Overview of the epidemiologic studies on the health effects of ELF magnetic and electric fields published in the fourth trimester of 2019

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1. <u>Reviews</u>

METHODOLOGICAL LIMITATIONS IN EXPERIMENTAL STUDIES ON SYMPTOM DEVELOPMENT IN INDIVIDUALS WITH IDIOPATHIC ENVIRONMENTAL INTOLERANCE ATTRIBUTED TO ELECTROMAGNETIC FIELDS (IEI-EMF) - A SYSTEMATIC REVIEW. Schmiedchen K, Driessen S, Oftedal G. Environ Health. 2019 Oct 22;18(1):88.

Hypersensitivity to electromagnetic fields (EMF) is a controversial condition. While individuals with idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF) claim to experience health complaints upon EMF exposure, many experimental studies have found no convincing evidence for a physical relation. The aim of this systematic review was to evaluate methodological limitations in experimental studies on symptom development in IEI-EMF individuals that might have fostered false positive or false negative results. Furthermore, the profiles of these limitations between studies with positive and negative results are compared. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guided the methodological conduct and reporting. Eligible were blinded experimental studies that exposed individuals with IEI-EMF to different EMF exposure levels and queried the development of symptoms during or after each exposure trial. Strengths and limitations in design, conduct and analysis of individual studies were assessed using a customized rating tool.

Twenty-eight studies met the eligibility criteria and were included in this review. In many studies, both with positive and negative results, methodological limitations that might have either fostered false or masked real effects of exposure were identified. The most common limitations were related to the selection of study participants, the counterbalancing of the exposure sequence and the effectiveness of blinding. Many studies further lacked statistical power estimates. Methodically sound studies indicated that an effect of exposure is unlikely.

Conclusions: Overall, the evidence points towards no effect of exposure. If physical effects exist, previous findings suggest that they must be very weak or affect only few individuals with IEI-EMF. Given the evidence that the nocebo effect or medical/mental disorders may explain the symptoms in many individuals with IEI-EMF, additional research is required to identify the various factors that may be important for developing IEI-EMF and for provoking the symptoms. The authors recommend the identification of subgroups and exploring IEI-EMF in the context of other idiopathic environmental intolerances. If further experimental studies are conducted, they should preferably be performed at the individual level. In particular, to increase the likelihood of detecting

hypersensitive individuals, if they exist, researchers are encouraged to achieve a high credibility of the results by minimizing sources of risk of bias and imprecision.

2. Residential exposure

None

3. Occupational exposure

MATERNAL CUMULATIVE EXPOSURE TO EXTREMELY LOW FREQUENCY ELECTROMAGNETIC FIELDS, PREMATURITY AND SMALL FOR GESTATIONAL AGE: A POOLED ANALYSIS OF TWO BIRTH COHORTS.

Migault L, Garlantézec R, Piel C, Marchand-Martin L, Orazio S, Cheminat M, Zaros C, Carles C, Cardis E, Ancel PY, Charles MA, de Seze R, Baldi I, Bouvier G.

Occup Environ Med. 2020 Jan;77(1):22-31.

The objective of this study was to examine the relation between maternal cumulative exposure to ELF-EMF during pregnancy and the risk of prematurity or small for gestational age (SGA) in a pooled analysis of two French birth cohorts. Elfe and Epipage2 are both population-based birth cohorts initiated in 2011 and included 18 329 and 8400 births, respectively. Health data and household, mother and child characteristics were obtained from medical records and questionnaires at maternity and during follow-up. A job exposure matrix was used to assess cumulative exposure to ELF-EMF during three periods: (1) until 15 weeks of gestation, (2) until 28 weeks of gestation and (3) until 32 weeks of gestation. Analyses were restricted to single live births in mainland France and to mothers with documented jobs (N=19 894). Adjusted logistic regression models were used.

According to the period studied, 3.2%-4% of mothers were classified as highly exposed. Results were heterogeneous. Increased risks of prematurity were found among low exposed mothers for the three periods, and no association was observed among the most exposed (OR1=0.92 (95% CI 0.74 to 1.15); OR2=0.98 (95% CI 0.80 to 1.21); OR3=1.14 (95% CI 0.92 to 1.41)). For SGA, no association was observed with the exception of increased risk among the low exposed mothers in period 2 and the most exposed in period 3 (OR=1.25 (95% CI 1.02 to 1.53)).

