American Journal of Epidemiology

Vol. 168, No. 10
DOI: 10.1093/aje/kwn230
Advance Access publication October 3, 2008

Original Contribution

Childhood Leukemia in Relation to Radio Frequency Electromagnetic Fields in the Vicinity of TV and Radio Broadcast Transmitters

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Received for publication February 27, 2008; accepted for publication July 7, 2008.

A case-control study of radio frequency electromagnetic fields (RF-EMFs) and childhood leukemia was conducted in West Germany. The study region included municipalities near high-power radio and TV broadcast towers, including 16 amplitude-modulated and 8 frequency-modulated transmitters. Cases were aged 0–14 years, were diagnosed with leukemia between 1984 and 2003, and were registered at the German Childhood Cancer Registry. Three age-, gender-, and transmitter-area-matched controls per case were drawn randomly from population registries. The analysis included 1,959 cases and 5,848 controls. Individual exposure to RF-EMFs 1 year before diagnosis was estimated with a field strength prediction program. Considering total RF-EMFs, the odds ratio derived from conditional logistic regression analysis for all types of leukemia was 0.86 (95% confidence interval: 0.67, 1.11) when upper (≥95%/0.701 V/m) and lower (<90%/0.504 V/m) quantiles of the RF-EMF distribution were compared. An analysis of amplitude-modulated and frequency-modulated transmitters separately did not show increased risks of leukemia. The odds ratio for all types of leukemia was 1.04 (95% confidence interval: 0.65, 1.67) among children living within 2 km of the nearest broadcast transmitter compared with those living at a distance of 10–<15 km. The data did not show any elevated risks of childhood leukemia associated with RF-EMFs.

child; electromagnetic fields; leukemia; radiation, radio; television

Abbreviations: AM, amplitude modulated; CI, confidence interval; FM, frequency modulated; ICCC, International Classification of Childhood Cancer; RF-EMF, radio frequency electromagnetic field.

For many decades, radio and TV broadcast stations have been emitting radio frequency electromagnetic fields (RF-EMFs) in the frequency range of 10 kHz–870 MHz. Amplitude-modulated (AM) transmitters are usually not located in populated areas but have large coverage areas and operate at relatively high power levels (1). In the vicinity of AM transmitters (100-m radius), high field strengths of more than 10 V/m can occur. Exposure decreases with increasing distance from the transmitter. Frequency-modulated (FM) radio and TV transmitters are usually located in urban areas. Maximum field strength is often observed at a distance of several hundred meters to several kilometers from the transmitter. In the vicinity of an FM/TV transmitter, the vertical radiation patterns give rise to high variability in the fields measured near ground level. Hence, there is a weak correlation between exposure and distance from the transmitter.

Some ecologic studies reported small to moderately increased incidence rates of childhood leukemia in association with proximity to broadcast towers (2–6). Other studies, however, reported no association (7, 8). Conflicting results are due to the limitations of geographic correlation studies. A case-control study on this topic was conducted in South Korea by using hospital-based controls. It included only AM transmitters and cases diagnosed between 1993 and 1999. An increased leukemia risk for children living within 2 km of an AM transmitter was observed, but no association with total RF-EMF exposure was found (9, 10).

Between 2005 and 2007, we conducted a case-control study in West Germany by using population-based controls.

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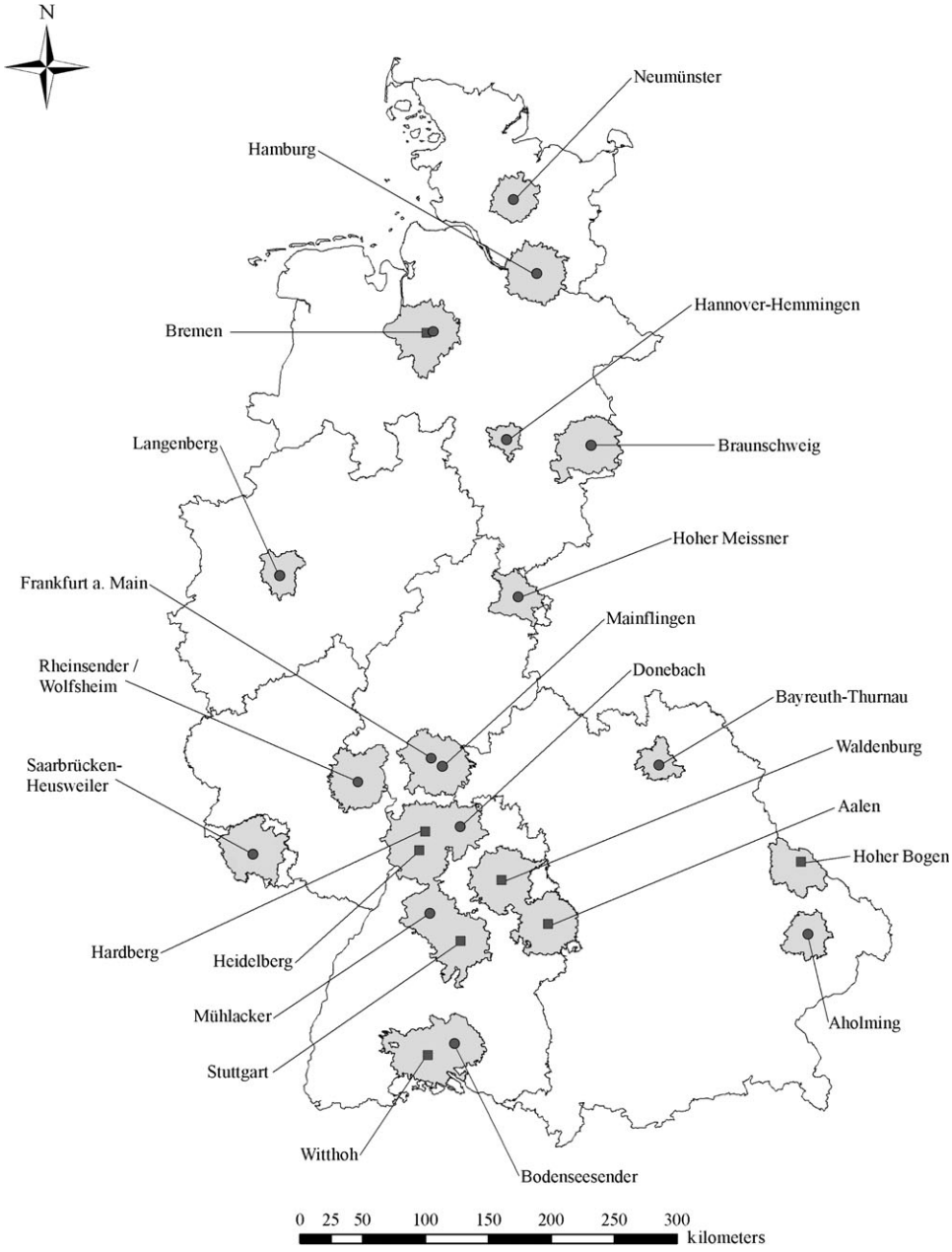

