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Archives of Environmental Health: An International Journal

ISSN: 0003-9896 (Print) Journal homepage: www.tandfonline.com/journals/vzeh20

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To cite this article: Bruce Hocking & Ian Gordon (2003) Decreased Survival for Childhood Leukemia in Proximity to Television Towers, Archives of Environmental Health: An International Journal, 58:9, 560-564, DOI: 10.3200/AEOH.58.9.560-564

To link to this article: https://doi.org/10.3200/AEOH.58.9.560-564

Published online: 07 Aug 2010.

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Decreased Survival for Childhood Leukemia in Proximity to Television Towers

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ABSTRACT. Previously, an increased risk of childhood leukemia was identified among children who resided in an inner ring (radius ~4 km) of 3 municipalities surrounding television towers, compared with children who resided in an outer ring (radius ~4–12 km) of 6 municipalities surrounding, but farther away from, the towers, which are situated in North Sydney, Australia. In the current study, the authors examined the survival experience of these children for all childhood leukemias, and for acute lymphatic leukemia (*International Statistical Classification of Diseases and Related Health Problems*, 9th revision [ICD-9] rubric 204.0) in particular. Of 123 cases of acute lymphatic leukemia, 29 cases (16 of whom died) were in the inner ring of municipalities nearest the towers, and 94 cases (34 of whom died) occurred in the outer, more-distant ring. There was a significant difference in survival rates between the 2 groups (log-rank test, $p = 0.03$; Wilcoxon, $p = 0.05$). The 5-yr survival in the inner ring of municipalities was 55%, and in the outer ring was 71% (i.e., subjects in the inner ring were 23% less likely to survive than those in the outer ring); at 10 yr, survival in the inner and outer rings was 33% and 62%, respectively. Following adjustment, the mortality rate ratio that the authors used to compare the inner ring with the outer ring was 2.1 (95% confidence interval = 1.1, 4.0). There was an association between residential proximity to the television towers and decreased survival among cases of childhood leukemia in North Sydney, Australia.
<Key words: Australia, childhood cancer, leukemia, radiofrequency radiation, survival>

CHILDHOOD LEUKEMIA rates (i.e., in the 0–14 yr age group) were reported previously as being increased in municipalities proximate to very high-frequency (VHF) television (TV) transmission towers in North Sydney, Australia.[1] This was a "greenfield" study, with no prior reports of clusters of leukemia. This finding was part of an assessment of health effects in communities exposed to low levels of radio frequency radiation (RFR). In the previous study,[1] an increased risk of childhood leukemia was identified among children who resided in an inner ring (radius ~4 km) of 3 municipalities surrounding television towers, compared with children who resided in an outer ring (radius ~4–12 km) of 6 municipalities surrounding but farther away from the TV towers, which are situated in North Sydney, Australia (for map, see reference 1). In this study,[1] it was determined that the inner ring of municipalities immediately surrounding the towers experienced an exposure of 8.0–0.2 μW/cm^2, compared with that of the outer ring (exposure: 0.2–0.02 μW/cm^2). Comparison of the inner ring with the outer ring produced an incidence rate ratio (RR) for lymphatic leukemia of 1.55 (95% confidence interval [CI] = 1.00, 2.41); the RR for mortality was 2.74 (95% CI = 1.42, 5.27). This greater mortality risk intimated a decrease in survival. In the current study, we have collected additional information about the aforementioned survival analysis.

Method

We analyzed survival data for all cases of childhood leukemia (*International Statistical Classification of Dis-*

eases and Related Health Problems, 9th revision [ICD-9] rubric 204.0)[2] that occurred in the study area, as recorded by the New South Wales (NSW) Cancer Registry for the period 1972–1993.[1] The NSW Cancer Registry is a population-based registry with multiple reporting sources for the entire state. Deidentified case data for childhood leukemia showed the type of leukemia, year of diagnosis, year of birth, year of death, age at diagnosis, age at death, sex, and municipality of residence at the time of diagnosis. The municipality at the time of death was not recorded and was not readily available because of privacy restraints. We researched movements of families from property to property in the areas, and we estimated that only a few families with children moved each year in this highly desirable area, implying, therefore, that there was continuity of exposure from time of diagnosis until death.

