

dr. Els De Waegeneer

Public Health Department

Ghent University

1. Reviews and meta-analyses

1.1 Environmental factors and risks of cognitive impairment and dementia: A systematic review and meta-analysis

Zhao, Y., Qu, Y., Ou, Y., Zhang, Y., Tan, L., Yu, J. (2021). *Ageing Research Reviews*, 72, 101504. <https://doi.org/10.1016/j.arr.2021.101504>

Background: Dementia is a challenging neurodegenerative disease. This systematic review aimed to summarize natural, physical, and social environmental factors that are associated with age-related cognitive impairment and dementia.

Methods: The authors systematically searched PubMed, EMBASE, Web of Science, and PsychINFO till January 11, 2021 for observational studies. The hazard ratio (HR), relative risk (RR), and odds ratio (OR) with 95% confidence interval (CI) were aggregated using random-effects methods. The quality of evidence for each association was evaluated.

Results: Of the 48,399 publications identified, there were 185 suitable for review across 44 environmental factors. Meta-analyses were performed for 22 factors. With high-to-moderate quality of evidence, risks were suggested in exposure to PM_{2.5} (HR=1.24, 95%CI: 1.17–1.31), NO₂ (HR=1.07, 95%CI: 1.02–1.12), aluminum (OR=1.35, 95% CI: 1.14–1.59), solvents (OR=1.14, 95%CI: 1.07–1.22), road proximity (OR=1.08, 95%CI: 1.04–1.12) and other air pollutions, yet more frequent social contact (HR=0.82, 95%CI: 0.76–0.90) and more greenness (OR=0.97, 95%CI: 0.95–0.995) were protective. With low-to-very low quality, electromagnetic fields, pesticides, SO₂, neighborhood socioeconomic status, and rural living were suggested risks, but more community cultural engagement might be protective. No significant associations were observed in exposure to PM₁₀, NO_x, noise, silicon, community group, and temperature. For the remaining 22 factors, only a descriptive analysis was undertaken as too few studies or lack of information.

Conclusions: This review highlights that air pollutions, especially PM_{2.5} and NO₂ play important role in the risk for age-related cognitive impairment and dementia. The studies providing findings for the effect of EMF on cognitive impairment and dementia were evaluated as low-to-very low quality.

1.2 Effect of electromagnetic field on abortion: A systematic review and meta-analysis.

Ghazanfarpour, M., Atarodi Kashani, Z., Pakzad, R., Abdi, F., Alsadat Rahnamaei, F., Akbari, P., Roozbeh, N. (2021). *Open Medicine*, 16(1), 1628-1641.

<https://doi.org/10.1515/med-2021-0384>

Background & Objective: The increasing use of new technologies by pregnant women inevitably exposes them to the risks of the electromagnetic fields (EMFs). This study was aimed to evaluate the effects of EMF exposure on abortion.

Methods: Web of Science, Cochrane Library, MEDLINE, PubMed, EMBASE, Scopus, and Google Scholar were searched until 2021. Pooled odds ratio (OR) with 95% confidence interval (CI) was estimated using a random-effects model. Heterogeneity was explored using Cochran's Q test and I² index. A meta-regression method was employed to investigate the factors affecting heterogeneity between the studies. The Newcastle-Ottawa scale was used to assess the credibility of the studies.

Results: Eligible studies (N = 17) were analyzed with a total of 57,693 participants. The mean maternal age (95% CI) was 31.06 years (27.32-34.80). Based on meta-analysis results, the pooled estimate for OR of EMF with its effects was 1.27 (95% CI: 1.10-1.46). According to the results of meta-regression, sample size had a significant effect on heterogeneity between studies (p: 0.030), but mother's age and publication year had no significant effect on heterogeneity (p-value of both were >0.05). No publication bias was observed.

Conclusion: The authors conclude that exposure to EMFs above 50 Hz or 16 mG is associated with 1.27× increased risk of abortion. However, it must be noted that a recall bias is plausible. Another limitation of the study is the methodological issue of self-reported exposure of the women involved and of the lack of consideration of the different categories and sources of EMF. More investigation on this issue is needed, especially since the results of this study aren't confirmed by other epidemiological studies, nor by animal studies on the topic.

