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Association between Childhood Leukaemia and Exposure to Power-frequency Magnetic Fields in Middle Europe.

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**Short form of the title**

Childhood leukaemia and power-frequency magnetic fields

## ABSTRACT

**Objective** Higher levels of exposure to extremely low-frequency magnetic fields (ELF-MF) are associated with a slightly increased risk of childhood leukaemia. Compared with more-developed Western countries, higher exposure levels are evident in the Czech Republic, probably because of the different types of housing. In light of this, we aimed to examine the association between ELF-MF exposure and childhood leukaemia in the Czech Republic.

**Methods** We conducted a paired case-control study. The cases (children with leukaemia) were age- sex- and permanent residence-matched to controls (children without leukaemia). Although this limited potential bias and confounding, it also limited our number of participants.

**Results** The matched analyses included 79 case-control pairs. No significant association between ELF-MF exposure and childhood leukaemia was observed for exposures over 0.2  $\mu\text{T}$  (odds ratio [OR] = 0.93, confidence interval [CI] = 0.45 – 1.93), 0.3  $\mu\text{T}$  (OR = 0.77, CI = 0.34 – 1.75) or 0.4  $\mu\text{T}$  (OR = 0.9, CI = 0.37 – 2.22).

**Conclusion** Despite higher levels of exposure in Middle and Eastern Europe, no indication of an association between ELF-MF exposure and childhood leukaemia was determined. This in contrast to the findings of previous studies conducted in different countries.

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## CHILDHOOD LEUKAEMIA AND EXTREMELY LOW-FREQUENCY MAGNETIC FIELDS

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**Objective** Higher levels of exposure to extremely low-frequency magnetic fields (ELF-MF) are associated with a slightly increased risk of childhood leukaemia. Compared with developed Western countries, higher exposure levels are evident in the Czech Republic, probably because of the different types of housing. In light of this, we aimed to examine the association between ELF-MF exposure and childhood leukaemia in the Czech Republic.

**Methods** We conducted a paired case-control study. The cases (children with leukaemia) were age- sex- and permanent residence-matched to controls (children without leukaemia). Although this limited potential bias and confounding, it also limited our number of participants. **Results** The matched analyses included 79 case-control pairs. No significant association between ELF-MF exposure and childhood leukaemia was observed for exposures over 0.2  $\mu\text{T}$  (odds ratio [OR] = 0.93, confidence interval [CI] = 0.45 – 1.93), 0.3  $\mu\text{T}$  (OR = 0.77, CI = 0.34 – 1.75) or 0.4  $\mu\text{T}$  (OR = 0.9, CI = 0.37 – 2.22). **Conclusion** Despite higher levels of exposure in Middle and Eastern Europe, no indication of an association between

ELF-MF exposure and childhood leukaemia was determined. This in contrast to the findings of previous studies conducted in different countries.

**Keywords:** Childhood leukaemia, power-frequency magnetic field exposure, extremely low-frequency magnetic field, housing types

## INTRODUCTION

Childhood leukaemia is a rare disease, and according to data from the Institute of Health Information and Statistics, each year there are about 40–70 new cases per 1.5–1.7 million children (see [1] for a detailed overview). In CZ during the period 1998–2008, the average number of new cases per year was about 34 per 1 million children, which is slightly lower than the number of new cases in the United Kingdom (approximately 42 cases per 1 million children [2-3]), and Germany (approximately 45 cases per 1 million children [3-4]).

Case-control epidemiological studies of the association between childhood leukaemia and power-frequency magnetic field exposure have been conducted in several developed countries (UK, Germany, USA, Canada, Japan, New Zealand, and others). Most of these studies [5-16] failed to detect a significant association, possibly because of their limited statistical power. After the publication of some pooled analyses [17-19] the International Agency of Research on Cancer (IARC) classified extremely low frequency magnetic fields (ELF-MF) as being “possibly carcinogenic to humans” (Group 2B in 2002) [20]. Slightly increased risks of childhood leukaemia have been estimated with an odds ratio (OR) of 2.0 (95% confidence interval [CI] = 1.27 – 3.13) for exposure levels  $> 0.4 \mu\text{T}$  [18], and of 1.7 (95% CI = 1.2 – 2.3) for exposure levels  $> 0.3 \mu\text{T}$  [19]. Following this classification, other studies attempted to clarify the existence of an association between ELF-MF and childhood leukaemia [21-25]. A pooled analysis [26] of these recent studies found a smaller, non-significant OR of 1.44 (95% CI = 0.88 – 2.36) for exposure levels  $> 0.3 \mu\text{T}$ . No attempts

