Appendix 7


Abstract:

Background: The present study was initiated to examine the claims of the residents of the Druze Isifya Village in Northern Israel that their high cancer rates were associated with the past exposures to radiation from radio and cellular transmitters. Objective: To investigate the association between past exposure to RF/MW transmitters and cancer risks, taking into account familial cancer history, occupational exposures and indicators of life-style. Methods: We carried out a population-based case-control study involving 307 residents, of whom 47 were diagnosed between 1989 and 2007 with different types of cancer and 260 controls. Cancer diagnoses were obtained from medical records. Exposure status of individual houses were determined from a map, based on the distances between each house and RF/MW antennas, and were calculated using geographic information systems (GIS) tools. Data on additional risk factors for cancer, like smoking and occupation, were obtained from individual questionnaires. The analysis was adjusted for measures of life style and occupational exposure, and Binary multiple logistic regressions was used, for all cancer sites and for individual cancer types for those cancers with at least 5 documented cases. Results: Past occupational exposures to chemicals (e.g., pesticides) and electronics, were found to be strongly associated with increased cancer risks (all sites: OR = 2.79; CI = 1.14–6.82; P < 0.05), but no discernible trend in overall cancer risk was associated with proximity to sources of past RF/MW radiation exposure (n = 47 OR = 1.00; CI = 0.99–1.02; P > 0.4). Colorectal cancer showed a negligible elevated adjusted risk associated with radiation intensity (n = 11 OR = 1.03; CI = 1.01–1.05; P < 0.01). Conclusion: There was evidence for an increased risk of cancers which were associated with chemicals in manufacturing and agriculture and electronics, where there may have been exposures to EMF, but the study did not confirm the suspicion of increased cancer risks associated with radiation for most cancer types in this village. Misclassification of past exposures could explain the negative finding.

Abstract:

We investigated the association between exposure to radio-frequency electromagnetic fields (RF-EMFs) from broadcast transmitters and childhood cancer. First, we conducted a time-to-event analysis including children under age 16 years living in Switzerland on December 5, 2000. Follow-up lasted until December 31, 2008. Second, all children living in Switzerland for some time between 1985 and 2008 were included in an incidence density cohort. RF-EMF exposure from broadcast transmitters was modeled. Based on 997 cancer cases, adjusted hazard ratios in the time-to-event analysis for the highest exposure category (>0.2 V/m) as compared with the reference category (<0.05 V/m) were 1.03 (95% confidence interval (CI): 0.74, 1.43) for all cancers, 0.55 (95% CI: 0.26, 1.19) for childhood leukemia, and 1.68 (95% CI: 0.98, 2.91) for childhood central nervous system (CNS) tumors. Results of the incidence density analysis, based on 4,246 cancer cases, were similar for all types of cancer and leukemia but did not indicate a CNS tumor risk (incidence rate ratio = 1.03, 95% CI: 0.73, 1.46). This large census-based cohort study did not suggest an association between predicted RF-EMF exposure from broadcasting and childhood leukemia. Results for CNS tumors were less consistent, but the most comprehensive analysis did not suggest an association.
Cancer risks in the Druze Isifya Village: Reasons and RF/MW antennas

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Abstract

Background: The present study was initiated to examine the claims of the residents of the Druze Isifya Village in Northern Israel that their high cancer rates were associated with the past exposures to radiation from radio and cellular transmitters. Objective: To investigate the association between past exposure to RF/MW transmitters and cancer risks, taking into account familial cancer history, occupational exposures and indicators of life-style. Methods: We carried out a population-based case-control study involving 307 residents, of whom 47 were diagnosed between 1989 and 2007 with different types of cancer and 260 controls. Cancer diagnoses were obtained from medical records. Exposure status of individual houses were determined from a map, based on the distances between each house and RF/MW antennas, and were calculated using geographic information systems (GIS) tools. Data on additional risk factors for cancer, like smoking and occupation, were obtained from individual questionnaires. The analysis was adjusted for measures of life style and occupational exposure, and Binary multiple logistic regressions was used, for all cancer sites and for individual cancer types for those cancers with at least 5 documented cases.

Results: Past occupational exposures to chemicals (e.g., pesticides) and electronics, were found to be strongly associated with increased cancer risks (all sites: OR = 2.79; CI = 1.14–6.82; \(P < 0.05\)), but no discernible trend in overall cancer risk was associated with proximity to sources of past RF/MW radiation exposure (\(n = 47\) OR = 1.00; CI = 0.99–1.02; \(P > 0.4\)). Colorectal cancer showed a negligible elevated adjusted risk associated with radiation intensity (\(n = 11\) OR = 1.03; CI = 1.01–1.05; \(P < 0.01\)). Conclusion: There was evidence for an increased risk of cancers which were associated with chemicals in manufacturing and agriculture and electronics, where there may have been exposures to EMF, but the study did not confirm the suspicion of increased cancer risks associated with radiation for most cancer types in this village. Misclassification of past exposures could explain the negative finding.

Keywords: Cancer; Agrochemicals; Electronics; Microwave radiation; RF/MW transmitters; Retrospective study

1. Introduction

The general public has become increasingly exposed to radio and microwave radiation at frequencies of 100 kHz–300 GHz from radio and cellular transmitters, wireless computers (Wi-Fi technology), wireless telephones with base stations in the house (the DECT technology), personal digital assistance (PDA) devices and cellular phones. There is uncertainty, however, as to whether these exposures pose risks for cancer and other health effects. Several studies have been published to date describing the relationship between RF/MW radiation exposure from base stations and different health symptoms, such as sleep disturbances, heart rhythm disruption, headaches, dizziness and depression (see \textit{inter alia} \cite{1–4}).

However, epidemiological evidence on community RF/MW radiation and cancer accumulated to date is based mainly on associations, and assessments of group exposures, without information on individual exposures, and therefore may be biased towards the null by exposure misclassification. Several studies indicated an increased risk for cancer associated with living in vicinity of transmitters, but these studies had less than complete information on exposure assessment and possible confounders \cite{5–10}.

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Isifya Village is located on the top of the Carmel Mountain (about 750 m above the sea level). Its hilltop location made it especially attractive for communication companies to erect their towers and antennas as they can cover wide distances with their services. The first radio transmitters in the village were erected in the beginning of the 1970s. Cellular antennas were added in the 1990s. In 2000, all the cellular antennas and radio transmitters in the village were destroyed by local residents who attributed different health symptoms to the radiation [11, 12].