Remarks:

- This publication shows significant shortcomings that undermine their claims. The authors fail to specify the type of radiation they are working on: e.g. they don't consistently and clearly differentiate between RF and ELF-EMF throughout the whole of the article, and in the discussion, they even introduce infrared waves and ionizing radiations. These types of radiation cannot be considered and examined as a whole when considering health effects. Next to this, they offer a blurred conclusion that arouses fear amongst the public without clearly identifying what exactly needs caution. The article must be met with the necessary reluctance.
- The suggested association has also been critiqued by other authors: Grimes, D.R., Heathers, J. (2021). Association between magnetic field exposure and miscarriage risk is not supported by the data. *Science Reports*, 11, 22143.

<https://doi.org/10.1038/s41598-021-01391-3>

2 Residential exposure

2.1 Potential factors affecting chronic chemical intolerance associated with constitutional predisposition or lifestyle and environment during childhood: From a six-year follow-up study.

Azuma, K., Uchiyama, I., Kunugita, N. (2021). *Journal of Psychosomatic Research*, 151. <https://doi.org/10.1016/j.jpsychores.2021.110665>

Background & Objective: The Japanese chemical intolerance (JCI) study was conducted in January 2012 with a cohort of 7245 adults from population-based sampling. This study aimed to investigate the childhood constitutional and environmental factors involved in the development of chronic CI from the prospective cohort study.

Methods: In the cohort, 4683 persons were identified after six years. Self-reported questionnaires were administered to the subjects to obtain information on CI status; medical history; constitution, lifestyle, and housing environment during childhood; and recent psychosomatic states. The authors assessed the differences between individuals with persisting CI status during the follow-up (defined as chronic CI) and controls not having CI status during the follow-up.

Results: A total of 2500 individuals responded. Multiple logistic regression analyses revealed significant associations between chronic CI and motion sickness to car or bus and allergic conjunctivitis during childhood. Significant associations between a possible increased risk of CI and the existence of high-voltage power lines close to housing, the use of vinyl covering in wall material, the use of strong perfume by a family member, and the experience of stinky odor of paint or wax at elementary school were observed. However, the use of carpet in floor material and plaster coating in wall material was associated with a possible decreased risk of CI. Some potential constitutional predisposition from childhood, including inherent susceptibility in the autonomic nervous system may be involved in the development of CI.

Conclusion: The results of a comprehensive pooled analysis on the association between childhood leukemia and distance to power lines suggested that the association was not explained by high magnetic fields and some other causes linked to the characteristics of power lines might be involved in the association. A systematic review did not indicate that static electric field has adverse biological effects in humans or animals. The evidence suggested the role of the superficial sensory stimulation of the hair and skin as the basis for the perception of the field. Possibly, such perception of sensory stimuli to the field from childhood may lead to the sensory sensitivity of the autonomic nervous system to exposure to extrinsic stimuli and CI development in the later life. Further research on such effect and biological mechanism is required.

3 Occupational exposure

3.1 Motor Neuron Disease Risk and Magnetic Field Exposures.

Sorahan, T., Nichols, L. (2021). *Occupational Medicine*, In press.

Background & Objective: Many studies have investigated magnetic field exposure and the risks of motor neuron disease (MND). Meta-analyses have found positive associations but a causal relationship has not been established. The aim of this study is to investigate the risks of MND and occupational exposure to magnetic fields in a large UK cohort.

Methods: Mortality of 37 986 employees of the former Central Electricity Generating Board of England and Wales was investigated for the period 1987–2018. Employees were first employed in the period 1942–82 and were still in employment on the 1 November, 1987. Detailed calculations enabled estimates to be made of magnetic field exposures. Observed deaths were compared with expected numbers based on mortality rates for the general population of England and Wales and Poisson regression was used to calculate rate ratios (relative risks) for categories of lifetime, lagged (distant) and lagged (recent) magnetic field exposure.

Results: Mortality from MND in the total cohort was similar to national rates (observed 69, expected 71.3, SMR 97, 95% CI 76–122). There were no statistically significant trends of risks increasing with lifetime, recent or distant magnetic field exposure, although positive associations were observed for some categories of recent exposure.

Conclusions: The study did not find that the cohort had elevated risks of MND as a consequence of occupational lifetime exposure to magnetic fields, although a possible role for recent exposures could usefully be investigated in other datasets.

3.2 Evaluating occupational morbidity among energy enterprise employees in industrial region of Kazakhstan.

Grebeneva, O.V., Rybalkina, D.H., Ibrayeva, L.K., Shadetova, A.Z., Drobchenko, E.A., Aleshina, N.Y. (2021). *Russian Open Medical Journal*, 10(3).

