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Overview of the epidemiologic studies on the health effects of ELF electric and magnetic fields (ELF-EMF) published in the third quarter of 2023.

dr. Els De Waegeneer

Department of Public Health

Ghent University

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1. Reviews and meta-analyses

1.1 Electromagnetic Radiation Exposure and Childhood Leukemia: Meta-analysis and Systematic Review.

Huaipeng, G., Lei, K., Weiwei, Q., Yahong, L. (2023). *Alternative Therapies*, in press.

Link

Background and objective: Leukemia is the most prevalent cancer among children and adolescents. This study investigated the potential association between exposure to magnetic fields and the risk of pediatric leukemia.

Methods: The authors conducted a comprehensive search of electronic databases, including Scopus, EMBASE, Cochrane, Web of Science, and Medline, up to December 15, 2022, to identify relevant studies examining the link between childhood leukemia and magnetic field exposure.

Results: The first meta-analysis revealed a statistically significant inverse association between pediatric leukemia and magnetic field strengths ranging from 0.4 µT to 0.2 µT, suggesting a reduced risk associated with this range. The second meta-analysis focused on wiring configuration codes and observed a potential link between residential magnetic field exposure and childhood leukemia. Pooled relative risk estimates were 1.52 (95% CI = 1.05-2.04, P = .021) and 1.58 (95% CI = 1.15-2.23, P = .006) for exposure to 24-hour magnetic field measurements, suggesting a possible causal relationship. In the third meta-analysis, the odds ratios for the exposure groups of 0.1 to 0.2 µT, 0.2 to 0.3 µT, 0.3 to 0.4 µT, and 0.4 µT above 0.2 µT were 1.09 (95% confidence interval = 0.82 to 1.43 µT), 1.14 (95% confidence interval = 0.68 to 1.92 µT), and 1.45 (95% confidence interval = 0.87 to 2.37 µT), respectively. In contrast to the findings of the three meta-analyses, there was no evidence of a statistically significant connection between exposure to 0.2 µT and the risk of juvenile leukemia. A further result showed no discernible difference between the two groups of children who lived less than 100 meters from the source of magnetic fields and those who lived closer (OR = 1.33; 95% CI = 0.98-1.73 µT).

Conclusions: The collective results of three metaanalyses, encompassing magnetic field strengths ranging from 0.1 µT to 2.38 µT, underscore a statistically significant association between the intensity of magnetic fields and the occurrence of childhood leukemia. However, one specific analysis concluded that no apparent relationship exists between exposure to 0.1 µT and an elevated risk of leukemia development in children.

1.2 Effect of extremely low-frequency electromagnetic radiation on pregnancy outcome: A meta-analysis.

Fangfang, Z.,, Chunlan, M., Yu, J.L., Miao, Z., Wenna, L. (2023). *African Journal of Reproductive Health, 27*(5), 95. https://doi.org/10.29063/ajrh2023/v27i5.9

Background and objective: Extremely low-frequency electromagnetic radiation (ELF-EMF) are generated by electrical devices and power systems (1 to 300 Hz). Although several studies have demonstrated that ELF-EMF may be associated with an increased risk of adverse pregnancy outcomes, other studies have shown no evidence of associations. This meta-analysis was conducted to assess the effect of extremely low frequency electromagnetic radiation on pregnancy outcomes.

Methods: The following electronic bibliographic databases were searched to identify relevant studies: PubMed, Web Of Science, Cochrane library, Embase, EBSCO. In addition, the manual retrieval of relevant references was conducted as a supplement. Select all eligible studies published from Database construction library to March 10, 2021. Search type for queue research on influence of electromagnetic field radiation on pregnancy results. Data were screened and extracted independently by two researchers. Review Manager 5.3 software was used for the meta-analysis.

Results: There was no significant increase in the risk of miscarriage, stillbirth, birth defects and preterm delivery in the pregnant women who lived near the electromagnetic fields compared with the control group.

Conclusions: No correlation has been found between maternal ELF-EMF exposure and miscarriage, stillbirth, neonatal birth defects and preterm delivery, while the effects on small gestational age and low birth weight are still uncertain. Related research with high-quality large samples and different regions are still needed for further verification.