According to the National Cancer Registry [13], there was an excess of cancer morbidity in Isifya, during the years 1998–2001, especially in men (RR = 1.57; CI (95%) = 1.12–2.02). There were specific types of cancer for which it was possible to make individual calculations. For lymphoma, in men on the basis of 7 cases in this period, RR was 2.28; (CI95%: 0.59–3.97) and colorectal cancer rate in men, on the basis of 8 cases, the RR was 2.01 (CI95% 0.62–3.4) ibid.

The aim of this study was to determine the possible reasons of cancers and if there were elevated cancer risks associated with living in proximity to non-ionizing radiation emitting transmitters. The study was carried out to address concerns of the local residents of the village about their exposure to radio and cellular transmitters.

2. Materials and methods

The present analysis is a retrospective follow up study. Because most houses in the village do not have street numbers, cancer registry data were unavailable for the study. Therefore, in the analysis, we relied on medical documents with confirmed diagnosis of cancer. Informed consent forms were signed by all the participants. The questionnaires were filled in face-to-face interviews by a single interviewer (IA) in the participant’s home. The questionnaires included questions about cancer history in the family; education;
marriage in the family (e.g., with cousins, which is not uncommon among the Druze); familial polyposis (a precancerous lesion); occupational exposures; smoking and passive smoking; duration of residence in the same house; alcohol consumption; nutritional habits; frequency of physical exercise; the use of cellular phones; exposure to wireless equipment in the house (such as digitally enhanced cordless telephones-DECT); use of oral contraceptives or hormones replacement therapy (HRT) and income (below average, average and above average). For deceased cancer patients, a family member was asked to fill in the questionnaire. Each visited house was marked on the map of the village, and the same process was used for controls.

The houses were then mapped in the ArcGIS9™ software using the building layer (map) provided by the local municipality. The radio and cellular transmitters, located in the village prior to 2000, were also mapped in the ArcGIS9™ software as a separate layer (Fig. 1). Information on the transmitters’ locations was confirmed by the municipality.

We discovered that several families in the village had antennas on their home’s roofs. These antennas were also mapped. The GIS layers for mapping antennas and houses were then used to calculate distances between each house and the nearest antenna. The study has 85.42% statistical power of detecting an odds ratio of 2.6 for 0.05 statistical significance level (Open Epi, Appendix A).

The study was approved by the Helsinki Committee of the local “Rambam” hospital. Informed consent forms were signed by all the participants.

2.1. Eligibility

Cancer cases were defined as eligible for inclusion on the basis of official medical documents and histopathology diagnosis of cancer. Altogether, 348 residents of the village were surveyed with a questionnaire that included the diagnosis details vs. controls, of whom 47 had cancer: colorectal [11], breast cancer [10], lymphoma [6], Leukemia [3], lungs [2], uterine [2], liver [2], stomach [2], ovarian [2], pancreas [2], prostate [2], cervix [1], brain [1], and bladder [1].

Excluded from analysis were residents who migrated to the area after the year 2000 and also patients without documents, which left us with 307 subjects, of whom 47 were diagnosed with cancer. There was only 1 cancer patient (male) among the 28 people who migrated to the area after 2000 (22 females and 6 males).

Houses built in the last 10–15 years were also excluded from the sample, to account for latency effects.

2.2. Exposure assessment

Individual exposure (E) was estimated using the following formula: \( E = 1/D^2 \), where \( D \) is distance (in meters) between a house and the closest transmitter, following studies reported observed intensity decreases in the inverse proportion to the squared distance from the radiation source (see inter alia [14]) remembering that the major transmitting power of the RF/MW antennas is, however, directed to the horizon while the cellular phone base stations are aimed at a proximal radius of downward sites.

2.3. Statistical analysis

For the statistical analysis of the questionnaire we used the binary logistic regression model in SPSS 15.0™, in which radiation intensity (see Section 2.2) was adjusted for individual variables associated with cancer risk: one of these variables, nutrition habits in the village were found to be quite uniform among the population with a high prevalence of meat eating, shifts from traditional foods and exposure to processed foods in recent years. Occupational exposure was classified into three groups: working in construction, with pesticides, electronics and industrial chemicals vs. occupations with no exposure to industrial or agriculture particular risk factors, and the unemployed.

3. Results

The general characteristics of the study population are reported in Table 1. 15.3% of the studied population was found to have cancer.

### Table 1

| Basic characteristics of the Isifya study population. |
|---|---|---|
| Parameter | No. | % |
| Age (for male and female) | | |
| Mean | 48 |  |
| Median | 48 |  |
| Gender | | |
| Male | 118 | 38.4 |
| Female | 189 | 61.6 |
| Marriage with cousins within the family | | |
| No | 252 | 82.1 |
| Yes | 55 | 17.9 |
| Smoking | | |
| No | 264 | 86 |
| Yes | 43 | 14 |
| Occupation | | |
| Chemicals and electronics | 43 | 14 |
| Other | 264 | 86 |
| Education | | |
| Elementary and high school | 217 | 70.7 |
| Higher education and no education | 90 | 29.3 |
| Exposure time (years) | | |
| Mean | 21.8 |  |
| Min | 1 |  |
| Max | 30 |  |
| Std. deviation | 8.689 |  |

Distribution of cancer cases by neighbourhood

| A: Old neighbourhood (more exposed) | 32 | 68% |
| B: Less exposed neighbourhood | 11 | 23% |
| C: Unknown exposure | 4 | 8.5% |
the most intense exposures. This neighbourhood was also the most densely populated. The first diagram shows a clear reduction in the number of all cancer cases with increasing distance, possible relationship between distance to antenna transmitters and the increasing risk of cancer. The lower diagram also shows the second peak of cancer prevalence (within 300–350 m range), which may indicate points where radiation beam hits the ground depending on the transmission frequency. In fact, the pattern is consistent with sinusoidal model [15]. But since we had no specific characteristics of the antennas, we could not analyze these relationships further.

The results of the binary logistic regression analysis are reported in Table 2. Data on cancer types of less than 5 cases were analyzed and there were no notable findings (Tables 3–5). We summarize the noteworthy findings. As Table 2 shows, age was weakly associated with risk of colorectal cancer (OR = 1.04; CI 95% = 0.99–1.10; \( P < 0.1 \)) and education was inversely associated with risks for cancer from all sites (OR = 0.49; CI 95% = 0.21–0.72; \( P < 0.1 \)).