have been made to examine ELF-MF and childhood cancer in the Middle or Eastern Europe, or the Czech Republic (CZ), even though the housing stock and related ELF-MF exposures in these areas differ from those in previously studied countries (because of the previous politico-economic system) [27-28]. We previously identified that average ELF-MF exposure levels were up to three times higher in CZ in comparison with developed Western countries [29]. For this reason, we conducted a case-control study to elucidate whether ELF-MF exposure in CZ was associated with an increased risk of childhood leukaemia.

## METHODS

### *Equipment and software*

The assessment of exposure to power-frequency magnetic fields was made using purpose-built equipment described elsewhere [29]. The epidemiological data were processed by the programs STATA (Stata Corp., Release 9, College Station, Texas U.S.A.) and OPENEPI [30].

### *Procedure*

A paired case-control study and logistic regression were used to examine the association between ELF-MF and childhood leukaemia. The study was conducted over approximately three years, and the participants were recruited from a range of housing types in the cities, towns and villages of CZ (see [29]).

### *Selection of cases*

The cases included children less than 15 years old, living permanently in CZ with leukaemia (predominantly acute lymphoblastic leukaemia) diagnosed by authorized physicians (diagnoses C91 – C95 [1]). The time since diagnoses was from several weeks up to 5 years for a few cases. Recent cases have been preferred. The quality of leukaemia diagnostics in CZ is very good; therefore, the identification of “cases” is reliable and specific.

Our study cases (n = 82) were identified from medical records of university hospitals. The number of cases was limited by the non-participation of some hospitals.

### ***Selection of controls***

Our controls were also identified from the medical records of university hospitals. Just two (Ostrava and Olomouc) of the five university hospitals (Prague, Hradec Kralove, Brno, Ostrava, Olomouc) provided data. The controls had visited a university hospital for reasons other than cancer (for instance, injury, respiratory or digestive illness). Controls (children without leukaemia) were age- sex- and permanent residence-matched to cases (children with leukaemia). Controls were selected from the same district (for village-based cases) or the same town as their matched case.

In total, 163 participants were recruited, 82 cases and 81 controls. No matches were made for 3 cases and 2 controls. Therefore, only 79 pairs, i.e. 79 cases and 79 controls, were included in the matched analyses.

### ***Exposure assessment***

A detailed description of the ELF-MF exposure assessment method is provided in our previous publication [29]. We divided all housing types into three categories (high-rise, multifamily and family housing) and measured ELF-MF in the participants' houses, in the vicinity of the houses, and inside the participants' schools in different seasons. Each measurement site corresponded with a case or control's permanent residence; therefore, we were able to evaluate individual exposure. The exposure duration was based on the participant's age (range 1–14 years).

### ***Epidemiological data analysis***

The association between ELF-MF exposure and childhood leukaemia occurrence was investigated using conditional logistic regression. We calculated ORs and CIs for various exposure cut points.

## RESULTS

The distribution of ELF-MF exposure by case-control pairs, and by case and control groups is presented in Tables 1 table 2.

**Table 1.** Distribution of ELF-MF exposure by case-control pairs (n = 79)

Case-control pairs		Controls					
Exposure		$\geq 0.2 \mu\text{T}$	$< 0.2 \mu\text{T}$	$\geq 0.3 \mu\text{T}$	$< 0.3 \mu\text{T}$	$\geq 0.4 \mu\text{T}$	$< 0.4 \mu\text{T}$
Cases	$\geq 0.2 \mu\text{T}$	17 pairs	14 pairs	----	----	----	----
	$< 0.2 \mu\text{T}$	15 pairs	33 pairs	----	----	----	----
	$\geq 0.3 \mu\text{T}$	----	----	7 pairs	10 pairs	----	----
	$< 0.3 \mu\text{T}$	----	----	13 pairs	49 pairs	----	----
	$\geq 0.4 \mu\text{T}$	----	----	----	----	4 pairs	9 pairs
	$< 0.4 \mu\text{T}$	----	----	----	----	10 pairs	56 pairs