Conclusions: Some heterogeneous associations between ELF-EMF exposure and prematurity and SGA were observed. However, due to heterogeneity (i.e., their independence regarding the level of exposure), associations cannot be definitely explained by ELF-EMF exposure.

CANCER INCIDENCE IN UK ELECTRICITY GENERATION AND TRANSMISSION WORKERS, 1973-2015.

Sorahan TM. Occup Med. 2019 Aug 22;69(5):342-351.

The aim of the study was to examine updated cancer incidence findings among a cohort of UK electricity generation and transmission workers. Cancer morbidity experienced by 81 616 employees of the former Central Electricity Generating Board of England and Wales was investigated for the period 1973-2015. All employees had worked for at least 6 months with some employment between 1973 and 1982. Standardized registration ratios (SRRs) were calculated based on national rates. Overall cancer morbidity was slightly below expectation in males. Significant excesses were found in male workers for mesothelioma (observed [Obs] 763, SRR 326), skin cancer (non-melanoma) (Obs 5616, SRR 106), and prostate cancer (Obs 4298, SRR 106), and in female workers for cancer of the small intestine (Obs 13, SRR 220), nasal cancer (Obs 11, SRR 407), and breast cancer (Obs 758, SRR 110). More detailed analyses showed important contrasts, particularly for mesothelioma, lung cancer, skin cancer, prostate cancer and breast cancer.

Conclusions: A clear occupational excess of mesothelioma was not matched by a corresponding excess of asbestos-induced lung cancer. Confident interpretation of the excesses of cancers of the nasal cavities and small intestine is not possible, although occupational exposures received in this industry may well not be involved. An excess of skin cancer in transmission workers may be associated with outdoor working. There was no excess for leukaemia.

DNA DAMAGE FROM LONG-TERM OCCUPATIONAL EXPOSURE TO EXTREMELY LOW FREQUENCY ELECTROMAGNETIC FIELDS AMONG POWER PLANT WORKERS. Bagheri Hosseinabadi M, Khanjani N, Mirzaii M, Norouzi P, Atashi A. *Mutat Res. 2019 Oct;846:403079.*

Extremely low frequency electromagnetic fields (ELF-EMFs) are not known as definite occupational carcinogens, but some studies have reported the genotoxic effects of these fields on cell lines. The present study aimed to evaluate the effects of long-term occupational exposure to these fields on DNA damage. In this cross-sectional study, blood samples were taken from 102 thermal power plant workers as the exposure group and 136 subjects as the unexposed group. DNA damage was evaluated using alkaline comet assay and flow cytometry. Exposure to ELF-EMFs was measured based on spot measurements and the IEEE Std C95.3.1 standard. The indices of comet assay, tail DNA percent, tail factor (%), and damage index were significantly higher in the exposed group compared to the unexposed group. Increased exposure to electric fields enhanced comet assay indices, except tail length; while exposure to electric fields had no significant effect on such indices. The percentage of cells at early apoptosis and late apoptosis phases caused by exposure to magnetic fields, respectively, decreased and increased significantly.

Conclusions: Long-term occupational exposure to ELF-EMFs can probably cause genotoxic effects.

4. Human experimental studies

None

5. Exposure assessment

CLUSTER ANALYSIS OF RESIDENTIAL PERSONAL EXPOSURE TO ELF MAGNETIC FIELD IN CHILDREN: EFFECT OF ENVIRONMENTAL VARIABLES. Tognola G, Chiaramello E, Bonato M, Magne I, Souques M, Fiocchi S, Parazzini M, Ravazzani P. Int J Environ Res Public Health. 2019 Nov 8;16(22).

Personal exposure to Extremely Low Frequency Magnetic Fields (ELF MF) in children is a very timely topic. The authors applied cluster analysis to 24 h indoor personal exposures of 884 children in France to identify possible common patterns of exposures. They investigated how electric networks near child home and other variables potentially affecting residential exposure, such as indoor sources of ELF MF, the age and type of the residence and family size, characterized the magnetic field exposure patterns.

