

## Original Contribution

# 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.

broadcast transmitters; central nervous system tumors; childhood leukemia; childhood neoplasms; electromagnetic fields; radio waves

Abbreviations: AM, amplitude modulation; CI, confidence interval; CNS, central nervous system; FM, frequency modulation; IARC, International Agency for Research on Cancer; ICC-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.

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

assignment, because children are not stationary at their place of residence.

Most previous studies on this topic used an ecological design, and leukemia rates were mostly found to be increased in the proximity of broadcast transmitters, reaching statistical significance in some (6–9) but not all (10–12) studies. However, lack of individual exposure data and lack of confounding adjustment limits interpretation. Further, some of these ecological studies were based on small sample sizes and were initiated because of previous cluster reports. Recently, the results of 2 more informative large case-control studies with individual exposure assessment based on modeling were published (13–15). A South Korean study (13, 14) with 1,928 childhood leukemia cases and an equal number of matched hospital-based controls found no association between childhood leukemia risk and the average predicted field strengths from 31 amplitude-modulation (AM) radio transmitters. However, children living within 2 km of the transmitters had a relative risk of 2.15 (95% confidence interval (CI): 1.00, 4.67) for all types of leukemia compared with children living more than 20 km away. The other large case-control study (15), conducted in the vicinity of 16 AM and 8 frequency-modulation (FM) broadcast transmitters in Germany, included 1,959 leukemia cases and 3 population-based controls per case, matched on age, sex, and transmitter area. That study found no indication for an association between RF-EMFs and childhood leukemia.

The aim of our study was to investigate, within a prospective, census-based cohort study design, the association between RF-EMF exposure from broadcast transmitters and childhood cancer, particularly leukemia and tumors of the central nervous system (CNS).

## METHODS

### Study population

The study was based on data from the Swiss Childhood Cancer Registry (SCCR) and the Swiss National Cohort. The SCCR includes cancer patients aged less than 21 years at diagnosis. For patients under age 16 years at diagnosis, at least 95% of incident cases are registered (16). The Swiss National Cohort is a database containing data on all Swiss buildings, households, and persons (17, 18). It is based on probabilistic record linkages of census data sets from 1990 and 2000 with each other and with national birth, mortality, and emigration data sets. Participation in the Swiss census is compulsory, and coverage for the 2000 census was estimated to be 98.6% (19).

We considered all cancer diagnoses made in Switzerland classified according to the *International Classification of Childhood Cancer, Third Edition* (ICCC-3) (20), with a special focus on leukemia (ICCC-3 code I), acute lymphoblastic leukemia (ICCC-3 code I.a), and CNS tumors (ICCC-3 code III), including benign tumors.

**Time-to-event analysis.** We used 2 strategies to analyze the data: a time-to-event analysis and an incidence density cohort analysis. For the time-to-event analysis, we included children who were under age 16 years and living in Switzerland on the date of the 2000 census (December 5, 2000).

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 (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.

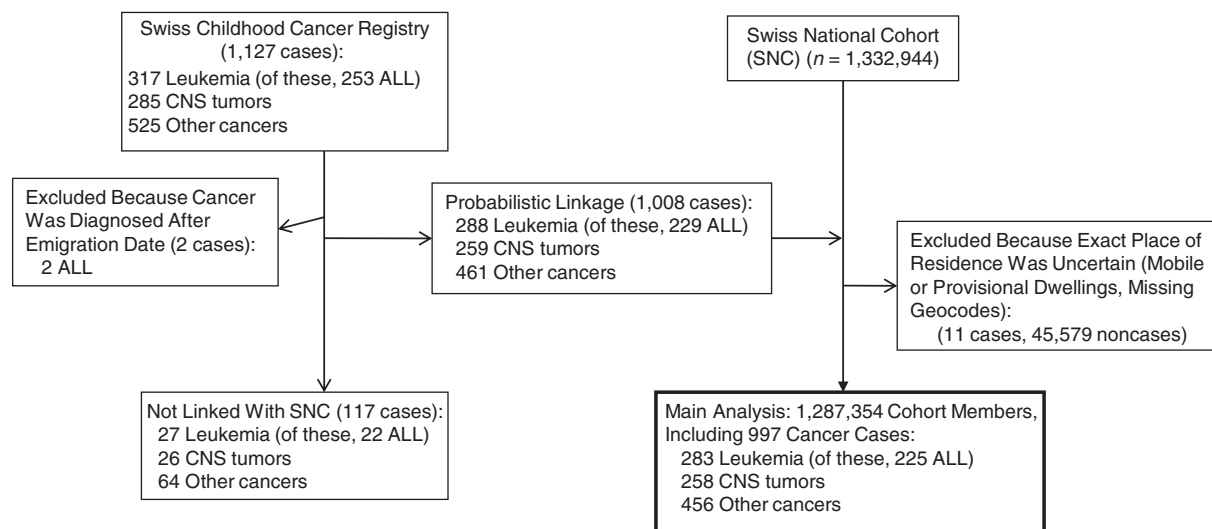
Geospatial data on potential confounders were extracted from digital maps using ArcGIS (ESRI, New York, New York), based on the place of residence. Data on background  $\gamma$  radiation were available from the Swiss radiation maps (24) with a grid cell resolution of 2 km. Digital maps with power lines 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  $\mu\text{m}$ , 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, Forests and Landscape (26, 27). Residential radon exposure was estimated from a nationwide radon prediction model (28, 29).