For all cancer sites, there was a statistically significant association between cancer and the occupational exposure to chemicals and electronics (\( n = 43; \) OR = 2.79;...
Table 5
Results of logistic regression for less than 5 cases.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pancreas, OR (95% CI)</th>
<th>Stomach, OR (95% CI)</th>
<th>Prostate, OR (95% CI)</th>
<th>Liver, OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of cases/controls</td>
<td>2/305</td>
<td>1/306</td>
<td>2/305</td>
<td>2/305</td>
</tr>
<tr>
<td>Age</td>
<td>1.02 (0.87–1.20)</td>
<td>1.09 (0.96–1.23)</td>
<td>1.10 (0.89–1.37)</td>
<td>0.96 (0.82–1.13)</td>
</tr>
<tr>
<td>Gender</td>
<td>0.00 (0.00)</td>
<td>9,569,283.1 (0.00)</td>
<td>0.00 (0.00)</td>
<td>1.04 (0.02–51.87)</td>
</tr>
<tr>
<td>Education</td>
<td>0.00 (0.00)</td>
<td>0.00 (0.00)</td>
<td>0.00 (0.00)</td>
<td>0.00 (0.00)</td>
</tr>
<tr>
<td>Marriage within family</td>
<td>0.00 (0.00)</td>
<td>0.00 (0.00)</td>
<td>0.00 (0.00)</td>
<td>0.00 (0.00)</td>
</tr>
<tr>
<td>Smoking</td>
<td>14.25 (0.03–5233.48)</td>
<td>0.93 (0.00)</td>
<td>1.67 (0.04–61.04)</td>
<td>12.45 (0.34–453.54)</td>
</tr>
<tr>
<td>Radiation intensity</td>
<td>1.11 (0.91–1.34)</td>
<td>0.99 (0.93–1.06)</td>
<td>0.97 (0.86–1.10)</td>
<td>0.96 (0.84–1.11)</td>
</tr>
<tr>
<td>Years of exposure to radiation</td>
<td>0.76 (0.48–1.18)</td>
<td>0.92 (0.79–1.08)</td>
<td>12.03 (0.00–5.6E+192)</td>
<td>7988.30 (0.00–7.2E+285)</td>
</tr>
<tr>
<td>Constant</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.59</td>
<td>0.25</td>
<td>0.54</td>
<td>0.40</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Brain, OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases/controls</td>
<td>1/306</td>
</tr>
<tr>
<td>Age</td>
<td>1.00 (0.84–1.20)</td>
</tr>
<tr>
<td>Gender</td>
<td>13,020,733 (0.00)</td>
</tr>
<tr>
<td>Education</td>
<td>0.00 (0.00)</td>
</tr>
<tr>
<td>Marriage within family</td>
<td>8.7E+009</td>
</tr>
<tr>
<td>Smoking</td>
<td>2.00 (0.00)</td>
</tr>
<tr>
<td>Occupation</td>
<td>5.07 (0.00)</td>
</tr>
<tr>
<td>Radiation intensity</td>
<td>1.06 (0.93–1.22)</td>
</tr>
<tr>
<td>Years of exposure to radiation</td>
<td>1.082 (0.66–1.76)</td>
</tr>
<tr>
<td>Constant</td>
<td>0.00</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.44</td>
</tr>
</tbody>
</table>

CI$_{95\%}$ = 1.14–6.82; $P < 0.05$). We had no data on the role of occupational non-ionizing radiation exposures in those reporting electronics exposures.

Estimated intensity of community radiation exposure was not associated with risk of all cancers ($n = 47; \text{OR} = 1.00; \text{CI}_{95\%} = 0.99–1.02; P > 0.4$) and a minor association for colorectal cancer ($n = 11; \text{OR} = 1.03; \text{CI}_{95\%} = 1.01–1.05; P < 0.05$). For breast cancer, there was an inverse association with estimated radiation intensity ($n = 10; \text{OR} = 0.84; \text{CI}_{95\%} = 0.72–0.79; P = 0.01$). Other results of note were related to age at start of exposure, for all sites cancer, with older age, higher risk ($n = 47; \text{OR} = 1.03; \text{CI}_{95\%} = 1.00–1.06; P < 0.05$), and for breast cancer ($n = 10; \text{OR} = 1.11; \text{CI}_{95\%} = 1.01–1.20; P < 0.05$). There was a strong but non significant association between occupational exposures and lymphoma ($n = 4; \text{OR} = 6.53; \text{CI}_{95\%} = 0.956–44.622; P < 0.1$).

The results were not changed for confidence intervals of 90% and 80%.

4. Discussion

Our study did not confirm the impression of an inverse association with proximity to estimated past locations of antennae (Fig. 2). The data did not also provide evidence for an increased risk of all cancers related to residents’ estimated past exposure to non-ionizing radiation from radio neither the cellular transmitters in the Isifya Village. However, we found a low and inconsequential but significantly increased risk of colorectal cancer related to estimated past exposure to radiation at 90% confidence intervals.

![Fig. 2. Ratios between the total numbers of detected cancer cases in different distance bands from the RF/MW transmitters, estimated respectively for the total number of residents in each distance band (top diagram) and for the total number of people covered by the survey (bottom diagram). The labels above the columns represent the number of cancer cases for each range of distance.](image-url)
to non-ionizing radiation. We did not find an association between colorectal cancer and familiar polyposis. We are aware of only one study on occupational exposure to RF/MW radiation that showed an increased risk for colorectal cancer [16]. Generally colorectal cancer is related to nutritional risk factors [17–21].

No increased risk was found for lymphoma and all sites cancer with relation to estimated past exposure to radiation. However a reduction of risk in relation to RF/MW was found for breast cancer. There is no indication for an inverse link between RF/MW and for breast cancer in the literature. The association of higher socioeconomic and the occurrence of breast cancer is well known. There is evidence in the literature of a correlation between higher incidence of breast cancer and high income populations [22,23].

We could not assess the role of lower socioeconomic status, but it cannot be ruled out as a possible explanation in the area closer to the antennas.

We found a high but non statistically significant association between occupational exposure to pesticides and industrial chemicals, including work with electronics and risk of lymphoma. The relationship between lymphoma and pesticides is consistent with findings from other studies [24,25] as well as the relationship with other cancers [26,27].

For all cancer sites, there was a statistically significant association between occupational exposure to chemicals and electronics. This finding is consistent with findings from experimental studies on an interaction between chemicals and microwave exposures: microwave fields interact at cell membranes with amplitude-modulated at ELF frequencies, and with chemical stimulations of chemical cancer promoters. [28]. Oxidative stress is increased from occupational exposures to EMF and chemicals [29]. Magnetic fields thus can act as a cancer promoter or work in synergy with other cancer promoters [30]. Microwave workers with more than 20 years of job experience, who were exposed to soldering fumes and/or electronic solvents, were found to have a 10-fold risk of brain tumors [31].

