Overview of the epidemiologic studies on the health effects of ELF electric and magnetic fields (ELF-EMF) published in the third trimester of 2021.

dr. Els de Waegeneer
Public Health Department
Ghent University

1. Reviews and meta-analyses

1.1.1 Pooled analysis of recent studies of magnetic fields and childhood leukemia.

Amoon A.T., Swanson J., Magnani C., Johansen C. (2021). Environmental Research, 204.
https://doi.org/10.1016/j.envres.2021.111993

Background & Objective: Over forty epidemiologic studies have addressed an association between measured or calculated extremely-low-frequency magnetic fields (MF) and childhood leukemia. These studies have been aggregated in a series of pooled analyses, but it has been 10 years since the last such.

Methodology: the authors present a pooled analysis combining individual-level data (24,994 cases, 30,769 controls) from four recent studies on MF and childhood leukemia.

Results: Unlike previous pooled analyses, the authors found no increased risk of leukemia among children exposed to greater MF: odds ratio (OR) = 1.01, for exposure ≥0.4 µT (µT) compared with exposures <0.1 µT. Similarly, no association was observed in the subset of acute lymphoblastic leukemia, birth homes, studies using calculated fields, or when geocoding accuracy was ignored. In these studies, there is a decline in risk over time, also evident when the authors compare three pooled analyses. A meta-analysis of the three pooled analyses overall presents an OR of 1.45 (95% CI: 0.95–2.20) for exposures ≥0.4 µT.

Conclusions: The results are **not** in line with previous pooled analysis and show a decrease in effect to no association between MF and childhood leukemia. This could be due to methodological issues, random chance, or a true finding of disappearing effect.

2. Residential exposure

None

3. Occupational exposure

None

4. Human experimental studies

None

5. Exposure assessment

None

6. Leukemia studies

6.1. Cadmium (Cd) and Lead (Pb) topsoil levels and incidence of childhood leukemias.

Asenjo S., Nunez O., Segu -Tell J., Pardo Romaguera E., Canete Nieto A., Martın-Mendez I., Bel-lan A., Garcıa-PerezJ., Carceles-Alvarez A., Ortega-Garcıa J.A., Ramis R. (2021). Environmental Chemistry and Health. https://doi.org/10.1007/s10653-021-01030-w

Background & Objective: There are few well-established risk factors for childhood leukemias. While the frequency of childhood leukemias might be partially attributable to some diseases (accounting for a small fraction of cases) or ionizing radiation, the role of heavy metals has not been assessed. The objective of this study was to assess the potential association between levels of cadmium (Cd) and lead (PB) in soil and childhood leukemias incidence.

Methodology: The authors conducted a population-based case–control study of childhood leukemia in Spain, covering 2897 incident cases gathered from the Spanish Registry of Childhood Tumors and including 14 Spanish Regions with a total population of 5,307,433 children (period 1996–2015). Cd and Pb bioavailable levels at every child's home address were estimated using data from the Geochemical Atlas of Spain. The authors used logistic regression to estimate odds ratios (ORs) and their 95% confidence intervals (95%CIs); they included as covariates: sex, rurality, employment rate and socioeconomic status. Metal levels were analyzed according to two definitions: as continuous variable assuming linearity and as categorical variables to explore a potentially nonlinear association (quantiles).

Results: Increases in both Cd and Pb topsoil levels were associated with increased probability of childhood leukemias incidence. The results for the models with the continuous variables showed that a unit increase on the topsoil level was associated with an OR of 1.11 for Cd (95%CI 1.00–1.24) and an OR of 1.10 for Pb (95%CI 0.99–1.21).

Conclusion: This study may point towards a possible link between residential Cd and Pb topsoil levels and the probability of childhood leukemias incidence. Residing in a location with the highest concentrations of these heavy metals compared to those locations with the lowest could increase the risk around a 20%, for both Cd and Pb.

