# Residential exposure to electromagnetic fields and childhood leukaemia: a meta-analysis

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Although individual epidemiological investigations have suggested associations between residential exposure to electromagnetic fields (EMFs) and childhood leukaemia, overall the findings have been inconclusive. Several of these studies do, however, lend themselves to application of the meta-analysis technique. For this purpose we carried out searches using MEDLINE and other sources, and 14 case–control studies and one cohort study were identified and evaluated for epidemiological quality and included in the meta-analysis. Relative risk estimates were extracted from each of the studies and pooled. Separate meta-analyses were performed on the basis of the assessed EMF exposure (wiring configuration codes, distance to power distribution equipment, spot and 24-h measures of magnetic field strength (magnetic flux density) and calculated magnetic field). The meta-analysis based on wiring configuration codes yielded a pooled relative risk estimate of 1.46 (95% confidence interval (CI) = 1.05–2.04, $P = 0.024$) and for that for exposure to 24-h measurements of magnetic fields, 1.59 (95% CI = 1.14–2.22, $P = 0.006$), indicating a potential effect of residential EMF exposure on childhood leukaemia. In most cases, lower risk estimates were obtained by pooling high-quality studies than pooling low-quality studies. There appears to be a clear trend for more recent studies to be of higher quality. Enough evidence exists to conclude that dismissing concerns about residential EMFs and childhood leukaemia is unwarranted. Additional high-quality epidemiological studies incorporating comparable measures for both exposure and outcomes are, however, needed to confirm these findings and, should they prove to be true, the case options for minimizing exposure should be thoroughly investigated to provide definitive answers for policy-makers.

**Keywords:** electromagnetic fields; leukaemia, radiation induced; meta-analysis; risk factors.

*Voir page 913 le résumé en français. En la página 913 figura un resumen en español.*

## Introduction

In 1979 Wertheimer & Leeper (*1*) published the first report that showed an increased risk of cancer mortality among children living near electrical wiring configurations and which were consistent with the presence of high currents. Although many studies linking exposure to electromagnetic fields (EMFs) with health effects have been conducted, there is still much debate over whether this exposure at the levels that occur in domestic settings can cause cancer, particularly childhood leukaemia. Some workers have recently called for an end to further research on exposure to magnetic fields (*2*), whereas others believe that abandoning research on this topic is premature (*3, 4*).

Meta-analysis is a quantitative approach for systematically combining the results of previous studies in order to arrive at conclusions that cannot be drawn from the results of any one study alone. Although it has been applied most often to combine the results of randomized trials, use of meta-analysis is not confined to the synthesis of information from experimental studies. A large number of studies that involve meta-analysis of nonexperimental data have been published in recent years, although such use of the technique is less accepted than it is in the analysis of data from clinical trials (*5*). Meta-analyses of observational epidemiological studies have also previously been carried out to examine the relationship between residential EMF exposure and childhood leukaemia (*6–11*). In general, such analyses have shown a significant increased risk of childhood leukaemia when residential exposure is assessed through the use of wiring configuration codes (a categorical exposure rating scheme based on wire size and distance from the residence), whereas the association with other related markers of exposure, such as proximity to power lines and calculated magnetic fields from power lines, appears less evident.

Several well-conducted epidemiological studies on the association between EMFs and childhood leukaemia were published after the above-mentioned meta-analyses appeared. The purpose of the present investigation was to reassess the risk of childhood leukaemia associated with residential EMF exposure in the light of these more recent publications. In so doing we hoped to be able to provide answers to the following questions.

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- Could the association between wire codes and childhood leukaemia be confirmed?
- Is there an association between childhood leukaemia and other markers of residential EMF exposure?
- What is the overall quality of existing studies and is there a relationship between the quality of studies and the magnitude of risk?
- What recommendations can we make for further studies, if warranted?

## Materials and methods

### Identification of relevant studies

Studies pertaining to the relationship between EMFs and childhood leukaemia were identified using a MEDLINE search of the medical literature published in English over the period 1966–98. Copies of the relevant articles were obtained and reviewed to identify additional references.

To be eligible for inclusion in the meta-analyses, studies had to satisfy the following criteria: be primary studies, not reanalyses or reviews; be of case–control, cohort, or cross-sectional design; examine residential-based exposures through wiring configuration codes, distance to power distribution equipment, spot and 24-h measures of magnetic field strength (magnetic flux density), and calculated magnetic fields; examine childhood leukaemia; report an odds ratio and its variance or sufficient data to estimate them; be in English, and be published before January 1999.

### Quality assessment

Each article was blinded with regard to authors, institution, and journal. The articles were read and scored for quality by two independent readers using a system that incorporates elements of methods developed by Chalmers et al. (*12*), Longnecker et al. (*13*), Morris et al. (*14*) and Villari et al. (*15*). The criteria employed are shown in the results section below. A quality score was calculated as the percentage of applicable criteria that were met in each study. Items concerned with efforts to minimize potential bias were given twice the weight of those evaluating data analysis.

