from the 22 towns to the Massachusetts Cancer Registry (MCR) since its founding in 1982. Five additional hospitals located on the outskirts of the 22-town area were also contacted, but two refused to participate, and three reported no cases. Given that several hospitals were unwilling to re-ascertain cases diagnosed during the years of mandatory reporting to the MCR, the registry constituted a major source of cases diagnosed after 1981.

Those cases who had been diagnosed between 1982 and 1984 and who had resided in Plymouth, Kingston, Duxbury, Marshfield, and Scituate (i.e, 27 of the 115 cases over age 12 y ascertained by the SMHS), had been used previously to demonstrate excessive leukemia incidence near Pilgrim.^{23,24} Two controls were matched to each case for age (within 5 y), sex, vital status, and year of death; in addition, each control must have been residing in 1 of the 22 towns during the same year the corresponding case was diagnosed with leukemia.

Controls for deceased cases (i.e., 88.6% of all cases) were selected by a stratified random-sampling procedure from a printout provided by the Massachusetts Registry of Vital Records and Statistics. All individuals were listed who had died of nonexcluded illnesses between 1978 and 1987 and who were permanent residents of the 22-town area. Excluded illnesses were those suspected of being associated with diseases or exposures under study (i.e., leukemia; chronic obstructive lung disease; tuberculosis; and cancers of the mouth, larynx, pharynx, esophagus, lung, pancreas, kidney, or bladder).

Controls for living cases were all over age 15 y, and all were selected randomly from the 1987 or 1988 town street directories. In accordance with state law, all town residents over age 16 y are listed in these directories. Four controls were selected for each case to help ensure the availability of 2 eligible participants from the original 4. Alternates in case-control sets in which the 2 first-choice controls had agreed to participate were not pursued unless needed to replace controls for cases for whom all 4 potential controls had been depleted.

Historical data pertaining to residence, occupation, health, and sociodemographics were collected from the subjects or their surrogates (when subjects were deceased) during a 45-min telephone interview conducted by trained staff. Introductory letters were sent to prospective respondents (i.e., case, control, or surrogate respondent) at least 10 d prior to the date of attempted telephone contact. In each letter, the aims of the study and data-collection process were explained, and respondents were advised about the types of questions that would be posed to them during the interview. Blank residential- and occupational-history forms were sent with the letters to encourage respondents to recall or obtain the required information before the interview.

Although the controversy surrounding plant safety had been covered by local media (as had the start of this health study), a conscious effort was made during communications with respondents to avoid mention of the outcome under investigation and the exposure of interest. More specifically, the study was introduced merely as a health survey, and no mention was made in letters or scripts of leukemia, nuclear power, or the

Pilgrim plant.

To keep interviewers blind to case-control status, we devised a coding scheme to distinguish cases from controls; however, many respondents were interviewed by individuals familiar with the study design and coding scheme. The interview began by ascertaining the subject's address during the case's diagnosis year, followed by a request for a list of all addresses at which the subject had resided during the preceding 40 y. With respect to each address listed, the following were noted: year the subject had moved to the residence, number of years at residence, and details about the home and the neighborhood during the subject's residence there. If there were any gaps in history, individuals were asked to focus on their own ages and the ages of their relatives during the period in question.

Potential for exposure to airborne radioactive noble gases emitted from Pilgrim was determined via two crude surrogate methods. In the first method, residential proximity to the plant between 1974 and 1977 (i.e., years of higher-than-normal radioactive releases) was used as the exposure-potential index. The distance used for individuals (6% of all subjects) who had occupied multiple residences during that time period was a weighted average of the distances applicable to all qualifying addresses. In a four-category parameterization of the proximity variable, 4 mi was selected arbitrarily as the cutoff point between those with the highest potential for exposure and those with less exposure potential. The other cutoff points corresponded to the 25th and 75th percentiles of the resi-

dential-proximity distribution.

