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Residential exposure to magnetic fields from high-voltage power lines and risk of childhood leukemia

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ABSTRACT

Background: Several studies have suggested an excess risk of leukemia among children living close to high-voltage power lines and exposed to magnetic fields. However, not all studies have yielded consistent results, and many studies may have been susceptible to confounding and exposure misclassification.

Methods: We conducted a case-control study to investigate the risk of leukemia associated with magnetic field exposure from high-voltage power lines. Eligible participants were children aged 0–15 years residing in the Northern Italian provinces of Modena and Reggio Emilia. We included all 182 registry-identified childhood leukemia cases diagnosed in 1998–2019, and 726 age-, sex- and province-matched population controls. We assessed exposure by calculating distance from house to nearest power line and magnetic field intensity modelling at the subjects' residence. We used conditional logistic regression models to estimate odds ratios (ORs) and 95% confidence intervals (CIs), with adjustment for potential confounders (distance from nearest petrol station and fuel supply within the 1000 m-buffer, traffic-related particulate and benzene concentrations, presence of indoor transformers, percentage of urban area and arable crops).

Results: In multivariable analyses, the OR comparing children living <100 m from high-voltage power-lines with children living ≥400 m from power-lines was 2.0 (95% CI 0.8–5.0). Results did not differ substantially by age at disease diagnosis, disease subtype, or when exposure was based on modeled magnetic field intensity, though estimates were imprecise. Spline regression analysis showed an excess risk for both overall leukemia and acute lymphoblastic leukemia among children with residential distances <100 m from power lines, with a monotonic inverse association below this cutpoint.

Conclusions: In this Italian population, close proximity to high-voltage power lines was associated with an excess risk of childhood leukemia.

1. Introduction

In modern society, exposure to magnetic fields is common. Public interest about electromagnetic fields from power-supply systems is increasing along with higher demand for electricity, wireless technologies, and changes in work systems and social behavior (Brabant et al.,

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2022; Seomun et al., 2021). Since 2002, low frequency magnetic fields (ELF-MF) have been classified by the International Agency for Research on Cancer (IARC) as possibly carcinogenic (group 2 B), based on pooled analyses of epidemiological studies on the association of average exposure to residential power-frequency magnetic field above 0.3 μT to childhood leukemia (WHO - IARC, 2002). These findings, combined with limited evidence in animal studies and methodological issues in human studies, were deemed insufficient to show a carcinogenic effect of ELF-MF. Few epidemiological studies have been performed since 2010, with inconsistent results (Amoon et al., 2022).

We investigated risk of childhood leukemia associated with ELF-MF exposure from high-voltage power lines in a case-control study among residents of Northern Italy.

2. Methods

2.1. Study population

Using an established population-based case-control study (Malagoli et al., 2010, 2015; Vinceti et al., 2012), we identified all cases of childhood leukemia (ICD-9 codes 204–208) diagnosed from 1998 through 2019 below the age of 15 among residents of the Modena and Reggio Emilia provinces (population around 1,200,000 of two provinces of Emilia-Romagna region in Northern Italy) in the nationwide hospital-based registry of childhood malignancies (Ferrari et al., 2009), following approval of the Modena Ethical Committee.

Using a computer-generated random process, we selected four controls for each case, matched on sex, year of birth, and province of residence at time of diagnosis, from all residents enrolled in the National Health Services directory of Modena and Reggio Emilia provinces.

2.2. Residences identification and geocoding

We ascertained residential address at time of diagnosis for cases and in the corresponding year for their matched controls by Local Health Units (Nation-wide-hospital-based registry of childhood malignancies managed by the Associazione Italiana Ematologia Oncologica Pediatrica-AIEOP). All residential addresses were first geocoded through their geographical coordinates by linkage to the Modena and Reggio Emilia Provinces Address Database, and then included in a Geographical Information System (GIS) using Arc-GIS software (version 10.1, ESRI, Redlands, CA 2012). We retrieved the satellite coordinates of the residences using methodology based on an official geocoding database made available by the Modena and Reggio Emilia Province and, for addresses not included in the database, through the Google Earth App or direct in loco measurement using a portable GPS device (GPSmap 60CSx, Garmin Int. Corp., Olathe, KS) (Malagoli et al., 2010, 2015; Malavolti et al., 2023; Vinceti et al., 2012). In particular, we performed in loco measurements to retrieve and map the geographical coordinates for 33 subjects.

2.3. ELF-MF modelling

We used a ELF-MF exposure modelling process as explained in detail elsewhere (Malagoli et al., 2010, 2012). Briefly, we used geodata about the high-voltage power lines (≥132 kV) located during 1998–2011 in the study area, made available by the Emilia-Romagna Regional Agency for Environmental Prevention and Energy (ARPAE). In this period, there were 194 lines operating in the study provinces (171 with 132–150 kV, 10 with 220 kV, and 13 with 380 kV), having a total length of 1125 km (579 and 546 for Modena and Reggio Emilia respectively), all of which had been already operating since 1998 (71% since 1979). Precision of geocoding was on the order of <1 m, and we used both Google Earth and on-site visits to evaluate the accuracy of the available data.