On the basis of preliminary analysis, concern was raised regarding an unexpectedly large fraction of cases with very brief survivals because these cases substantially influenced the survival curves. There were 11 cases who survived 1 mo or less (6 of whom resided in the inner ring). We manually searched the case records of these individuals to check diagnosis and database accuracy, and to determine whether any diagnoses were made at the time of autopsy. All data were found to be correct, and only 1 case from the inner ring was diagnosed at autopsy. The latter case was excluded from analysis; we regarded the 10 remaining cases as valid for the purpose of survival analysis, and we retained them for analysis with the other cases.

Data were described by standard Kaplan-Meier curves for the inner and outer rings for all cases of childhood leukemia, and for a subset of cases that reflected acute lymphatic leukemia only. We used the log-rank test and Wilcoxon tests to compare groups and to test difference(s) between them. We applied Cox's proportional hazards model to the data to control for possible confounding by age at diagnosis, sex, and year of diagnosis. The aforementioned model allows for varying durations of follow-up, and includes subjects who remain alive at the conclusion of the follow-up period. Subjects who were alive at the end of 1993 were censored on December 31, 1993—the latest date on which a death could be reported into the database.

Results

We examined 160 cases of leukemia (any type [ICD-9, rubrics 204–208]) in the study area (Table 1). Of these, 36 cases (21 of whom died) resided in the inner ring, and 124 cases (53 deaths) resided in the outer ring.

There was a significant difference between the 2 survival curves for all cases of childhood leukemia (Fig. 1; log-rank test, $p = 0.04$; Wilcoxon test, $p = 0.05$). The 5-yr survival in the inner ring of municipalities was 49%, and it was 62% in the outer ring (i.e., the outcome in the inner ring was 21% worse than in the outer ring); at 10 yr, the survival was 33% and 55%, respectively (i.e., the outcome in the inner ring was 40% worse than in the outer ring). We used Cox's proportional hazards model to adjust for the potential confounders, and the resulting mortality RR comparing the inner ring with the outer ring was 1.8 (95% CI = 1.0, 3.0).

There were 123 diagnosed cases of acute lymphatic leukemia (ICD-9, rubric 204.0), of which 29 cases (16 deaths) were in the inner ring of municipalities and 94 cases (34 deaths) were in the outer ring. There was a significant difference in survival between groups (Fig. 2; log-rank test, $p = 0.03$; Wilcoxon test, $p = 0.05$). The 5-

Table 1.—Number of Cases of Childhood Leukemia, by Municipal Ring,* Sex, Vital Status, and ICD-9 Classification

			ICD-9 Classification							
Ring*	Sex	Vital status	204.0	204.9	205.0	205.1	206.0	208.0	208.9	Total
Outer	Male	Alive	30	0	3	1	1	0	1	36
		Dead	18	0	3	1	0	7	0	29
	Female	Alive	30	0	2	2	1	0	0	35
		Dead	16	1	3	2	0	2	0	24
Inner	Male	Alive	8	0	0	0	0	0	0	8
		Dead	9	0	0	0	0	2	0	11
	Female	Alive	5	0	2	0	0	0	0	7
		Dead	7	0	1	2	0	0	0	10
		Total	123	1	14	8	2	11	1	160

Note: ICD-9 = *International Statistical Classification of Diseases and Related Health Problems*, 9th revision.[2]
*"Ring" refers to either (1) municipalities in Sydney that were within a 4-km radius of 3 television transmission towers (i.e., inner ring), or (2) municipalities that were in areas 4–12 km from the 3 television transmission towers (i.e., outer ring).