2. Residential exposure

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3. Occupational exposure

3.1 Occupational exposure to extremely low-frequency magnetic fields and follicular lymphoma risk: a family case–control study.

Odutola, M.K., Van Leeuwen, M.T., Bruinsma, F.J. et al. (2023). *Occupational & Environmental Medicine, 80*, 599–602. https://doi.org/10.1136/oemed-2023-108949

Background and objective: This study aimed to examine the relationship between occupational exposure to extremely lowfrequency magnetic fields (ELF-MFs) and follicular lymphoma (FL) risk.

Methods: The authors conducted a family case–control study between 2011 and 2016 in Australia and included 681 cases. Controls were either a family member of cases (related (n=294), unrelated (n=179)) or were unrelated recruited for a similarly designed Australian multiple myeloma study (n=711). The authors obtained detailed job histories using lifetime work calendars. Exposure to ELF-MFs was assigned using an enhanced job exposure matrix, with a lag period of 10 years. The authors examined associations with FL risk using logistic regression accounting for relatedness between cases and controls. Sensitivity analyses were performed, including by control type, by sex, complete case analyses, ELF-MF exposure percentiles in addition to quartiles, ELF-MF exposure in the maximum exposed job, a shorter lag period (1 year) and the cumulative exposure in the most recent time period (1–9 years).

Results: No association was observed with the average intensity, duration or lifetime cumulative exposure to occupational ELF-MF exposure in the primary or sensitivity analyses.

Conclusions: These findings do not support an association between occupational ELF-MF exposure and FL risk. Although the inclusion of family members as part of the larger control group may have biased our risk estimates towards the null, findings were similar in sensitivity analyses restricted to cases and unrelated controls. Further research incorporating enhanced exposure assessment to ELF-MF is warranted to inform occupational safety regulations and any potential role in lymphomagenesis.

4. Exposure Assessment

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5. Leukaemia Studies

5.1 Environmental, social and behavioral risk factors in association with spatial clustering of childhood cancer incidence.

Hüls, A., Van Cor, S., Christensen, G.M. et al. (2023). *Spatial and Spatio-temporal Epidemiology, 45*, 100582. https://doi.org/10.1016/j.sste.2023.100582

Background and objective: Childhood cancer incidence is known to vary by age, sex, and race/ethnicity, but evidence is limited regarding external risk factors. The authors aim to identify harmful combinations of air pollutants and other environmental and social risk factors in association with the incidence of childhood cancer based on 2003–2017 data from the Georgia Cancer Registry.

Methods: The authors calculated the standardized incidence ratios (SIR) of Central Nervous System (CNS) tumors, leukemia and lymphomas based on age, gender and ethnic composition in each of the 159 counties in Georgia, USA. County-level information on air pollution, socioeconomic status (SES), tobacco smoking, alcohol drinking and obesity were derived from US EPA and other public data sources. Two unsupervised learning tools (self-organizing map [SOM] and exposure-continuum mapping [ECM]) were applied to identify pertinent types of multi-exposure combinations. Spatial Bayesian Poisson models (Leroux-CAR) were fit with indicators for each multi-exposure category as exposure and SIR of childhood cancers as outcomes.

Results: The authors identified consistent associations of environmental (pesticide exposure) and social/behavioral stressors (low socioeconomic status, alcohol) with spatial clustering of pediatric ancer class II (lymphomas and reticuloendothelial neoplasms), but not for other cancer classes. More research is needed to identify the causal risk factors for these associations.

5.2 Pesticides as a potential independent childhood leukemia risk factor and as a potential confounder for electromagnetic fields exposure.

Nguyen, A., Crespi, C.M., Vergara, X., Kheifets, L. (2023). *Environmental Research, 238.* https://doi.org/10.1016/j.envres.2023.116899

Background and objective: Both pesticides and high magnetic fields are suspected to be childhood leukemia risk factors. Pesticides are utilized at commercial plant nurseries, which sometimes occupy the areas underneath high-voltage powerlines. This study wants to evaluate whether potential pesticide exposures (intended use, chemical class, active ingredient) utilized at plant nurseries act as an independent childhood leukemia risk factor or as a confounder for proximity to, or magnetic fields exposure from, high-voltage powerlines.