To assess ELF-MF exposure around the high-voltage power lines, we used the current intensity for each line measured every 15 min (4 data per hour) for all days in 2001, modelling the average ELF-MF induction in the corridors at 8 m in height. We performed this calculation using a 2D freeware software simulation package named 'CAMPI' predicting magnetic field yielded by high-voltage power lines (Andreuccetti, 2002), a method that has been validated within the Emilia-Romagna region (Violanti, 2003). We inputted into the model the phases and disposition of conductors and the average current characterizing each power line in 2001, the earliest period for which we had available data (Malagoli et al., 2010, 2012). The ELF-MF corridors were at intensities <0.1, 0.1–0.2, 0.2–0.4 and ≥ 0.4 μT. However, in the study area, there was limited variability over time of current flows in the power lines. For example, during the 1986–2007 period, the power line flow increased by about 3% per year (Vinceti et al., 2012), and then remained stable in the most recent years with limited variability.

2.4. Distance to nearest high-power line

We calculated the distance from the subject's residence at diagnosis to the nearest ≥132 kV power line in ArcGIS. Due to the uncertainties about the amount of ELF-MF exposure relevant for childhood leukemia risk (Fews et al., 1999; Henshaw et al., 1996), we extended the corridors surrounding the power lines up to a distance of 400 m and divided it into three categories (Rothman, 2014) (<100 m, 100-<200 m, and 200-<400 m), using cutpoints provided by earlier studies (Amoon et al., 2018; Pedersen et al., 2014; Wunsch-Filho et al., 2011). Subjects who lived ≥400 m away from the nearest transmission line were considered unexposed. GIS handling and exposure assessment were performed blindly to the subject's case/control status.

2.5. Confounders

We considered several environmental factors as potential confounders in the multivariable analysis. We modeled outdoor air concentration of particulate matter with diameter <10 μm (PM_{10}) at the residence of each child (Filippini et al., 2019), using the CAlifornia LINE Source Dispersion Model, version 4 (CALINE4 - Sacramento CA, Dept. of trasportation, Division of New Technology and Research, 1989), a line source air quality model, based on vehicular traffic flow parameters and meteorological data (Vinceti et al., 2012). Roads, including names, technical and administrative classification were also obtained from the cartographic archive of Emilia Romagna Region Agency. We considered exposure to emissions from petrol stations, assuming as exposed children residing within a 100 m buffer from a gas station (Malavolti et al., 2023); we also considered, as a potential source of exposure misclassification, the presence of indoor transformer stations within the building of residence, using information about the transformer location made available by ARPAE. We also determined the urban and arable crop density around the subject's residences by calculating the percentage of the land use type in proximity to each geocoded home, based on a circular area with a radius of 100 m around the house of residence. Specifically, we used the 2014 Land Use Map (available at https://geoportale.regione.emilia-romagna.it), which contained a detailed description of land use according to the specifications of Corine Land Cover. With a coupled GIS/Python procedure, we defined a circular buffer with a 100-m radius around each subject's home. For arable crop-type and urban-type identification analysis, we used the predefined land use subtypes named 'Rural area' and "Urban area" (Andreuccetti, 2002; Malagoli et al., 2015, 2016; Vinceti et al., 2017).

We collected information about socio-demographic factors, i.e. maternal age and ethnicity, and paternal income for the index year (a proxy for annual household income), using birth certificates from the Local Health Units of Modena and Reggio Emilia, and the directory of the Revenue Agency of the Ministry of Finance, respectively.

2.6. Data analysis

We divided ELF-MF intensities into four categories (<0.1, 0.1 - <0.2, 0.2 - <0.4 and ≥ 0.4 μT), assuming as reference group a ELF-MF <0.1 μT. Distance from homes to the nearest transmission line was categorized into five groups (<100, 100-<200, 200-<400 and ≥ 400 m), and homes located ≥400 m from transmission lines constituted the reference group in this analysis. We estimated the risk ratio for childhood leukemia in relation to ELF-MF and distance to power lines by calculating the odds ratio (OR) of the disease in unadjusted and multivariable conditional logistic regression models matched on sex, age and province of residence. In the multivariable model, we adjusted for outdoor benzene and PM_{10} concentrations (as continuous variable), percentage of urban area and arable crops within the 100 m-buffer around the house, maternal age at delivery (continuous) (Rothman and Mosquin, 2013; Rothman et al., 2021), race (categorized as White, Black or Asian), and paternal annual income (continuous). We performed unadjusted conditional logistic regression analysis for individual confounding factors. We also conducted stratified analyses by subject's age of diagnosis for cases or year of sampling for controls (<5 vs. ≥5 years), and for the acute lymphoblastic leukemia subtype (ALL). The precision of ORs was evaluated by computing their 95% confidence intervals (CIs). Finally, we modeled the association between distance from residential address to the nearest power line and odds of leukemia using a restricted cubic spline regression model (Orsini and Greenland, 2011) by selecting the optimal number of knots according to Akaike's information criterion (AIC) and using the knot-placement method previously recommended (Harrel, 2001). We applied three knots: at 100, 200 and 400 m. For this analysis, we used the 'sample', 'mkspline' e 'xblc' routines of Stata-17.0 statistical package (Stata Corp., College Station, TX 2022).