Exposure was also assessed by a score, calculated from each individual's residential and worksite histories and meteorologic and emissions data supplied by plant officials. The inverse square law26,27 was applied to the distances between the plant and each residence and worksite occupied for at least 3 mo during the period of interest. The resultant terms were weighted by factors representing (a) the proportion of time typically spent at work (1/3) and at home (2/3), (b) the percentage of time each location was downwind of Pilgrim during the specified year, and (c) the extent to which reported emissions of noble gases for the year exceeded a "normal" level. In all years, except for the mid-1970s, emissions of radioactive noble gases were kept at or below 1 000 TBq,²⁸⁻³⁰ which was considered "normal" for exposure-assessment purposes. Levels reported during the mid-1970s ranged from 2 000 to 15 000 TBq. Annual emissions-weighting factors equaled the amount of radioactivity (in TBq) in the form of noble gases emitted in a given year divided by 1 000. Annual exposure scores were summed over the years of interest to yield each individual's summary exposure score. Unbiased division of the continuum into four categories was accomplished by establishing cutoff points at the 25th, 50th, and 75th percentiles of the distribution. The scores were not intended to represent radiation doses; instead, they were used to provide a proximity-based—but more refined—alternative to residential proximity

alone as a crude surrogate for exposure.

Risks were estimated by conditional logistic regression, as performed by the proportional-hazards general linear modeling program of the Statistical Analysis System (SAS).³¹ Candidate terms for the final model were selected a priori and included terms for work in a priori–specified "high-risk" occupations and industries, work in occupations and industries associated with leukemia risk in this data set, cigarette smoking, and socioeconomic status (SES). The stratification of SES was accomplished using Hollingshead and Redlich's method,³² which is a numerical scoring system in which values are assigned to educational level and occupation, after which they are combined via a simple formula into an index of social position.

To account for induction time, we ignored the portion of the subject's (case's or control's) history that occurred within 5 y of the case's leukemia diagnosis. To determine whether control replacement and the use of deceased controls had biased the comparison group geographically, we compared the proportion of the 208 participating controls that had resided in each town during the matched case's diagnosis year to the townspecific proportion of the 22-town population (i.e., the sum over the 22 towns of the averages of the towns' 1980 and 1985 populations). We grouped towns into zones, based on proximity to Pilgrim, so that group comparisons could also be made. Towns that did not fit entirely into a zone were assigned to the zone to which most of the town's population was attributable. The population of Hanson, which was bisected by a demarcation line, was split between two zones.

Results

Ascertainment of cases. A total of 115 cases of nonchronic lymphocytic leukemia were ascertained for the 1978–1986 period. Forty-three cases had been diagnosed between 1978 and 1981, and 72 had been diagnosed between 1982 and 1986. The majority (70%) had myelogenous cell types, and the remaining 30% was split approximately equally between acute lymphocytic-type leukemia and rare or unclassifiable forms.

Response rate. Interviews were completed successfully for 105 (91%) of the 115 cases of nonchronic lymphocytic leukemia ascertained. Prospective respondents for 313 controls were contacted to complete 208 control interviews (control response rate = 66%), resulting in 2 matched controls for each of the 103 (of 105) cases and 1 matched control for each of the remaining 2 cases. Sixty-four percent of the nonresponses reflected a refusal to be interviewed; 34% resulted from the failure to locate a subject or a surrogate respondent.

Control distribution versus expectation. The proportion of participating controls that resided in each town and in each proximity grouping (or zone) during the matched case's diagnosis year (Table 1) was similar to the corresponding proportion of the 1980–1985 22town population.

Potential confounders and matching factors. Cases and controls were well matched with respect to matching factors (Table 2). Relaxation of the vital-status matching criterion for young subjects, however, biased the control group slightly toward living subjects. Despite the stricter residence requirements imposed on controls versus cases by the sampling frames, controls resembled cases according to various indices of residential history in the study area. A statistically significantly greater percentage of controls versus cases had smoked, and a statistically significantly greater percentage of cases versus controls had been employed in a priori–specified "high-risk" occupations or industries (i.e., those that afforded opportunity for exposure to chemicals, fumes, or radiation).