Methods: A state-wide records-based case-control study was conducted for California with 5788 childhood leukemia cases and 5788 controls that examined specific pesticide use, magnetic field exposures and distances to both powerlines and plant nurseries. Exposure assessment incorporated geographic information systems, aerial satellite images, and other historical information.

Results: Childhood leukemia risk was potentially elevated for several active pesticide ingredients: permethrin (odds ratio (OR) 1.49, 95% confidence interval (CI) (0.83–2.67), chlorpyrifos (OR 1.29, 95% CI 0.89–1.87), dimethoate (OR 1.79, 95% CI 0.85–3.76), mancozeb (OR 1.41, 95% CI 0.85–2.33), oxyfluorfen (OR 1.41, 95% CI 0.75–2.66), oryzalin (OR 1.60, 95% CI 0.97–2.63), and pendimethalin (OR 1.82, 95% CI 0.81–2.25). Rodenticide (OR 1.42, 95% CI 0.78–2.56) and molluscicide (OR 1.22, 95% CI 0.82–1.81) exposure also presented potentially elevated childhood leukemia risks. Childhood leukemia associations with calculated fields or powerline proximity did not materially change after adjusting for pesticide exposure. Childhood leukemia risks with powerline proximity remained similar when pesticide exposures were excluded.

Conclusion: Pesticide exposure may be an independent childhood leukemia risk factor. Childhood leukemia risks for powerline proximity and magnetic fields exposure were not explained by pesticide exposure.

5.3 Microbiota, Diet and Acute Leukaemia: Tips and Tricks on Their Possible Connections.

Furci, F., Cicero, N., Allegra, A., Gangemi, S. (2023). *Nutrients*, *15*(19),4253.

https://doi.org/10.3390/nu15194253

Background and objective: Acute leukaemia is probably one of the most recurrent cancers in children and younger adults, with an incidence of acute lymphoblastic leukaemia in 80% of cases and an incidence of acute myeloid leukaemia in 15% of cases. Yet, while incidence is common in children and adolescents, acute leukaemia is a rare disease whose aetiology still requires further analysis.

Methods: This study presents an examination of information found in literature regarding the role of dietary factors and gut microbiota alterations in the development of leukaemia.

Results: Many studies have investigated the aetiology of acute leukaemia, reporting that the formation of gut microbiota may be modified by the start and development of many diseases. Considering that in patients affected by acute lymphoblastic leukaemia, there is an inherent disequilibrium in the gut microbiota before treatment compared with healthy patients, increasing evidence shows how dysbiosis of the gut microbiota provokes an inflammatory immune response, contributing to the development of cancer.

Conclusion: This analysis suggests the key role of gut microbiota in the modulation of the efficacy of leukaemia treatment as well as in the progress of many cancers, such as acute leukaemia.

5.4 Association between Residential Proximity to Viticultural Areas and Childhood Acute Leukemia Risk in Mainland France: GEOCAP Case-Control Study, 2006–2013.

Mancini, M., Hémon, D., de Crouy-Chanel, P., et al. (2023). Environmental Health Perspectives, 131(10). https://doi.org/10.1289/EHP12634

Background and objective: Pesticide exposures are suspected of being a risk factor for several childhood cancers, particularly acute leukemia (AL). Most of the evidence is based on self-reported parental domestic use of pesticides, but some studies have also addressed associations with agricultural use of pesticides near the place of residence. The objective of the study was to evaluate the risk of AL in children living close to vines, a crop subject to intensive pesticide use.

Methods: Data were drawn from the national registry-based GEOCAP study. The authors included all of the AL cases under the age of 15 years diagnosed in 2006–2013 (n= 3,711) and 40,196 contemporary controls representative of the childhood population in France. The proximity of the vines (probability of presence within 200, 500, and 1,000 m) and the viticulture density (area devoted to vines within 1,000 m) were evaluated around the geo-coded addresses in a geographic information system combining three national land use maps. Logistic regression models were used to estimate odds ratios (ORs) for all AL and for the lymphoblastic (ALL) and myeloid (AML) subtypes. Heterogeneity between regions was studied by stratified analyses. Sensitivity analyses were carried out to take into account, in particular, geocoding uncertainty, density of other crops and potential demographic and environmental confounders.