Experimental studies on RF and immunity, both epidemiological [32,33] and experimental studies [34–37] showed contradictory effects. For example, Cleary et al. [35] found both an increase and decrease of proliferation of T-lymphocytes, and Phillips et al. (1998) found both an increase and decrease of DNA damage.

Although smoking is a known, recognized significant factor in the development of many cancers [38–40], we did not find a statistically significant association between self reported smoking and cancer risk in this study, neither for individual cancers nor all sites.

Despite the impressions suggested by the mapping data, our logistic regression analysis did not discover an overall relationship between cancer and estimated past exposure to non-ionizing radiation.

Our study’s strength is the inclusion of multiple risk factors such lifestyle, occupational exposures and genetic factors and the use of GIS, which enabled us to provide past individual exposure estimates and minimize exposure misclassification [41].

Our data analysis enabled us to exclude the possibilities that ethnic background, parity, age, birth rate, accounted for differences, as these factors were controlled for in the statistical analysis.

5. Study limitations

This study’s major limitation is that we cannot exclude the possibility of exposure misclassification because of multiple sources (cellular and radio), influence of topographic factors, angle of beam in relation to residence of exposed subjects, and the lack of individual data on round the clock proximity to sources.

The lack of data on past actual radiation levels was a consequence of the fact that antennae were removed before the start of the study. Thus, there was the possibility of errors in reconstructing past exposures based on distance alone.

We recognize that distance is not a totally reliable proxy exposure indicator for RF-EMF exposure. Distance was found to be a good exposure proxy for a single AM transmitter and of limited informative value in studies involving several transmitters, especially when they operate in different frequency bands [42].

Another limitation is the small study population size and thus low statistical power. Our study was also limited by small number of cases from the types of cancer believed to associate with exposure – i.e., leukemia and lymphomas [7,10,43,44].

The study did not include the new metric, called GS units, measured with Graham/Stetzer meter, and reflecting average rate of change of high frequency voltage transients from electrical power wiring, that are caused by interruption of electrical current flow (“dirty electricity”). A recent study found that dirty electricity was related to increased cancer risk [45].

6. Conclusion

We observed an increased risk from occupational chemicals and electronics exposures, for breast cancer and all sites cancer, but no clear indication of increased risk of cancer (all sites) among residents of Isifya attributed to past estimated RF exposure to broadcasting towers.

Competing interests

The authors declare that they have no competing interests.
Acknowledgements

The study was supported by a scholarship from the University of Haifa. Our gratitude is due to Suleiman Abu Rukan, Mira Abu Zalef and the village women’s committee, for their initiative in promoting this study.

Appendix A. Explanation of questionnaire variables

Age – at start of exposure.
Education level – no education, elementary school, high school, non academic above high school, and academic degree.
History of cancer – cancer in the family (first degree).
Marriage in the family – marriage to cousins or parents are cousins.
Occupation – housewives, unemployed, working at risk conditions (chemicals, radiation), and other – non risk exposure at work.
Smoking – never, used to smoke and stopped, smoking. Amount of cigarettes per day was not included in final analysis.
Passive smoking (exposure in house as a child).
Number of children (for number of pregnancies).
Nutrition
(A) Carnivore, vegetarian or vegan;
(B) Frequency of vegetables consumption;
(C) Frequency of industrial (processed) food consumption.
Alcohol – frequency and amount of consumption.
Time of exposure – years of exposure to transmitters.

Appendix B. Power calculation by Open Epi programme

Two-sided confidence interval (%) 95
Number of cases 47
Percent of exposure among cases (%) 68
Number of controls 260
Percent of exposure among controls (%) 44.6
Odds ratio 2.6

Power based on:
Normal approximation 85.42%
Normal approximation with continuity correction 81.1%

References


Exposure to Radio-Frequency Electromagnetic Fields From Broadcast Transmitters and Risk of Childhood Cancer: A Census-based Cohort Study

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We investigated the association between exposure to radio-frequency electromagnetic fields (RF-EMFs) from broadcast transmitters and childhood cancer. First, we conducted a time-to-event analysis including children under age 16 years living in Switzerland on December 5, 2000. Follow-up lasted until December 31, 2008. Second, all children living in Switzerland for some time between 1985 and 2008 were included in an incidence density cohort. RF-EMF exposure from broadcast transmitters was modeled. Based on 997 cancer cases, adjusted hazard ratios in the time-to-event analysis for the highest exposure category (>0.2 V/m) as compared with the reference category (<0.05 V/m) were 1.03 (95% confidence interval (CI): 0.74, 1.43) for all cancers, 0.55 (95% CI: 0.26, 1.19) for childhood leukemia, and 1.68 (95% CI: 0.98, 2.91) for childhood central nervous system (CNS) tumors. Results of the incidence density analysis, based on 4,246 cancer cases, were similar for all types of cancer and leukemia but did not indicate a CNS tumor risk (incidence rate ratio = 1.03, 95% CI: 0.73, 1.46). This large census-based cohort study did not suggest an association between predicted RF-EMF exposure from broadcasting and childhood leukemia. Results for CNS tumors were less consistent, but the most comprehensive analysis did not suggest an association.

Original Contribution

Radio-frequency electromagnetic fields (RF-EMFs) from broadcast transmitters (radio and television transmitters) have been hypothesized to cause childhood cancer, although a biological mechanism has not been identified for low exposure levels (1, 2). The International Agency for Research on Cancer (IARC) has classified RF-EMFs as “possibly carcinogenic to humans (group 2B)” based on positive associations between glioma and acoustic neuroma and exposure to RF-EMFs from wireless telephones (3). Regarding studies on the possible association between cancer and exposure to RF-EMFs from fixed-site transmitters, the IARC Working Group found the available evidence insufficient to draw a conclusion.

The output power of broadcast transmitters can be high, in order to cover large geographical areas. Thus, they are spaced far apart, and field levels can be relatively high in the immediate vicinity at ground level. As a consequence, epidemiologic exposure assessment for these sources is less vulnerable to exposure misclassification than that for other environmental RF-EMF sources such as mobile-phone base stations, which display a much higher spatial variation (4, 5). High spatial heterogeneity is a challenge for modeling but also for exposure

Abbreviations: AM, amplitude modulation; CI, confidence interval; CNS, central nervous system; FM, frequency modulation; IARC, International Agency for Research on Cancer; ICCC-3, International Classification of Childhood Cancer, Third Edition; RF-EMF(s), radio-frequency electromagnetic field(s); SCCR, Swiss Childhood Cancer Registry; UHF, ultra-high frequency; VHF very high frequency.
Time at risk started on the date of the census and lasted until the date of diagnosis, death, emigration, the child’s 16th birthday, or December 31, 2008, whichever occurred first. Incident cancer cases in the Swiss National Cohort were identified by means of a probabilistic linkage with the SCCR using information on date of birth, sex, place of residence, place of birth, and parents’ birthdates if available. The resulting data set contained the diagnosis date of cancer cases and information on potential confounders for all study participants: sex, birth order (within each household), socioeconomic status of the parents (highest education, socioprofessional category), and geospatial data for place of residence on the census date.

