Leukemia, Lymphomas, and Myeloma Mortality in the Vicinity of Nuclear Power Plants and Nuclear Fuel Facilities in Spain[1]

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Abstract

Mortality due to hematological tumors in towns near Spain's seven nuclear power plants and five nuclear fuel facilities during the period 1975–1993 was ascertained. The study was based on 610 leukemia-, 198 lymphoma-, and 122 myeloma-induced deaths in 489 towns situated within a 30-km radius of such installations. As control areas, we used 477 towns lying within a 50- to 100-km radius of each installation, matched by population size and a series of sociodemographic characteristics (income level, proportion of active population engaged in farming, proportion of unemployed, percentage of illiteracy, and province). Relative risk (RR) for each area and the trends in risk with increasing proximity to an installation were analyzed using log-linear models. None of the nuclear power plants registered an excess risk of leukemia-induced mortality in any of the surrounding areas. Excess risk of leukemia mortality was, however, observed in the vicinity of the uranium-processing facilities in Andújar [RR, 1.30; 95% confidence interval, 1.03–1.64] and Ciudad Rodrigo (RR, 1.68; 95% confidence interval, 0.92–3.08). Excess risk of multiple-myeloma mortality was found in the area surrounding the Zorita nuclear power plant. Statistical testing revealed that, with the single exception of multiple myeloma, none of the tumors studied showed evidence of a rise in risk with proximity to an installation. No study area yielded evidence of a raised risk of leukemia mortality among persons under the age of 25 years. More specific studies are called for in areas near installations that have been fully operational for longer periods. In this connection, stress should be laid on the importance of using dosimetric information in all future studies.

Introduction

Because of the contradictory nature of their results, studies into cancer incidence and mortality in areas near nuclear installations have not served to dispel existing doubts as to the possible adverse population effects of radioactive discharges emanating from the routine running of such installations. The report that appeared in late 1983 concerning a cluster of leukemias in young residents living in the vicinity of a nuclear fuel reprocessing plant in Sellafield (England) resulted in a considerable amount of investigation. In the main, this research has tended to focus on leukemias in persons under the age of 25. There has been confirmation of excess risk of childhood leukemias in areas near the Sellafield plant (1, 2), the Dounreay and Hunterston facilities in Scotland (3–6), and the Aldermaston Atomic Weapons Establishment (7, 8) in England. Reports have also been received of excess risk of leukemia- and lymphoma-related mortality in the proximity of some NPPs[3] (9–11). Etiological studies have in turn been conducted in an effort to ascertain the role played by radiation from such installations in disease (12–15). A considerable number of studies carried out in different countries have reported an absence of risk in areas around NFFs and NPPs (16–24). Radioactive discharges in the vicinity of these kinds of installations involve very low doses, far below the level of natural background radiation. It has, therefore, been argued that these doses are unable to account for the excess risk of the incidence of certain malignancies, thus giving rise to a number of alternative hypotheses (10, 13, 25).

Whatever the case, the role played by exposure to low levels of ionizing radiation in the etiology of cancer continues to stimulate debate and study. The epidemiological designs most favored for the purpose of investigating this possible relationship are: (*a*) follow-up of worker cohorts with dosimetric controls (26–30); (*b*) case-control studies, basically of childhood leukemias (8, 12, 13, 31, 32); and (*c*) cancer incidence and mortality studies in populations residing near and around nuclear installations (9, 17, 33–35).

Spain currently has 7 NPPs, with a total of 10 reactors (9 fully operational and 1 in the process of being dismantled) and nine nuclear fuel facilities (three fully operational, one shut down and five in the process of being dismantled). Although the country's first NPP came into operation in 1968, no study has ever been conducted to assess the specific risk faced by populations residing near these kinds of installations. Mortality drawn from death certificates was the only nation-wide source of information in Spain, on which a first analysis of this nature could be based. We, therefore, proceeded to carry out a cancer mortality study covering towns situated in the proximity of NPPs and NFF. This paper reports on the results of that study

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[3] The abbreviations used are: NPP, nuclear power plant; NFF, nuclear fuel facility; NWSF, nuclear waste storage facility; SMR, standardized mortality ratio; ICD, International Classification of Diseases; RR, relative risk; CI, confidence interval.

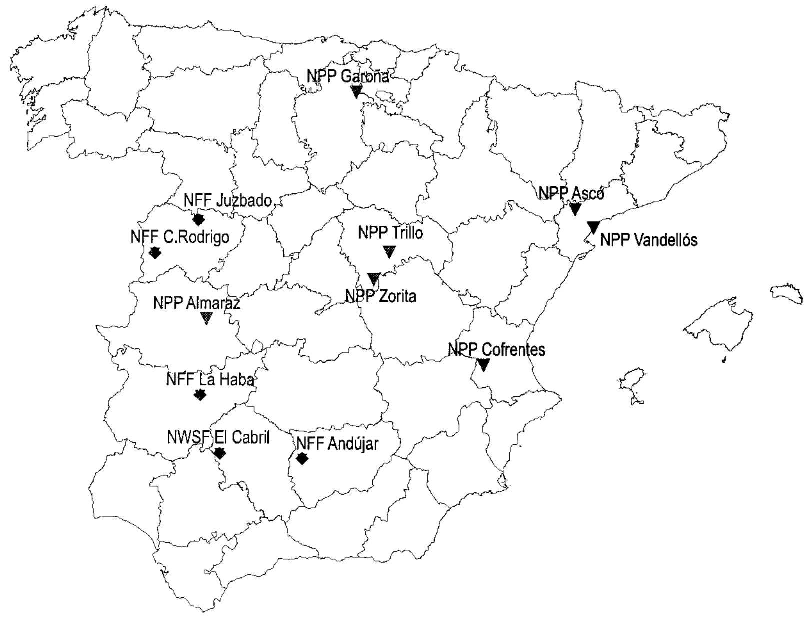

Fig. 1. Sites of NPPs and NFFs in Spain.

with respect to leukemia, lymphomas, and multiple-myeloma mortality. The analysis presented here sought: (*a*) to quantify the RR of death in the vicinity of such installations; (*b*) to ascertain said risk before and after the date on which these installations first came into operation; (*c*) to study changes in risk in accordance with the subjects' relative proximity to the respective installations; and (*d*) given the descriptive and exploratory nature of this study, to provide additional pointers for new research.

Materials and Methods

We studied cancer mortality in towns situated near 7 NPPs with 10 reactors that had been operational in the period 1975–1993 and 5 NFFs that had been operational in the same period. With the exception of El Cabril, which is a NWSF built on the site of an abandoned uranium mine, the NFFs are uranium-concentrate processing facilities located in mining areas where the ore is extracted. Of the remaining installations, three were excluded because they were experimental research reactors and a fourth because it came into service in 1993. Fig. 1 shows the site of these installations. This was a retrospective cohort study whose population base was made up of the inhabitants of towns neighboring the nuclear installations under review. For the purposes of description and analysis, the area falling within a 30-km radius of any such installation was called the "exposed zone"; and towns (selected as outlined below) lying within a 50–100-km radius of said installation were called the "reference zone." Although the choice of a 30-km radius was arbitrary, it roughly coincides with the area used in other studies.