### Data extraction

A number of different methods were used to measure EMF exposure in the studies examined. In the absence of a unique criterion, not all studies examining EMF exposure and childhood leukaemia risk could be included in a single analysis. Exposure assessment methods were aggregated into the following categories: wiring configuration codes; distance to power distribution equipment; spot and 24-h measures of magnetic field strength; calculated indices of magnetic field strength using distance to power distribution equipment; and historic load data. To aggregate exposure categories across studies, we dichotomized exposure strata using the cut-off points that were common to most of the studies. More specifically, in studies where the exposure status was assessed through the wiring code or distance criterion, subjects were considered exposed if they were living in homes with high current configurations or at a distance of less than 50 m from any electrical sources, respectively. Similarly, in studies where the assessment of exposure was made via spot, 24-h measurements or historical calculation of magnetic field strength, a cut-off point of 0.2 μT was used.

For each blinded study, data were extracted in a contingency table format, and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Data extraction was carried out independently by two readers. After completing data extraction, the two readers met to resolve any differences and arrive at a consensus.

### Statistical pooling

The random effects model described by DerSimonian & Laird (*16*) was used to combine the collected values. This procedure yields a single estimate of the OR for leukaemia in children exposed to EMFs compared with nonexposed children. It also enables testing the homogeneity across the individual studies (using the Q statistics); the heterogeneity, if not zero, is then incorporated into the pooled variance estimate.

We avoided pooling results obtained through the use of different exposure criteria, and instead carried out separate meta-analyses based on exposure assessment methods, using the cut-off points specified above. Studies that used more than one method of EMF measurement were included in more than one meta-analysis. In order to test all decision rules that we used in extracting OR data, we performed additional meta-analyses using, for each exposure assessment method, data that in the single studies gave the lowest OR (best scenario) and the highest OR (worst scenario).

Finally, studies were also divided into two groups and analysed according to their quality score: the potential impact of the quality of studies on the results was assessed by comparing pooled results from studies with scores above the median to studies whose scores were equal to or below the median.

## Results

### Literature search

The literature search identified 14 case–control studies (*1*, *17–29*) and one cohort study (*30*) that investigated the relationship between residential magnetic-field exposures and childhood leukaemia and which met our inclusion criteria. Of these studies, 10 employed only one method of EMF measurement (*1, 17, 18, 20, 22, 24, 26, 27, 29, 30*), three used two methods (*19, 25, 28*), and two studies used three methods (*21, 23*). Thus, six studies were

available for the meta-analysis evaluating exposure through wiring configuration codes (*1, 17, 19, 21, 25, 27*) and five studies for the meta-analysis in which the exposure was determined by spot measures (*18, 19, 21, 23, 28*), whereas meta-analyses based on distance from electrical sources (*20, 23, 24, 26*), 24-h measurements of magnetic fields (*21, 25, 28, 29*) and calculated magnetic fields (*22, 23, 26, 30*) comprised four studies each.

The inclusion of the studies by Tomenius (*18*) and Feychting & Ahlbom (*23*) in the meta-analysis based on spot measurements of magnetic fields was problematic, since a partial overlap of their data cannot be excluded. Therefore, we included in our main analysis only the Feychting & Ahlbom study, testing the impact of this choice in a sensitivity analysis.

Magnetic field strength was not dichotomized at the 0.2 μT level in four studies reporting spot or 24-h measures and calculated indices (Tomenius (*18*) = 0.3 μT; London et al. (*21*) = 0.125 and 0.264 μT for spot and 24-h measurements, respectively; Olsen et al. (*22*) = 0.25 μT; Tynes & Haldorsen (*26*) = 0.14 μT). In order to include in the meta-analyses all available data, we assumed that the exposure cut-off points used in these studies were comparable to the 0.2 μT exposure.

## Quality assessment

Table 1 shows the results of the quality scoring procedure. The potential for selection bias may be a concern in the individual studies considered. Although 11 of the 14 case–control studies used population-based cancer registries to identify cases, there are a number of important concerns about the control selection. Only five studies used a population register to identify controls. If the ascertainment of