Incidence density cohort analysis. For the incidence density cohort analysis, no linkage between SCCR and Swiss National Cohort data was necessary. We included in this cohort all SCCR-registered patients diagnosed between January 1985 and December 2008 and residing in Switzerland at the time of diagnosis. For a Poisson regression analysis, person-years at risk accrued during a census year (1990, 2000) were calculated for each cell of a cross-tabulation between exposure categories, sex, and 1-year age strata. Cell-specific person-years for noncensus years were then estimated by inter-/extrapolation from corresponding values in the census years, with adjustments for national population-level changes by sex and age, which were known for all years. Details on this procedure are provided by Spycher et al. (21).

Exposure assessment

For this study, we focused on broadcast transmitters emitting medium-wave (0.5–1.6 MHz), short-wave (6–22 MHz), very high frequency (VHF; 174–230 MHz), and ultra-high frequency (UHF; 470–862 MHz) EMFs, which includes analogous television transmitters (VHF and UHF bands), terrestrial digital audio broadcast transmitters (VHF band), and digital terrestrial video broadcast transmitters (UHF band). All models considered antenna height, transmission duration, the horizontal and vertical directions of the emissions, and local topography. We included all VHF and UHF transmitters in Switzerland with an output power of more than 100 kW (11 transmitters), as well as transmitters with an output power between 10 kW and 100 kW if more than 30,000 persons lived within a 5-km radius (11 transmitters). Population density was considered as a selection criterion because transmitters in a highly populated area may cause relevant exposure, whereas remote transmitters (mainly in the alpine region) were not expected to be relevant for population exposure. RF-EMF levels from these transmitters were modeled by the Federal Office of Communications for an area with a radius of 10 km around each transmitter for the years 1990 and 2000. For the modeling, the Institut für Rundfunktechnik 2-dimensional model (IRT_2d) model (22) was applied using CHIR plus_BC software from LS Telecom (Lichtenau, Germany).

RF-EMF exposure levels from all Swiss short- and medium-wave radio transmitters with an output power greater than 1 kW (9 transmitters) were modeled on the basis of the Fresnel Deygout method (23) using ICS-Telecom software from ATDI (Paris, France). For these transmitters, modeling was carried out within a radius of 20 km for the years 1993.
and 1997. For overlapping modeled areas, the exposure levels of all transmitters were summed.

In the time-to-event analysis, RF-EMF exposure to radio and television transmitters at baseline was assessed for each study participant at the place of residence using the modeled RF-EMFs from 2000 and 1997, respectively. In the incidence density cohort analysis, place of residency on the date of diagnosis was used for exposure assignment. For children diagnosed before 1995, exposure assessment was based on the models for 1990 and 1993. Thereafter, RF-EMF exposure was assessed using the modeled RF-EMFs from 2000 and 1997, respectively.

Geospatial data on potential confounders were extracted from digital maps using ArcGIS (ESRI, New York, New York), based on the place of residence. Data on background γ radiation were available from the Swiss radiation maps (24) with a grid cell resolution of 2 km. Digital maps with power lines with a resolution of 1:25,000 were provided by the Federal Inspectorate for Heavy Current Installations. We extracted distances to the traffic network in 2000 from digital maps on the traffic network with a resolution of 1:25,000 (VECTOR25-maps), published by the Federal Office of Topography. Data on distances to the nearest orchards, vineyards, and golf courses, for the estimation of exposure to agricultural pesticides, were obtained from the Swiss land-use statistics (Arealstatistik Schweiz) for the year 1997, published by the Swiss Federal Statistical Office, with a grid cell resolution of 100 m. We geocoded the location of the pediatric cancer centers manually (25). Data on ambient benzene, particulate matter with an aerodynamic diameter less than 10 μm, and nitrogen dioxide exposure were available from a digital map with a grid cell resolution of 100 m (benzene: 400 m), published by the Swiss Agency for the Environment, Forestry and Landscape (26, 27). Residential radon exposure was estimated from a nationwide radon prediction model (28, 29).

### Statistical analysis

For the time-to-event and incidence density cohort analyses, the same RF-EMF exposure categories were used with a priori chosen cutpoints at 0.05 V/m and 0.2 V/m to differentiate between low, medium, and high exposure. All study participants living in an area not covered by the modeling were included in the reference category. A cutpoint of 0.05 V/m for the reference category was chosen because this value is unlikely to be exceeded due to broadcasting outside the modeling area (30). A cutpoint of 0.2 V/m for high exposure corresponds roughly to the first quartile of the study population being exposed to RF-EMF levels of more than 0.05 V/m.

For the time-to-event analysis, Cox proportional hazards regression models were applied using age as the underlying time scale. Period effects were considered by splitting the follow-up time into two 4-year blocks. The basic models always included adjustment for sex. Furthermore, we decided a priori to adjust for exposure to the potential leukemia risk factors benzene, natural background ionizing γ radiation, distance to the nearest high-voltage power line, and degree of urbanization (31–33). We tested the relevance of additional potential confounding factors in the time-to-event analysis by including one confounder at a time in the model and applying a change-in-estimation criterion of 10% (34). We also conducted a sensitivity time-to-event analysis that excluded

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**Figure 1.** Linkage of the database of the Swiss Childhood Cancer Registry to that of the Swiss National Cohort (SNC) for a study of radiofrequency electromagnetic fields and childhood cancer, Switzerland, 2000–2008. ALL, acute lymphoblastic leukemia; CNS, central nervous system.
all children not living in an area covered by the exposure modeling (i.e., >10 km or >20 km from any transmitter).

For the incidence density analysis, we conducted a Poisson regression analysis that adjusted for sex, age, and calendar year. Separate analyses were conducted for the period up to 1995 and the period after 1995. Results of the incidence density analysis for leukemia were also stratified by age, using 1 and 6 years of age as cutpoints.