UTM-format (Universal Transversa Mercator projection) centroid coordinates for municipal population centers were furnished by the National Geographical Institute (*Instituto Geográfico Nacional*). With the aid of a Geographic Information System, these coordinates were used to measure the distance from the population centroids to the nuclear installations. Distances so calculated were then subjected to quality control, involving manual checking of the accuracy of measurement against a random sample of 50 population centroids plotted on Army Geographical Unit maps, drawn to a scale of 1:50,000 and showing the precise position of the NPPs. The measurements obtained proved accurate in all cases.

Follow-up covered the period January 1, 1975, to December 31, 1993. For all of the NPPs as a whole, 316 towns within a 30-km radius and 303 within a 50 to 100-km radius were included in the study, matched by income level, number of inhabitants, proportion of the active population engaged in farming, proportion of unemployed, percentage of illiteracy, and province. These towns were selected at random from among all of those that met the matching conditions. For all of the nuclear fuel facilities as a whole, 173 (there were originally 177, but four towns merged with another two) and 174 towns in the exposed and reference zones, respectively, were included in the study, matched as above. The small disparities in the number of towns were attributable to changes in municipal boundary lines between 1981 and 1991 or to the impossibility of matching. The study covered a total of 644,044 persons in the exposed zone for all types of installations. Sociodemographic data were taken from the 1991 census (36) and information on income levels was taken from the Spanish Market Yearbook (*Anuario del Mercado Español*; Ref. 37). The distance chosen excluded all of the towns lying between 30 and 50 kms of any nuclear facility.

This paper presents the results on mortality due to leukemias (ICD-8 204–207, ICD-9 204–208), Hodgkin's disease (ICD 201), non-Hodgkin's lymphomas (ICD 200, 202) and multiple myeloma (ICD 203). The latency periods used were 1 year for leukemias (38) and 10 years for all other tumors. A latency period of 10 years rules out the possibility of studying cancer mortality other than that due to leukemias for the areas surrounding the Ascó, Cofrentes, Trillo and Juzbado facilities, because all these plants were inaugurated relatively recently. Data specific to this study were supplied on computer files by the National Statistics Institute (*Instituto Nacional de Estadística*). Individual records were broken down by cause, sex, age group, year of death and town of residence. Town-of-residence data for deceased persons are treated as confidential in Spain in the case of towns having fewer than 10,000 inhabitants, thus calling for a special agreement with the National Statistics Institute for the purposes of this study.

To obtain a population breakdown by sex, age, and year for towns included in the study, recourse was had to the 1981 population census, 1986 municipal roll, and 1991 census, as furnished by the National Statistics Institute. 1981-census data were restricted to towns of over 5000 inhabitants, so that the 1981 age-based distribution of populations in towns of under 5000 inhabitants had to be estimated on the basis of the 1986 and 1991 distributions, by categorizing age into 5-year age groups (18 groups) and using a procedure appropriate for small localities (39). Relying on a log-linear polynomial regression model (39), interpolation was used to estimate annual municipal population figures for the period 1981–1991. Pre-1981 and post-1991 populations were extrapolated by adopting a linear procedure, allocating more weight to the nearest census year. With the annual population estimates for each town, person-years for each age band (0–4, 5–14, 15–24, 25–34, 35–44, 45–54, 55–64, 65–74, and 75+), sex, and period (1975–1978, 1979–1983, 1984–1988, and 1989–1993) were then calculated, taking into account those variables that had changed over time, such as operational start-up of reactors and installations.

For analysis purposes, log-linear models were fitted on the assumption that the number of deaths per stratum followed a Poisson distribution. In these models, observed cases were the dependent variable and, as an external standard (40), concurrent Spanish cause-specific mortality rates were used, with expected cases being computed by age, sex, and time period for each town in the exposed and reference (control) zones. Expected cases were included as offset in the models. A term that we called "exposure" (a radius of 30 km or less from the facility), was included as the independent variable. The regression coefficient of this exposure term provided us with the logarithm of the ratio between the respective SMRs for the exposed and reference zones, something that we, in a departure from the traditional use of the term, called "relative risk" (RR). This estimator was adjusted for age, sex, time period, and matching variables. In the case of leukemia-related mortality, results specific to the under-25 age group are shown.

Similar models were fitted to study the effect of distance on mortality. This variable was constructed by categorizing distances in the 0–30-km belt into 5 levels (consisting of circular sectors having equal surface areas) and using towns situated at a distance of 50–100 km as the reference level. Expressed in kilometers, the cutoff points for the intervals were as follows: 0-, 13.4-, 19.6-, 23.2-, 26.8–30, and 50–100. This was included in all of the models both as a categorical and as a continuous variable (in kilometers), which rendered it possible: (*a*) in the former case, to estimate the effect for the respective distances; and (*b*) in the latter case, to ascertain the existence of radial effects (rise in RR with increasing proximity to an installation) and, by applying the likelihood ratio test, the statistical significance of such distance-induced effects. Matching variables were included in this analysis as continuous covariates centered around their mean to ensure control of possible gradients in these variables with proximity to the installation. In view of the heterogeneity of the installations, we ran specific analyses on individual installations and a joint analysis on all the installations.

We studied changes in risk by comparing the position before and after the date on which NPPs and fuel facilities first came into operation (start-up), taking latency periods into account. These periods were included in the assessment of risk before start-up. The statistical significance of this change was obtained by means of the likelihood ratio test, which evaluates the interaction term, *exposure* × *plant operation*, in regression models.

RR CIs were calculated using the SEs of the parameters yielded by the model. Model results were checked and corrected for over-dispersion problems (41) using the robust methods recommended by Breslow (42) for the purpose because these methods are insensitive to the form adopted by variance.

Results

Table 1 sets out the socioeconomic characteristics of populations residing near nuclear installations. According to the 1991 census, the study populations in 30-km belts totaled 302,861 and 341,203 for NPPs and NFFs, respectively. Furthermore, Table 1 shows these contributions to the study in terms of person-years.

Tables 2 and 3 show the number of observed deaths, SMRs, for the reference zones and areas in a radius of 0–15 and 0–30 km of each installation, and the RRs and CIs yielded by comparison with the reference zones for both sexes and across all of the age groups, for the different causes studied. Table 4 shows RR by reference to the distance from the respective installations, for tumors causing a minimum of 10 deaths. The results of the pre-and post-start-up analyses are quoted in Table 5.

NPPs. In essence, the results (Table 2) revealed excess risk of multiple myeloma mortality in the Zorita power plant area. This was the sole tumor to register a mortality higher than expected, and one that was statistically significant in the context of this installation's surroundings. The RR for leukemias in the area nearest the plant (0–15 km) was 1.58 (95% CI, 0.81–3.67). Analysis of the distance variable (Table 4) showed a statistically significant increase in myeloma with proximity to the installation and a RR rising to a maximum in the 13–19-km sector.

In the exposed zone around the Vandellós power plant (Table 2), the RR for leukemias was 1.19 (95% CI, 0.82–1.73). Within a 15-km radius, the RR for leukemias was 1.59. Yet on categorization and application of the statistical test, none of these diseases appeared to evince (distance-related) radial effects (Table 4).

Because of the fact that Ascó, Cofrentes, and Trillo came into operation relatively recently, only the results for leukemias are shown (Tables 2 and 4). In no case did the pattern of risk prove remarkable.

The results for leukemias among the under-25 age group are shown in Table 2. The number of cases was very low overall, Garoña being the only installation where the RR exceeded 1, though even here, the excess risk was not statistically significant.