Table 1. **Items used in quality scoring for studies of the association between exposure to residential electromagnetic fields (EMF) and childhood leukaemia**

| Quality scoring item | % of studies complying[a] |
|---|---|
| **Case–control studies** | |
| Cases either randomly selected or selected to include all cases in a specific population | 79 |
| Cases identified without knowledge of exposure status | 100 |
| Response rate for identified cases > 75% | 64 |
| Control drawn randomly from the same population of cases | 36 |
| No known association between control status and exposure | 93 |
| Response rate for identified controls > 75% | 50 |
| **Cohort studies** | |
| Initial response rate > 75% | 100 |
| Comparison of persons who did and did not participate | 0 |
| Follow-up rate > 75% | 100 |
| Comparison of who were and were not lost to follow-up | 0 |
| Exposed/nonexposed subjects identified without knowledge of disease status | 100 |
| No known association between nonexposed status and disease | 100 |
| **All studies** | |
| Subjects unaware of specific associations of interest insofar as possible | 67 |
| Exposure/disease assessment made blindly with respect to the case–control/exposure status of subjects | 53 |
| Specific disease criteria given | 33 |
| Disease validated by histology or other gold standard | 53 |
| Exposure evaluations made in relation to the time of diagnosis | 67 |
| Differential mobility among cases and controls (or among exposed and nonexposed) considered | 80 |
| Age considered as potential confounder | 100 |
| Sex considered as potential confounder | 93 |
| Socioeconomic status considered as potential confounder | 87 |
| Parental occupational exposure to EMF considered as potential confounder | 20 |
| Indicators of air quality (e.g. traffic density) considered as potential confounder | 40 |
| Competing carcinogenic exposures considered as potential confounder | 40 |
| Demographic data listed | 53 |
| Statistical analysis of demographic data | 7 |
| Power calculations performed | 13 |
| Precise *P*-values and/or confidence interval given | 87 |
| Test statistic specified | 93 |
| Appropriate statistical analysis | 80 |

[a] If compliance was not specifically indicated in the text, noncompliance was assumed.

cases as well as the population register is complete, these studies should be free of selection biases. In most studies, however, controls were selected in less desirable ways, such as using regional birth certificate files, random digit dialing or other cancer cases. Response rates for cases and controls were frequently less than 75%, particularly in studies requiring subject interviews or magnetic field measurements.

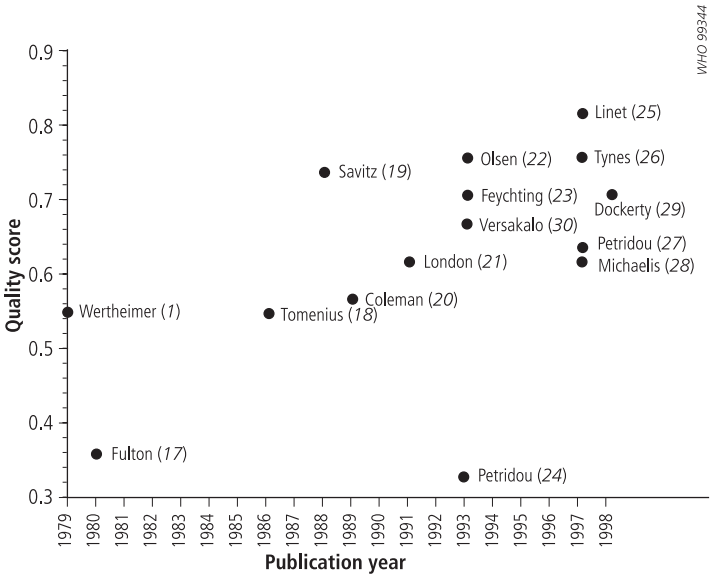
Misclassification bias cannot be considered negligible. Although few studies specified disease criteria or clearly stated that cancer diagnosis was validated by histology or some other gold standard, diseases like leukaemia are subject to relatively little misclassification (false negatives are unlikely given the severity of the disease, and false positives are unlikely given the medical scrutiny of suspected cases). By contrast, exposure misclassification is a pervasive concern in case–control studies of the effect of exposure to EMFs. Unfortunately, not all studies made serious efforts to collect as much of the exposure data as possible while being unaware of the case–control status of the subjects. Use of such a procedure does not ensure the absence of errors but makes it highly probable that errors would be independent of case or control status and therefore that the results would be biased towards the null.

Information bias associated with failure to consider confounding variables may have been more of a problem. With the exception of age (100% of studies), sex (93%) and socioeconomic status (87%), less than half of the studies considered potentially confounding variables such as traffic density (40%), parental occupational exposure to EMFs (20%) or other competing carcinogenic exposures (40%). Although attempts made to adjust for those variables have produced evidence against the presence of substantial confounding, such attempts are severely hampered by the scarcity of established or even strongly suspected causes of childhood leukaemia.

Statistical analysis was judged appropriate in most studies. Although the majority of studies listed *P* values and/or 95% CI, very few listed or analysed demographic data. Only two studies provided power calculations.

Quality scores for the individual studies ranged from 0.33 to 0.82, and there was a clear tendency for more recent studies to be of better quality (Fig. 1).

Fig. 1. **Relationship between year of publication and quality score of studies relating electromagnetic field (EMF) and childhood leukaemia.** Individual studies are identified by the name of the first author (figures in parentheses are the literature references).