Stepwise selection of model terms. Terms that added significantly to a model that already included terms for proximity or for the Pilgrim-exposure score were those that pertained to work history and cigarette smoking. Terms for SES did not add to the model, and their removal did not alter main-effect estimates.

Results of proximity-based analyses. The ORs relating leukemia risk for all subjects to residential proximity to Pilgrim (Table 3) were consistently greater than 1.0 and tended to increase as proximity to Pilgrim increased. The small group of subjects that had resided within 4 mi of Pilgrim had 3.88 (95% CI = 0.81–10.64) times the leukemia risk of those who had lived ≥ 23 mi from Pilgrim.

Results obtained for males were similar to results obtained for females, the only exception being the magnitude of the OR associated with the highest exposure-potential category (i.e., 5.14 [95% CI = 0.31–84.17] for males and 3.46 [95% CI = 0.50–23.73] for females). None of the individual ORs were statistically significantly greater than 1.0, but, for the full data set, the ORs increased significantly as proximity to the plant increased. Results of distance-based analyses were generally similar for two separate time periods (Table 4), during each of which approximate the content of th

mately half the cases were diagnosed.

Results of score-based analyses. We also used the exposure score as an index of exposure potential (Table 3), and all ORs exceeded 1.0 when effects of higher exposure potential were compared with effects of lower exposure potential. Furthermore, when data for all males and females were combined, we observed a statistically significant linear trend in the ORs, and 95% Cls for ORs excluded 1.0. Although all relative risk estimates for males exceeded 2.0-and CIs excluded or nearly excluded 1.0-a linear trend was not obvious. The ORs estimated for female subjects, however, exhibited a strong linear trend, and individuals with the highest exposure scores had a statistically significantly greater risk of leukemia (OR = 5.19, 95% CI = 1.83-15.70) than did individuals with the lowest exposure scores.

Table 1.—Distribution of the 208 Participating Controls, by Town of Residence for Cases at Time of Diagnoses (y) Versus the Source Population*

Proximity Zone†	Miles between zone boundary and Pilgrim	Town‡	Population (%)	Controls (%	
1	≤ 8.0	Plymouth	14.1	13.0	
2	8.1-13.2	Carver	2.7	3.8	
		Duxbury	4.5	2.9	
		Kingston	2.9	2.4	
		Marshfield	7.8	9.1	
		Plympton	0.8	0.5	
		Total	18.7	18.7	
3	13.3-17.0	Halifax	2.1	1.0	
		Hanson (eastern)	1.6	0.0	
		Pembroke	4.9	5.8	
		Wareham	7.1	9.6	
		Total	15.7	16.4	
3	> 17.0	Bridgewater	7.3	5.3	
		East Bridgewater	3.8	3.4	
		Hanson	4.2	4.8	
		Hanson (western)	1.6	3.8	
		Lakeville	2.4	3.8	
		Marion	1.6	1.9	
		Mattapoisett	2.2	3.4	
		Middleboro	6.2	5.8	
		Norwell	3.4	3.8	
		Rochester	1.2	1.4	
		Rockland	5.9	5.8	
		Scituate	6.7	5.3	
		Whitman	5.0	3.4	
		Total	46.5	48.5	

*Town-specific 1980/1985 average population aged ≥ 13 y.

†Proximity zones were defined by drawing concentric circles around Pilgrim.

‡A town's assigned zone was the zone that contained most of its population.