The last column in Table 4 shows the *P* for trend of the effect according to distance. The only malignancy to register a clear and statistically significant distance-induced gradient (radial effect) was multiple myeloma in Zorita.

With respect to leukemias, the pre-and post-start-up mortality levels proved very similar for the three areas in which the study was feasible. In the case of multiple myeloma, the post-start-up risk proved higher for the Zorita and Garoña catchment areas, yet the increase was not statistically significant.

NFFs. Table 3 shows the RRs for the nuclear fuel facilities. The Andújar area registered excess leukemia mortality (RR 1.30; 95% CI 1.03–1.64). In the 15-km sector surrounding the Ciudad Rodrigo facility, the RR was 1.68 (95% CI, 0.92–3.08). In all, 14 of the 30 deaths took place in the Ciudad Rodrigo metropolitan area.

Table 1 General characteristics of populations studied in areas adjacent to nuclear power plants and fuel facilities

	Population[a]		Person-years (thousands)		Percent			Average income	Average population
	Total	<25 yr	Latency 1y[b]	Latency 10y[c]	Illiteracy	Unemployed	Farming		
NPPs[d]									
Zorita (1968)[e]									
0–30 km	25,816	7,305	538.9	415.8	5.6	10.4	22.7	6.2	461.0
50–100 km	29,914	9,293	558.5	440.5	4.5	10.9	18.8	6.5	564.4
Garoña (1971)									
0–30 km	57,625	20,236	1,328.2	897.5	1.3	13.4	12.7	6.7	992.3
50–100 km	50,060	15,475	987.9	670.2	1.1	14.7	23.4	7.0	725.7
Vandellós (1972)									
0–30 km	73,594	26,161	1,474.3	930.4	3.1	13.5	16.8	6.2	2,628.4
50–100 km	43,373	14,675	801.0	513.8	2.6	12.9	11.3	6.6	1,606.4
Almaraz (1981)									
0–30 km	47,637	17,672	571.9	143.2	5.4	30.3	32.7	5.6	1,488.7
50–100 km	45,946	16,390	561.8	138.0	5.2	27.5	31.0	5.8	1,584.3
Ascó (1983)									
0–30 km	49,049	13,410	499.9	0	1.9	10.7	27.1	6.5	876.7
50–100 km	61,594	19,275	603.3	0	2.1	9.7	23.5	6.6	1,162.2
Cofrentes (1984)									
0–30 km	35,881	11,733	331.9	0	4.0	17.8	16.8	6.8	1,888.5
50–100 km	71,975	27,159	649.3	0	4.0	19.0	10.6	6.1	4,498.4
Trillo (1988)									
0–30 km	13,259	3,312	68.0	0	3.2	11.2	25.5	5.4	232.6
50–100 km	12,976	3,392	66.3	0	2.4	11.4	26.2	5.7	231.7
Total									
0–30 km	302,861	100,075	4,813.1	2,386.9					
50–100 km	315,838	105,702	4,228.0	1,762.5					
NFFs[f]									
Andújar (1959)									
0–30 km	126,063	50,411	2,386.2	2,386.2	8.4	22.4	30.7	5.1	6,003.0
50–100 km	152,673	58,224	2,918.8	2,918.8	8.8	21.6	31.8	5.3	7,270.1
El Cabril (1961)									
0–30 km	38,781	13,545	764.7	764.7	9.7	34.8	25.2	5.1	4,309.0
50–100 km	44,373	18,114	814.7	814.7	10.2	35.6	39.0	4.5	5,546.6
La Haba (1977)									
0–30 km	111,456	41,790	1,825.5	791.4	6.2	27.5	26.5	5.5	4,458.2
50–100 km	151,289	59,682	2,407.5	1,079.6	6.0	26.5	21.0	5.6	6,051.6
Ciudad Rodrigo (1978)									
0–30 km	32,276	9,393	484.0	163.7	2.7	18.7	24.2	5.8	733.6
50–100 km	35,848	10,556	525.4	180.5	2.1	19.9	19.8	5.7	833.7
Juzbado (1985)									
0–30 km	32,627	11,151	261.6	0	0.8	16.2	26.9	5.6	429.2
50–100 km	36,713	10,832	302.4	0	1.2	16.6	30.1	5.8	476.8
Total									
0–30 km	341,203	126,290	4,029.4	2,911.6					
50–100 km	420,896	157,408	4,889.6	2,386.2					

[a] 1991 census.
[b] Person-years assuming a latency period of 1 year.
[c] Person-years assuming a latency period of 10 years.
[d] The study covered 316 towns in the exposed zone (0–30 km) and 303 in the reference zone (50–100 km).
[e] In parentheses, year of start-up.
[f] The study covered 173 towns in the exposed zone (0–30 km) and 174 in the reference zone (50–100 km).

Table 4 reports the results of the analysis of risk in accordance with the distance to the uranium-concentrate processing plants and the El Cabril NWSF. None of the causes studied registered a pattern that indicated a rise in risk with proximity and at the same time proved statistically significant with the test used. The El Cabril storage facility is located in a relatively deserted area, only 9 towns lying within a 30-km radius; the nearest is over 16 kms away. For distances under 20 kms, the of leukemias was in excess of 2.

We were able to study the start-up effect (Table 5) in the case of the La Haba, Ciudad Rodrigo, and Juzbado facilities. Available data failed to show evidence of a statistically significant rise in mortality.

Discussion

Overall, the results point to a rise in risk of death from multiple myeloma in the area surrounding the Zorita NPP. Similarly, the possible existence of excess risk of leukemias in the proximity of the Andújar and Ciudad Rodrigo facilities argues in favor of more specific studies in areas adjacent to nuclear fuel facilities.

The validity of death-certificate diagnoses for investigating cancer is generally accepted (17, 19, 35, 43). Mortality data, although showing a high degree of accuracy in cancers of the lymphatic tissue and hematopoietic system (43, 44), are nevertheless not the most ideal means for studying diseases such as childhood leukemia because of therapeutic improvements that

Table 2 Mortality by cause in areas within a 15- and 30-km radius of NPPs, taking as reference (control) towns lying within a radius of 50–100 kilometers[a]