## Statistical analysis

Table 2 lists the OR estimates with their respective 95% CIs extracted from each study and shows the results of pooling data from all studies according to the five different methods of exposure assessment. Although 17 of these 23 estimates (73.9%) had ORs greater than 1.00, only 5 (21.7%) were significantly greater than this ($P < 0.05$). The overall OR estimates of these meta-analyses were always greater than 1.00, indicating a potential effect of residential EMF exposure on childhood leukaemia risk. However, this effect is statistically significant only for meta-analyses based on wiring configuration codes (pooled OR = 1.46; 95% CI = 1.05–2.04; $P = 0.024$) and 24-h measurements of magnetic fields (pooled OR = 1.59; 95% CI = 1.14–2.22; $P = 0.006$). In the meta-analysis of studies in which the exposure assessment was made through spot measurements of magnetic field, the exclusion of the Feychting & Ahlbom study (*23*) and the inclusion of that by Tomenius (*18*) decreased the overall OR below 1.00 (pooled OR = 0.94; 95% CI = 0.50–1.77; $P = 0.850$). Individual studies included in the different meta-analyses appear heterogeneous ($P < 0.05$) only in the case of exposure assessment performed with wiring configuration codes or by distance.

Even in the presence of predefined and well-established criteria, we encountered in many studies more than one possibility for data extraction. For example, in the study by Wertheimer & Leeper (*1*), exposure assessment was performed both at birth and death addresses, which resulted in OR estimates of 2.28 and 2.97, respectively; Linet et al. (*25*) calculated results using unmatched analysis as well as analysis of matched case–control pairs, with corresponding OR estimates of 1.19 and 1.39. To test the sensitivity of our results to the different choices of data extraction, we performed separate meta-analyses using, for each exposure assessment method, data that gave the lowest (best scenario) and the highest (worst scenario) OR estimates. The impact of the different choices of data extraction did not seem to be substantial (Table 3). The overall ORs resulting from studies based on wiring configuration codes and 24-h measurements of magnetic fields were always significantly different from 1.00, ranging from 1.33 to 1.58 and from 1.50 to 1.95, respectively. Interestingly, the heterogeneity of studies included in the meta-analysis based on wiring configuration codes, compared with the baseline analysis, tended to decrease, and in the best-scenario hypothesis,

Table 2. **Summary of studies included in the meta-analyses relating electromagnetic fields (EMFs) and childhood leukaemia according to EMF measurement methods**