Results: In all, about 10% of the controls lived within 1 km of vines. While no evidence of association between proximity to vines and AL was found, viticulture density was positively associated with ALL [OR = 1:05 (1.00–1.09) for a 10% increase in density], with a statistically significant heterogeneity across regions. No association with AML was observed. The results remained stable in all the sensitivity analyses.

Conclusion: This study evidenced a slight increase in the risk of ALL in children living in areas with high viticulture density. This finding supports the hypothesis that environmental exposure to pesticides may be associated with childhood ALL.

5.5 Synthesized evidence for childhood acute lymphoblastic leukemia.

Onyije, F.M., Olsson, A., Bouaoun, L., Schüz, J. (2023). *Frontiers in Pediatrics, 11*. https://doi.org/10.3389/fped.2023.1209330

Background and objective: Childhood leukemia is the most common type of cancer among children globally. In this study, the auhtors evaluated the strength of evidence and magnitude of risk factors for childhood acute lymphoblastic leukemia (ALL) using relevant systematic reviews and pooled analyses that were not part of their previously published umbrella review. The authors also estimated the prevalence in the French population as an example of the relevance of different risk factors.

Methods: The strength of the association was evaluated using the summary RR/OR values of the various meta-analyses and categorized as very strong (RR > 5), strong (RR > 2), moderate (RR > 1.5), modest (RR > 1.2), and weak (RR > 1). The strength of association, heterogeneity across studies, and number of studies were used to evaluate the strength of evidence. The evidence was categorized into "strong" (consistently strong or very strong risk estimates in quality systematic review and meta-analysis), "some" (consistently moderate risk estimates in quality systematic review and meta-analysis), "little" (consistently low risk estimates), "no" (consistently no association), and "conflicting." The category of "conflicting" was used when systematic reviews on the same subject came to different conclusions.

Results and conclusion: The first update is on maternal exposure to pesticides during preconception or pregnancy. A recently published systematic review confirmed the author's previous assessment of convincing evidence of an increased ALL risk. The second update is on childhood exposure to domestic radon and the risk of leukemia. In their previous review, the auhtors concluded "conflicting evidence" based on a meta-analysis of cohort studies (two studies; OR = 0.97, 95% CI: 0.81–1.15) and of case–control studies (eight studies; OR = 1.22, 95% CI: 1.01–1.42), with somewhat conflicting results. In recent systematic reviews and meta-analyses, Moon and Yoo reported a summary risk estimate of 1.03 (95% CI: 1.01–1.06) per 100 Bq/m^3 radon increase based on eight case–control studies with moderate heterogeneity across studies. Ngoc et al. evaluated eight case–control studies, yielding a summary risk estimate of 1.43 (95% CI: 1.19–1.72). As the case–control studies included in those meta-analyses only partly overlapped with our previous review, the authors repeated their meta-analysis with 12 case–control studies, observing an increased summary risk estimate of 1.36 (95% CI: 1.11–1.66), with a heterogeneity of 52.8%, *P*-value = 0.02. Based on this finding, they upgraded radon to "little" evidence. Further updates are on cesarean delivery and maternal diabetes. The evidence was categorized as "little" for cesarean delivery (OR: 1.18, 95% CI: 1.07–1.31) and "some" for maternal diabetes (OR: 1.46, 95% CI: 1.28–1.67), as reported in our previous review. These findings remained unchanged even after the addition of new studies. In addition, with regard to exposure to extremely low-frequency magnetic fields (ELF-MF), the earlier evaluation of "some" evidence remained unchanged even after the inclusion of an additional systematic review. The prevalence of the highlighted risk factors in France varied from "common" to "high," except for electromagnetic field exposure, which is rare, confirming the importance of risk identification in any primary prevention.

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