Installation/Cause	Control		0–15 km		0–30 km		0–15 km		0–30 km	
	Obs[b]	SMR[c]	Obs	SMR	Obs	SMR	RR[d]	95% CI	RR	95% CI
All NPPs										
Non-Hodgkin's lymphomas	55	0.795	9	0.729	63	0.686	0.920	0.453–1.868	0.835	0.581–1.201
Hodgkin's disease	11	0.672	2	0.691	19	0.865	1.037	0.228–4.714	1.239	0.589–2.608
Myeloma	26	0.540	8	0.904	51	0.801	1.616	0.728–3.584	1.472	0.918–2.360
Leukemias	251	0.892	57	1.027	273	0.834	1.127	0.844–1.506	0.956	0.804–1.136
Leukemias <25[e]	34	1.128	7	1.470	27	0.776	1.214	0.529–2.787	0.703	0.418–1.181
Zorita										
Non-Hodgkin's lymphomas	13	0.727	5	1.075	13	0.689	1.479	0.527–4.148	0.949	0.440–2.046
Hodgkin's disease	2	0.452	2	1.754	5	1.100	1.715	0.801–3.670	2.432	0.475–12.453
Myeloma	4	0.308	6	1.744	19	1.343	5.653	1.610–19.851	4.354	1.497–12.663
Leukemias	29	0.708	12	1.117	34	0.767	1.578	0.809–3.076	1.083	0.663–1.770
Leukemias <25	8	2.002	2	2.050	4	1.096	1.024	0.218–4.821	0.547	0.165–1.814
Garoña										
Non-Hodgkin's lymphomas	24	0.942	2	0.618	20	0.571	0.656	0.156–2.765	0.606	0.335–1.096
Hodgkin's disease	5	0.800	0	0.000	3	0.352			0.440	0.105–1.840
Myeloma	6	0.340	1	0.406	15	0.614	1.195	0.144–9.899	1.808	0.702–4.658
Leukemias	45	0.709	8	0.971	54	0.620	1.370	0.646–2.906	0.874	0.590–1.296
Leukemias <25	5	0.669	1	2.222	10	1.022	3.321	0.388–28.425	1.528	0.523–4.470
Vandellós										
Non-Hodgkin's lymphomas	15	0.773	2	0.557	30	0.947	0.720	0.165–3.144	1.225	0.662–2.268
Hodgkin's disease	3	0.656	0	0.000	11	1.411			2.150	0.604–7.647
Myeloma	14	1.048	1	0.421	16	0.755	0.402	0.053–3.056	0.721	0.354–1.469
Leukemias	41	0.810	12	1.291	82	0.965	1.593	0.837–3.029	1.191	0.819–1.732
Leukemias <25	9	1.448	3	2.264	9	0.740	1.563	0.423–5.771	0.511	0.203–1.283
Almaraz										
Non-Hodgkin's lymphomas	3	0.467	0	0.000	0	0.000				
Hodgkin's disease	1	0.893	0	0.000	0	0.000				
Myeloma	2	0.486	0	0.000	1	0.255			0.525	0.049–5.672
Leukemias	34	0.930	3	0.585	35	0.995	0.630	0.196–2.022	1.07	0.668–1.714
Leukemias <25	2	0.496	0	0.000	0	0.000				
Ascó										
Leukemias	54	1.205	14	0.917	41	0.953	0.761	0.423–1.369	0.791	0.528–1.187
Leukemias <25	3	0.844	1	0.882	2	0.770	1.045	0.109–10.041	0.913	0.153–5.449
Cofrentes										
Leukemias	44	1.164	5	1.023	21	0.818	0.879	0.349–2.214	0.703	0.418–1.181
Leukemias <25	7	1.530	0	0.000	2	0.975			0.637	0.132–3.064
Trillo										
Leukemias	4	0.56	3	1.554	6	0.838	2.777	0.622–12.394	1.497	0.423–5.298
Leukemias <25	0	0.00	0	0.000	0	0.000				

[a] It was assumed that there was a latency period of 1 year for leukemias and 10 years for all other tumors.
[b] Obs, observed cases.
[c] SMR is the ratio of the number of observed : expected deaths at concurrent Spanish mortality rates.
[d] RR compares risk in study *versus* reference areas. The RR for combined facilities was obtained from a regression model, including the facilities as a factor, and differs from the simple ratio of the SMRs.
[e] Leukemias <25, deaths from leukemia at ages under 25 years.

have succeeded in lowering mortality without altering incidence. Yet, with the single exception of Tarragona, none of the provinces studied are equipped with population-based cancer registries that would otherwise enable cancer incidence to be studied in these areas.

In the calculation of person-years, interpolation and extrapolation techniques had to be used. These techniques were applied in the same way to all of the provinces and towns included in the various studies. Hence, any possible deviations that are inherent in the estimates will be equally present in all of the areas compared.

Specific methodological problems are posed by investigation into relatively rare diseases in areas adjacent to sources of contamination. Stress has been laid on the importance of ascertaining disease-frequency and -distribution in other areas similar in size to those being studied (45), a suggestion that was followed in our design. Indeed, a great part of the SMRs obtained from comparison with overall Spanish mortality were under 1 for the exposed and reference zones (Tables 2 and 3). Diagnostic verification of all of the cases is essential, because findings yielded by small areas are more sensitive to errors of classification, diagnosis, and reporting than those obtained for larger areas (45). Here however, case-diagnosis verification was ruled out by the very nature of our study, yet possible errors of classification would necessarily affect exposed and nonexposed towns in each region alike. In general, the areas compared in this study were rural. Reference towns were matched to exposed towns by sociodemographic variables and would, thus, indirectly maintain their comparability insofar as diagnostic accuracy and accessibility to the healthcare system are concerned. Sociodemographic information for the entire study period was not available. However, bearing in mind the characteristics of the Spanish National Health System, we would have no reason to suspect that there might be differential access to health care and diagnosis between exposed and reference areas.

Table 3 Mortality by cause in areas within a 15- and 30-km radius of NFFs, taking as reference (control) towns lying within a radius of 50–100 km[a]

Installation/Cause	Control		0–15 km		0–30 km		0–15 km		0–30 km	
	Obs[b]	SMR[c]	Obs	SMR	Obs	SMR	RR[d]	95% CI	RR	95% CI
All NFFs										
Non-Hodgkin's lymphomas	89	0.577	22	0.555	85	0.643	1.045	0.646–1.690	1.101	0.817–1.482
Hodgkin's disease	40	0.960	11	1.006	31	0.873	0.991	0.502–1.956	0.931	0.582–1.488
Myeloma	74	0.727	22	0.844	71	0.799	1.133	0.695–1.846	1.089	0.785–1.509
Leukemias	372	0.902	101	0.980	337	0.957	1.137	0.907–1.425	1.062	0.916–1.231
Leukemias <25[e]	70	1.181	18	1.217	57	1.191	1.040	0.608–1.780	1.015	0.716–1.440
Andújar										
Non-Hodgkin's lymphomas	41	0.499	13	0.447	34	0.524	0.896	0.481–1.669	1.050	0.667–1.653
Hodgkin's disease	26	1.035	8	0.886	16	0.800	0.856	0.389–1.883	0.772	0.415–1.436
Myeloma	38	0.691	18	0.950	34	0.792	1.373	0.784–2.405	1.146	0.722–1.818
Leukemias	138	0.829	61	1.030	142	1.074	1.242	0.919–1.679	1.296	1.025–1.638
Leukemias <25	33	1.255	13	1.231	30	1.344	0.981	0.517–1.863	1.071	0.654–1.754
El Cabril[f]										
Non-Hodgkin's lymphomas	15	0.695			19	0.741			1.067	0.543–2.097
Hodgkin's disease	3	0.450			6	0.795			1.768	0.442–7.065
Myeloma	11	0.779			16	0.872			1.120	0.521–2.408
Leukemias	40	0.913			55	1.058			1.159	0.289–4.646
Leukemias <25	6	0.794			7	1.149			1.446	0.490–4.268
La Haba										
Non-Hodgkin's lymphomas	28	0.705	4	0.663	25	0.788	0.941	0.334–2.653	1.117	0.652–1.915
Hodgkin's disease	11	1.354	1	0.876	7	1.103	0.647	0.084–4.998	0.814	0.316–2.101
Myeloma	16	0.629	2	0.484	16	0.772	0.770	0.177–3.345	1.226	0.615–2.445
Leukemias	142	1.057	19	0.923	97	0.890	0.874	0.541–1.410	0.842	0.651–1.090
Leukemias <25	29	1.421	2	0.944	16	1.085	0.664	0.160–2.756	0.763	0.416–1.402
Ciudad Rodrigo										
Non-Hodgkin's lymphomas	5	0.461	5	1.105	7	0.697	2.397	0.697–8.238	1.511	0.483–4.733
Hodgkin's disease	0	0.000	2	2.626	2	1.231				
Myeloma	9	1.222	2	0.667	5	0.728	0.546	0.118–2.525	0.596	0.201–1.763
Leukemias	25	0.598	18	1.006	30	0.758	1.683	0.919–3.082	1.268	0.746–2.153
Leukemias <25	0	0.000	3	1.738	3	0.986				
Juzbado										
Leukemias	27	1.044	3	0.556	13	0.670	0.533	0.165–1.721	0.642	0.333–1.237
Leukemias <25	11	1.293	1	1.301	5	0.616	1.006	0.130–7.770	0.477	0.167–1.363