Figure 1. Location of the 24 broadcast transmitters with >200 kW effective monopole radiated power (amplitude modulated (AM)) and >200/>500 kW effective radiated power (frequency modulated (FM)/TV), Germany, 1984–2003 (●, AM transmitters; ■, FM/TV transmitters).

The study involved cases diagnosed between 1984 and 2003 and included both AM and FM/TV transmitters. In this paper, we report the results.

MATERIALS AND METHODS

Transmitter selection and definition of the study region

Because it is possible to receive public TV and radio programs everywhere in Germany, RF-EMF exposure at some similar background level is ubiquitous, with little variation in exposure except in the vicinity of broadcast transmitters. Therefore, an efficient study design was developed by defining the study area as municipalities in the vicinity of Germany's strongest transmitters. Transmitters located in East Germany were not included because random sampling of historical controls was not possible for the former German Democratic Republic. High-output-power AM transmitters were identified in West Germany according to an effective monopole radiated power of at least 200 kW. In addition,

FM/TV transmitters with an aggregated effective radiated power of at least 200 kW (FM) or 500 kW (TV) were identified. Five transmitters in sparsely populated regions providing only 27 additional cases over the entire study period were not considered because of time restrictions and financial aspects related to recruitment of controls. A total of 16 AM transmitters and 8 FM/TV transmitters were finally selected.

RF-EMF model calculations and measurements were conducted during a pilot study. A critical value for AM transmitters is a field strength of 1 V/m because it exceeds field strengths usually detected in the environment, such as in the proximity of mobile phone base stations (11, 12). To define the transmitter area, the radius centered upon each AM transmitter was determined by an approximate 1-V/m radius calculated by its effective monopole radiated power and the assumption of propagation over flat and ideal ground. To include low exposed areas, this radius was doubled. For FM transmitters, different technology had to be considered. Here, an approximate 0.03-V/m (90 dB(μV/m)) radius was calculated (13). All municipalities within or at least partially within the respective circles were defined as the study region, resulting in 805 municipalities (Figure 1).

Study population

All cases were selected from the virtually complete German Childhood Cancer Registry (14). Our study included incident cases with leukemia diagnosed between January 1, 1984, and December 31, 2003. According to the International Classification of Childhood Cancer (ICCC), the following diagnoses were considered: lymphoid leukemia (ICCC Ia), acute myeloid leukemia (ICCC Ib), chronic myeloproliferative diseases (ICCC Ic), myelodysplastic syndrome and other myeloproliferative diseases (ICCC Id), and unspecified and other specified leukemias (ICCC Ie) (15). Eligible cases were less than age 15 years and lived in the study region at the time of diagnosis.

For each case, 3 individually matched controls were drawn randomly from the population living in the same transmitter area at the time of diagnosis of the case, of the same sex, and born as close in time as possible to the respective case but with a difference of 1 year at most. Communities were selected randomly by population size (considering sex, age, year of diagnosis, study region) and were asked to provide addresses and names of children fulfilling the matching criteria. A total of 82% of controls lived in areas with access to historical population records and could be selected even if they had moved out of the study area after the case was diagnosed. Controls who lived in study areas in which no historical population registries were available (18%) were selected from among those who were residentially stable.

It was not possible to obtain participants' full residential history. However, the date that they moved to the address where they were diagnosed (corresponding date for controls) was collected. Hence, it was possible to subdivide the study population into those who moved between birth and diagnosis and those who did not.

A total of 2,086 eligible cases were identified. Cases for whom address information was incomplete were excluded

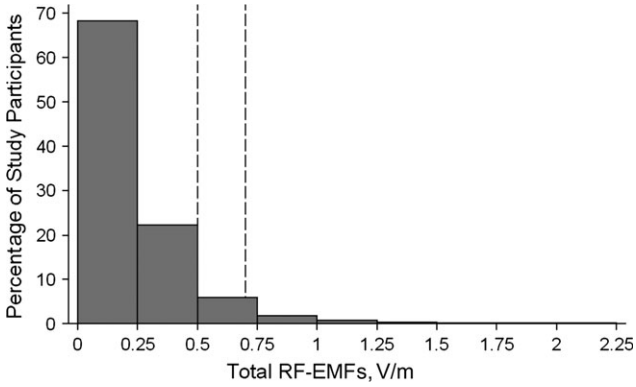

Figure 2. Distribution of total radio frequency electromagnetic fields (RF-EMFs) in the study population, Germany, 1984–2003. Dashed lines: 90% quantile and 95% quantile.