RESULTS

For the time-to-event analysis, 1,332,944 children aged ≤15 years on the census date were identified in the Swiss National Cohort database. Of these, 45,590 children with an unclear place of residence were excluded from the analysis (Figure 1). In total, 1,287,354 children with 7,627,646 person-years accumulated during the study period were considered for the analysis. We identified 1,127 cancer cases in the SCCR that were diagnosed between the 2000 census date and 2008 (Figure 1). Of these, 997 could be linked to the Swiss National Cohort database (283 leukemia cases and 258 CNS tumor cases).

Figure 2 shows the total field levels by distance to the closest transmitter for all residences in the modeled study area. The Spearman correlation between total field levels and

![Figure 2. Modeled strengths of radio-frequency electromagnetic fields according to distance from children’s households to the nearest broadcast transmitter within the modeled areas, Switzerland, 1997–2000.](image)

### Table 1. Hazard Ratio for Childhood Cancer According to Exposure to Radio-Frequency Electromagnetic Fields in Time-to-Event Analysis (Cox Regression), Switzerland, 2000–2008

<table>
<thead>
<tr>
<th>Cancer Type and Exposure Category</th>
<th>No. of Cases</th>
<th>Baseline HR&lt;sup&gt;a&lt;/sup&gt;</th>
<th>95% CI</th>
<th>Adjusted HR&lt;sup&gt;b&lt;/sup&gt;</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cancers, V/m</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.05</td>
<td>830</td>
<td>1</td>
<td>Referent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.05–0.2</td>
<td>127</td>
<td>1.17</td>
<td>0.97, 1.40</td>
<td>1.14</td>
<td>0.94, 1.38</td>
</tr>
<tr>
<td>&gt;0.2</td>
<td>40</td>
<td>1.06</td>
<td>0.77, 1.45</td>
<td>1.03</td>
<td>0.74, 1.43</td>
</tr>
<tr>
<td>Per 0.1 V/m</td>
<td>997</td>
<td>1.02</td>
<td>0.97, 1.08</td>
<td>1.02</td>
<td>0.96, 1.08</td>
</tr>
<tr>
<td>All types of leukemia, V/m</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.05</td>
<td>251</td>
<td>1</td>
<td>Referent</td>
<td>1</td>
<td>Referent</td>
</tr>
<tr>
<td>0.05–0.2</td>
<td>25</td>
<td>0.75</td>
<td>0.50, 1.13</td>
<td>0.70</td>
<td>0.46, 1.07</td>
</tr>
<tr>
<td>&gt;0.2</td>
<td>7</td>
<td>0.60</td>
<td>0.28, 1.28</td>
<td>0.55</td>
<td>0.26, 1.19</td>
</tr>
<tr>
<td>Per 0.1 V/m</td>
<td>283</td>
<td>0.85</td>
<td>0.70, 1.03</td>
<td>0.82</td>
<td>0.67, 1.01</td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia, V/m</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.05</td>
<td>199</td>
<td>1</td>
<td>Referent</td>
<td>1</td>
<td>Referent</td>
</tr>
<tr>
<td>0.05–0.2</td>
<td>20</td>
<td>0.76</td>
<td>0.48, 1.20</td>
<td>0.73</td>
<td>0.45, 1.17</td>
</tr>
<tr>
<td>&gt;0.2</td>
<td>6</td>
<td>0.65</td>
<td>0.29, 1.46</td>
<td>0.62</td>
<td>0.27, 1.43</td>
</tr>
<tr>
<td>Per 0.1 V/m</td>
<td>225</td>
<td>0.89</td>
<td>0.73, 1.08</td>
<td>0.88</td>
<td>0.72, 1.08</td>
</tr>
<tr>
<td>CNS tumors, V/m</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.05</td>
<td>207</td>
<td>1</td>
<td>Referent</td>
<td>1</td>
<td>Referent</td>
</tr>
<tr>
<td>0.05–0.2</td>
<td>36</td>
<td>1.32</td>
<td>0.93, 1.89</td>
<td>1.35</td>
<td>0.94, 1.95</td>
</tr>
<tr>
<td>&gt;0.2</td>
<td>15</td>
<td>1.59</td>
<td>0.94, 2.68</td>
<td>1.68</td>
<td>0.98, 2.91</td>
</tr>
<tr>
<td>Per 0.1 V/m</td>
<td>258</td>
<td>1.05</td>
<td>1.00, 1.10</td>
<td>1.05</td>
<td>1.00, 1.10</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; CNS, central nervous system; HR, hazard ratio.

<sup>a</sup> Adjusted for sex and period effects; age was used as the underlying time scale.

<sup>b</sup> Additionally adjusted for environmental γ radiation, benzene exposure, distance to the nearest high-voltage power line, and degree of urbanization.
distance to the closest transmitter was $-0.462$ (95% CI: $-0.464, -0.460$). Eleven percent of all children were exposed to a predicted RF-EMF between $0.05 \text{ V/m}$ and $0.2 \text{ V/m}$, and 4% were exposed above $0.2 \text{ V/m}$. From the whole study sample, 51% lived within the modeled area. Arithmetic mean exposure for this sample within the modeled area was $0.14 \text{ V/m}$, with a median value of $0.02 \text{ V/m}$, a 90th percentile value of $0.16 \text{ V/m}$, and a maximum value of $9.77 \text{ V/m}$. Mean exposure was higher in urban areas ($0.17 \text{ V/m}$) than in suburban ($0.14 \text{ V/m}$) and rural ($0.08 \text{ V/m}$) areas.

Results from the time-to-event analysis are shown in Table 1. Compared with the group of children exposed to a predicted RF-EMF between $0.05 \text{ V/m}$ and $0.2 \text{ V/m}$, hazard ratios for the highest exposure category ($\geq 0.2 \text{ V/m}$) were $1.03$ (95% CI: $0.74, 1.43$) for all cancers, $0.55$ (95% CI: $0.26, 1.19$) for leukemia, $0.62$ (95% CI: $0.27, 1.43$) for acute lymphoblastic leukemia, and $1.68$ (95% CI: $0.98, 2.91$) for CNS tumors when considering all transmitters (Table 1). The linear exposure-response analyses provided a result pattern similar to that of the categorical analyses, although the positive correlation with CNS tumors reached statistical significance for all types of transmitters. The linear analyses indicated that none of the additional potential confounding factors materially altered the hazard ratios (Figure 3). Restricting the analysis to children who were living within the modeled exposure area had virtually no impact on the results (data not shown).