## Statistical analysis

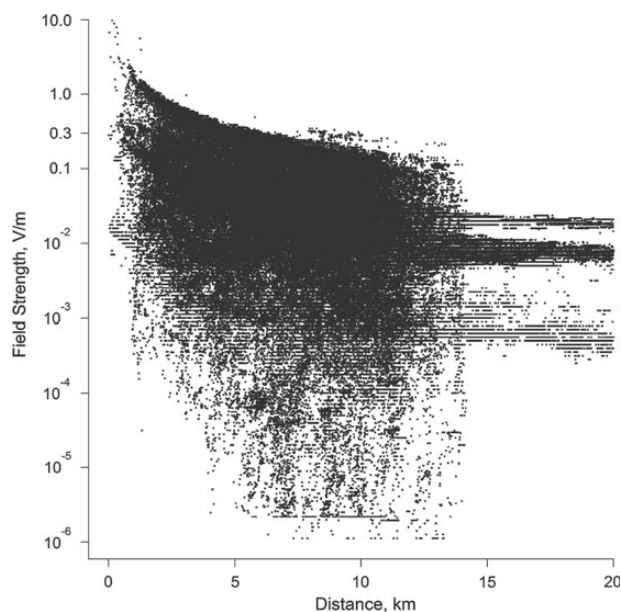
For the time-to-event and incidence density cohort analyses, the same RF-EMF exposure categories were used with a priori chosen cutpoints at 0.05 V/m and 0.2 V/m to differentiate between low, medium, and high exposure. All study participants living in an area not covered by the modeling were included 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 short- and medium-wave transmitters, the exposure variable was dichotomized at 0.05 V/m because of the lower levels.

In addition to categorical exposure classification, we also carried out linear exposure-response modeling in the time-to-event analysis using exposure to the broadcast transmitters as a continuous predictor and expressing the hazard ratio per 0.1-V/m increase in exposure. For these analyses, exposure levels outside the modeled area were set to 0.001 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  $\gamma$  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



**Figure 1.** Linkage of the database of the Swiss Childhood Cancer Registry to that of the Swiss National Cohort (SNC) for a study of radio-frequency electromagnetic fields and childhood cancer, Switzerland, 2000–2008. ALL, acute lymphoblastic leukemia; CNS, central nervous system.



**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.

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

**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

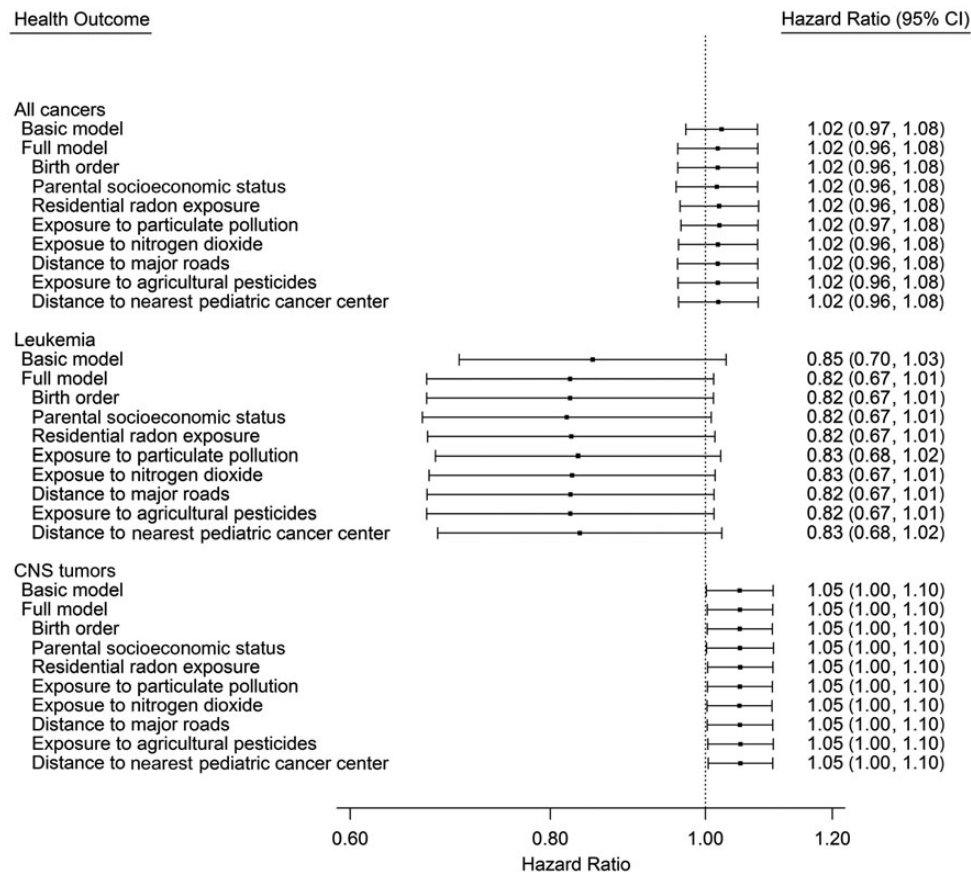
Cancer Type and Exposure Category	No. of Cases	Baseline HR <sup>a</sup>	95% CI	Adjusted HR <sup>b</sup>	95% CI
All cancers, V/m					
<0.05	830	1	Referent		
0.05–0.2	127	1.17	0.97, 1.40	1.14	0.94, 1.38
>0.2	40	1.06	0.77, 1.45	1.03	0.74, 1.43
Per 0.1 V/m	997	1.02	0.97, 1.08	1.02	0.96, 1.08
All types of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