(45 cases, no name and address; 82 cases, insufficient information on the address). A total of 1,959 cases and 5,848 controls were included in the analysis. Almost all cases had 3 controls (98.7%), 1.1% had 2 controls, and 0.2% had 1 control. Each address of cases and controls as well as all transmitter coordinates were converted to Cartesian coordinates, which alleviated calculation of distances. Quality assessment showed that 99.5% of the coordinates were exact on the house level, the others on the street level (midpoint).

Retrospective exposure estimation

All relevant transmitter operators supplied data describing the operating characteristics of their transmitters between 1983 and 2002. Individual RF-EMF exposure was calculated with a field strength prediction program. This prediction software has been developed to assure adequate coverage for all radio/TV consumers in Germany. An incorporated geographic information system based on Cartesian coordinates allowed exposure estimation for the given places of residence of cases and controls, which was calculated under blinded conditions.

The nationwide coverage of AM radio and FM radio and TV is the reason for a mixed exposure situation. However, it was possible to compute AM and FM/TV separately. For AM transmitters, MININEC modeling was used in combination with propagation over spherical earth of finite ground conductivity. Field strengths were calculated for 1.5 m above ground (16, 17). For FM/TV transmitters, a Meeks algorithm was applied to compute the average of the field strength 10 m above ground over pixels of 100×100 m^2 (18, 19) and was scaled down to 1.5 m by applying an empirical correction of -10 dB.

RF-EMFs are emitted by not only those high-power transmitters that were used to define the study region (referred to as ''main transmitters''). Broadcast towers with power comparable to or lower than that of the main transmitters within the study region had to be considered as well as transmitters outside the study region that emitted relevant radiation into

Table 1. Characteristics of Leukemia Cases and Matched Population Controls Aged <15 Years in Broadcast Transmitter Areas in Germany, 1984–2003

	Controls[a] (*n* = 5,848)		Leukemia Cases[b]							
			All Cases (*n* = 1,959)		Lymphoid Leukemia (*n* = 1,586)		Myeloid Leukemia (*n* = 336)		Others (*n* = 37)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Age at diagnosis, years										
0	322	5.5	108	5.5	47	3.0	56	16.7	5	13.5
1–4	2,745	47.0	920	47.0	795	50.1	117	34.8	8	21.6
5–9	1,593	27.2	535	27.3	459	28.9	69	20.5	7	18.9
10–14	1,188[c]	20.3	396	20.2	285	18.0	94	28.0	17	46.0
Sex										
Male	3,308	56.6	1,109	56.6	898	56.6	192	57.1	19	51.4
Female	2,540	43.4	850	43.4	688	43.4	144	42.9	18	48.6
Time period of diagnosis										
1984–1992	2,407	41.2	808	41.2	659	41.6	129	38.4	20	54.1
1993–2003	3,441	58.8	1,151	58.8	927	58.4	207	61.6	17	45.9
Transmitter area										
AM	3,878	66.3	1,326	67.7	1,057	66.6	249	74.1	20	54.1
FM/TV	1,970	33.7	633	32.3	529	33.4	87	25.9	17	45.9
Population density[d]										
Low	1,946	33.3	658	33.6	520	32.8	123	36.6	15	40.6
Medium	1,939	33.1	695	35.5	568	35.8	119	35.4	8	21.6
High	1,963	33.6	606	30.9	498	31.4	94	28.0	14	37.8

Abbreviations: AM, amplitude modulated; FM, frequency modulated.
[a] Matched to cases according to age, sex, transmitter region, and time of diagnosis.
[b] All cases: International Classification of Childhood Cancer (ICCC) I; lymphoid leukemia: ICCC Ia; myeloid leukemia: ICCC Ib, ICCC Id; others: ICCC Ic, ICCC Ie.
[c] Included 2 controls aged 15 years.
[d] Low: 0–1,293/km^2; medium: 1,294–3,600/km^2; high. 3,601–9,911/km^2.

the study region. Hence, in addition to the 24 main transmitters, exposure data from an additional 312 transmitters were included in the exposure estimation.

For the whole exposure period, calculated exposure data were available for each month, with the cumulated local average field strength (V/m) referring to AM transmitters, the cumulated local average field strength (V/m) referring to FM/TV transmitters, and the exposure for both transmitter types (total RF-EMFs). For cumulation, field strength values were converted to power flux density throughout.

The quality of the RF-EMF predictions was evaluated in a validation study (Sven Schmiedel, Danish Cancer Society, unpublished data), in which the prediction algorithm was tested against 477 RF-EMF measurements conducted in the study region. The measurements were performed during a measurement survey independently of the case-control study (20). Estimated RF-EMFs and measured RF-EMFs were highly correlated, with a Spearman rank correlation coefficient (r) of 0.80 (95% confidence interval (CI): 0.76, 0.83), which was clearly better than the correlation between measured RF-EMFs and distance to the transmitter ($r = 0.54$, 95% CI: 0.47, 0.60). Dichotomized at the 90% quantile, estimated and measured RF-EMFs revealed a satisfactory agreement (Cohen's kappa coefficient = 0.74, 95% CI: 0.64, 0.84).

Statistical analysis

Lymphoid leukemia represents approximately 80% of all cases of leukemia in children (14) and was considered separately. Myelodysplastic syndromes and acute myeloid leukemia were combined into 1 group (referred to as ''myeloid leukemia'') (21).