Background & Objective: This research project was aimed at studying the effects of an electromagnetic field of industrial frequency (EMF-IF) on employees of an energy company in Kazakhstan. The object of the study was the health status of electricians (morbidity with temporary disability – MTD), engaged in the maintenance of power lines, relay protection systems and substations (220 and 500 kV) at an energy enterprise in Kazakhstan.

Methods: The interrelation and dependence of the intensive MTD indicators on the hygienic factors at the workplace were determined, and the risks were calculated from the obtained data.

Results: Unfavorable workplace conditions caused an increase in disorders of the musculoskeletal system (up to 77%), blood circulation (up to 65%), nervous system (up to 52%), skin diseases (up to 46.4%), as well as the manifold rise of the likelihood of neoplasm

growth and respiratory diseases. For electricians, the relationships between the nervous system disorders ($r=0.792$), the circulatory system diseases ($r=0.573$), the musculoskeletal system ailments ($r=0.672$) and the EMF-IF parameters were discovered. At the same time, the dependence of the incidence rates of various diseases in workers on EMF, as well as moderate to high computed relative risks, implied the occupational genesis of workplace ailments: for nervous system – $R2 = 0.628$, cardiovascular system – $R2 = 0.709$, skin – $R2 = 0.729$, and musculoskeletal system – $R2 = 0.413$.

Conclusion: As preventive measures for electricians, the authors recommend to wear individual exposure meters, to limit work in contact with EMF, to include an oncologist in the medical commission, and for trainees, to screen for oxidative stress proteins and chaperone proteins to exclude a predisposition to oncogenesis.

4 Human Experimental Studies

5 Exposure Assessment

6 Leukemia Studies

6.1 External background ionizing radiation and childhood cancer: update of a nationwide cohort analysis.

Mazzei-Abba, A., Folly, C.L., Kreis, C., Ammann, R.A., Adam, C., Brack, E., Egger, M., Kuehni, C., Spycher, B.D. (2021). *Journal of Environmental Radioactivity*, 238-239.

doi: [10.1016/j.jenvrad.2021.106734](https://doi.org/10.1016/j.jenvrad.2021.106734)

Background & Objective: Exposure to high doses of ionizing radiation is known to cause cancer. Exposure during childhood is associated with a greater excess relative risk for leukemia and tumors of the central nervous system (CNS) than exposure in later life. Cancer risks associated with low-dose exposure (<100 mSv) are uncertain. The authors previously investigated the association between the incidence of childhood cancer and levels of exposure to external background radiation from terrestrial gamma and cosmic rays in Switzerland using data from a nationwide census-based cohort study. Here, they provide an update of that study using an extended follow-up period and an improved exposure model.

Methods: All children 0-15 years of age registered in the Swiss national censuses 1990, 2000, and 2010-2015, were included. The authors identified incident cancer cases during 1990-2016 using probabilistic record linkage with the Swiss Childhood Cancer Registry. Exposure to terrestrial and cosmic radiation at children's place of residence was estimated using geographic exposure models based on aerial spectrometric gamma-ray measurements. The authors estimated and included the contribution from ^{137}Cs deposition after the Chernobyl accident. The authors created a nested case-control sample and fitted conditional logistic regression models adjusting for sex, year of birth, neighborhood socioeconomic position,

and modelled outdoor NO₂ concentration. They also estimated the population attributable fraction for childhood cancer due to external background radiation.

Results: The authors included 3,401,113 children and identified 3,137 incident cases of cancer, including 951 leukemia, 495 lymphoma, and 701 CNS tumor cases. Median follow-up in the cohort was 6.0 years (interquartile range: 4.3-10.1) and median cumulative exposure since birth was 8.2 mSv (range: 0-31.2). Hazard ratios per 1 mSv increase in cumulative dose of external background radiation were 1.04 (95% CI: 1.01-1.06) for all cancers combined, 1.06 (1.01-1.10) for leukemia, 1.03 (0.98-1.08) for lymphoma, and 1.06 (1.01-1.11) for CNS tumors. Adjustment for potential confounders had little effect on the results. Based on these results, the estimated population attributable fraction for leukemia and CNS tumors due to external background radiation was 32% (7-49%) and 34% (5-51%), respectively.

Conclusions: These results suggest that background ionizing radiation contributes to the risk of leukemia and CNS tumors in children.