**Table 2.** Distribution of ELF-MF exposure by case (n = 82) and control (n = 81) groups

	Cases			Controls		
ELF-MF Exposure	$\geq 0.2 \mu\text{T}$	$\geq 0.3 \mu\text{T}$	$\geq 0.4 \mu\text{T}$	$\geq 0.2 \mu\text{T}$	$\geq 0.3 \mu\text{T}$	$\geq 0.4 \mu\text{T}$
Number of participants	32	18	14	33	21	15
ELF-MF Exposure	$< 0.2 \mu\text{T}$	$< 0.3 \mu\text{T}$	$< 0.4 \mu\text{T}$	$< 0.2 \mu\text{T}$	$< 0.3 \mu\text{T}$	$< 0.4 \mu\text{T}$
Number of participants	50	64	68	48	60	66

**Table 3.** Summary of logistic regression analysis results

Number of participants	Cut point	Odds Ratio	95% Confidence Interval

79 case-control pairs	0.2 $\mu$ T	0.933	0.451 – 1.933
	0.3 $\mu$ T	0.769	0.337 – 1.754
	0.4 $\mu$ T	0.900	0.366 – 2.215
82 cases and 81 controls, unmatched	0.2 $\mu$ T	0.931	0.474 – 1.828
	0.3 $\mu$ T	0.805	0.365 – 1.759
	0.4 $\mu$ T	0.906	0.373 – 2.191

The logistic regression results are presented in Table 3. Odd ratios were calculated for the matched data (case-control pairs) as well as for the unmatched data. All of the 95% CIs contained 1, implying that there is no association between ELF-MF exposure at any of the examined cut points and childhood leukaemia.

## DISCUSSION

### *Main finding of this study*

Although higher ELF-MF exposure levels were found in CZ in comparison with developed Western countries [29], we did not identify an association between exposure to power-frequency magnetic fields and childhood leukaemia. This finding is at odds with other studies [18-19] that report a significantly increased risk of childhood leukaemia with higher ELF-MF exposure. However, our results are in agreement with the findings of a recent pooled analysis [26]. Considering the aetiology of childhood leukaemia [34-41], and the very important role of infections [42-45], any contribution of ELF-MF to the most frequent childhood malignant disease is probably minor.

### *What is already known on this topic*

IARC classified ELF-MF as “possibly carcinogenic to humans” in group 2B in 2002 [20] based on some pooled analyses. The true association may actually be weaker than those reported in the earlier pooled analyses [18-19], and possibly not statistically significant,



because the most recent pooled analysis of over ten thousand participants generated an OR of 1.44 and 95% CI of 0.88 – 2.36 [26].

### ***What this study adds***

Primarily, the CZ context provided the opportunity to execute a case-control study under higher exposure conditions (see Tables 1 and 2, and [29]). Many previous studies were limited by very low numbers of participants in relatively higher exposures [12]. This study was carefully designed to decrease unwanted impacts, e.g. comparatively uneven distribution of disease in the population, variation in age and sex, and impacts of some chemical agents. We successfully reduced possible bias and environmental confounding factors by our paired selection of cases and controls. In addition, this is the first study of ELF-MF and childhood leukaemia in Middle and Eastern Europe, where the characteristics of housing and related ELF-MF exposures are unique [27-28].

### ***Limitation of this study***

This study was limited by the inclusion of only a small number of participants. This occurred because the number of new diagnoses of childhood leukaemia is low in CZ and some data are not available. Unavailability of data was caused by the refusal of cooperation of several university hospitals. Our use of matched pairs increased the validity of our study, but we did not account for their socioeconomic status and related factors. Nevertheless, our results may be suitable for use in a pooled analysis.

## CONCLUSIONS

A low delay between diagnosis and exposure assessment, and the use of matched case-control pairs ensured a higher validity of this study. Although power-frequency magnetic field exposures appear a little higher in CZ in comparison with some Western

countries, no indication of any association between exposure levels and childhood leukaemia was found for exposure levels over 0.2  $\mu\text{T}$ , 0.3  $\mu\text{T}$  or 0.4  $\mu\text{T}$  in our study.

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