Conditional logistic regression was used to estimate odds ratios and their 95% confidence intervals for average exposure in the month 1 year before diagnosis. Case-control status was the dependent variable.

The distribution of exposure from total RF-EMFs was skewed to the left (Figure 2), with a majority of study participants being exposed to background fields. For that reason, the ''high-exposure'' category was defined by the ≥90% quantile (0.504–7.742 V/m for total RF-EMFs). This group was further subdivided into the 90%–<95% and 95%–≤100% quantiles. To investigate a possible dose-response-relation,

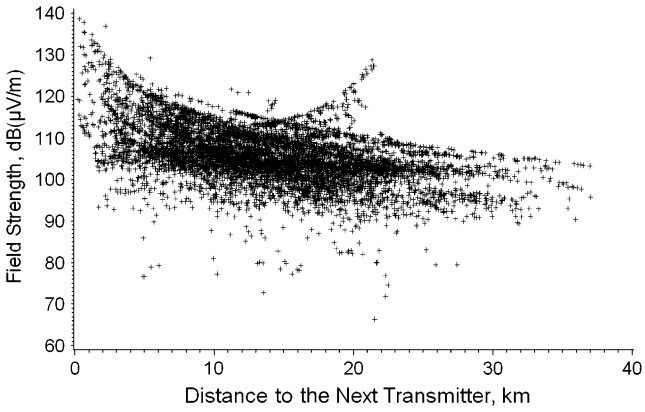

Figure 3. Scatter plot of total radio frequency electromagnetic fields in relation to distance of study subjects' place of residence to the nearest main transmitter, Germany, 1984–2003. For example, 120 dB(μV/m) ≙ 1 V/m.

RF-EMF was introduced as a continuous variable in a fractional polynomial model (22, 23). Furthermore, data for AM and FM/TV transmitters were analyzed separately.

Sensitivity analyses were conducted by looking at relevant subgroups. From 1983 until the early 1990s, RF-EMFs were almost exclusively due to broadcast transmitter emission. Afterward, an additional contribution came from the development of cellular telephone networks and cordless phones. Therefore, 2 exposure periods were formed (1983–1991, 1992–2002) and were analyzed separately. Since there are possibly distinctive etiologies for infant leukemia and childhood leukemia (24), and to account for a latency period of at least 1 year, the age group 1–4 years (peak of incidence of childhood leukemia) was analyzed separately. Furthermore, the analysis was restricted to cases and controls who did not move from their residences between birth and diagnosis.

Distance between the family's place of residence at the time of diagnosis (corresponding date for controls) and the nearest main transmitter was assessed. The distance was included as a categorized variable in the regression model (0–<2 km, 2–<6 km, 6–<10 km, 10–<15 km, ≥15 km). Because not all transmitter regions included areas ≥15 km away, a distance of 10–<15 km was used as the reference category.

Population density was considered as a possible confounder and was included in the regression model categorized in tertiles according to the distribution of controls. However, after adjustment for population density, the effect estimate was altered only marginally (<1%). Thus, this factor was not included in the final regression models.

SAS for Windows, version 9.1 software (SAS Institute, Inc., Cary, North Carolina) was used for all analyses.

RESULTS

Table 1 shows the main characteristics of the leukemia cases (n = 1,959) and their matched controls (n = 5,848). The most frequent diagnosis was lymphoid leukemia, with 1,586 cases (81.0%). There were 1,028 patients (52.5%) with leukemia diagnosed between 0 and 4 years of age. A total of 808 cases (41.2%) were diagnosed between 1984 and 1992. Figure 3 shows the distribution between RF-EMFs

Table 2. Estimated Risk of Childhood Leukemia Associated With Exposure to RF-EMFs Emitted From Radio and TV Broadcast Transmitters, Germany, 1984–2003

	All Cases				Lymphoid Leukemia				Myeloid Leukemia			
	No. of Controls	No. of Cases	OR	95% CI	No. of Controls	No. of Cases	OR	95% CI	No. of Controls	No. of Cases	OR	95% CI
AM and FM/TV[a]												
0–<90%	5,263	1,772	1.00	Reference	4,269	1,437	1.00	Reference	891	301	1.00	Reference
90–<95%	292	101	1.02	0.80, 1.31	224	79	1.05	0.79, 1.38	64	21	0.95	0.55, 1.65
95–≤100%	293	86	0.86	0.67, 1.11	238	70	0.86	0.65, 1.15	51	14	0.80	0.42, 1.50
AM[b]												
0–<90%	5,263	1,770	1.00	Reference	4,268	1,435	1.00	Reference	892	301	1.00	Reference
90–<95%	292	100	1.01	0.79, 1.30	224	79	1.05	0.79, 1.38	64	20	0.91	0.52, 1.59
95–≤100%	293	89	0.89	0.69, 1.15	239	72	0.89	0.67, 1.18	50	15	0.87	0.47, 1.63
FM/TV[c]												
0–<90%	5,263	1,770	1.00	Reference	4,270	1,429	1.00	Reference	896	308	1.00	Reference
90–<95%	292	98	0.99	0.78, 1.27	230	80	1.05	0.79, 1.38	53	14	0.74	0.39, 1.37
95–≤100%	293	91	0.92	0.71, 1.19	231	77	1.01	0.76, 1.33	57	14	0.67	0.35, 1.27

Abbreviations: AM, amplitude modulated; CI, confidence interval; FM, frequency modulated; OR, odds ratio; RF-EMFs, radio frequency electromagnetic fields.

[a] Quantiles of median exposure (V/m) to RF-EMFs 1 year before diagnosis of the case, AM, FM/TV: 0.004–<0.504, 0.504–<0.701, 0.701–7.742.