6.2 Childhood cancer and residential proximity to petrol stations: a nationwide registry-based case-control study in Switzerland and an updated meta-analysis.

Mazzei, A., Konstantinoudis, G., Kreis, C., Diezi, M., Ammann, R.A., Zwahlen, M., Kühni, C., Spycher, B.D. (2021). *International Archives of Occupational and Environmental Health*, doi: [10.1007/s00420-021-01767-y](https://doi.org/10.1007/s00420-021-01767-y).

Background & Objective: Benzene is a known carcinogen for adult leukemia. Exposure to benzene through parental occupation and the use of household products has been associated with childhood leukemia (CL). Ambient benzene has also been associated with CL and central nervous system (CNS) tumors. This study aimed to investigate whether the higher ambient levels of benzene in proximity of petrol stations are associated with a greater risk of childhood cancers, leukemia, and CNS tumors.

Methods: The authors identified children diagnosed with cancer at age 0-15 years during 1985-2015 from the Swiss Childhood Cancer Registry and selected 10 age and sex-matched controls per case from national censuses. They calculated the distance from children's home to the nearest petrol station using precise geocodes. The authors estimated odds ratios using conditional logistic regression adjusting for ambient levels of NO₂, distance to highways, level of urbanization, and presence of a cantonal cancer registry. In addition, they ran a meta-analysis pooling current results for CL with those of previous studies.

Results: The authors identified 6129 cases, of which 1880 were leukemias and 1290 CNS tumors. 24 cases lived within 50 m from a petrol station. The adjusted odds ratio of a cancer diagnosis for children thus exposed compared to unexposed children (> 500 m) was 1.29 (0.84-1.98) for all cancers combined, 1.08 (0.46-2.51) for leukemia, and 1.30 (0.51-3.35) for CNS tumors. During 2000-2015, when exposure assessment was more precise, the adjusted odds ratio for any cancer diagnosis was 1.77 (1.05-2.98). The summary relative risk estimate for CL in the meta-analysis including four studies was 2.01 (1.25-3.22).

Conclusions: The study provides weak support for an increased risk of childhood cancers among children living close to petrol stations. A meta-analysis including our study suggests an increased risk for CL.

6.3 Epidemiological studies of CT scans and cancer risk: the state of the science.

Berrington de Gonzalez, A., Pasqual, E., Veiga, L. (2021). *British Journal of Radiology*, 94(1126), 20210471. doi: [10.1259/bjr.20210471](https://doi.org/10.1259/bjr.20210471)

Background & Objective: 20 years ago, 3 manuscripts describing doses and potential cancer risks from CT scans in children raised awareness of a growing public health problem. The authors reviewed the epidemiological studies that were initiated in response to these concerns that assessed cancer risks from CT scans using medical record linkage.

Methods: The authors evaluated the study methodology and findings and provide recommendations for optimal study design for new efforts. 17 eligible studies were identified; 13 with published risk estimates, and 4 in progress.

Results: There was wide variability in the study methodology, however, which made comparison of findings challenging. Key differences included whether the study focused on childhood or adulthood exposure, radiosensitive outcomes (*e.g.* leukemia, brain tumors) or all cancers, the exposure metrics (*e.g.* organ doses, effective dose or number of CTs) and control for biases (*e.g.* latency and exclusion periods and confounding by indication). The authors were able to compare results for the subset of studies that evaluated leukemia or brain tumors. There were eight studies of leukemia risk in relation to red bone marrow (RBM) dose, effective dose or number of CTs; seven reported a positive dose-response, which was statistically significant ($p < 0.05$) in four studies. Six of the seven studies of brain tumors also found a positive dose-response and in five, this was statistically significant. Mean RBM dose ranged from 6 to 12 mGy and mean brain dose from 18 to 43 mGy. In a meta-analysis of the studies of childhood exposure the summary ERR/100 mGy was 1.78 (95%CI: 0.01-3.53) for leukemia/myelodysplastic syndrome ($n = 5$ studies) and 0.80 (95%CI: 0.48-1.12) for brain tumors ($n = 4$ studies) (p -heterogeneity > 0.4). Confounding by cancer pre-disposing conditions was unlikely in these five studies of leukemia. The summary risk estimate for brain tumors could be overestimated, however, due to reverse causation.

Conclusion: there is growing evidence from epidemiological data that CT scans can cause cancer. The absolute risks to individual patients are, however, likely to be small. Ongoing large multicenter cohorts and future pooling efforts will provide more precise risk quantification.