[a] It was assumed that there was a latency period of 1 year for leukemias and 10 years for all other tumors.
[b] Obs, observed cases.
[c] SMR is the ratio of the number of observed : expected deaths at concurrent Spanish mortality rates.
[d] RR compares risk in study *versus* reference areas. The RR for combined facilities was obtained from a regression model including the facilities as a factor and differs from the simple ratio of the SMRs.
[e] Leukemias <25, deaths from leukemia at ages under 25 years.
[f] No towns within 15 km of the installation.

In theoretical terms, comparison of SMRs are open to criticism on the basis that, internally, the SMRs use different standard populations. In this study, thanks to the matching procedure followed in the design, differences in structure between the populations compared were not very marked. The method of comparison of SMRs adopted in the presentation of these results was chosen because: (*a*) it was the same as that used in the references (9, 17); (*b*) it included the comparison with Spanish mortality, and (*c*) it allowed all of the age strata to be collapsed, thereby reducing sensitivity to instability in age-specific rates (40). Moreover, analysis based on comparison of mortality rates (rate ratios) via models that use person-years as offset and include age, was found to yield equivalent results.

The study of the distance variable seeks to associate mortality with the nuclear installation as the putative source of contamination. Distance to the installation tends to be used as a surrogate variable for exposure in cases in which dosimetric information or the radiological history of an installation's environs is not forthcoming (46, 47), with reconstruction of such data constituting a field of investigation in itself (48). Indeed, in this respect, the study is "ecological," in that individual levels of exposure are unknown and the inhabitants of any given town are thus implicitly assumed to have received similar exposures. There will inevitably be persons who have resided for part of their lives in exposed towns and then moved to nonexposed areas and *vice versa*.

The Zorita power plant's area in the Province of Guadalajara showed evidence of an excess risk of multiple myeloma cases. Although not statistically significant, this excess risk remained in evidence even when the whole country was taken as reference. Yet, analysis adjusted for geographical location is nevertheless, to be preferred. Excess risk of myeloma connected with ionizing radiation has been documented in follow-up studies of Japanese atomic-bomb survivors (49) and nuclear industry workers (50–53). A raised risk has also been found in populations residing near English-based nuclear installations that were commissioned before 1955 (9). Guadalajara is a province with a myeloma mortality risk verging on the average for Spain (54), yet its municipal pattern of distribution is marked by a cluster in the southwest of the province where the NPP is situated. There are no grounds for thinking that different biological and/or genetic determinants may have a nonhomogeneous distribution in the natural agrarian region to

Table 4 RR according to distance of population centroids to NPPs and NFFs[a]

Installation[b]/Cause	Distance, km (reference >50 km)[c]					
	26.8–30	23.2–26.7	19–23.1	13.4–18.9	0–13.3	*P* for trend
All NPPs						
Non-Hodgkin's lymphomas	0.696	2.021	0.800	0.706	0.939	0.2272
Hodgkin's disease	0.754	1.169	0.957	2.178	1.121	0.3526
Myeloma	1.070	0.738	1.341	2.128	1.533	0.2403
Leukemias	0.778	0.984	1.105	0.965	1.034	0.9852
Leukemias <25[d]	0.285	1.618	0.735	0.413	1.272	0.2702
Zorita						
Non-Hodgkin's lymphomas	0.342	2.334	0.602	2.382	1.163	0.9136
Myeloma	1.310	2.712	2.565	8.120	4.917	0.0164
Leukemias	0.777	1.351	1.086	0.718	1.495	0.8028
Garoña						
Non-Hodgkin's lymphomas	0.555	2.361	0.655	0.263	1.034	0.1842
Myeloma	1.125	0.004	1.575	1.182	2.530	0.3983
Leukemias	0.947	0.002	1.128	1.381	0.778	0.4307
Vandellós						
Non-Hodgkin's lymphomas	0.722	2.506	1.582	0.859	0.612	0.9807
Myeloma	0.822	0.347	0.273	0.837	0.341	0.0292
Leukemias	0.739	0.813	1.541	0.878	1.360	0.5291
Almaraz						
Leukemias	1.106	2.071	1.162	0.943	0.782	0.9083
Ascó						
Leukemias	0.303	0.951	0.848	0.934	0.637	0.2219
Cofrentes						
Leukemias	0.687	1.521	2.953	0.402	1.529	0.7614
Trillo						
Leukemias	0.001	1.577	0.953	1.609	6.874	0.3064
All NFFs						
Non-Hodgkin's lymphomas	1.022	0.985	1.013	1.216	1.178	0.9147
Hodgkin's disease	0.740	1.251	1.093	0.617	1.080	0.8968
Myeloma	1.026	0.636	1.098	1.323	1.188	0.4224
Leukemias	0.943	0.924	1.037	1.192	1.125	0.3971
Leukemias <25	1.065	0.849	0.707	1.323	0.957	0.7386
Andújar						
Non-Hodgkin's lymphomas	1.127	1.618	0.863	1.449	0.827	0.7260
Hodgkin's disease	0.366	1.354	0.916	0.001	0.940	0.9845
Myeloma	0.373	0.747	1.460	0.820	1.343	0.3254
Leukemias	1.033	1.087	1.499	1.624	1.137	0.1077
Leukemias <25	1.296	0.904	0.979	1.466	0.886	0.9340
El Cabril						
Non-Hodgkin's lymphomas	0.658	0.194	0.288	0.731		0.3179
Myeloma	0.679	0.001	0.239	3.293		0.8628
Leukemias	1.229	0.593	2.436	2.372		0.4156
La Haba						
Non-Hodgkin's lymphomas	1.125	0.002	0.913	1.074	2.228	0.8382
Myeloma	2.142	0.003	1.008	1.177	0.000	0.9397
Leukemias	0.800	0.552	0.558	0.987	0.756	0.1231
Leukemias <25	1.141	0.001	0.000	1.077	0.000	0.3643
Ciudad Rodrigo						
Leukemias	0.648	1.027	0.851	0.600	2.063	0.2084
Juzbado						
Leukemias	0.731	0.998	0.001	1.480	0.533	0.5364

[a] It was assumed that there was a latency period of 1 year for leukemias and 10 years for all other tumors.
[b] Only sites with 10 or more observed deaths are shown.
[c] Estimates have been adjusted for matching variables. The most distant towns (radius, 50–100 km) are taken as reference.
[d] Leukemias <25, deaths from leukemia at ages under 25 years.