[b] Quantiles of median exposure (V/m) to RF-EMFs 1 year before diagnosis of the case, AM: 0–<0.488, 0.488–<0.683, 0.683–7.741.

[c] Quantiles of median exposure (V/m) to RF-EMFs 1 year before diagnosis of the case, FM/TV: <0.001–<0.164, 0.164–<0.198, 0.198–0.815.

Table 3. Estimated Risk of Childhood Leukemia Associated With Exposure to RF-EMFs Emitted From Radio and TV Broadcast Transmitters, by Time Period and Restricted to Children Who Did Not Move From Their Residence and to Children Aged 1–4 Years, Germany, 1984–2003

	All Cases				Lymphoid Leukemia				Myeloid Leukemia			
	No. of Controls	No. of Cases	OR	95% CI	No. of controls	No. of cases	OR	95% CI	No. of Controls	No. of Cases	OR	95% CI
Exposure time period: 1983–1991[a]												
0–<90%	2,166	729	1.00	Reference	1,765	598	1.00	Reference	347	114	1.00	Reference
90–<95%	120	49	1.23	0.85, 1.76	92	35	1.13	0.74, 1.72	26	13	1.56	0.74, 3.29
95–≤100%	121	30	0.72	0.47, 1.10	105	26	0.71	0.45, 1.11	12	2	0.55	0.12, 2.53
Exposure time period: 1992–2002[b]												
0–<90%	3,096	1,031	1.00	Reference	2,507	830	1.00	Reference	539	184	1.00	Reference
90–<95%	172	64	1.13	0.82, 1.54	131	52	1.22	0.86, 1.74	40	12	0.85	0.42, 1.73
95–≤100%	173	56	0.98	0.71, 1.36	131	45	1.07	0.74, 1.53	42	11	0.74	0.36, 1.52
Children who did not move[c]												
0–<90%	2,531	1,034	1.00	Reference	2,001	838	1.00	Reference	483	181	1.00	Reference
90–<95%	141	45	0.94	0.62, 1.43	109	30	0.83	0.51, 1.35	31	12	1.42	0.57, 3.50
95–≤100%	141	38	0.82	0.53, 1.24	116	35	0.93	0.59, 1.45	24	1	0.15	0.02, 1.18
Children aged 1–4 years[d]												
0–<90%	2,470	833	1.00	Reference	2,137	721	1.00	Reference	311	104	1.00	Reference
90–<95%	137	53	1.13	0.79, 1.59	116	44	1.10	0.75, 1.60	21	9	1.31	0.53, 3.23
95–≤100%	138	34	0.72	0.48, 1.07	117	30	0.75	0.49, 1.14	19	4	0.63	0.21, 1.94

Abbreviations: CI, confidence interval; OR, odds ratio; RF-EMFs, radio frequency electromagnetic fields.

[a] Quantiles of median exposure (V/m) to RF-EMFs 1 year before diagnosis of the case, 1983–1992: 0.004–<0.546, 0.546–<0.779, 0.779–7.022.

[b] Quantiles of median exposure (V/m) to RF-EMFs 1 year before diagnosis of the case, 1993–2002: 0.005–<0.468, 0.468–<0.653, 0.653–7.742.

[c] Quantiles of median exposure (V/m) to RF-EMFs 1 year before diagnosis of the case, subjects who did not move between birth and diagnosis: 0.004–<0.553, 0.553–<0.788, 0.788–7.742.

[d] Quantiles of median exposure (V/m) to RF-EMFs 1 year before diagnosis of the case, children aged 1–4 years: 0.004–<0.520, 0.520–<0.751, 0.751–7.742.

(dB(μV/m)) from all transmitters 1 year before diagnosis and the distance of the places of residence of the study subjects to the nearest main transmitter. By comparing residences at a 2-km distance with residences at a 30-km distance from a transmitter, it is shown that distance of an individual place of residence to the transmitter is an important determinant of exposure to RF-EMFs. On the other hand, at intermediate distances such as 20 km, considerable variation in exposure, from 85 dB(μV/m) to >120 dB(μV/m), was observed. Hence, other transmitter-related factors also influence the individual exposure situation to a great extent, mainly the output power of the main transmitter, the antenna characteristics, and emissions from further low-power transmitters in the study region.

For total RF-EMF exposure, the 95–≤100% quantiles were compared with the lower quantile (<90%) (Table 2). The corresponding odds ratio for all leukemias was 0.86 (95% CI: 0.67, 1.11). Additionally, no statistically significant associations were observed by transmitter type (AM and FM/TV) or by subtype of leukemia. A possible dose-response relation was investigated by using field strengths (dB(μV/m)) as a continuous variable. The odds ratio for all types of leukemia in increments of 1 dB(μV/m) was 0.99 (95% CI: 0.98, 1.00). The dose-response-relation was also investigated by using fractional polynomials, but there was no significant increase in the model fit, suggesting that the log-linear model was adequate.

An analysis by time period showed no difference between the 2 exposure time periods considered, with no significantly increased risk for all types of leukemia or subgroups of leukemia (Table 3). A total of 57% of the cases and 48% of the controls were residentially stable. A subgroup analysis restricted to these children yielded results comparable to those for the whole data set (Table 3). For children between 1 and 4 years of age, the odds ratio for all types of leukemia was 0.72 (95% CI: 0.48, 1.07).