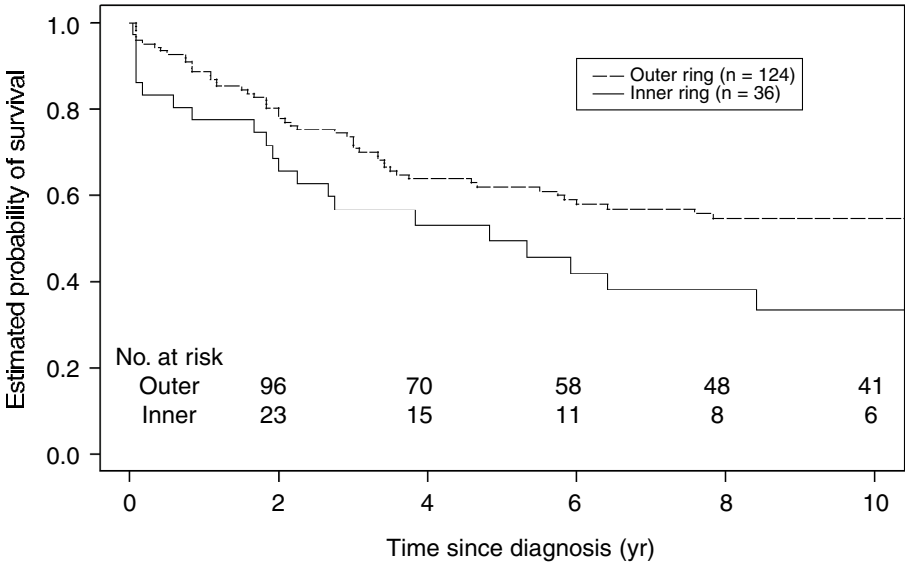

Fig. 1. Survival curves for all types of childhood leukemias in North Sydney, Australia (1972–1993), by geographic area of exposure.

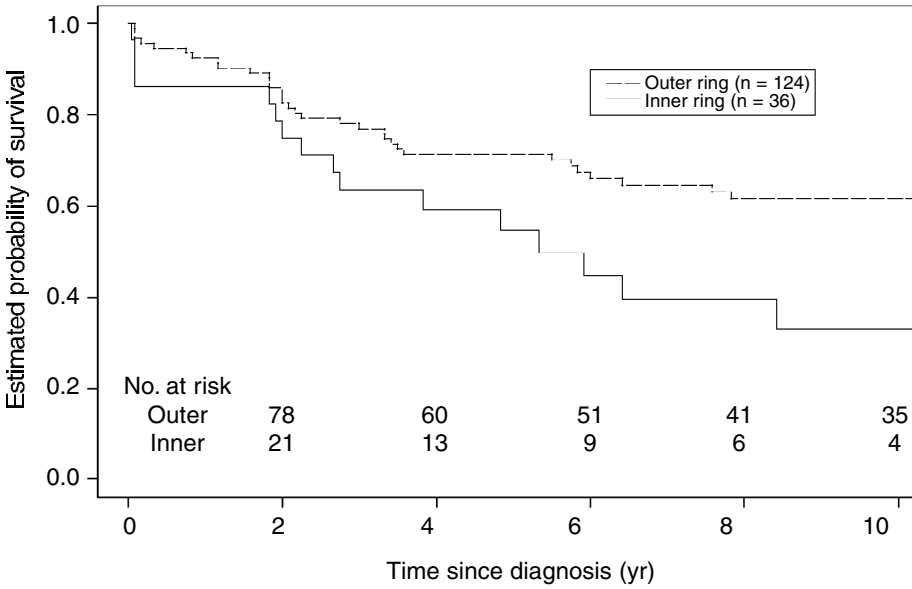

Fig. 2. Survival curves for acute lymphatic leukemia (*International Statistical Classification of Diseases and Related Health Problems*, 9th revision [ICD-9] rubric 204.0) in North Sydney, Australia (1972–1993), by geographic area of exposure.

yr survival in the inner ring of municipalities was 55%, and in the outer ring it was 71% (i.e., the inner ring was 23% worse); at 10 yr, the survival was 33% and 62%, respectively (the inner ring was 47% worse). Following adjustment for the potential confounders, we used Cox's model to compare the mortality RR in the inner ring with that of the outer ring (RR = 2.1 [95% CI = 1.1, 4.0]). There were too few cases of acute myeloid leukemia for accurate analysis.

A possible concern about the data is that 9 cases were diagnosed prior to 1972—before the registry was truly population-based. All 9 of these cases died. We, therefore, excluded the 9 cases and repeated the analyses; the resulting mortality RR for all leukemias was 1.8

(95% CI = 1.1, 3.2), which represented 35 cases (20 deaths) in the inner ring and 116 cases (45 deaths) in the outer ring. The RR for acute lymphatic leukemia was 2.2 (95% CI = 1.1, 4.3), which represented 28 cases (15 deaths) in the inner ring and 90 cases (30 deaths) in the outer ring.

Discussion

The groups of municipalities proximate and more distal to the TV towers differed with respect to the survival experience of children with leukemia: the inner ring had a worse survival rate than the outer ring. Very early deaths made a substantial contribution to this difference, but the gap in survival increased from 5 yr (more than 20% worse) to 10 yr (more than 40% worse)—suggesting that distance from the towers had an ongoing influence on survival.