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  $\gamma$  radiation, benzene exposure, distance to the nearest high-voltage power line, and degree of urbanization.





**Figure 3.** Impact of various confounding factors on the hazard ratio for childhood cancer per 0.1-V/m increase in exposure to radio-frequency electromagnetic fields in time-to-event analysis, Switzerland, 2000–2008. Potential confounding factors were added to the full model one at a time. The basic model adjusted for age and sex. The full model additionally adjusted for environmental  $\gamma$  radiation, benzene exposure, distance to the nearest high-voltage power line, and degree of urbanization. The relevance of additional potential confounding factors was tested by including one confounder at a time in the model. Linear adjustment was used for birth order (within each household), radiation, benzene, particulate matter with an aerodynamic diameter less than 10  $\mu\text{m}$ , and nitrogen dioxide. Categorical adjustment was used for distance to highways (<40 m, 40–<100 m, 100–400 m, or >400 m), distance to class 1 roads (<20 m, 20–<50 m, 50–200 m, or >200 m), distance to high-voltage railway lines (<50 m, 50–<200 m, 200–600 m, or >600 m), exposure to agricultural pesticides (<50 m, 50–<100 m, 100–200 m, or >200 m to orchards; <100 m, 100–<250 m, 250–500 m, or >500 m to vineyards; <750 m, 750–<1,500 m, 1,500–3,000 m, or >3,000 m to golf courses), distance to the nearest pediatric medical center (<5 km, 5–<15 km, 15–30 km, or >30 km), domestic radon exposure (50th (77.7 Bq/m<sup>3</sup>) and 90th (139.9 Bq/m<sup>3</sup>) percentiles), parental socioeconomic status (low, medium, high, or no information), and parental job position (low, medium, high, unemployed/retired/housewife/volunteer work, or no information). Bars, 95% confidence intervals (CIs).

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 V/m and 0.2 V/m, and 4% were exposed above 0.2 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 V/m, with a median value of 0.02 V/m, a 90th percentile value of 0.16 V/m, and a maximum value of 9.77 V/m. Mean exposure was higher in urban areas (0.17 V/m) than in suburban (0.14 V/m) and rural (0.08 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 below 0.05 V/m, hazard ratios for the highest exposure category ( $\geq 0.2$  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

**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

Cancer Type and Exposure Category	Time Period								
	1985–2008			1985–1995			1996–2008		
	No. of Cases	IRR <sup>a</sup>	95% CI	No. of Cases	IRR <sup>a</sup>	95% CI	No. of Cases	IRR <sup>a</sup>	95% CI
All cancers, V/m									
<0.05	3,591	1	Referent	1,433	1	Referent	2,158	1	Referent
0.05–0.2	511	1.09	1.00, 1.20	202	1.11	0.96, 1.28	309	1.09	0.96, 1.22
>0.2	144	0.90	0.76, 1.06	76	1.23	0.98, 1.55	68	0.69	0.54, 0.87
All types of leukemia, V/m									
<0.05	1,149	1	Referent	478	1	Referent	671	1	Referent
0.05–0.2	138	0.92	0.77, 1.10	58	0.96	0.73, 1.26	80	0.90	0.71, 1.14
>0.2	39	0.76	0.55, 1.05	23	1.13	0.74, 1.71	16	0.52	0.32, 0.85
Acute lymphoblastic leukemia, V/m									
<0.05	917	1	Referent	378	1	Referent	539	1	Referent
0.05–0.2	112	0.94	0.77, 1.14	45	0.94	0.69, 1.28	67	0.94	0.73, 1.21
>0.2	33	0.81	0.57, 1.14	21	1.30	0.84, 2.02	12	0.48	0.27, 0.86
CNS tumors, V/m									
<0.05	718	1	Referent	247	1	Referent	471	1	Referent
0.05–0.2	108	1.16	0.95, 1.42	35	1.12	0.78, 1.59	73	1.18	0.92, 1.51
>0.2	33	1.03	0.73, 1.46	17	1.60	0.98, 2.61	16	0.75	0.45, 1.23

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

<sup>a</sup> Adjusted for age, calendar year, and sex.

associated with predicted RF-EMFs. There was no indication of association 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 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

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

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

<sup>a</sup> 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 to the overall RF-EMF exposure of the population. This reduced the potential for exposure misclassification. In Switzerland, RF-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 may 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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