Results of the analysis of distance of place of residence to the nearest main transmitter at the time of diagnosis are shown in Table 4. A statistically nonsignificantly increased risk of all types of leukemia was apparent for children whose residence was located within a 2-km distance of the nearest AM transmitter compared with those children

Table 4. Estimated Risk of Childhood Leukemia by Proximity to Radio and TV Broadcast Transmitters, Germany, 1984–2003

Distance, km[a]	All Cases				Lymphoid Leukemia				Myeloid Leukemia			
	No. of Controls	No. of Cases	OR	95% CI	No. of Controls	No. of Cases	OR	95% CI	No. of Controls	No. of Cases	OR	95% CI
AM or FM/TV transmitter												
0–<2	67	25	1.04	0.65, 1.67	51	24	1.31	0.80, 2.15	14	1	0.19	0.02, 1.47
2–<6	587	172	0.81	0.66, 0.99	473	141	0.82	0.66, 1.03	101	27	0.75	0.45, 1.24
6–<10	1,096	314	0.79	0.67, 0.93	881	241	0.76	0.63, 0.91	188	66	1.00	0.68, 1.47
10–<15	1,549	551	1.00	Reference	1,254	446	1.00	Reference	268	93	1.00	Reference
≥15	2,457	866	1.00	0.88, 1.14	1,995	708	1.01	0.87, 1.16	420	144	0.99	0.72, 1.37
AM transmitter[b]												
0–<2	33	14	1.15	0.60, 2.22	23	13	1.56	0.77, 3.16	10	1	0.24	0.03, 1.96
2–<6	322	102	0.80	0.62, 1.05	253	81	0.82	0.61, 1.11	63	20	0.77	0.42, 1.43
6–<10	766	237	0.84	0.69, 1.02	604	178	0.81	0.65, 1.01	149	53	0.94	0.62, 1.44
10–<15	1,140	420	1.00	Reference	911	332	1.00	Reference	213	82	1.00	Reference
≥15	1,525	522	0.94	0.80, 1.10	1,226	427	0.96	0.80, 1.14	277	88	0.87	0.60, 1.27
FM/TV transmitter												
0–<2	34	11	1.03	0.50, 2.13	28	11	1.19	0.56, 2.50	4	0	0.00	0.00, 9.57[c]
2–<6	265	70	0.80	0.57, 1.12	220	60	0.80	0.55, 1.14	38	7	0.82	0.27, 2.47
6–<10	330	77	0.69	0.50, 0.96	277	63	0.67	0.47, 0.95	39	13	1.48	0.55, 4.00
10–<15	409	131	1.00	Reference	343	114	1.00	Reference	55	11	1.00	Reference
≥15	932	344	1.13	0.89, 1.45	769	281	1.08	0.83, 1.41	143	56	1.88	0.86, 4.11

Abbreviations: AM, amplitude modulated; CI, confidence interval; FM, frequency modulated; OR, odds ratio.
[a] Distance to the nearest main transmitter at the time of diagnosis of the case.
[b] Not considered were 31 cases and 92 controls because of the temporary shutdown of 2 transmitters.
[c] Exact confidence interval.

living at a distance of 10–<15 km, a risk that became slightly stronger when we repeated this analysis for lymphoid leukemia only. For FM/TV transmitters or both transmitter types combined, there was a statistically nonsignificantly increased risk of lymphoid leukemia. However, some odds ratios for lymphoid leukemia and all leukemias at distances of 2–10 km were statistically significantly decreased.

The analysis of distance was based on few cases living in the 2-km circumference of AM transmitters ($n = 14$); therefore, a risk increase in the main analysis (Table 2) may have been missed by using the 95% quantile (0.683 V/m) as a too-low cutoff point. For that reason, the analysis comparing high and low AM-related RF-EMF exposure was repeated by using the upper 99% quantile as the ''high'' and the lower 90% quantile as the ''low'' exposure category (≥99% percent quantile: 1.72–7.74 V/m), giving 16 exposed cases. The corresponding odds ratio for all types of leukemia was 0.80 (95% CI: 0.46, 1.40).

DISCUSSION

This study did not show any significant increase in risk associated with exposure to RF-EMFs emitted by broadcast towers and leukemia in children. The results were similar for total RF-EMFs from all transmitters and for AM and FM/TV separately; hence, the modulation mode and frequency range of the RF-EMF signal had no impact on disease risk. No elevated risks of leukemia were found for the time period 1983–1991, which was characterized by an exposure without major contributions from mobile phone communication technology.

Lifetime RF-EMF exposure from transmitters could not be estimated since residential history of the study subjects was not available. However, a subgroup analysis including only those subjects who lived at the same address from birth to diagnosis did not show an increased risk of childhood leukemia.

The causes of childhood leukemia are poorly understood (24). There is no plausible biologic mechanism for an association between RF-EMFs and childhood leukemia, and it is not known whether a susceptible time window for children is of relevance. In this study, average RF-EMF exposure 1 year before diagnosis was assessed for cases and controls. Broadcast towers provide steadily uninterrupted service to their consumers. For that reason, the average sum exposure at a given place of residence varies very little with time in general. This conclusion is reflected in the individual history of operation provided by the network operators for each transmitter. In rare instances, AM transmitters have been switched off, rebuilt, or displaced. These events noticeably

Table 5. Results Regarding Total RF-EMF Exposure From AM Transmitters and Risk of Childhood Leukemia Comparing 2 Case-Control Studies Conducted in Germany (1984–2003) and Korea (1993–1999)

	Germany	95% CI	Korea	95% CI
Total RF-EMF exposure[a]				
Reference category (quartile 1)	<0.518 V/m		<0.518 V/m	
High-exposure category (quartile 4)	≥0.917 V/m		≥0.917 V/m	
Odds ratio and 95% CI (all cases)	0.88	0.63, 1.22	0.83	0.63, 1,08
Odds ratio and 95% CI (lymphoid leukemia)	0.99	0.70, 1.39	0.93	0.67, 1.29
Distance to the nearest AM transmitter				
Reference category	10–<15 km		>20 km	
High-exposure category	<2 km		≤2 km	
Odds ratio and 95% CI (all cases)	1.15	0.60, 2.22	2.15	1.00, 4.67
Odds ratio and 95% CI (lymphoid leukemia)	1.56	0.77, 3.16	1.60	0.69, 3.72

Abbreviations: AM, amplitude modulated; CI, confidence interval; RF-EMF, radio frequency electromagnetic field.