3. Results

We identified 182 incident cases of childhood leukemia (details of diagnosis reported in Supplementary Table S1) during the study period (average age at diagnosis: 6.2 years), including 148 ALL cases (6.3 years). The case/control distributions of the study population by distance from home of the nearest high-voltage power line, and by ELF-MF exposure category, are reported in Table 1. Risk of childhood leukemia was positively associated with three confounding factors included in the multivariable model: exposure to arable crops, indoor transformer stations, and residence in an urban area (Supplementary Table S2). The corresponding leukemia ORs and 95% CIs for magnetic field exposure in both unadjusted and multivariable models are reported in Table 2. Compared with children living ≥400 m from a power line, ORs for leukemia among children residing <100 m from the nearest power line were 2.1 (95% CI: 0.9–5.2) in the unadjusted analysis and 2.0 (95% CI: 0.8–5.0) in the multivariable model. Restricting the analysis to the ALL subtype, these respective ORs were 2.3 (95% CI: 0.9–6.1) and 2.2 (95% CI: 0.8–6.0) (Table 2). Cases of myeloid leukemia were too few to permit an analysis restricted to this disease subtype.

In age-stratified analyses, ORs for overall leukemia were slightly stronger among younger children, living <100 m (vs. ≥400 m) from a power line, with ORs of 2.4 (95% CI: 0.4–14.6) among children aged <5 years and 1.8 (95% CI: 0.6–5.4) among children aged ≥5 years in the multivariable model (Table 2). Conversely, for the ALL subtype, the OR was slightly stronger among older children (≥5 years: multivariable OR

Table 2
Odds ratio of childhood leukemia and acute lymphoblastic leukemia (ALL) subtype according to distance from home to the nearest high-voltage power line.

Distance to the nearest high-voltage power line, m	All subjects	<5 years	≥5 years
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Unadjusted analysis[a]			
Leukemia			
≥400 (Referent)	1.0	1.0	1.0
200 - <400	0.9 (0.5–1.6)	1.1 (0.5–2.4)	0.7 (0.3–1.7)
100 - <200	0.9 (0.4–2.0)	0.4 (0.1–3.2)	1.1 (0.4–2.8)
<100	2.1 (0.9–5.2)	2.6 (0.4–15.5)	1.9 (0.7–5.3)
ALL			
≥400 (Referent)	1.0	1.0	1.0
200 - <400	1.0 (0.5–1.8)	1.0 (0.5–3.1)	0.7 (0.3–1.9)
100 - <200	0.7 (0.3–1.7)	0.5 (0.1–3.7)	0.8 (0.3–2.3)
<100	2.3 (0.9–6.1)	1.9 (0.2–21.1)	2.3 (0.8–6.5)
Multivariable analysis[b]			
Leukemia			
≥400 (Referent)	1.0	1.0	1.0
200 - <400	0.9 (0.5–1.6)	1.2 (0.5–2.6)	0.8 (0.3–1.9)
100 - <200	0.9 (0.4–2.0)	0.4 (0.0–3.0)	1.2 (0.5–3.2)
<100	2.0 (0.8–5.0)	2.4 (0.4–14.6)	1.8 (0.6–5.4)
ALL			
≥400 (Referent)	1.0	1.0	1.0
200 - <400	1.0 (0.5–1.9)	1.5 (0.6–3.7)	0.8 (0.3–2.2)
100 - <200	0.7 (0.3–1.8)	0.5 (0.1–3.6)	0.9 (0.3–2.7)
<100	2.2 (0.8–6.0)	1.8 (0.2–20.0)	2.0 (0.6–6.4)

Abbreviations: ALL, acute lymphoblastic leukemia; CI, confidence interval; OR, odds ratio.
[a] Matched on sex, age, and province of residence.
[b] Adjusted for distance from the nearest petrol station and fuel supply within the 1000 m-buffer, PM_{10}, benzene, indoor transformer stations, urban area, and land farm arable crops.

Table 1
Distribution by distance from home to the nearest high-voltage power line, by estimated magnetic field exposure.

	All leukemias			Acute lymphoblastic leukemia (ALL)		
	All subjects (cases/controls)	<5 years	≥5 years	All subjects (cases/controls)	<5 years	≥5 years
Distance to the nearest high-voltage power line, m						
≥400	150/603	70/282	80/321	122/489	56/227	66/262
200 - <400	17/75	10/36	7/39	14/58	8/25	6/33
100 - <200	7/33	1/11	6/22	5/31	1/10	4/21
<100	8/15	2/3	6/12	7/12	1/2	6/10
All subjects	182/726	83/332	99/394	148/590	66/264	82/326
Magnetic Fields, μT						
<0.1	180/725	83/332	97/393	146/589	66/264	80/325
0.1 - <0.2	0/1	0/0	0/1	0/1	0/0	0/1
0.2 - <0.4	1/0	0/0	1/0	1/0	0/0	1/0
≥0.4	1/0	0/0	1/0	1/0	0/0	1/0
All subjects	182/726	83/332	99/394	148/590	66/264	82/326

= 2.0, 95% CI: 0.6–6.4) than among younger children (<5 years: multivariable OR = 1.8, 95% CI: 0.2–20.0).