| Study | Country | Age of study subjects (years) | No. of cases[a] | No. of controls[a] | OR[b] |
|---|---|---|---|---|---|
| **Wiring configuration codes**[c] | | | | | |
| Wertheimer & Leeper (ref. *1,* 1979) | USA | <19 | 155 (63, 40.6%) | 155 (29, 18.7%) | 2.98; *1.78–4.98* |
| Fulton et al. (ref. *17,* 1980) | USA | <21 | 198 (103, 52.0%) | 225 (112, 50.0%) | 1.09; *0.75–1.60* |
| Savitz et al. (ref. *19,* 1988) | USA | <15 | 97 (27, 27.8%) | 259 (52, 20.1%) | 1.54; *0.90–2.63* |
| London et al. (ref. *21,* 1991) | USA | <11 | 211 (122, 57.8%) | 205 (92, 44.9%) | 1.68; *1.14–2.48* |
| Linet et al. (ref. *25,* 1997) | USA | <15 | 402 (111, 27.6%) | 402 (113, 28.1%) | 0.98; *0.72–1.33* |
| Petridou et al. (ref. *27,* 1997) | Greece | <15 | 117 (11, 9.4%) | 202 (14, 6.9%) | 1.39; *0.61–3.18* |
| *Overall* | | | 1 180 (437, 37.0%) | 1 448 (412, 28.4%) | 1.46; *1.05–2.04*[d] |
| **Distance from power distribution equipment**[e] | | | | | |
| Coleman et al. (ref. *20,* 1989) | England | <18 | 84 (14, 16.7%) | 141 (15, 10.6%) | 1.68; *0.77–3.68* |
| Feychting & Ahlbom (ref. *23,* 1993) | Sweden | <16 | 38 (6, 15.8%) | 554 (34, 6.1%) | 2.87; *1.12–7.33* |
| Petridou et al. (ref. *24,* 1993) | Greece | <15 | 136 (96, 70.6%) | 187 (132, 70.6%) | 1.00; *0.62–1.62* |
| Tynes & Haldorsen (ref. *26,* 1997) | Norway | <15 | 148 (9, 6.1%) | 579 (55, 9.5%) | 0.62; *0.30–1.28* |
| *Overall* | | | 406 (125, 30.8%) | 1 461 (236, 16.1%) | 1.23; *0.70–2.18*[f] |
| **Spot measurements of magnetic fields**[g] | | | | | |
| Tomenius (ref. *18*, 1986) | Sweden | <19 | 243 (4, 1.6%) | 212 (10, 4.7%) | 0.34; *0.10–1.09* |
| Savitz et al. (ref. *19,* 1988) | USA | <15 | 36 (5, 13.9%) | 207 (16, 7.7%) | 1.93; *0.66–5.63* |
| London et al. (ref. *21,* 1991) | USA | <11 | 140 (16, 6.7%) | 109 (11, 10.1%) | 1.15; *0.51–2.59* |
| Feychting & Ahlbom (ref. *23,* 1993) | Sweden | <16 | 24 (4, 16.7%) | 344 (70, 20.3%) | 0.78; *0.26–2.36* |
| Michaelis et al. (ref. *28*, 1997) | Germany | <15 | 176 (6, 3.4%) | 414 (16, 3.9%) | 0.88; *0.34–2.28* |
| *Overall* | | | 376 (31, 8.2%) | 1 074 (113, 10.5%) | 1.11; *0.68–1.79*[f] |
| **24-h measurements of magnetic fields**[g] | | | | | |
| London et al. (ref. *21*, 1991) | USA | <11 | 164 (20, 12.2%) | 144 (11, 7.6%) | 1.68; *0.78–3.64* |
| Linet et al. (ref. *25,* 1997) | USA | <15 | 463 (58, 12.5%) | 463 (44, 9.5%) | 1.36; *0.90–2.07* |
| Michaelis et al. (ref. *28*, 1997) | Germany | <15 | 176 (9, 5.1%) | 414 (8, 1.9%) | 2.74; *1.04–7.21* |
| Dockerty et al. (ref. *29*, 1998) | New Zealand | <15 | 40 (7, 17.5%) | 40 (3, 7.5%) | 2.62; *0.63–10.95* |
| *Overall* | | | 843 (94, 11.1%) | 1 061 (66, 6.2%) | 1.59; *1.14–2.22*[f] |
| **Calculated magnetic fields**[g] | | | | | |
| Feychting & Ahlbom (ref. *23*, 1993) | Sweden | <16 | 37 (7, 18.9%) | 554 (46, 8.3%) | 2.58; *1.07–6.19* |
| Olsen et al. (ref. *22*, 1993) | Denmark | <15 | 833 (3, 0.4%) | 1 666 (4, 0.2%) | 1.50; *0.34–6.73* |
| Verkasalo et al. (ref. *30*, 1993) | Finland | <20 | 35 (3, 8.6%) | 134 797 (7297, 5.4%) | 1.64; *0.50–5.35* |
| Tynes & Haldorsen (ref. *26*, 1997) | Norway | <15 | 148 (1, 0.7%) | 579 (14, 2.4%) | 0.27; *0.04–2.10* |
| *Overall* | | | 1 053 (14, 1.3%) | 137 596 (7 361,5.3%) | 1.55; *0.73–3.32*[f] |

[a] Figures in parentheses are the number and percentage of exposed subjects.

[b] Figures in italics are 95% confidence intervals.

[c] Exposure strata dichotomized in low current configuration vs high current configuration.

[d] Random effects model, as described by DerSimonian & Laird (ref. *16*).

[e] Exposure strata dichotomized as distance <50 m vs ⩾50 m.

[f] Summary odds ratio (random effects model, as described by DerSimonian & Laird (ref. *16*)).

[g] Exposure strata dichotomized as magnetic field strength <0.2 μT vs ⩾0.2 μT.

[h] Calculation performed excluding the study by Tomenius (ref. *18),* because of data overlapping with Feychting & Ahlbom's study (ref. *23).*

became not significant ($P < 0.05$). In contrast, the heterogeneity of studies in which the exposure was assessed by 24-h EMF measures, although not significant, tended to increase slightly either in the best-case or worst-case scenario.

The quality of the studies does seem to have a substantial impact on our summary estimates, particularly in meta-analyses based on wiring configuration codes, 24-h measurements of magnetic fields, and calculated magnetic fields, since high-quality-score studies have lower risk estimates than low-quality-score studies (Table 4).

## Discussion

By the end of 1998, 15 studies had been published that provided relevant data on the association between