[a] Korea: root-sum mean square of the maximum-adjusted electric field of each transmitter established before subjects' year of diagnosis. Germany: root-sum mean square of the adjusted average electric field of each transmitter 1 year before diagnosis.

altered exposure levels, but virtually no AM transmitter was affected more than 3 times during the exposure period (1983–2002). After German reunification in 1989, some transmitters were adjusted to provide lower output power. However, analysis of the exposure time period 1992–2002 did not show any pattern in the risk estimates different from that in the previous 10 years (Table 3).

A strength of the recent study is the availability of individual RF-EMF exposure data. Exposure estimation was based on detailed historical operating characteristics of the included transmitters. The quality of the field-strength predictions was validated with field measurements, demonstrating a good agreement. For the exposure estimation, all relevant broadcasting sources of exposure to RF-EMFs were considered. High-output-power AM and FM/TV transmitters were included, as well as the contribution of transmitters outside of the study region but emitting relevant radiation into the study region. Transmitters located in sparsely populated areas were not considered. This omission did not introduce any bias because the excluded transmitters did not differ from the included transmitters regarding their exposure impact, and only 27 additional cases would have been obtained.

The study included 1,959 cases and 5,848 individually population-based, matched controls, which provided sufficient statistical power for detecting a possible relation between disease and exposure even in subgroup analyses. Sensitivity and specificity for total RF-EMFs were 76.6% (95% CI: 62.0, 87.7) and 97.4% (95% CI: 95.5, 98.7), respectively, leading to an exposure misclassification that still enabled us to detect a true odds ratio of 1.4 with statistical power greater than 80%. It is very unlikely that exclusion of a few cases (45 without name and address, 82 with incomplete addresses) caused any selection bias.

Study results may possibly have been influenced by confounders such as social class or immune-system-related variables. Population density was considered a proxy for such possible confounders. However, when population density was considered, the observed associations changed only marginally. Ionizing radiation is the only established risk factor for childhood leukemia (24, 25), but a correlation between sufficient doses of ionizing radiation and RF-EMFs is highly unlikely. In addition, extremely low-frequency electromagnetic fields are not a plausible confounder because elevated fields are very rare in Germany (0.2% of houses with exposures of >0.4 μT) (26), and there is no reason to think that fields from power lines or indoor wiring are correlated with RF-EMFs from transmitters.

This study has some limitations. Children naturally spend time at places other than their home address, with a possibly different exposure situation compared with estimated exposure at their place of residence. On the other hand, children less than age 5 years usually spend most of their time at home, and residential exposure might be a good predictor of individual exposure (27). Nevertheless, odds ratios were similar for children less than 5 years of age and those in older age groups. Furthermore, it should be considered that indoor levels of RF-EMFs are often lower by orders of magnitude because buildings shield the fields. In this study with a 20-year exposure period, indoor exposure could not be estimated because detailed knowledge on characteristics of the residences, such as building materials, was not available. However, there is no reason to assume differential misclassification between cases and controls. Furthermore, the study did not consider other sources of RF-EMFs such as mobile phones, cordless phones, or their base stations. However, an increased risk in the time period before the widespread use of these technologies was not found. Finally,

a study that considers all high-power transmitters in Germany would have been preferable. On the other hand, sufficient statistical power was achieved for the current transmitter selection, yielding an efficient study setting.

In a recent case-control study from South Korea (9), the investigators found a significantly higher risk of all types of leukemia for children residing within 2 km of the nearest AM transmitter compared with children residing more than 20 km away from it. For total RF-EMF exposure, no increased odds ratio for lymphoid leukemia or all types of leukemia was observed when the upper quartile was compared with the lowest quartile (10). Table 5 shows the main results of the Korean and German case-control study for total RF-EMFs from AM transmitters using the same cutoff points. The results are consistent; in particular, both studies do not show an increased childhood leukemia risk at exposures above 0.917 V/m.

In conclusion, our study provides little evidence for an association between exposure to RF-EMFs and the risk of childhood leukemia. The population-based case-control approach with large numbers of subjects, a long study period (1984–2003), and individual exposure estimation is superior to that of previous studies. The results weaken the evidence from earlier reports on increased childhood leukemia incidence rates in the vicinity of broadcast transmitters.

ACKNOWLEDGMENTS

Author affiliations: Institute of Medical Biostatistics, Epidemiology and Informatics, University Mainz, Mainz, Germany (Hiltrud Merzenich, Sabrina Bennack, Maria Blettner); Institute of Cancer Epidemiology, Danish Cancer Society, Copenhagen, Denmark (Sven Schmiedel, Joachim Schüz); Lower Saxony Water Management, Coastal Defense and Nature Conservation Agency, Hildesheim, Germany (Hauke Brüggemeyer); and Südwestrundfunk [the public broadcasting corporation of southwest Germany], Department of Frequency and Coverage Planning, Stuttgart, Germany (Johannes Philipp).

The study was funded by the Federal Office for Radiation Protection (BfS, Oberschleißheim/Munich) as part of the German Mobile Telecommunication Research Programme.