When basing exposure assessment on fixed ELF-MF cut-points, we identified two exposed case children (both affected by ALL), one belonging to the 0.2–0.4 μT corridor and the other to the ≥0.4 μT corridor, and one control child, in the 0.1–0.2 μT corridor. The unadjusted OR of leukemia associated with ELF-MF exposure ≥0.1 μT was 8.0 (95% CI: 0.7–88.2), as shown in Table 3. Sensitivity analyses among subjects with complete data on demographic variables, specifically maternal race and paternal income, showed similar though less precise results (Supplementary Table S3).

In the dose-response spline model, we observed a strong though imprecise association between distance from power lines and an excess risk of leukemia among children residing within close proximity to the lines, i.e. <100 m, in both unadjusted and multivariable analysis, while there was no such indication at distance greater than 150 m (Fig. 1). Adjustment for potential confounders had little influence on this pattern (Fig. 1B). We found comparable trends when ALL is considered only (Supplementary Figure S1).

4. Discussion

In this study, we observed an increased odds of childhood leukemia among those who resided in close proximity, i.e. <100 m, from a high-voltage power line. Over the last four decades, residential exposure to extremely low frequency magnetic fields, including those generated by power lines, has been associated with childhood leukemia in several epidemiological studies, though there have been some inconsistencies in results, likely owing to small sample sizes, selection and information biases, and residual confounding (Abdul Rahman et al., 2008; Crespi et al., 2016; Draper et al., 2005; Feychting and Ahlbom, 1993; Kabuto et al., 2006; Kleinerman et al., 2000; McBride et al., 1999; Olsen et al., 1993; Pedersen et al., 2014; Petridou et al., 1997; Schuz and Erdmann, 2016; Sermage-Faure et al., 2013; Tomenius, 1986; Tynes and Haldorsen, 1997; UK Childhood Cancer Study Investigators, 2000; Wunsch-Filho et al., 2011). In biological studies, there is some evidence of small carcinogenic effects related to magnetic fields of low intensity (Chen et al., 2020; Kapri-Pardes et al., 2017). In 2001, the International Agency for Research on Cancer (IARC) classified ELF-MF as possibly carcinogenic to humans (WHO - IARC, 2002), mainly based on consistent findings yielded by pooled analysis (Ahlbom et al., 2000; Greenland et al., 2000) reporting a higher risk of childhood leukemia associated with long-term exposure to ELF-MF above 0.3/0.4 μT. Comparable results were obtained ten years later in a pooled analysis comprising 10,

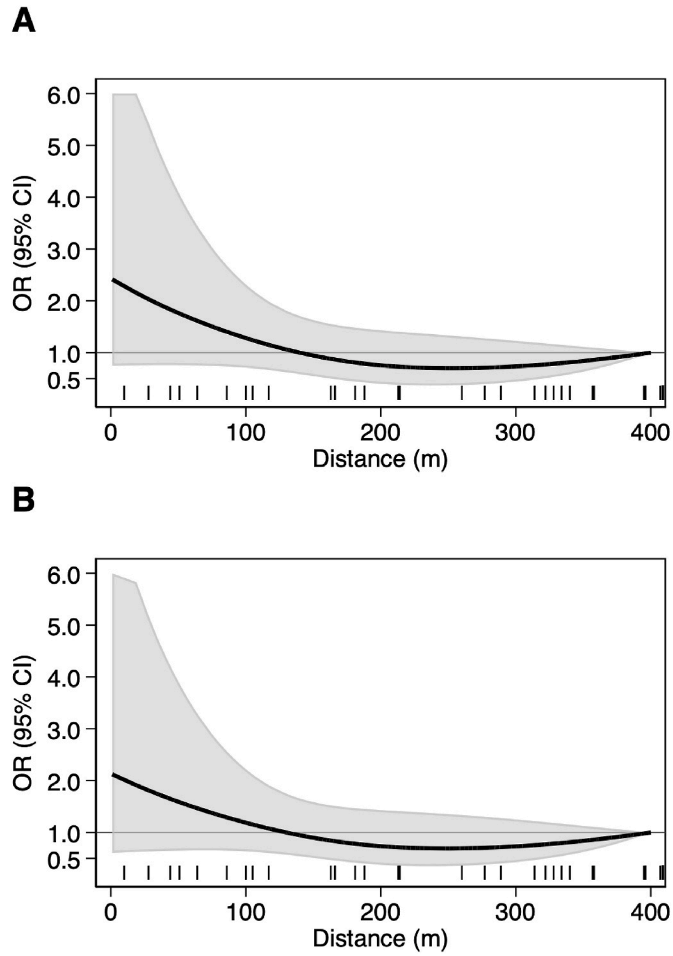

Fig. 1. Restricted cubic splines of childhood leukemia risk according to distance of residence from high-voltage power line matched on sex, age and province of residence (A) and additionally adjusted for distance from the nearest petrol station and fuel supply within the 1000 m-buffer, PM_{10}, benzene, indoor transformer stations, urban area, and land farm arable crops (B). Solid black line and gray shaded area indicate the odds ratio (OR) and the 95% confidence interval (CI), respectively.

Table 3
Odds ratio of childhood leukemia and the acute lymphoblastic leukemia (ALL) subtype according to magnetic field exposure.