Discussion

Our findings were generally supportive of the hypothesis that the diagnosis of adult nonchronic lymphocytic leukemia between 1978 and 1986 in southeastern Massachusetts was related to both residential proximity to Pilgrim during the "high-emissions" years and to a score designed to account for residential and worksite proximity and downwind time for the plant's entire operating history. Several factors, however, do not support a causal interpretation of these unexpected results. Among such factors is the Nuclear Regulatory Commission's estimated dose of 120 person-rem for the 22-town population, resulting from Pilgrim's 1972-1981 reported radioactive releases.33 This estimated dose represents an elevation over background levels, the possible effect of which has been likened to that of residing in Denver, Colorado (e.g., at high altitude) versus Boston.34 Consequently, without hypothesizing unreported emissions, a radionuclide-concentrating mechanism, or a previously unknown effect of exposure to low levels of ionizing radiation, the associations described here could not be explained by Pilgrim's radioactive releases. Although in some studies

leukemia occurrence has been linked to residence near nuclear plants,^{3,5–10,15} interpretation of these studies has remained very controversial.³⁵ Furthermore, the bulk of the research focused on childhood leukemia, and, in most cases, the facilities in question released high levels of radioactivity from nuclear-fuel reprocessing. Sellafield—the most studied of the plants—also experienced a major accident. There have also been problems at Pilgrim, but the plant had been cited by the Nuclear Regulatory Commission for management problems (and not radioactive releases),³⁶ and a proposed wind-mediated radionuclide-concentrating mechanism^{23,25} has failed to garner support from the scientific community.^{37,38}

The highest ORs reported were obtained from comparisons involving small numbers of exposed subjects. Furthermore, results of subgroup analyses tended to vary somewhat, depending on the category cut points used.

We considered the estimation of individual radiation doses to be beyond the scope of this state-funded study; nevertheless, there was potential for misclassification from the use of crude surrogate measures, thus

Table 2.—Case-Control Comparisons: Matching Factors and Other Attributes

	Cases (n = 105	Controls ($n = 208$		
Factor	No.	%	No.	%	
Gender					
Male	64	61.0	126	60.6	
Female	41	39.0	82	39.4	
Vital Status					
Living	12	11.4	34	16.3	
Deceased	93	88.6	174	83.7	
Age (y)					
13-18	6	5.7	5	2.4	
19–24	5	4.8	12	5.8	
25-39	10	9.5	23	11.1	
40-54	20	19.0	34	16.3	
55-69	26	24.8	62	29.8	
70-84	26	24.8	55	26.4	
≥ 85	12	11.4	17	8.2	
Mean age (SD)*	59 (21.7)		59 (20.4)		
SES† percentile					
Below 25th	25	23.8	50	24.0	
25th -75th	52	49.5	108	51.9	
Above 75th	26	24.8	50	24.0	
Unknown	2	1.9	O	0.0	
Cigarette smoking‡	54	51.4	128	61.5	
"High-risk" work history§	40	38.1	50	24.0	
Residence in study area since plant start-up	75	71.4	150	72.1	
Mean y in area (SD)*	18 (12.7)		19 (11.4)		
Residence in one zone since start-up Number of addresses	71	67.6	135	64.9	
occupied within 40 y of case diagnosis < 4	59	56.2	107	E1 W	
4-5	26	24.8	52	51.4 25.0	
4-3 ≥ 5	20	19.0	49	23.6	
Number of jobs held within 40 y of case	20	13,0	43	23.0	
diagnosis					
0	11	10.5	26	12.5	
1-2	50	47.6	96	46.2	
3-4	29	27.6	56	26.9	
≥ 5	15	14.3	30	14.4	

^{*}p > .05 for t test comparing means.

constituting a major methodologic weakness. To model exposure potential, we relied—as have many others—on plant proximity; only crude attempts were made to factor in meteorologic and emissions data, and certain variables (e.g., terrain, elevation) were ignored, even in the scoring system. Another potential source of misclassification bias was the reliance on self- and surrogate-reported data. Although inaccurate reporting of residence was unlikely,³⁹ misclassification of occupation and/or SES might have effected incomplete control

of confounding by these factors. Gender differences noted in results gleaned from score-based analyses may have reflected misclassification of males because of their greater tendency to have worked, compared with females.