which the Zorita area belongs. Apart from ionizing radiation, known risk factors for myeloma include certain specific occupational exposures, such as pesticides, benzene, paints and solvents, and engine exhausts (55). Increased risk of myeloma has been reported for farm workers and workers in the petroleum refining, rubber and plastics manufacturing, and wood products industries. There are no petroleum refineries or plastics-related industries in this area. The exposed and reference towns were matched according to the proportion of farm workers. Moreover, based on the information available, no differences in crop cultivation were identified as between the areas compared. The data (in conjunction with the presence of a radial pattern peaking at a distance of 14 km from the plant), though not technically attributable to the nuclear installation by

Table 5 Estimated relative risk for study areas before and after the date on which nuclear facilities first came into operation (pre- and post-start-up)[a]

	Pre-start-up						Post-start-up		Homogeneity
	Control		0–30 km				0–30 km		P
	Obs[b]	SMR[c]	Obs	SMR	RR[d]	95% CI	RR	95% CI	
NPPS									
Zorita						1975–78[e]		1979–93	
Non-Hodgkin's lymphomas	1	0.397	0	0.000			0.949	0.440–2.046	0.2324
Hodgkin's disease	1	0.670	1	0.599	0.894	0.056–14.257	2.432	0.475–12.453	0.5443
Myeloma	1	0.570	1	0.479	0.840	0.053–13.398	4.354	1.497–12.663	0.2939
Garoña						1975–80		1981–93	
Non-Hodgkin's lymphomas	2	0.315	6	0.679	2.155	0.439–10.581	0.606	0.335–1.096	0.1205
Hodgkin's disease	3	0.880	6	1.276	1.450	0.364–5.766	0.440	0.105–1.840	0.2306
Myeloma	4	0.930	2	0.330	0.355	0.066–1.909	1.808	0.702–4.658	0.0891
Vandellós						1975–81		1982–93	
Non-Hodgkin's lymphomas	2	0.340	7	0.688	2.022	0.423–9.660	1.225	0.662–2.268	0.5483
Hodgkin's disease	2	0.666	5	0.935	1.403	0.276–7.138	2.150	0.604–7.647	0.6898
Myeloma	4	0.981	6	0.895	0.912	0.257–3.229	0.721	0.354–1.469	0.7510
Almaraz						1975–90 (75–80)		1991–93 (81–93)	
Non-Hodgkin's lymphomas	15	0.726	9	0.459	0.632	0.277–1.443			
Hodgkin's disease	8	1.119	5	0.725	0.648	0.213–1.967			
Myeloma	5	0.345	8	0.592	1.713	0.562–5.217	0.525	0.049–5.672	0.3665
Leukemias	15	0.819	16	0.908	1.109	0.550–2.237	1.070	0.668–1.714	0.9331
Leukemias <25	5	1.462	4	1.128	0.771	0.208–2.864			
Ascó						1975–93 (75–83)		(84–93)	
Non-Hodgkin's lymphomas	26	0.673	24	0.632	0.939	0.539–1.635			
Hodgkin's disease	8	0.707	13	1.181	1.670	0.696–4.008			
Myeloma	17	0.625	18	0.648	1.037	0.535–2.011			
Leukemias	29	0.922	21	0.638	0.692	0.396–1.211	0.791	0.528–1.187	0.7052
Leukemias <25	4	0.924	2	0.547	0.592	0.109–3.226	0.913	0.153–5.449	0.7308
Cofrentes						1975–93 (75–85)		(86–93)	
Non-Hodgkin's lymphomas	34	0.948	24	0.969	1.022	0.607–1.721			
Hodgkin's disease	11	0.971	8	1.090	1.123	0.454–2.774			
Myeloma	22	0.950	18	1.023	1.077	0.578–2.006			
Leukemias	32	0.918	20	0.807	0.879	0.503–1.535	0.703	0.418–1.181	0.5655
Leukemias <25	8	1.049	7	1.875	1.787	0.648–4.927	0.637	0.132–3.064	0.2611
Trillo						1975–93 (75–88)		(89–93)	
Non-Hodgkin's lymphomas	3	0.248	2	0.169	0.681	0.116–3.999			
Hodgkin's disease	1	0.301	2	0.609	2.020	0.185–22.069			
Myeloma	3	0.326	6	0.672	2.063	0.518–8.212			
Leukemias	13	0.751	12	0.710	0.944	0.431–2.068	1.497	0.423–5.298	0.5414
NFFs									
La Haba						1975–86 (75–78)		1987–93 (79–93)	
Non-Hodgkin's lymphomas	27	0.734	13	0.418	0.570	0.295–1.101	1.117	0.652–1.915	0.1179
Hodgkin's disease	24	1.554	13	0.999	0.643	0.329–1.256	0.814	0.316–2.101	0.6902
Myeloma	18	0.719	15	0.690	0.960	0.485–1.898	1.226	0.615–2.445	0.6216
Leukemias	20	0.985	17	0.965	0.980	0.518–1.853	0.842	0.651–1.090	0.6707
Leukemias <25	5	1.006	1	0.259	0.258	0.030–2.186	0.763	0.416–1.402	0.2960
Ciudad Rodrigo						1975–88 (75–79)		1989–93 (80–93)	
Non-Hodgkin's lymphomas	13	0.804	7	0.458	0.569	0.227–1.424	1.511	0.483–4.733	0.1874
Hodgkin's disease	4	0.675	3	0.538	0.797	0.178–3.559			
Myeloma	6	0.488	7	0.596	1.222	0.412–3.625	0.596	0.201–1.763	0.3579
Leukemias	8	0.664	10	0.866	1.304	0.515–3.304	1.268	0.746–2.153	0.9582
Leukemias <25	1	0.547	1	0.608	1.110	0.070–17.694			
Juzbado						1975–93 (75–86)		(87–93)	
Non-Hodgkin's lymphomas	14	0.492	12	0.589	1.198	0.555–2.585			
Hodgkin's disease	6	0.724	5	0.839	1.159	0.354–3.794			
Myeloma	16	0.772	11	0.759	0.984	0.457–2.116			
Leukemias	24	0.761	22	1.003	1.319	0.740–2.352	0.642	0.333–1.237	0.1050
Leukemias <25	3	0.787	4	1.389	1.763	0.398–7.811	0.511	0.046–5.629	0.3784

[a] It was assumed that there was a latency period of 1 year for leukemias and 10 years for all other tumors.
[b] Obs, observed cases.
[c] SMR is the ratio of the number of observed : the number of expected deaths at concurrent Spanish mortality rates.
[d] RR compares risk in study *versus* reference areas. The RR for combined facilities was obtained from a regression model including the facilities as a factor and differs from the simple ratio of the SMRs.
[e] Years included for lymphomas and myeloma. Years included for leukemias are in parentheses.
[f] Leukemias <25, deaths from leukemia at ages under 25 years.

virtue of the nature of this study, nevertheless, lend heightened interest to using case-by-case diagnostic verification to ascertain the true incidence of this disease in the province.

With respect to leukemia-related mortality, mention should be made of: (*a*) excess risks observed in the environs of the Andújar facility; and (*b*) figures on the borderline of statistical significance in the Vandellós, Zorita, and Ciudad Rodrigo catchment areas. In this analysis, no distinction was drawn between types of leukemia because of the importance of the number of deaths certified as leukemia of unspecified cell type. Nevertheless, exploratory exclusion of specified chronic lymphatic leukemia produced very similar results.