	All subjects		<5 years		≥5 years	
	Cases/Controls	OR (95% CI)	Cases/Controls	OR (95% CI)	Cases/Controls	OR (95%CI)
Unadjusted model[a]						
Leukemia						
<0.1 (Referent)	180/725	1.0	83/332	1.0	97/393	1.0
≥0.1	2/1	8.0 (0.7–88.2)	0/0	–	2/1	8.0 (0.7–88.2)
ALL						
<0.1 (Referent)	146/589	1.0	66/264	1.0	80/325	1.0
≥0.1	2/1	8.0 (0.7–88.2)	0/0	–	2/1	8.0 (0.7–88.2)
Multivariable model[a]						
Leukemia						
<0.1 (Referent)	180/725	1.0	83/332	1.0	97/393	1.0
≥0.1	2/1	7.6 (0.7–83.8)	0/0	–	2/1	8.0 (0.7–89.3)
ALL						
<0.1 (Referent)	146/589	1.0	66/264	1.0	80/325	1.0
≥0.1	2/1	7.5 (0.7–82.8)	0/0	–	2/1	8.1 (0.7–90.3)

Abbreviations: ALL, acute lymphoblastic leukemia; CI, confidence interval; OR, odds ratio.
[2] Adjusted for distance from the nearest petrol station and fuel supply within the 1000 m-buffer, PM_{10}, benzene, indoor transformer stations, urban area and arable crops.
[a] Matched on sex, age and province of residence.

818 cases with leukemia (Kheifets et al., 2010). Similarly, a recent systematic review and meta-analysis reported an increased risk of developing leukemia in children due to exposure to ELF-MF higher than 0.4 μT as well as living within 50 m from the power lines (Brabant et al., 2022). In addition, our estimates are roughly comparable to a previous study carried out in the same area in the period 1986–2007 that showed high risk of all leukemia and acute lymphoblastic leukemia, thus confirming the high risk for children exposed to levels $\geq$0.1 μT (Malagoli et al., 2010). Also, a previous study in another Italian region (Lombardy) using similar cutoff ($<$0.1 and $\geq$ 0.1 μT) showed a strong association between such amount of exposure and disease risk (Bianchi et al., 2000). Overall, these suggest that risk of childhood leukemia may start to increase already at ELF-MF exposure $\geq$0.1 μT.

We found slightly higher excess risk among children younger than five years of age compared with children $\geq$5 years, but these results were imprecise due to the low number of exposed children. Such observations, however, only partially support a greater susceptibility to chemical and physical toxicants in the youngest children (Borsari et al., 2018; Malagoli et al., 2016; Sangun et al., 2015; Vinceti et al., 2012). Our results may have been prone to historical exposure misclassification (e.g., prenatal and early postnatal exposure to magnetic fields), which could have been differential according to participants' age, thus reducing our capacity to detect potential interactions between age and exposure on disease risk.

Our study covered an entire geographical region based in two provinces of Italy, relying on registry data and not on active participation by study subjects and therefore avoiding selection bias. In addition, cases were drawn from a hospital-based high-quality disease registry covering the entire country, thus ensuring nearly complete registration of all childhood leukemia cases. Furthermore, exposure assessment (both ELF-MF modelling and distance) was done blindly as to case/control status.

Among the study limitations, we acknowledge the potential for residual confounding, though accounted for several socioeconomic and environmental risk factors for childhood leukemia. For instance, certain characteristics such as radiation exposure history or parental occupation exposure were unavailable for many study participants, and other provided incomplete information (e.g., paternal income vs. household income). However, a sensitivity analysis limited to subjects accounting for all potential confounders measured yielded similar results to the main analysis, suggesting confounding for these demographic factors should not have been a major source of bias.

We also acknowledge the small number of incident cases, and particularly of ELF-MF exposed participants, leading to statistical instability of the OR estimates and thereby considerably limiting our capacity to smoothly assess dose-response relations and small changes in risk to carry out stratified analyses. Finally, we could not perform a subgroup analysis for myeloid childhood leukemia, due to the limited number of cases and the lack of exposed children.

In conclusion, in this Italian population, residence within 100 m of high-voltage power lines was associated with an increased risk of childhood leukemia. These results showed a clear dose-response relation below that cutpoint, though the results were imprecise. Our findings are generally consistent with findings obtained in several studies worldwide.

Credit author statement

MV and CM conceived the study. Material preparation and data collection were performed by MM, CM, TF, SF, ST, GP, MC, MP, PZ, BN and AC. Data analyses were performed by MM, CM, TF and MV. The first draft of the manuscript was written by MM and CM with the contribution of TF, LAW, EB and MV. All authors commented on previous versions of the manuscript and all authors read and approved the final manuscript.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr. Wise is a consultant for AbbVie Inc, and the Gates Foundation. Her institution also receives NIH funding for studies outside of this work. Finally, Dr. Wise receives in-kind donations for primary data collection in the PRESTO cohort (Swiss Precision Diagnostics and Kindara.com). All other authors declare that they have no competing interests.

Data availability

The data that have been used are confidential.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2023.116320.