Conclusions: Three indoor personal exposure patterns were identified: children living near overhead lines of high (63-150 kV), extra-high (225 kV) and ultra-high voltage (400 kV) were characterized by the highest exposures; children living near underground networks of low (400 V) and mid voltage (20 kV) and substations (20 kV/400 V) were characterized by mid exposures; children living far from electric networks had the lowest level of exposure. The harmonic component was not relevant in discriminating the exposure patterns, unlike the 50 Hz or broadband (40-800 Hz) component. Children using electric heating appliances, or living in big buildings or in larger families had generally a higher level of personal indoor exposure. Instead, the age of the residence was not relevant in differentiating the exposure patterns.

LOW FREQUENCY MAGNETIC FIELDS INSIDE CARS.

Pääkkönen R, Korpinen L. Radiat Prot Dosimetry. 2019 Nov 7.

Magnetic fields were compared inside passenger seats of electric, petrol and hybrid cars. While driving about 5 km in an urban environment, values were recorded and compared between car types. The magnetic flux densities of the cars were less than 2.6 μ T. The magnitudes of the magnetic fields of petrol cars and hybrid cars were about the same and slightly lower for electric cars. Based on these measurements, exposure was less than 3% of the guidelines given for the general population or people using pacemakers.

6. Leukaemia studies

PATERNAL SMOKING BEFORE CONCEPTION AND DURING PREGNANCY IS ASSOCIATED WITH AN INCREASED RISK OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: A SYSTEMATIC REVIEW AND META-ANALYSIS OF 17 CASE-CONTROL STUDIES.

Cao Y, Lu J, Lu J. J Pediatr Hematol Oncol. 2020 Jan;42(1):32-40.

Current evidence regarding the association between paternal smoking before conception or during pregnancy and the risk of childhood acute lymphoblastic leukemia (ALL) are inconsistent. This study aimed to systematically summarize the current evidence regarding this potential association. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Meta-analysis of Observational Studies in Epidemiology (MOOSE), the authors systematically retrieved PubMed, Embase, Web of Science, and Scopus, screened relevant literature, and assessed the methodologic quality of the included studies. Pooled estimates were calculated using random-effects models. Statistical heterogeneity was assessed by I values and χ tests for the Cochrane Q statistic. The dose-response relation was investigated using 2-stage nonlinear models. A total of 17 case-control studies were identified, and the synthesized risk ratios (RRs) for smoking before conception (RR=1.15, 95% confidence interval: 1.04-1.27) and during pregnancy (RR=1.20, 95% confidence interval: 1.12-1.28) were both statistically significant. Moreover, the dose-response analysis showed a positive association as well.

Conclusions: Current evidence from observational studies suggests the association between paternal smoking before conception or during pregnancy and the increased risk of childhood ALL, which needs to be confirmed in prospective studies.

MATERNAL INFECTION IN PREGNANCY AND CHILDHOOD LEUKEMIA: A SYSTEMATIC REVIEW AND META-ANALYSIS.

He JR, Ramakrishnan R, Hirst JE, Bonaventure A, Francis SS, Paltiel O, Håberg SE, Lemeshow S, Olsen S, Tikellis G, Magnus P, Murphy MFG, Wiemels JL, Linet MS, Dwyer T. *J Pediatr. 2019 Dec 3.*

The objective of this study was to summarize the published evidence regarding the association between maternal infection during pregnancy and childhood leukemia. The authors searched PubMed and Embase to identify relevant studies for a systematic review and meta-analysis. They included human studies that reported associations of at least one measure of maternal infection during pregnancy with acute lymphoblastic leukemia (ALL) or all childhood leukemias in the offspring. One reviewer extracted the data first using a standardized form, and the second reviewer independently checked the data for accuracy. Two reviewers used the Newcastle-Ottawa Scale to assess the quality of included studies. A random effects meta-analyses was conducted to pool the ORs of specific type of infection on ALL and childhood leukemia.