6.2. Exposure to pesticides and childhood leukemia risk: A systematic review.

Karalexi M.A., Tagkas C.F., Markozannes G., Tseretopoulou X., Hernandez A.F., Schüz J., Halldorsson T.I., Psaltopoulou T., Petridou E.T., Tzoulaki I., Ntzani E.E. (2021). Environmental Pollution, 285. https://doi.org/10.1016/j.envpol.2021.117376

Background & Objective: Despite the abundance of epidemiological evidence concerning the association between pesticide exposure and adverse health outcomes including acute childhood leukemia (AL), evidence remains inconclusive, and is inherently limited by heterogeneous exposure assessment and multiple statistical testing. The authors performed a literature search of peer-reviewed studies, published until January 2021, without language restrictions.

Methodology: Summary odds ratios (OR) and 95% confidence intervals (CI) were derived from stratified random-effects meta-analyses by type of exposure and outcome, exposed populations and window of exposure to address the large heterogeneity of existing literature. Heterogeneity and small-study effects were also assessed.

Results: The authors identified 55 eligible studies (n = 48 case-control and n = 7 cohorts) from over 30 countries assessing >200 different exposures of pesticides (n = 160,924 participants). The summary OR for maternal environmental exposure to pesticides (broad term) during pregnancy and AL was 1.88 (95%CI: 1.15–3.08), reaching 2.51 for acute lymphoblastic leukemia (ALL; 95%CI: 1.39–4.55). Analysis by pesticide subtype yielded an increased risk for maternal herbicide (OR: 1.41, 95%CI: 1.00–1.99) and insecticide (OR: 1.60, 95%CI: 1.11–2.29) exposure during pregnancy and AL without heterogeneity (p = 0.12–0.34). Meta-analyses of infant leukemia were only feasible for maternal exposure to pesticides during pregnancy. Higher magnitude risks were observed for maternal pesticide exposure and infant ALL (OR: 2.18, 95%CI: 1.44–3.29), and the highest for infant acute myeloid leukemia (OR: 3.42, 95%CI: 1.98–5.91). Overall, the associations were stronger for maternal exposure during pregnancy compared to childhood exposure. For occupational or mixed exposures, parental, and specifically paternal, pesticide exposure was significantly associated with increased risk of AL ($OR_{parental}$: 1.75, 95%CI: 1.08–2.85; $OR_{paternal}$: 1.20, 95%CI: 1.07–1.35).

Conclusion: The epidemiological evidence, supported by mechanistic studies, suggests that pesticide exposure, mainly during pregnancy, increases the risk of childhood leukemia, particularly among infants. Sufficiently powered studies using repeated biomarker analyses are needed to confirm whether there is public health merit in reducing prenatal pesticide exposure.

6.3. Residential proximity to plant nurseries and risk of childhood leukemia.

Nguyen A., Crespi C.M., Vergara X., Chun N., Kheifets L. (2021). Environmental Research, 200. https://doi.org/10.1016/j.envres.2021.111388

Background: Pesticides are a potential risk factor for childhood leukemia. Studies evaluating the role of prenatal and/or early life exposure to pesticides in the development of childhood leukemia have produced a range of results. In addition to indoor use of pesticides, higher risks have been reported for children born near agricultural crops. No studies have looked at pesticide exposure based on proximity of birth residence to commercial plant nurseries, even though nurseries are located much closer to residences than agricultural crops and can potentially result in chronic year-round pesticide exposure.

Objectives: To evaluate whether risk of childhood leukemia is associated with pesticide use as determined by distance of residence at birth to commercial, outdoor plant nurseries.

Methodology: The authors conducted a large statewide, record-based case-control study of childhood leukemia in California, which included 5788 childhood leukemia cases and an equal number of controls. Pesticide exposure was based on a spatial proximity model, which combined geographic information system data with aerial satellite imagery.

Results: Overall, the results supported an increased childhood leukemia risk only for birth residences very close to nurseries. For birth residences less than 75 m from plant nurseries, the authors found an increased risk of childhood leukemia (odds ratio (OR) 2.40, 95% confidence interval (CI) 0.99-5.82) that was stronger for acute lymphocytic leukemia (OR 3.09, 95% CI 1.14-8.34).