The major factors affecting survival in childhood leukemia are age at diagnosis, refractory disease that particularly relates to leukocyte count and cytogenetics of the cells,[3] and access to good health care. We adjusted for age at diagnosis, sex, and year of diagnosis. Clinical data that contained details about these deaths were unavailable to us, but they warrant additional examination with respect to leukemia subtype, cytogenetic abnormalities, and concurrent illnesses (e.g., Down syndrome), which would contribute to a better understanding of our observations. Differences in survival rates between populations may be associated with early diagnosis and treatment. Both the inner and outer rings we studied are located within high socioeconomic areas; therefore, it is unlikely that access to care produced a significant bias.[1] Treatment for childhood leukemia is usually conducted at 1 of 2 major centers (not in the study area) that use standard protocols; therefore, it is unlikely that therapy is biased. Mortality in the outer ring was determined previously to be similar to that of the entire state[1] and is, therefore, a valid comparison with the inner-ring experiences.

Our original study was criticized by McKenzie et al.,[4] who claimed that the excess incidence in the inner area could be attributed to 1 municipality—Lane Cove. They did not comment on mortality in the inner ring. In our previous study, we reported that our test for homogeneity ($p = 0.10$ for incidence and $p = 0.13$ for mortality) showed that the rates in all 3 municipalities in the inner ring were consistent with a constant underlying elevated risk.[1] There is, therefore, no prima facie case for considering the municipalities individually.[5] Our original data were basic in construction and constrained by municipal boundaries; therefore, any true association underlying our estimate was likely greater than that observed as a result of nondifferential misclassification. Our original study design also assumed uniform distribution of RFR over the survey area, but the undulations of terrain and the high-rise buildings of the inner ring likely created uneven exposures between municipalities. If the exposures are causal, possible cases and RRs would vary. We also analyzed our data for trends in incidence over time and found no significant trend, which argues against a cluster.[1]

To our knowledge, survival data have not been analyzed previously with respect to exposure to electromagnetic fields. On the basis of adverse cancer mortality trends in some Australian states associated with increased broadcasting services, Holt[6] suggested that RFR may promote the development of cancer. The mechanism whereby RFR at these low levels may contribute to causation or progression of leukemia is unknown. Recently, acute childhood leukemia has been shown to be initiated frequently by a chromosome translocation event in utero[7]; studies of identical twins have shown that such an event is insufficient for clinical leukemia, and that a promotional event is also required.[8] Adey[9] reviewed the various processes whereby low-level RFR affects cell membranes and may dispose to disease by various mechanisms, such as promoting and/or facilitating cancer progression by influencing cell proliferation and/or inhibiting defenses (e.g., apotosis, immunological surveillance). In our previous study, we noted that TV signals have deep, 50-Hz amplitude modulations that are pulsed to assist in synchronization of the receiving TV set.[1] This fact is of interest because low-level (4-mG) 50-Hz fields have recently been classified as a possible carcinogen by the International Agency for Research on Cancer.[10]

Dolk et al.[11,12] examined cancer data in relation to 1 major and several other ultra high-frequency (UHF) TV and frequency modulation (FM) radio transmitters in the United Kingdom, and no excess in the incidence of childhood leukemia was found. It should be noted, however, that the authors did not examine survival or mortality data. Australian TV uses VHF that, because of its longer (i.e., ~3-m to 5-m) wavelength, has increased coupling with, and hence increased energy deposition into, the whole body by an order of magnitude greater than UHF and, therefore, exposures are not strictly comparable. Chagnaud et al.[13] reported that short-term exposures to RFR have no effect on the life expectancy of rats injected with benzo[*a*]pyrene to induce tumors. However, researchers did not expose the rats after the onset of tumors was recognized. Our observations were related to the survival of children in proximity to an RFR source after their leukemia was diagnosed and treated.

The data presented here do not establish a causal relationship between cancer and RFR. However, our observations of increased incidence and decreased survival, which worsens during the period of follow-up among children who reside near TV transmitters, are congruent with the possibility that RFR acts as a facilitator of cancer.

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The authors thank the NSW Cancer Council for providing the data for analysis.

Submitted for publication August 23, 2002; revised; accepted for publication January 17, 2003.

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