References

Abdul Rahman, H.I., Shah, S.A., Alias, H., Ibrahim, H.M., 2008. A case-control study on the association between environmental factors and the occurrence of acute leukemia among children in Klang Valley, Malaysia. Asian Pac. J. Cancer Prev. APJCP 9, 649–652.

Ahlbom, A., Day, N., Feychting, M., Roman, E., Skinner, J., Dockerty, J., Linet, M., McBride, M., Michaelis, J., Olsen, J.H., Tynes, T., Verkasalo, P.K., 2000. A pooled analysis of magnetic fields and childhood leukaemia. Br. J. Cancer 83, 692–698. https://doi.org/10.1054/bjoc.2000.1376.

Amoon, A.T., Crespi, C.M., Ahlbom, A., Bhatnagar, M., Bray, I., Bunch, K.J., Clavel, J., Feychting, M., Hemon, D., Johansen, C., Kreis, C., Malagoli, C., Marquant, F., Pedersen, C., Raaschou-Nielsen, O., Roosli, M., Spycher, B.D., Sudan, M., Swanson, J., Tittarelli, A., Tuck, D.M., Tynes, T., Vergara, X., Vinceti, M., Wunsch-Filho, V., Kheifets, L., 2018. Proximity to overhead power lines and childhood leukaemia: an international pooled analysis. Br. J. Cancer 119, 364–373. https://doi.org/10.1038/s41416-018-0097-7.

Amoon, A.T., Swanson, J., Magnani, C., Johansen, C., Kheifets, L., 2022. Pooled analysis of recent studies of magnetic fields and childhood leukemia. Environ. Res. 204, 111993 https://doi.org/10.1016/j.envres.2021.111993.

Andreuccetti, D., 2002. Manuale Programma CAMPI Version 4.1. Consiglio Nazionale delle Ricerche, Firenze.

Bianchi, N., Crosignani, P., Rovelli, A., Tittarelli, A., Carnelli, C.A., Rossitto, F., Vanelli, U., Porro, E., Berrino, F., 2000. Overhead electricity power lines and childhood leukemia: a registry-based, case-control study. Tumori 86, 195–198. https://doi.org/10.1177/030089160008600303.

Borsari, L., Malagoli, C., Werler, M.M., Rothman, K.J., Malavolti, M., Rodolfi, R., De Girolamo, G., Nicolini, F., Vinceti, M., 2018. Joint effect of maternal tobacco smoking and pregestational diabetes on preterm births and congenital anomalies: a population-based study in Northern Italy. J. Diabetes Res. 2018, 2782741 https://doi.org/10.1155/2018/2782741.

Brabant, C., Geerinck, A., Beaudart, C., Tirelli, E., Geuzaine, C., Bruyere, O., 2022. Exposure to magnetic fields and childhood leukemia: a systematic review and meta-analysis of case-control and cohort studies. Rev. Environ. Health. https://doi.org/10.1515/reveh-2021-0112.

Chen, L., Xia, Y., Lu, J., Xie, Q., Ye, A., Sun, W., 2020. A 50-Hz magnetic-field exposure promotes human amniotic cells proliferation via SphK-S1P-S1PR cascade mediated ERK signaling pathway. Ecotoxicol. Environ. Saf. 194, 110407 https://doi.org/10.1016/j.ecoenv.2020.110407.

Crespi, C.M., Vergara, X.P., Hooper, C., Oksuzyan, S., Wu, S., Cockburn, M., Kheifets, L., 2016. Childhood leukaemia and distance from power lines in California: a population-based case-control study. Br. J. Cancer 115, 122–128. https://doi.org/10.1038/bjc.2016.142.

Draper, G., Vincent, T., Kroll, M.E., Swanson, J., 2005. Childhood cancer in relation to distance from high voltage power lines in England and Wales: a case-control study. BMJ 330, 1290. https://doi.org/10.1136/bmj.330.7503.1290.

Ferrari, A., Dama, E., Pession, A., Rondelli, R., Pascucci, C., Locatelli, F., Ferrari, S., Mascarin, M., Merletti, F., Masera, G., Arico, M., Pastore, G., 2009. Adolescents with cancer in Italy: entry into the national cooperative paediatric oncology group AIEOP trials. Eur. J. Cancer 45, 328–334. https://doi.org/10.1016/j.ejca.2008.12.003.

Fews, A.P., Henshaw, D.L., Wilding, R.J., Keitch, P.A., 1999. Corona ions from powerlines and increased exposure to pollutant aerosols. Int. J. Radiat. Biol. 75, 1523–1531. https://doi.org/10.1080/095530099139124.

Feychting, M., Ahlbom, A., 1993. Magnetic fields and cancer in children residing near Swedish high-voltage power lines. Am. J. Epidemiol. 138, 467–481. https://doi.org/10.1093/oxfordjournals.aje.a116881.

Filippini, T., Hatch, E.E., Rothman, K.J., Heck, J.E., Park, A.S., Crippa, A., Orsini, N., Vinceti, M., 2019. Association between outdoor air pollution and childhood leukemia: a systematic review and dose-response meta-analysis. Environ. Health Perspect. 127, 46002. https://doi.org/10.1289/EHP4381.