Conclusion: The association was robust to choices of reference group, cut points and data quality. The findings suggest that close proximity to plant nurseries may be a risk factor for childhood leukemia and that this relationship should be further evaluated.

6.4. 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.E., Spycher B.D. (2021). Journal of Environmental Radioactivity, 238-239. 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.

Methodology: The authors included all children 0–15 years of age registered in the Swiss national censuses 1990, 2000, and 2010–2015. They 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. A nested case-control sample was created and fitted conditional logistic regression models adjusting for sex, year of birth, neighborhood socioeconomic position, and modelled outdoor NO_2 concentration. The authors also estimated the population attributable fraction for childhood cancer due to external background radiation.

Results: The investigators 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: The results suggest that background ionizing radiation contributes to the risk of leukemia and CNS tumors in children.

6.5. Cannabinoid exposure as a major driver of pediatric acute lymphoid Leukaemia rates across the USA: combined geospatial, multiple imputation and causal inference study.

Reece A.S. & Hulse G.K. (2021). BMC Cancer, 21. https://doi.org/10.1186/s12885-021-08598-7

Background & Objective: Acute lymphoid leukaemia (ALL) is the commonest childhood cancer whose incidence is rising in many nations. In the USA, between 1975 and 2016, ALL rates (ALLRs) rose 93.51% from 1.91 to 3.70/100,000 < 20 years. ALL is more common in Caucasian-Americans than amongst minorities. The cause of both the rise and the ethnic differential is unclear, however, prenatal cannabis exposure was previously linked with elevated childhood leukaemia rates. The authors investigated epidemiologically if cannabis use impacted nationally on ALLRs, its ethnic effects, and if the relationship was causal.

Methodology**:** State data on overall, and ethnic ALLR from the Surveillance Epidemiology and End Results databank of the Centre for Disease Control (CDC) and National Cancer Institute (NCI) were combined with drug (cigarettes, alcoholism, cannabis, analgesics, cocaine) use data from the National Survey of Drug Use and Health; 74.1% response rate. Income and ethnicity data was from the US Census bureau. Cannabinoid concentration was from the Drug Enforcement Agency Data. Data was analyzed in R by robust and spatiotemporal regression.

Results: In bivariate analyses a dose-response relationship was demonstrated between ALLR and Alcohol Use Disorder (AUD), cocaine and cannabis exposure, with the effect of cannabis beingstrongest (β-estimate = 3.33(95%C.I. 1.97, 4.68), P = 1.92×10^{-6}). A strong effect of cannabis use quintile on ALLR was noted (Chi.Sq. = 613.79, P = 3.04×10^{-70}). In inverse probability weighted robust regression adjusted for other substances, income and ethnicity, cannabis was independently significant (β-estimate = 4.75(0.48, 9.02), P = 0.0389). In a spatiotemporal model adjusted for all drugs, income, and ethnicity, cannabigerol exposure was significant (β-estimate = 0.26(0.01, 0.52), P = 0.0444), an effect increased by spatial lagging (THC: β-estimate = 0.47(0.12, 0.82), P = 0.0083). After missing data imputation ethnic cannabis exposure was significant (β-estimate = 0.64(0.55, 0.72), P = 3.1×10^{-40}). 33/35 minimum e-Values ranged from 1.25 to 3.94×10^{36} indicative of a causal relationship. Relaxation of cannabis legal paradigms had higher ALLR (Chi.Squ.Trend = 775.12, P = 2.14×10^{-112}). Cannabis legal states had higher ALLR (2.395 ± 0.039 v. 2.127 ± 0.008 / 100,000, P = 5.05×10^{-10}).

Conclusions: Data show that ALLR is associated with cannabis consumption across space-time, is associated with the cannabinoids, THC, cannabigerol, cannabinol, cannabichromene, and cannabidiol, contributes to ethnic differentials, demonstrates prominent quintile effects, satisfies criteria for causality and is exacerbated by cannabis legalization.