This review included 20 studies (ALL, n = 15; childhood leukemia, n = 14) reported in 32 articles. Most (>65%) included studies reported a positive association between infection variables and ALL or childhood leukemia. Among specific types of infection, the authors found that influenza during pregnancy was associated with higher risk of ALL (pooled OR, 3.64; 95% CI, 1.34-9.90) and childhood leukemia (pooled OR, 1.77; 95% CI, 1.01-3.11). Varicella (pooled OR, 10.19; 95% CI, 1.98-52.39) and rubella (pooled OR, 2.79; 95% CI, 1.16-6.71) infections were also associated with higher childhood leukemia risk.

Conclusions: These findings suggest that maternal infection during pregnancy may be associated with a higher risk of childhood leukemia.

PREDICTING RESIDENTIAL RADON CONCENTRATIONS IN FINLAND: MODEL DEVELOPMENT, VALIDATION, AND APPLICATION TO CHILDHOOD LEUKEMIA. Nikkilä A, Arvela H, Mehtonen J, Raitanen J, Heinäniemi M, Lohi O, Auvinen A.

Scand J Work Environ Health. 2019 Nov 25.

Inhaled radon gas is a known alpha-emitting carcinogen linked especially to lung cancer. Studies on higher concentrations of indoor radon and childhood leukemia have conflicting but largely negative results. In this study, the authors aimed to create a sophisticated statistical model to predict indoor radon concentrations and apply it to a Finnish childhood leukemia case-control dataset. Prediction was based on ~80 000 indoor radon measurements, which were linked to national registries for potential indoor radon predictors based on the literature. In modelling, the authors used classical methods, random forests and deep neural networks. They had 1093 cases and 3279 controls from a nationwide case-control study. Odds ratio (OR) for childhood leukemia were estimated using conditional logistic regression adjusted for potential confounders. The r² of the final log-linear model was 0.21 for houses and 0.20 for apartments. Using random forest method, The authors were able to obtain slightly better fit for both houses (r^2 = 0.28) and apartments (r^2 = 0.23). In a risk analysis based on the casecontrol data with log-linear model, a non-significant (P=0.54) increase with predicted radon concentrations was observed [OR for the 2nd quartile 1.08, 95% confidence interval (CI) 0.77-1.50, OR 1.10 with 95% CI 0.79-1.53 for the 3rd, and 1.29 with 95% CI 0.93-1.77 for the highest guartile].

Conclusions: This modelling and the previously published models performed similarly, involve major uncertainties, and the results should be interpreted with caution. A slight non-significant increase in risk of childhood leukemia related to higher average indoor radon concentrations was observed.

PARENTAL OCCUPATIONAL EXPOSURE TO DIESEL ENGINE EXHAUST IN RELATION TO CHILDHOOD LEUKAEMIA AND CENTRAL NERVOUS SYSTEM CANCERS: A REGISTER-BASED NESTED CASE-CONTROL STUDY IN DENMARK 1968-2016. Volk J, Heck JE, Schmiegelow K, Hansen J. Occup Environ Med. 2019 Nov;76(11):809-817.

Using nationwide register data, the authors investigated the association between maternal and paternal perinatal employment in industries with exposure to diesel engine exhaust and risk of leukaemia and central nervous system (CNS) cancers, including certain subtypes. Children aged \leq 19 years and diagnosed with childhood cancer from 1968 to 2016 were identified in the Danish Cancer Registry and 25 randomly selected cancer-free controls per case were matched by age and sex. Parents were identified in the Danish Civil Registration System and employment histories were retrieved from a nationwide mandatory pension fund. The probability of exposure to diesel engine exhaust was assessed using a validated job exposure matrix. Conditional logistic regression was used for estimation of ORs, including their 95% CIs. Maternal employment in industries with diesel engine exhaust exposure was associated with an increased risk of CNS cancers (OR 1.31, 95% CI 0.99 to 1.74) and of astrocytoma (OR 1.49, 95% CI 1.04 to 2.14) in offspring. The highest OR for these cancers were seen for mothers with highest probability of exposure to diesel engine exhaust. For fathers, ORs for cancers under study were close to one. No increased risks of leukaemias were found for either mothers or fathers employed in diesel industries.

Conclusions: Risks were increased for CNS and astrocytoma for maternal employment in industries with diesel engine exhaust. No increased risks of leukaemias were found.