Table 3. **Sensitivity of summary results of meta-analyses relating electromagnetic fields (EMFs) and childhood leukaemia, according to choices of data extraction**

| EMF measurement method | No. of studies | Summary OR[a] | *P*-value | Heterogeneity | |
|---|---|---|---|---|---|
| | | | | $\chi^2$ test | *P*- value |
| **Wiring configuration codes** | | | | | |
| Best scenario | 6 | 1.33; *1.00–1.76*[b] | 0.048 | 10.86 (5)[c] | 0.054 |
| Baseline analysis | 6 | 1.46; *1.05–2.04* | 0.024 | 16.00 (5) | 0.007 |
| Worst scenario | 6 | 1.58; *1.14–2.21* | 0.007 | 14.65 (5) | 0.011 |
| **Distance from power distribution equipment** | | | | | |
| Best scenario | – | – | – | – | – |
| Baseline analysis | 4 | 1.23; *0.70–2.18* | 0.47 | 8.46 (3) | 0.037 |
| Worst scenario | – | – | – | – | – |
| **Spot measurements of magnetic fields** | | | | | |
| Best scenario | 4 | 1.03; *0.63–1.70* | 0.9 | 0.81 (3) | 0.847 |
| Baseline analysis | 4 | 1.11; *0.68–1.79* | 0.68 | 1.73 (3) | 0.63 |
| Worst scenario | – | – | – | – | – |
| **24-h measurements of magnetic fields** | | | | | |
| Best scenario | 4 | 1.50; *1.03–2.19* | 0.034 | 3.96 (3) | 0.266 |
| Baseline analysis | 4 | 1.59; *1.14–2.22* | 0.006 | 2.55 (3) | 0.466 |
| Worst scenario | 4 | 1.95; *1.11–3.40* | 0.019 | 6.04 (3) | 0.109 |
| **Calculated magnetic fields** | | | | | |
| Best scenario | – | – | – | – | – |
| Baseline analysis | 4 | 1.55; *0.73–3.32* | 0.25 | 6.10 (3) | 0.107 |
| Worst scenario | – | – | – | – | – |

[a] Summary odds ratio (random effects model, using the method described by DerSimonian & Laird, ref. *16*).

[b] Figures in italics are 95% confidence intervals.

[c] Figures in parentheses are degrees of freedom.

residential exposure to EMF and childhood leukaemia: nine in Europe, five in the USA, and one in New Zealand. The majority of these studies appeared between 1986 and 1993, and five studies were published in the period 1997–98. All but one were case–control studies, most of which were based on a comprehensive case ascertainment in a geographically defined population. Exposure assessment was based on a variety of methods, including wiring configuration codes, distance to power distribution equipment, spot and 24-h measures of magnetic field strength, and calculated indices using distance to power distribution equipment and historical load data. One-third of the studies employed more than one method of EMF measurement.

In the present investigation, pooling results arising from the use of different exposure criteria was avoided, and we performed separate meta-analyses for each method of exposure assessment. The meta-analysis based on wiring configuration codes confirmed the 1.5-fold statistically significant excess of childhood leukaemia already documented in previous studies (*7–11*). The exposure rates among control subjects in the individual studies varied from 6.9% to 50%, and the heterogeneity was found to be statistically significant. The ca. 1.5-fold risk of childhood leukaemia was also reported in meta-analyses based on calculated magnetic fields and 24-h measurements of magnetic fields. This excess risk was significant only in the analysis of studies relying on 24-h measurements of magnetic fields, in which the exposure rate among controls varied from 1.9% to 9.5%, and the heterogeneity was not statistically significant. Meta-analyses based on distance and spot measurements of magnetic fields produced ORs of lower magnitude and not significantly different from unity.

Other meta-analyses of the association between exposure to residential electromagnetic fields and childhood leukaemia have been carried out. For example, Washburn et al. (*6*), combining results of studies published before 1992, found increased risks for leukaemia, lymphoma, and nervous system cancers, although the risk of lymphoma was not significant. Miller et al. (*7*), in separate meta-analyses of studies published before 1993 according to EMF measurement methods, documented statistically significant increased risks for childhood leukaemia for wiring configuration codes, and distance and calculated indices, whereas spot measures consistently showed non-significant odds ratios. On the basis of studies published before 1994, Meinert & Michaelis (*8*) confirmed the significant association between childhood leukaemia and residential EMF

Table 4. **Sensitivity of summary results of meta-analyses relating electromagnetic fields (EMFs) and childhood leukaemia to quality scores of individual studies**