The incidence density cohort analysis accumulated 30.2 million person-years at risk and comprised 4,246 cancer cases, including 971 cases from the time-to-event analyses with geocoded addresses at the time of diagnosis. Results for the whole study period and for period-stratified analyses are shown in Table 2. Again leukemia tended to be negatively
There was no indication of a relationship between CNS tumor risk and predicted RF-EMF exposure from all transmitters. However, analyses restricted to the period up to 1995 yielded borderline-significant increased incidence rate ratios for all cancers in the high exposure category (incidence rate ratio = 1.23, 95% CI: 0.98, 1.55). For the period after 1995, the corresponding incidence rate ratio was significantly decreased (incidence rate ratio = 0.69, 95% CI: 0.54, 0.87). Stratifying the analyses for leukemia into different age groups that might represent different etiologies did not indicate effect modification by age (Table 3).

The results were similar when we restricted the analyses to VHF and UHF transmitters (see Web Tables 1 and 2, available at http://aje.oxfordjournals.org/). For short- and medium-wave transmitters, hazard ratios in the time-to-event analysis tended to be somewhat higher but not statistically significant, based on few cases, and without indications of a linear exposure-response association.

### Table 2. Incidence Rate Ratio for Cancer Among Children Under Age 16 Years in Incidence Density Cohort Analysis, by Exposure Category and Time Period, Switzerland, 1985–2008

<table>
<thead>
<tr>
<th>Cancer Type and Exposure Category</th>
<th>Time Period</th>
<th>No. of Cases</th>
<th>IRR*</th>
<th>95% CI</th>
<th>No. of Cases</th>
<th>IRR*</th>
<th>95% CI</th>
<th>No. of Cases</th>
<th>IRR*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cancers, V/m</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.05</td>
<td>3,591</td>
<td>1 Referent</td>
<td>1,433</td>
<td>1 Referent</td>
<td>2,158</td>
<td>1 Referent</td>
<td>1961</td>
<td>1 Referent</td>
<td>1,090</td>
<td>0.96, 1.22</td>
</tr>
<tr>
<td>0.05–0.2</td>
<td>511</td>
<td>1.09 1.00, 1.20</td>
<td>202</td>
<td>1.11 0.96, 1.28</td>
<td>309</td>
<td>1.09 0.96, 1.22</td>
<td></td>
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</tr>
<tr>
<td>&gt;0.2</td>
<td>144</td>
<td>0.90 0.76, 1.06</td>
<td>76</td>
<td>1.23 0.98, 1.55</td>
<td>68</td>
<td>0.69 0.54, 0.87</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All types of leukemia, V/m</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.05</td>
<td>1,149</td>
<td>1 Referent</td>
<td>478</td>
<td>1 Referent</td>
<td>671</td>
<td>1 Referent</td>
<td>1,433</td>
<td>1 Referent</td>
<td>1,090</td>
<td>0.96, 1.22</td>
</tr>
<tr>
<td>0.05–0.2</td>
<td>138</td>
<td>0.92 0.77, 1.10</td>
<td>58</td>
<td>0.96 0.73, 1.26</td>
<td>80</td>
<td>0.90 0.71, 1.14</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0.2</td>
<td>39</td>
<td>0.76 0.55, 1.05</td>
<td>23</td>
<td>1.13 0.74, 1.71</td>
<td>16</td>
<td>0.52 0.32, 0.85</td>
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<td></td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia, V/m</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.05</td>
<td>917</td>
<td>1 Referent</td>
<td>378</td>
<td>1 Referent</td>
<td>539</td>
<td>1 Referent</td>
<td>917</td>
<td>1 Referent</td>
<td>1,149</td>
<td>1 Referent</td>
</tr>
<tr>
<td>0.05–0.2</td>
<td>112</td>
<td>0.94 0.77, 1.14</td>
<td>45</td>
<td>0.94 0.69, 1.28</td>
<td>67</td>
<td>0.94 0.73, 1.21</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0.2</td>
<td>33</td>
<td>0.81 0.57, 1.14</td>
<td>21</td>
<td>1.30 0.84, 2.02</td>
<td>12</td>
<td>0.48 0.27, 0.86</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>CNS tumors, V/m</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt;0.05</td>
<td>718</td>
<td>1 Referent</td>
<td>247</td>
<td>1 Referent</td>
<td>471</td>
<td>1 Referent</td>
<td>718</td>
<td>1 Referent</td>
<td>1,149</td>
<td>1 Referent</td>
</tr>
<tr>
<td>0.05–0.2</td>
<td>108</td>
<td>1.16 0.95, 1.42</td>
<td>35</td>
<td>1.12 0.78, 1.59</td>
<td>73</td>
<td>1.18 0.92, 1.51</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0.2</td>
<td>33</td>
<td>1.03 0.73, 1.46</td>
<td>17</td>
<td>1.60 0.98, 2.61</td>
<td>16</td>
<td>0.75 0.45, 1.23</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** CI, confidence interval; CNS, central nervous system; IRR, incidence rate ratio.

* Adjusted for age, calendar year, and sex.

### Table 3. Incidence Rate Ratio for Leukemia Among Children Under Age 16 Years in Incidence Density Cohort Analysis, by Exposure Category and Age Group, Switzerland, 1985–2008

<table>
<thead>
<tr>
<th>Cancer Type and Exposure Category</th>
<th>Age Group, years</th>
<th>No. of Cases</th>
<th>IRR*</th>
<th>95% CI</th>
<th>No. of Cases</th>
<th>IRR*</th>
<th>95% CI</th>
<th>No. of Cases</th>
<th>IRR*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1</td>
<td></td>
<td></td>
<td></td>
<td>1–5</td>
<td></td>
<td></td>
<td>6–15</td>
<td></td>
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<tr>
<td>All types of leukemia, V/m</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.05</td>
<td>46</td>
<td>1 Referent</td>
<td>523</td>
<td>1 Referent</td>
<td>1,149</td>
<td>1 Referent</td>
<td>1,090</td>
<td>1 Referent</td>
<td>1,090</td>
<td>0.96, 1.22</td>
</tr>
<tr>
<td>0.05–0.2</td>
<td>4</td>
<td>0.63 0.23, 1.74</td>
<td>61</td>
<td>0.89 0.68, 1.16</td>
<td>138</td>
<td>0.92 0.77, 1.10</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&gt;0.2</td>
<td>1</td>
<td>0.44 0.06, 3.19</td>
<td>25</td>
<td>1.07 0.71, 1.59</td>
<td>39</td>
<td>0.76 0.55, 1.05</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia, V/m</td>
<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>&lt;0.05</td>
<td>22</td>
<td>1 Referent</td>
<td>463</td>
<td>1 Referent</td>
<td>917</td>
<td>1 Referent</td>
<td>1,149</td>
<td>1 Referent</td>
<td>1,090</td>
<td>0.96, 1.22</td>
</tr>
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<td>0.05–0.2</td>
<td>2</td>
<td>0.65 0.15, 2.76</td>
<td>57</td>
<td>0.94 0.71, 1.24</td>
<td>112</td>
<td>0.94 0.77, 1.14</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0.2</td>
<td>0</td>
<td>0.00 0.00, ∞</td>
<td>23</td>
<td>1.11 0.73, 1.68</td>
<td>33</td>
<td>0.81 0.57, 1.14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** CI, confidence interval; IRR, incidence rate ratio.