We assumed a 5-y latent period for leukemia after radiation exposure. This implied that subjects were considered unexposed if their entire period of residence near Pilgrim had occurred within 5 y of diagnosis. If the latent period was often shorter than 5 y, subjects may have been misclassified. The potential for misclassification of residence was limited, however, because of the brief period of interest (i.e., 1972 to 5 or 2 y before diagnosis). Only 11 cases and 13 controls would have been classified differently with respect to residence during the "high-emissions" years under a 2-y versus 5-y latency assumption. Crude analyses in which case-control status was related to residential proximity during the mid-1970s revealed higher values for 11 of 15 ORs calculated under a 2-y latency assumption; only 1 value was found to be lower.

The following three design features could have resulted in spuriously elevated ORs that related plant proximity to case-control status: (1) exclusion of Cape Cod cases from the study, (2) heavy reliance on MCR data for case finding, and (3) use of a geographically limited selection of hospitals. Hospital and MCR data and population figures lead us to suggest that, had the four qualifying Cape Cod towns been included, ORs ratios would have been lower than reported. Such ecological comparisons can be misleading, however, because they are based on aggregate statistics, which can be inaccurate, and because they ignore the influence of potentially confounding factors. Furthermore, although news reports of elevated cancer rates near Pilgrim—and the hypothesis that Pilgrim was the cause-might have resulted in geographically biased reporting of leukemia cases to the MCR, neither reviews of leukemia death certificates nor analyses of discharge data from hospitals not used for case finding provided evidence of biased ascertainment. Also reassuring was the fact that 91% of the nonchronic lymphocytic leukemia cases, that were from the MCR as 1982–1986 diagnoses attributable to the 22-town area, were diagnosed at a major Boston hospital, a Brockton hospital, or at one of three southeastern Massachusetts hospitals; all of these hospitals were included in the case-finding effort.

Bias could also have been introduced by the use of a deceased control group, by the imposition on controls (but not cases) of a 1987–1988 22-town residence requirement, and by low response from controls. It was clear from the smoking data that use of deceased controls resulted in case-control differences. It has been demonstrated previously that an unhealthy lifestyle (particularly one that features cigarette smoking) is associated with premature death. ⁴⁰ This does not automatically imply, however, that deceased controls would be different from the target population in every important respect. Results of our comparison of the geographic distribution of controls to the distribution of the 22-town population supported the contention that the con-

tSES determined by Hollingshead Index.

[‡]Cases were less likely to have smoked than controls (p < .05). §Cases were more likely than controls (p < .05) to have been employed for ≥ 6 mo in a job or industry likely to result in exposure to chemicals, fumes, or radiation.

Table 3.—Relative Risk* of Leukemia, by Distance from Pilgrim During High-Emissions Years, and by Pilgrim-Exposure Score

	Distance-based analyses					Score-based analyses				
Subjects	Distance (mi)	Cases (n = 105)	Controls $(n = 208)$	OR	95% CI	Exposure score	Cases (n = 105)	Controls $(n = 208)$	OR	95% CI
Males and	≥ 23.0	21	57	1.00		≤ 0.04	16	61	1.00	
femalest	13.0-22.9	52	109	1.44	0.68 - 3.01	0.04-0.28	28	48	2.12	1.02-4.39
	4.0-12.9	27	39	2.25	0.96 - 3.63	0.29 - 0.72	30	55	2.77	1.20-6.39
	< 4.0	5	3	3.88	0.81 - 10.64	≥ 0.73	31	44	3.46	1.50-7.96
Males	≥ 23	12 32	33	1.00		≤ 0.04	9	37	1.00	
	13.0-22.9	32	65	1.53	0.53 - 4.40	0.04-0.28	18	25	2.61	0.98 - 6.97
	4.0 - 12.9	18	27	2.29	0.71 - 7.37	0.29 - 0.72	20	33	3.19	1.08-9.39
	< 4.0	2	1	5.14	0.31 - 84.87	≥ 0.73	17	31	2.83	0.95 - 8.41
Subtotal		64	126				64	126		
Females‡	≥ 23.0	9	24	1.00		≤ 0.04	7	24	1.00	
	13.0-22.9	20	44	1.32	0.45 - 3.88	0.04 - 0.28	10	23	1.53	0.49-4.73
	4.0 - 12.9	9	12	2.31	0.62 - 8.70	0.29-0.72	10	22	2.16	0.56-8.23
	< 4.0	3	2	3.46	0.50-23.73	≥ 0.73	14	13	5.19	1.83-14.70
Subtotal		41	82				41	82		