No excess risk of leukemia-related mortality was detected in the population aged 0–24 years residing within a 30-km radius of any NPP. The only area to register a high RR was that of Garoña, but here, the excess risk failed to attain statistical significance. Joint analysis registered: an RR of 0.70 for areas surrounding the different NPPs and 1.02 for areas surrounding the different NFFs. In view of the length of the follow-up period, the statistical power of the studies on the respective installations is low with respect to the under-25 age group. With a total of 40 expected cases for all of the NPP catchment areas, the probability (power) of detecting a 50% rise in risk (RR = 1.5) is 86% (with a type I error of 5%).

Exposure to environmental radon is the greatest single source of human exposure to ionizing radiation (56). The influence of natural radiation on mortality could not be incorporated into this analysis. All of the towns selected (exposed and reference zones) in the Zorita and Vandellós areas lie in localities that have extremely low levels of natural radiation. Rates of exposure are below 10 μRoentgen/h, equivalent to an average effective dose of 1.09 μSievert/year (109 mrem/year; Ref. 57). We, therefore, think that adjusting the effect estimates for levels of natural radiation in these two areas would have no influence whatsoever on the results. However, such an adjustment may well be of greater interest in the case of uranium-concentrate and NFF catchment areas located in parts of the country with high levels of natural radiation (Ciudad Rodrigo, Juzbado, and Andújar).

The results reported here have to be interpreted with a great deal of caution, because of the nature of the study and the limitations described above. Being an ecological and exploratory study, any possible deduction linking the presence of nuclear installations to cancer mortality in their environs, must be viewed as largely speculative. More specific studies are called for in the Vandellós, Zorita, and Garoña areas, sites of the first NPPs to be built in Spain. In this connection, stress should be laid on the importance of using dosimetric information in all future studies.

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References

1. Draper, G. J., Stiller, C. A., Cartwright, R. A., Craft, A. W., and Vincent, T. J. Cancer in Cumbria and in the vicinity of the Sellafield nuclear installation, 1963–90. Br. Med. J., *306:* 89–94, 1993.

2. Bithell, J. F., Dutton, S. J., Draper, G. J., and Neary, N. M. Distribution of childhood leukaemias and non-Hodgkin's lymphomas near nuclear installations in England and Wales. Br. Med. J., *309:* 501–505, 1994.

3. Black, R. J., Sharp, L., Harkness, E. F., and McKinney, P. A. Leukaemia and non-Hodgkin's lymphoma: incidence in children and young adults resident in the Dounreay area of Caithness, Scotland in 1968–91. J. Epidemiol. Community Health, *48:* 232–236, 1994.

4. Heasman, M. A., Urquhart, J. D., Black, R. J., Kemp, I. W., Glass, S., and Gray, M. Leukaemia in young persons in Scotland: a study of its geographical distribution and relationship to nuclear installations. Health Bull. (Edinb.), *45:* 147–151, 1987.

5. Heasman, M. A., Kemp, I. W., Urquhart, J. D., and Black, R. Childhood leukaemia in northern Scotland. Lancet, *1:* 266, 1986.

6. Sharp, L., Black, R. J., Harkness, E. F., and McKinney, P. A. Incidence of childhood leukaemia and non-Hodgkin's lymphoma in the vicinity of nuclear sites in Scotland, 1968–93. Occup. Environ. Med., *53:* 823–831, 1996.

7. Roman, E., Beral, V., Carpenter, L., Watson, A., Barton, C., Ryder, H., and Aston, D. L. Childhood leukaemia in the West Berkshire and Basingstoke and North Hampshire District Health Authorities in relation to nuclear establishments in the vicinity. Br. Med. J. Clin. Res. Ed., *294:* 597–602, 1987.

8. Roman, E., Watson, A., Beral, V., Buckle, S., Bull, D., Baker, K., Ryder, H., and Barton, C. Case-control study of leukaemia and non-Hodgkin's lymphoma among children aged 0–4 years living in west Berkshire and north Hampshire health districts. Br. Med. J., *306:* 615–621, 1993.

9. Forman, D., Cook-Mozaffari, P., Darby, S., Davey, G., Stratton, I., Doll, R., and Pike, M. Cancer near nuclear installations. Nature (Lond.), *329:* 499–505, 1987.

10. Ewings, P. D., Bowie, C., Phillips, M. J., and Johnson, S. A. Incidence of leukaemia in young people in the vicinity of Hinkley Point nuclear power station, 1959–86. Br. Med. J., *299:* 289–293, 1989.

11. Clapp, R. W., Cobb, S., Chan, and Walker, B., Jr. Leukaemia near Massachusetts nuclear power plant. Lancet, *2:* 1324–1325, 1987.

12. Urquhart, J. D., Black, R. J., Muirhead, M. J., Sharp, L., Maxwell, M., Eden, O. B., and Jones, D. A. Case-control study of leukaemia and non-Hodgkin's lymphoma in children in Caithness near the Dounreay nuclear installation. Br. Med. J., *302:* 687–692, 1991.

13. Gardner, M. J., Snee, M. P., Hall, A. J., Powell, C. A., Downes, S., and Terrell, J. D. Results of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria. Br. Med. J., *300:* 423–429, 1990.

14. Gardner, M. J., Hall, A. J., Downes, S., and Terrell, J. D. Follow up study of children born elsewhere but attending schools in Seascale, West Cumbria (schools cohort). Br. Med. J. Clin. Res. Ed., *295:* 819–822, 1987.

15. Gardner, M. J., Hall, A. J., Downes, S., and Terrell, J. D. Follow up study of children born to mothers resident in Seascale, West Cumbria (birth cohort). Br. Med. J. Clin. Res. Ed., *295:* 822–827, 1987.

16. Baron, J. A. Cancer mortality in small areas around nuclear facilities in England and Wales. Br. J. Cancer, *50:* 815–824, 1984.

17. Jablon, S., Hrubec, Z., and Boice, J. D., Jr. Cancer in populations living near nuclear facilities. A survey of mortality nationwide and incidence in two states. J. Am. Med. Assoc., *265:* 1403–1408, 1991.

18. Darby, S. C., and Doll, R. Fallout, radiation doses near Dounreay, and childhood leukaemia. Br. Med. J. Clin. Res. Ed., *294:* 603–607, 1987.

19. Hattchouel, J. M., Laplanche, A., and Hill, C. Cancer mortality around French nuclear sites. Ann. Epidemiol., *6:* 126–129, 1996.

20. McLaughlin, J. R., Clarke, E. A., Nishri, E. D., and Anderson, T. W. Childhood leukemia in the vicinity of Canadian nuclear facilities. Cancer Causes Control, *4:* 51–58, 1993.

21. Waller, L. A., Turnbull, B. W., Gustafsson, G., Hjalmars, U., and Andersson, B. Detection and assessment of clusters of disease: an application to nuclear power plant facilities and childhood leukaemia in Sweden. Stat. Med., *14:* 3–16, 1995.

22. Hattchouel, J. M., Laplanche, A., and Hill, C. Leukaemia mortality around French nuclear sites. Br. J. Cancer, *71:* 651–653, 1995.

23. Michaelis, J., Keller, B., Haaf, G., and Kaatsch, P. Incidence of childhood malignancies in the vicinity of West German nuclear power plants. Cancer Causes Control, *3:* 255–263, 1992.

24. Prindull, G., Demuth, M., and Wehinger, H. Cancer morbidity rates of children from the vicinity of the nuclear power plant of Wurgassen (FRG). Acta Haematol. (Basel), *90:* 90–93, 1993.