* Adjusted for age, calendar year, and sex.
DISCUSSION

This large census-based cohort study did not suggest increased childhood leukemia risk from exposure to broadcasting-related RF-EMFs. We observed an elevated risk of CNS tumors in the time-to-event analysis, but this finding could not be confirmed in the incidence density analysis, which was based on a substantially higher number of cases and a longer follow-up period.

The main strength of this study was that it was based on registry data, without the requirement to contact study participants. As a consequence, a high proportion of all eligible study participants could be included, which prevented participation bias. In addition, we were able to individually assess RF-EMF exposure based on established models and did not have to rely on rough exposure proxies, such as distance, which have been used in many previous studies (6–11, 13, 14). The exposure distribution of radio and television transmitters is complex, and our analyses indicated only a moderate correlation between the modeled field strengths and the distance to the nearest broadcast transmitters.

We applied 2 cohort analysis approaches, both with advantages and disadvantages. The time-to-event analysis allowed for consideration of numerous potential confounding factors, which was not done in 2 previous case-control studies (13–15). With this approach, we could demonstrate that the evaluated confounding factors are not crucial for this type of exposure-response analysis. Thus, our second approach with basic confounding adjustment in the incidence density cohort is considered reliable. The incidence density cohort covered a longer follow-up period and included more than 4,000 childhood cancer cases. A further strength of the incidence density analysis was separate consideration of data from the period before 1996, when use of cordless and mobile phones was less prevalent and broadcast transmitter emissions contributed to a larger proportion of the overall RF-EMF exposure of the population. This reduced the potential for exposure misclassification. In Switzerland, RM-EMFs from broadcasting were found to account for 12% of the total environmental RF-EMF exposure between 2007 and 2008 (35). Ideally, for the period after 1995, the contributions of exposure from wireless phone use and mobile-phone base stations should be considered in the analyses. However, this is very complex, and such data were not available for this nationwide cohort.

A limitation of the incidence density cohort analysis was the estimation of aggregated person-years by inter- and extrapolation of census data from 1990 and 2000. Although this interpolation adjusted for national sex- and age-specific population levels in noncensus years, we could not account for localized population fluctuations between census years, leaving some uncertainty in the denominator of the incidence rate calculations. However, this would only have biased the results if it differed systematically by exposure category. On the other hand, a limitation of the time-to-event analyses was the probabilistic record linkage of cases with the Swiss National Cohort. Some cases could not be linked, and some mismatches may have occurred as well. Both of these errors will have caused some misclassification of outcomes and exposure, but it was most likely nondifferential.

A limitation of the exposure assessment is that transmitter data were only available from 2 years during the study period. However, year-to-year changes in emissions from transmitters were generally relatively low until 2008, except for the shutdown of a short-wave transmitter (in Schwarzenburg) in 1998, which was considered in the exposure assessment. To consider shielding, diffraction, or the reflection of RF-EMFs in the modeling, one needs data on local meteorology, morphology, vegetation, and soil conductivity (4), which were not available for the whole study period. The introduced uncertainty is of particular concern for high exposure values. For this reason, we decided to conduct the primary analysis based on categorized exposure data, which is a more robust approach with regard to potential outliers.

Our study showed no indications of an increased leukemia risk with respect to RF-EMF exposure from broadcast transmitters. A lack of association between RF-EMFs and childhood leukemia is in line with the results of 2 previous case-control studies (13–15) with similar methodological features. In the German case-control study, Merzenich et al. (15) modeled RF-EMF exposure for each month during the study period and also conducted analyses stratified according to age and period; as in our study, they did not find any indication of effect modification by age or an increased risk for the early period (1983–1991) before mobile communication was introduced. Our results for leukemia are also in line with animal, in vitro, and laboratory studies that did not find a biological mechanism for long-term exposure to low levels of RF-EMFs (1, 36, 37).

With respect to CNS tumors, our results were less consistent. Borderline significant indications of an association with RF-EMFs were found in both the time-to-event analysis and the incidence density cohort analyses restricted to the time period up to 1995. However, incidence rate ratios were not increased for the entire incidence density cohort analysis comprising the whole study period from 1985 to 2008. This incidence density cohort analysis was based on the highest number of exposed cases and thus is considered the most reliable, whereas chance might be an explanation for the associations observed in the smaller data sets. On the other hand, one might give more weight to the early data, where exposure misclassification was reduced because broadcasting was the main source of environmental exposure (35). However, in-depth analyses of the statistically significant linear exposure-response relationship in the time-to-event analysis showed that the result was strongly affected by 2 highly exposed (>1 V/m) CNS cases (0.8% of all cases), as compared with only 0.1% of the study participants exposed above this level. Because no highly exposed leukemia case was observed, confidence intervals for the CNS analyses were considerably narrower than those for the leukemia analyses, despite similar numbers of cases.

The time-to-event analysis and the incidence density cohort analysis used different exposure time windows. The time-to-event analysis considered baseline exposure at the time of the 2000 census, whereas the incidence density analyses considered exposure at the time of diagnosis. Ideally, one would consider full residential history, but these data were not available.

An association between CNS tumors and RF-EMFs was not supported by the results of a South Korean case-control
study on broadcast transmitters (13, 14) or a British case-control study on mobile-phone base-station exposure (38). Childhood CNS tumors are almost always found in the brain (39, 40). Thus, if low RF-EMF levels, as observed in our study, caused CNS tumors in children, one would also expect increased risks from use of wireless phones, which lead to substantially higher exposure to the head. However, such an association was not observed in a previous case-control study (41), and CNS tumor incidence rates were not found to be increased among children aged 7–19 years in Northern European countries between 1990 and 2009 (42). Finally, neither animal studies nor in-vivo or in-vitro studies have identified a mechanism which would support an association at these low RF-EMF levels (1, 43).

In summary, this study did not find evidence of an association between RF-EMF exposure from broadcast transmitters and incidence of childhood leukemia. Results for CNS tumors were less consistent, but the most comprehensive analysis in terms of number of cases and observation period did not support an association.

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