Greenland, S., Sheppard, A.R., Kaune, W.T., Poole, C., Kelsh, M.A., 2000. A pooled analysis of magnetic fields, wire codes, and childhood leukemia. Childhood Leukemia-EMF Study Group. Epidemiology 11, 624–634. https://doi.org/10.1097/00001648-200011000-00003.

Harrel, F.E., 2001. Regression Modeling Strategies. Springer Cham, Switzerland. https://doi.org/10.1007/978-3-319-19425-7.

Henshaw, D.L., Ross, A.N., Fews, A.P., Preece, A.W., 1996. Enhanced deposition of radon daughter nuclei in the vicinity of power frequency electromagnetic fields. Int. J. Radiat. Biol. 69, 25–38. https://doi.org/10.1080/095530096146156.

Kabuto, M., Nitta, H., Yamamoto, S., Yamaguchi, N., Akiba, S., Honda, Y., Hagihara, J., Isaka, K., Saito, T., Ojima, T., Nakamura, Y., Mizoue, T., Ito, S., Eboshida, A., Yamazaki, S., Sokejima, S., Kurokawa, Y., Kubo, O., 2006. Childhood leukemia and magnetic fields in Japan: a case-control study of childhood leukemia and residential power-frequency magnetic fields in Japan. Int. J. Cancer 119, 643–650. https://doi.org/10.1002/ijc.21374.

Kapri-Pardes, E., Hanoch, T., Maik-Rachline, G., Murbach, M., Bounds, P.L., Kuster, N., Seger, R., 2017. Activation of signaling cascades by weak extremely low frequency electromagnetic fields. Cell. Physiol. Biochem. 43, 1533–1546. https://doi.org/10.1159/000481977.

Kheifets, L., Ahlbom, A., Crespi, C.M., Draper, G., Hagihara, J., Lowenthal, R.M., Mezei, G., Oksuzyan, S., Schuz, J., Swanson, J., Tittarelli, A., Vinceti, M., Wunsch Filho, V., 2010. Pooled analysis of recent studies on magnetic fields and childhood leukaemia. Br. J. Cancer 103, 1128–1135. https://doi.org/10.1038/sj.bjc.6605838.

Kleinerman, R.A., Kaune, W.T., Hatch, E.E., Wacholder, S., Linet, M.S., Robison, L.L., Niwa, S., Tarone, R.E., 2000. Are children living near high-voltage power lines at increased risk of acute lymphoblastic leukemia? Am. J. Epidemiol. 151, 512–515. https://doi.org/10.1093/oxfordjournals.aje.a010237.

Malagoli, C., Fabbi, S., Teggi, S., Calzari, M., Poli, M., Ballotti, E., Notari, B., Bruni, M., Palazzi, G., Paolucci, P., Vinceti, M., 2010. Risk of hematological malignancies associated with magnetic fields exposure from power lines: a case-control study in two municipalities of northern Italy. Environ. Health 9, 16. https://doi.org/10.1186/1476-069X-9-16.

Malagoli, C., Crespi, C.M., Rodolfi, R., Signorelli, C., Poli, M., Zanichelli, P., Fabbi, S., Teggi, S., Garavelli, L., Astolfi, G., Calzolari, E., Lucenti, C., Vinceti, M., 2012. Maternal exposure to magnetic fields from high-voltage power lines and the risk of birth defects. Bioelectromagnetics 33, 405–409. https://doi.org/10.1002/bem.21700.

Malagoli, C., Malavolti, M., Costanzini, S., Fabbri, S., Tezzi, S., Palazzi, G., Arcolin, E., Vinceti, M., 2015. Increased incidence of childhood leukemia in urban areas: a population-based case-control study. Epidemiol. Prev. 39, 102–107.

Malagoli, C., Costanzini, S., Heck, J.E., Malavolti, M., De Girolamo, G., Oleari, P., Palazzi, G., Teggi, S., Vinceti, M., 2016. Passive exposure to agricultural pesticides and risk of childhood leukemia in an Italian community. Int. J. Hyg Environ. Health 219, 742–748. https://doi.org/10.1016/j.ijheh.2016.09.015.

Malavolti, M., Malagoli, C., Filippini, T., Wise, L.A., Bellelli, A., Palazzi, G., Cellini, M., Costanzini, S., Teggi, S., Vinceti, M., 2023. Residential proximity to petrol stations and risk of childhood leukemia. Eur. J. Epidemiol. https://doi.org/10.1007/s10654-023-01009-0.

McBride, M.L., Gallagher, R.P., Theriault, G., Armstrong, B.G., Tamaro, S., Spinelli, J.J., Deadman, J.E., Fincham, S., Robson, D., Choi, W., 1999. Power-frequency electric and magnetic fields and risk of childhood leukemia in Canada. Am. J. Epidemiol. 149, 831–842. https://doi.org/10.1093/oxfordjournals.aje.a009899.

Olsen, J.H., Nielsen, A., Schulgen, G., 1993. Residence near high voltage facilities and risk of cancer in children. BMJ 307, 891–895. https://doi.org/10.1136/bmj.307.6909.891.

Orsini, N., Greenland, S., 2011. A procedure to tabulate and plot results after flexible modeling of a quantitative covariate. STATA J. 11, 1–29.