| EMF measurement method | No. of studies | Summary OR[a] | *P*-value | Heterogeneity | |
|---|---|---|---|---|---|
| | | | | $\chi^2$ test | *P*-value |
| **Wiring configuration codes** | | | | | |
| All studies | 6 | 1.46; *1.05–2.04*[b] | 0.024 | 16.00 (5)[c] | 0.007 |
| Low-quality studies | 3 | 1.72; *1.01–2.93* | 0.045 | 9.29 (2) | 0.009 |
| High-quality studies | 3 | 1.15; *0.85–1.55* | 0.37 | 2.42 (2) | 0.298 |
| **Distance from power distribution equipment** | | | | | |
| All studies | 4 | 1.23; *0.70–2.18* | 0.47 | 8.46 (3) | 0.037 |
| Low-quality studies | 2 | 1.18; *0.73–1.89* | 0.68 | 1.24 (1) | 0.265 |
| High-quality studies | 2 | 1.29; *0.29–5.81* | 0.74 | 6.93 (1) | 0.008 |
| **Spot measurements of magnetic fields** | | | | | |
| All studies | 4 | 1.11; *0.68–1.79* | 0.68 | 1.73 (3) | 0.63 |
| Low-quality studies | 2 | 1.03; *0.55–1.91* | 0.93 | 0.18 (1) | 0.671 |
| High-quality studies | 2 | 1.24; *0.51–2.99* | 0.63 | 1.47 (1) | 0.225 |
| **24-h measurements of magnetic fields** | | | | | |
| All studies | 4 | 1.59; *1.14–2.22* | 0.006 | 2.55 (3) | 0.466 |
| Low-quality studies | 2 | 2.03; *1.11–3.71* | 0.022 | 0.93 (1) | 0.335 |
| High-quality studies | 2 | 1.43; *0.96–2.14* | 0.08 | 0.71 (1) | 0.399 |
| **Calculated magnetic fields** | | | | | |
| All studies | 4 | 1.55; *0.73–3.32* | 0.25 | 6.10 (3) | 0.107 |
| Low-quality studies | 2 | 2.21; *1.07–4.58* | 0.033 | 0.65 (1) | 0.42 |
| High-quality studies | 2 | 0.74; *0.14–3.83* | 0.72 | 1.57 (1) | 0.21 |

[a] Summary odds ratio (random effects model, calculated using the method described by DerSimonian & Laird, ref. *16*).

[b] Figures in italics are 95% confidence intervals.

[c] Figures in parentheses are degrees of freedom.

exposure measured through wiring configuration codes, whereas no association was found with distance; the meta-analysis of studies in which the EMF exposure was either measured directly or calculated did not show an increase of childhood leukaemia with higher cut-off points. More recently, Wartenberg (*9*, *11*) documented that wiring codes and related markers of exposure, such as proximity to power lines and calculated magnetic fields from power lines, were associated with an approximate 1.5-fold excess risk of childhood leukaemia, whereas the evidence of an association with magnetic fields measured directly was not, in the aggregate, supported. None of these previous meta-analyses provided overall risk estimates from studies in which the exposure assessment was performed through 24-h measurements of magnetic fields.

The quality of the individual studies included in our meta-analyses was assessed on the basis of their statistical analyses and the efforts made to minimize potential for selection bias, misclassification bias related to exposure as well as disease, and information bias due to failure to consider potential confounding variables. Items concerned with efforts to minimize potential bias were given twice the weight of items evaluating data analysis. Since there appears to be no "gold standard" at present for EMF measurement, we did not evaluate the operational definition of exposure (e.g., all EMF measurements methods were assumed to be equally valid). It is well known that all quality assessment systems have a subjective component, none have yet been validated, and efforts to correlate quality scores with direction or size of effect have had mixed findings (*31, 32*). Therefore, we did not use quality scores to determine studies to be included in the meta-analysis or to assign statistical weights.

Despite these limitations, assessment of the quality of the individual studies used in our meta-analysis allowed us to draw the following conclusions:

- there has been improvement in study design and reporting, since findings published more recently tended to receive a higher quality rating;
- the possibility of selection bias, misclassification bias related to exposure, and information bias related to failure to consider potential confounders cannot be ruled out;
- most importantly, pooling high-quality-score studies resulted in lower risk estimates than did pooling low-quality-score studies.

If high-quality studies are more likely to yield valid information than low-quality studies, we can con-

clude that currently available data do not permit exact quantification of the true excess risk of childhood leukaemia due to residential EMF exposure.

An important limitation of the meta-analytical approach is related to publication bias. This occurs if positive results are more likely to be published than negative ones (*33–35*). In the case of residential EMF exposure and childhood leukaemia, there is an important factor that may mitigate the tendency for negative findings to be excluded from the published literature. In view of the considerable interest in this topic, it seems unlikely that any investigator would have trouble in getting even a negative study published. Indeed, the great majority of the studies that we included in our meta-analyses reported risk estimates with *P* values greater than 0.05, suggesting that non-significant results are readily publishable.

Several conclusions may be drawn from the results of this study.

- First, an association between residential EMF exposure and childhood leukaemia may exist. This possibility is supported by the statistically significant risk estimates obtained by pooling results of studies in which the exposure was assessed not only indirectly with markers such as wiring configuration codes but also through direct measurements of magnetic field for at least a 24-h period.
- Second, the magnitude of this excess risk, if any, is at present unknown, given the possibility of selection bias, exposure misclassification, and the existence of confounding variables in the individual studies.
- Third, there appears to be a clear trend for the more recent publications to be of better quality. If this trend continues, new good-quality studies can be expected in the future.
- Finally, enough evidence exists to lead us to conclude that dismissing concerns about EMF and childhood leukaemia is unwarranted. What is required is the publication of new state-of-the-art epidemiological studies that incorporate comparable measures for both exposure and outcomes in order to facilitate future meta-analyses. If this excess risk of childhood leukaemia is confirmed, we should thoroughly investigate, also from a cost-effectiveness point of view, possible options for minimizing exposure in order to provide definitive answers for policy-makers. ■