^{*}Odds ratio (OR), adjusted for the matching factors, cigarette smoking, and "high-risk" work.

Table 4.—Relative Risk* of Leukemia, by Distance from Pilgrim During High-Emissions Years and Time Period

Distance (mi)	1978–1982†				1983-1986†			
	Cases (n = 52)	Controls $(n = 104)$	OR	95% CI	Cases (n = 53)	Controls $(n = 104)$	OR	95% CI
≥ 23.0	14	31	1.00		7	26	1.00	
13.0-22.9	21	50	1.18	0.37 - 3.72	31	59	1.72	0.64-4.58
4.0 - 12.9	15	22	2.13	0.62 - 7.31	13	17	2.44	0.74 - 8.09
< 4.0	2	1	5.21	0.35-77.82	-3	2	3.46	0.50-24.05

^{*}Odds ratio (OR), adjusted for the matching factors, cigarette smoking, and "high-risk" work.

trol group was not biased geographically. Furthermore, most case-control comparisons provided evidence against the hypothesis that case and control groups differed; the two groups resembled each other with respect to SES, number of job changes, and residential history. On the other hand, controls were less likely than cases to have been employed in "high-risk" jobs or industries. However, the specific jobs and industries responsible for this difference (i.e., driving; precision production work; and employment in the transportation, leather, and shoe industries) implied a causal association, rather than bias.⁴¹

Possible leukemia correlates, other than exposure to Pilgrim's radioactive releases, that might have varied geographically included exposure to pesticides sprayed on cranberry bogs, exposure to radiation from medical procedures, exposure to electric and magnetic fields, and exposure to environmental pollutants other than radiation. A term for potential exposure to cranberry bogs (parameterized as "residence within half a mile of a bog") did not enter multivariate models. Nor did a term that crudely accounted for medical radiation exposure (i.e., number of radiographic procedures weighted for exposure differences among different types of procedures). Both terms, however, were derived from interview data that could have been inaccurate for these variables. We did not collect data on other sources of radiation or on other environmental pollutants.

Finally, we address the questionable practice discussed by Black⁴² and MacMahon³⁵ of selecting study areas based on prior information regarding disease occurrence. Although this research may not have been undertaken had Clapp et al.²³ not reported in 1987 that leukemia occurrence was elevated near Pilgrim, the hypothesis we addressed was generated by the British studies of the early 1980s—and not by the data of Clapp

[†]p < .05 for test for linear trend over distance and score categories.

 $[\]pm p < .05$ for test for linear trend over score categories.

tp > .05 for test for linear trend over distance categories.

et al. The data of Clapp et al generated a controversial hypothesis pertaining to the capabilities of sea breezes that we chose not to address. Instead, our goal was to apply a stronger study design (i.e., an analytical one) to the hypothesis that had been addressed previously only by the descriptive-level data of Poole et al.24

The methods employed in this investigation were superior to those used in many other studies of this problem, but the exposure-assessment scheme was still crude, and findings should be interpreted cautiously. We recommend analytic studies of populations that reside near other U.S. nuclear facilities and the use of more sophisticated exposure-assessment methods, when feasible.

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