Pedersen, C., Raaschou-Nielsen, O., Rod, N.H., Frei, P., Poulsen, A.H., Johansen, C., Schuz, J., 2014. Distance from residence to power line and risk of childhood leukemia: a population-based case-control study in Denmark. Cancer Causes Control 25, 171–177. https://doi.org/10.1007/s10552-013-0319-5.

Petridou, E., Trichopoulos, D., Kravaritis, A., Pourtsidis, A., Dessypris, N., Skalkidis, Y., Kogevinas, M., Kalmanti, M., Koliouskas, D., Kosmidis, H., Panagiotou, J.P., Piperopoulou, F., Tzortzatou, F., Kalapothaki, V., 1997. Electrical power lines and childhood leukemia: a study from Greece. Int. J. Cancer 73, 345–348. https://doi.org/10.1002/(SICI)1097-0215(19971104)73:3<345::AID-IJC7>3.0.CO;2-%23.

Rothman, K.J., Mosquin, P.L., 2013. Sparse-data bias accompanying overly fine stratification in an analysis of beryllium exposure and lung cancer risk. Ann. Epidemiol. 23, 43–48. https://doi.org/10.1016/j.annepidem.2012.11.005.

Rothman, K.J., 2014. Six persistent research misconceptions. J. Gen. Intern. Med. 29, 1060–1064. https://doi.org/10.1007/s11606-013-2755-z.

Rothman, K.J., Greenland, S., Lash, T., 2021. Modern Epidemiology (Philadelphia).

Sangun, O., Dundar, B., Comlekci, S., Buyukgebiz, A., 2015. The effects of electromagnetic field on the endocrine system in children and adolescents. Pediatr. Endocrinol. Rev. 13, 531–545.

Schuz, J., Erdmann, F., 2016. Environmental exposure and risk of childhood leukemia: an overview. Arch. Med. Res. 47, 607–614. https://doi.org/10.1016/j.arcmed.2016.11.017.

Seomun, G., Lee, J., Park, J., 2021. Exposure to extremely low-frequency magnetic fields and childhood cancer: a systematic review and meta-analysis. PLoS One 16, e0251628. https://doi.org/10.1371/journal.pone.0251628.

Sermage-Faure, C., Demoury, C., Rudant, J., Goujon-Bellec, S., Guyot-Goubin, A., Deschamps, F., Hemon, D., Clavel, J., 2013. Childhood leukaemia close to high-voltage power lines–the Geocap study, 2002-2007. Br. J. Cancer 108, 1899–1906. https://doi.org/10.1038/bjc.2013.128.

Tomenius, L., 1986. 50-Hz electromagnetic environment and the incidence of childhood tumors in Stockholm County. Bioelectromagnetics 7, 191–207. https://doi.org/10.1002/bem.2250070209.

Tynes, T., Haldorsen, T., 1997. Electromagnetic fields and cancer in children residing near Norwegian high-voltage power lines. Am. J. Epidemiol. 145, 219–226. https://doi.org/10.1093/oxfordjournals.aje.a009094.

UK Childhood Cancer Study Investigators, 2000. Childhood cancer and residential proximity to power lines. Br. J. Cancer 83, 1573–1580. https://doi.org/10.1054/bjoc.2000.1550.

Vinceti, M., Rothman, K.J., Crespi, C.M., Sterni, A., Cherubini, A., Guerra, L., Maffeis, G., Ferretti, E., Fabbi, S., Teggi, S., Consonni, D., De Girolamo, G., Meggiato, A., Palazzi, G., Paolucci, P., Malagoli, C., 2012. Leukemia risk in children exposed to benzene and PM(10) from vehicular traffic: a case-control study in an Italian population. Eur. J. Epidemiol. 27, 781–790. https://doi.org/10.1007/s10654-012-9727-1.

Vinceti, M., Filippini, T., Violi, F., Rothman, K.J., Costanzini, S., Malagoli, C., Wise, L.A., Odone, A., Signorelli, C., Iacuzio, L., Arcolin, E., Mandrioli, J., Fini, N., Patti, F., Lo Fermo, S., Pietrini, V., Teggi, S., Ghermandi, G., Scillieri, R., Ledda, C., Mauceri, C., Sciacca, S., Fiore, M., Ferrante, M., 2017. Pesticide exposure assessed through agricultural crop proximity and risk of amyotrophic lateral sclerosis. Environ. Health 16, 91. https://doi.org/10.1186/s12940-017-0297-2.

Violanti, S., 2003. EMF in urban areas, a study to assess low frequency fields in Bologna. ARPARivista 1, 30–31.

WHO - IARC, 2002. Non-Ionizing Radiation, Part 1: Static and Extremely Low-Frequency (ELF) Electric and Magnetic Fields. IARC*Press*, Lyon.

Wunsch-Filho, V., Pelissari, D.M., Barbieri, F.E., Sant'Anna, L., de Oliveira, C.T., de Mata, J.F., Tone, L.G., Lee, M.L., de Andrea, M.L., Bruniera, P., Epelman, S., Filho, V. O., Kheifets, L., 2011. Exposure to magnetic fields and childhood acute lymphocytic leukemia in Sao Paulo, Brazil. Cancer Epidemiol 35, 534–539. https://doi.org/10.1016/j.canep.2011.05.008.