The authors thank all transmitter operators for providing historical exposure data. They also thank Dr. Jost Wendler (Südwestrundfunk), Wolfgang Schröter, and Harry Korr (T-Systems – International) for technical recommendations and support of the study. The study cases were recruited through the German Childhood Cancer Registry (Mainz). The authors are grateful to Dr. Peter Kaatsch (head of the German Childhood Cancer Registry) and Dr. Claudia Spix (German Childhood Cancer Registry) for their support.

Conflict of interest: none declared.

REFERENCES

1. Dahme M. Residential RF exposure. *Radiat Prot Dosimetry.* 1999;83:113–117.
2. Maskarinec G, Cooper J, Swygert L. Investigation of increased incidence in childhood leukemia near radio towers in Hawaii: preliminary observations. *J Environ Pathol Toxicol Oncol.* 1994;13(1):33–37.
3. Hocking B, Gordon JR, Grain HL, et al. Cancer incidence and mortality and proximity to TV towers. *Med J Aust.* 1996; 165(11–12):601–605.
4. Dolk H, Shaddick G, Walls P, et al. Cancer incidence near radio and television transmitters in Great Britain, I. Sutton Coldfield transmitter. *Am J Epidemiol.* 1997;145(1):1–9.
5. Michelozzi P, Capon A, Kirchmayer U, et al. Adult and childhood leukemia near a high-power radio station in Rome, Italy. *Am J Epidemiol.* 2002;155(12):1096–1103.
6. Park SK, Ha M, Im HJ. Ecological study on residences in the vicinity of AM radio broadcasting towers and cancer death: preliminary observation in Korea. *Int Arch Occup Environ Health.* 2004;77(6):387–394.
7. Dolk H, Elliot P, Shaddick G, et al. Cancer incidence near radio and television transmitters in Great Britain. II. All high power transmitters. *Am J Epidemiol.* 1997;145:10–17.
8. McKenzie DR, Yin Y, Morrell S. Childhood incidence of acute lymphoblastic leukemia and exposure to broadcast radiation in Sydney—a second look. *Aust N Z J Public Health.* 1998; 22(3 suppl):360–367.
9. Ha M, Im H, Lee M, et al. Radio-frequency radiation exposure from AM radio transmitters and childhood leukemia and brain cancer. *Am J Epidemiol.* 2007;166(3):270–279.
10. Ha M, Im H, Kim BC, et al. Five authors reply [letter]. *Am J Epidemiol.* 2008;167(7):884–885.
11. Schüz J, Mann S. A discussion of potential exposure metrics for use in epidemiological studies on human exposure to radiowaves from mobile phone base stations. *J Expo Anal Environ Epidemiol.* 2000;10(6 pt 1):600–605.
12. Neubauer G, Feychting M, Hamnerius Y, et al. Feasibility of future epidemiological studies on possible health effects of mobile phone base stations. *Bioelectromagnetics.* 2007;28(3): 224–230.
13. International Telecommunication Union. Method for point-to-area predictions for terrestrial services in the frequency range 30 MHz to 3000 MHz. (Recommendation ITU-R P.1546-1, ITU, Geneva, Switzerland; 2003). (www.itu.int/publ/R-REC).
14. Kaatsch P, Spix C. *German Childhood Cancer Registry. Annual Report 2005.* Mainz, Germany: University Mainz; 2005.
15. Steliarova-Foucher E, Stiller C, Lacour B, et al. International Classification of Childhood Cancer, third edition. *Cancer.* 2005;103(7):1457–1467.
16. Rockway JW, Logan JC. MININEC Professional for Windows. Carson City, NV: EM Scientific Inc; 1995.
17. International Telecommunication Union. Ground-wave propagation curves for frequencies between 10 kHz and 30 MHz. (Recommendation ITU-R P.368-8, ITU, Geneva, Switzerland; 2005). (www.itu.int/publ/R-REC).
18. Philipp J, Merzenich H, Brüggemeyer H, et al. Retrospective exposure assessment for radio frequency electromagnetic fields from broadcast transmitters in a case-control study [in German]. *Adv Radio Sci.* 2007;5:1–10.
19. Meeks ML. VHF propagation over hilly, forested terrain. *IEEE Trans Ant Pr.* 1983;31:483–489.
20. Landesanstalt für Umweltschutz [Federal office for environment protection]. Spacious investigation of radio waves in Baden-Württemberg [in German]. (http://www2.lubw.baden-wuerttemberg.de/public/abt3/funkwellen [in German]) (Accessed February 5, 2008).
21. Niemeyer CM, Baumann I. Myelodysplastic syndrome in children and adolescents. *Semin Hematol.* 2008;45(1):60–70.

22. Greenland S. Dose-response and trend analysis in epidemiology: alternatives to categorical analysis. *Epidemiology.* 1995; 6(4):356–365.
23. Royston P, Ambler G, Sauerbrei W. The use of fractional polynomials to model continuous risk variables in epidemiology. *Int J Epidemiol*. 1999;28(5):964–974.
24. Greaves M. Infection, immune responses and the etiology of childhood leukemia. *Nat Rev Cancer.* 2006;6(3): 193–203.
25. Lightfoot TJ, Roman E. Causes of childhood leukaemia and lymphoma. *Toxicol Appl Pharmacol*. 2004;199(2):104–117.
26. Schüz J. Implications from epidemiologic studies on magnetic fields and the risk of childhood leukemia on protection guidelines. *Health Phys.* 2007;92(6):642–648.
27. Forssén UM, Ahlbom A, Feychting M. Relative contribution of residential and occupational magnetic field exposure over twenty-four hours among people living close to and far from a power line. *Bioelectromagnetics*. 2002;23(3):239–244.