## Résumé

### Méta-analyse de la relation entre leucémie de l'enfant et exposition à des champs électromagnétiques du fait du lieu de résidence

Les études épidémiologiques consacrées à la relation entre leucémie de l'enfant et exposition à des champs électromagnétiques du fait du lieu de résidence sont suggestives sans toutefois être concluantes. Un certain nombre d'entre elles se prêtent cependant à la technique de la méta-analyse. Nous avons effectué une recherche bibliographique au moyen de MEDLINE et d'autres sources de données pour retenir 14 études cas-témoins et une étude de cohorte dont nous avons évalué la qualité épidémiologique et que nous avons soumises ensuite à une méta-analyse. Nous avons tiré de chacune d'entre elles une estimation du risque relatif et nous avons réuni ces valeurs. Une méta-analyse distincte a été effectuée selon le mode d'évaluation du champ électromagnétique (code de configuration du bobinage, distance au centre de distribution, mesures ponctuelles ou sur 24 h de l'intensité du champ magnétique (densité de flux magnétique) ou détermination de ce champ par le calcul). La méta-analyse basée sur les codes de configuration a donné une estimation combinée du risque relatif égale à 1,46 (intervalle de confiance (IC) à 95% = 1,05–2,04, p = 0,024); celle qui prenait en compte la mesure du champ sur 24 h donnant une valeur de 1,59 (IC à 95 % = 1,14–2,22, p = 0,006 ) et indiquant donc la possibilité d'une relation entre exposition au champ magnétique et leucémie chez l'enfant). Dans la plupart des cas, le regroupement des résultats des études de très bonne qualité a donné une estimation du risque plus faible que dans le cas des études de qualité médiocre. On constate une nette tendance à l'amélioration de la qualité dans les études récentes. On a en tout cas suffisamment de preuves pour pouvoir conclure qu'il n'est pas justifié de faire bon marché des craintes qui se sont exprimées au sujet du risque de leucémie chez les enfants exposés à des champs électromagnétiques du fait de leur lieu de résidence. Il est nécessaire d'effectuer d'autres études épidémiologiques de très bonne qualité basées sur des mesures comparables de l'exposition et de son résultat pour pouvoir confirmer ces observations. Dans l'éventualité d'une confirmation de cet excès de risque, il faudrait étudier minutieusement les possibilités de réduction de l'exposition afin que les décideurs puissent disposer de conclusions définitives.

## Resumen

### Exposición a campos electromagnéticos en zonas de residencia y leucemia infantil: metanálisis

Las diversas investigaciones epidemiológicas realizadas sobre la relación entre la exposición a campos electromagnéticos (CEM) en zonas de residencia y la leucemia infantil se han saldado con indicios no concluyentes. Varios de esos trabajos, sin embargo, se prestan a ser estudiados mediante técnicas de metanálisis. En el

presente metanálisis se incluyeron 14 estudios de casos y testigos y un estudio de cohortes identificados a través de MEDLINE y de otras fuentes, previa evaluación de su calidad epidemiológica. Se combinaron las estimaciones del riesgo relativo obtenidas en cada uno de los estudios y se realizaron diversos metanálisis basados en las distintas evaluaciones de la exposición a los CEM (códigos de configuración del cableado, distancia a las instalaciones de distribución de la energía, mediciones puntuales y de 24 horas de la potencia de los campos electromagnéticos (densidad de flujo magnético), campos magnéticos calculados). El metanálisis basado en los códigos de configuración del cableado arrojó una estimación del riesgo relativo de 1,46 (IC95%: 1,05 - 2,04, p = 0,024), y en el caso de las mediciones de 24 horas de los campos electromagnéticos se obtuvo un valor de 1,59 (IC95%: 1,14-2,22, p = 0,006), lo que indica una posible relación entre la exposición a CEM en zonas de residencia y la aparición de leucemia infantil. En la mayoría de los casos las combinaciones de estudios de alta calidad dieron estimaciones del riesgo más bajas que las combinaciones de estudios de baja calidad. Se observa una clara tendencia a una mayor calidad en los estudios más recientes. Existen datos suficientes para concluir que no puede descartarse una relación entre la influencia de los campos electromagnéticos en la zona de residencia y la leucemia infantil. Es necesario realizar nuevos estudios epidemiológicos de gran calidad, con mediciones comparables tanto de la exposición como de los resultados, para corroborar estos resultados. Si se confirmara el posible exceso de riesgo, habría que investigar a fondo las alternativas para reducir al mínimo la exposición y proporcionar respuestas definitivas a los formuladores de políticas.

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