25. Kinlen, L. Evidence for an infective cause of childhood leukaemia: comparison of a Scottish new town with nuclear reprocessing sites in Britain. Lancet, *2:* 1323–1327, 1988.

26. IARC. Direct estimates of cancer mortality due to low doses of ionising radiation: an international study. IARC Study Group on Cancer Risk among Nuclear Industry Workers. Lancet, *344:* 1039–1043, 1994.

27. Checkoway, H., Pearce, N., Crawford-Brown, D. J., and Cragle, D. L. Radiation doses and cause-specific mortality among workers at a nuclear materials fabrication plant. Am. J. Epidemiol., *127:* 255–266, 1988.

28. Alexander, V. Brain tumor risk among United States nuclear workers. Occup. Med. (Phila.), *6:* 695–714, 1991.

29. Helton, J. C., Muller, A. B., and Bayer, A. Contamination of surface-water bodies after reactor accidents by the erosion of atmospherically deposited radionuclides. Health Physics, *48:* 757–771, 1985.

30. Rodriguez-Artalejo, F., Castaño-Lara, S., de-Andres-Manzano, B., García-Ferruelo, M., Iglesias-Martin, L., and del Rey-Calero, J. Occupational exposure to ionising radiation and mortality among workers of the former Spanish Nuclear Energy Board. Occup. Environ. Med., *54:* 202–208, 1997.

31. Carpenter, A. V., Flanders, W. D., Frome, E. L., Crawford-Brown, D. J., and Fry, S. A. CNS cancers and radiation exposure: a case-control study among workers at two nuclear facilities. J. Occup. Med., *29:* 601–604, 1987.

32. McLaughlin, J. R., King, W. D., Anderson, T. W., Clarke, E. A., and Ashmore, J. P. Paternal radiation exposure and leukaemia in offspring: the Ontario case-control study. Br. Med. J., *307:* 959–966, 1993.

33. Mangano, J. J. Cancer mortality near Oak Ridge, Tennessee. Int. J. Health Serv., *24:* 521–533, 1994.

34. Crump, K. S., Ng, T. H., and Cuddihy, R. G. Cancer incidence patterns in the Denver metropolitan area in relation to the Rocky Flats plant. Am. J. Epidemiol., *126:* 127–135, 1987.

35. Cook-Mozaffari, P. J., Darby, S. C., Doll, R., Forman, D., Hermon, C., Pike, M. C., and Vincent, T. Geographical variation in mortality from leukaemia and other cancers in England and Wales in relation to proximity to nuclear installations, 1969–78. Br. J. Cancer, *59:* 476–485, 1989.

36. Instituto Nacional de Estadística. Censo de Población 1991. Saeta municipal. Madrid: Instituto Nacional de Estadística, 1995.

37. Ayuso Orejana, J., Fernández Cuesta, J. A., and Plaza Ibeas, J. L. Anuario del Mercado Español. Madrid: Banco Español de Crédito, 1993.

38. Parkin, D. M., Clayton, D., Black, R. J., Masuyer, E., Friedl, H. P., Ivanov, E., Sinnaeve, J., Tzvetansky, C. G., Geryk, E., Storm, H. H., Rahu, M., Pukkala, E., Bernard, J. L., Carli, P. M., L'Huilluier, M. C., Menegoz, F., Schaffer, P., Schraub, S., Kaatsch, P., Michaelis, J., Apjok, E., Schuler, D., Crosignani, P., Magnani, C., and Bennett, B. G. Childhood leukaemia in Europe after Chernobyl: 5 year follow-up. Br. J. Cancer, *73:* 1006–1012, 1996.

39. Aickin, M., Dunn, C. N., and Flood, T. J. Estimation of population denominators for public health studies at the tract, gender, and age-specific level. Am. J. Public Health, *81:* 918–920, 1991.

40. Breslow, N., and Day, N. Statistical Methods in Cancer Research. II. The Design and Analysis of Cohort Studies. IARC Scient Publ. No. 82. Lyon, France: IARC, 1987.

41. Breslow, N. Extra-Poisson variation in log-linear models. Appl. Stat., *33:* 38–44, 1984.

42. Breslow, N. Regression and other quasi-likelihood models. J. Am. Stat. Assoc., *85:* 565–571, 1990.

43. Percy, C., Stanek, E., and Gloeckler, L. Accuracy of cancer death certificates and its effect on cancer mortality statistics. Am. J. Public Health, *71:* 242–250, 1981.

44. Benavides, F. G., Bolumar, F., and Peris, R. Quality of death certificates in Valencia, Spain. Am. J. Public Health, *79:* 1352–1354, 1989.

45. Beral, V. Childhood leukemia near nuclear plants in the United Kingdom: the evolution of a systematic approach to studying rare disease in small geographic areas. Am. J. Epidemiol., *132:* S63–68, 1990.

46. Diggle, P., Morris, S., Elliot, P., and Shaddick, G. Regression modelling of disease risk in relation to point sources. J. R. Stat. Soc. *160:* 491–505, 1997.

47. Lawson, A. On the analysis of mortality events associated with a prespecified fixed point. J. R. Stat. Soc. A, *156:* 363–377, 1993.

48. Shleien, B., Ruttenber, A. J., and Sage, M. Epidemiologic studies of cancer in populations near nuclear facilities. Health Physics, *61:* 699–713, 1991.

49. Kato, H., and Schull, W. J. Studies of the mortality of A-bomb survivors. 7. Mortality, 1950–1978: Part I. Cancer mortality. Radiat. Res., *90:* 395–432, 1982.

50. Smith, P. G., and Douglas, A. J. Mortality of workers at the Sellafield plant of British Nuclear Fuels. Br. Med. J. Clin. Res. Ed., *293:* 845–854, 1986.

51. Gilbert, E. S., Fry, S. A., Wiggs, L. D., Voelz, G. L., Cragle, D. L., and Petersen, G. R. Analyses of combined mortality data on workers at the Hanford Site, Oak Ridge National Laboratory, and Rocky Flats Nuclear Weapons Plant. Radiat. Res., *120:* 19–35, 1989.

52. Douglas, A. J., Omar, R. Z., and Smith, P. G. Cancer mortality and morbidity among workers at the Sellafield plant of British Nuclear Fuels. Br. J. Cancer, *70:* 1232–1243, 1994.

53. Tolley, H. D., Marks, S., Buchanan, J. A., and Gilbert, E. S. A further update of the analysis of mortality of workers in a nuclear facility. Radiat. Res., *95:* 211–213, 1983.

54. López-Abente, G., Pollán, M., Escolar, A., Abraira, V., and Errezola, M. Atlas de mortalidad por cáncer y otras causas en España, 1978–1992. Madrid: Fundación Científica de la Asociación Española Contra el Cáncer, 1996.

55. Herrington, L. J., Weiss, N. S., and Olshan, A. F. Mutiple myeloma. *In:* D. Schottenfeld, and J. F. Fraumeni, Jr. (eds), Cancer Epidemiology and Prevention, pp. 946–970. New York: Oxford University Press, 1996.

56. National Research Council Committee on the Biological Effects of Ionizing Radiation. Health effects of exposure to low levels of ionizing radiation. BEIR V. National Research Council. Washington DC: National Academy Press, 1990.

57. Suárez Mahou, E., and Fernández Amigot, J. A. Mapas provinciales a escala 1/1.000.000 de tasa de exposición. Resultados y aplicaciones del proyecto Marna. Madrid: Consejo de Seguridad Nuclear, 1997.