

Overview of the epidemiologic studies on the health effects of ELF electric and magnetic fields (ELF-EMF) published in the first quarter of 2024.

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### 1. Reviews and meta-analyses

# 1.1 Recent Research on EMF and Health Risk, Seventeenth report from SSM's Scientific Council on Electromagnetic Fields, 2022

Swedish Radiation Safety Autority (2024). Recent Research on EMF and Health Risk, Seventeenth report from SSM's Scientific Council on Electromagnetic Fields. <u>2024:05 Recent Research on EMF and Health Risk, Seventeenth report from SSM's Scientific Council on Electromagnetic Fields, 2022 -</u> <u>Strålsäkerhetsmyndigheten (stralsakerhetsmyndigheten.se)</u>

Background and objective: The Swedish Radiation Safety Authority's (SSM) Scientific Council on Electromagnetic Fields monitors current research on potential health risks in relation to exposure to electromagnetic fields and provides the authority with advice on assessing possible health risks. The Council gives guidance when the authority must give an opinion on policy matters when scientific testing is necessary. The council is required to submit a written report each year on the current research and knowledge situation. This is a consensus report. This means that all members of the Scientific Council agree with the complete report. This increases the strength of the given conclusions.

The report has the primary objective of covering the previous year's research in the area of electromagnetic fields (EMF) and health but also to place this in the context of present knowledge. The report gives the authority an overview and provides an important basis for risk assessment.

Methods: This report reviews studies on electromagnetic fields (EMF) and health risks, published from January 2021 up to and including December 2021. The report is the seventeenth in a series of annual scientific reviews which consecutively discusses and assesses relevant new studies and put these in the context of available information. The report covers different areas of EMF (static, low frequency, intermediate and radio frequency fields) and different types of studies such as biological, human and epidemiological studies. The result will be a gradually developing health risk assessment of exposure to EMF.

Results: No new established causal relationships between EMF exposure and health risk have been identified. The studies presented in this report do not resolve whether the consistently observed association between ELF magnetic field (ELF-MF) exposure and childhood leukaemia in epidemiology is causal or not. New research on brain tumours and mobile phone use is in line with previous research suggesting mostly an absence of risk. The thyroid gland is potentially highly exposed during mobile phone calls but little research on thyroid cancer has been conducted so far. Concerning studies on animals, it is difficult to draw general conclusions other than that under certain circumstances some effects from RF-EMF exposure are observed in experimental animals. The observations of increased oxidative stress reported in previous SSM reports continue to be found, some even below current reference levels. Oxidative stress is a natural biological process that can sometimes be involved in pathogenesis, but under what circumstances oxidative stress due to weak radio wave exposure may affect human health remains to be investigated. It is notable that new studies revealed that perception thresholds are lower in hybrid exposure conditions than in DC or AC field exposure alone.

Despite the increasing use of applications in the intermediate frequency (IF) range of the electromagnetic spectrum (300 Hz-10 MHz), scientific evaluation of potential health risks in that range

is scarce. However, the few studies identified by the council in this area have not indicated any health effects below current reference levels. The annual report also includes a section where studies that lack satisfactory quality have been listed. This year, as well as last year, many studies have been excluded due to poor quality. From a scientific perspective, studies of poor quality are irrelevant. They are also a waste of money, human resources and, in many cases, experimental animals.

Conclusions: The results of the research review give no reason to change any reference levels or recommendations in the field. However, the observations of biological effects in animals due to weak radio wave exposure clearly show the importance of maintaining the Swedish Environmental Code precautionary thinking. SSM's hands-free recommendation for mobile phone calls remains even though trends of glioma incidences do not provide support for an increasing risk caused by mobile phone radio wave exposure. However, observed biological effects and uncertainties regarding possible long term effects justify caution. No new findings that clearly change the suspicion of a causal link between weak low-frequency magnetic fields and childhood leukaemia have emerged in the report. The Swedish authorities' recommendation to generally limit exposure to low frequency magnetic fields due to the observed increased incidence of childhood leukaemia close to power lines remains unchanged.

# 1.2 Electromagnetic Field Exposure and Abortion in Pregnant Women: A Systematic Review and Meta-Analysis

Irani, M., Aradmehr, M., Ghorbani, M. et al. (2023). Electromagnetic Field Exposure and Abortion in Pregnant Women: A Systematic Review and Meta-Analysis. *Malaysian Journal of Medical Sciences*, 30(5), 70–80. <u>https://doi.org/10.21315/mjms2023.30.5.6</u>

Background and objective: This study examined the effects of exposure to electromagnetic fields (EMF) on pregnancy and the risk of miscarriage.

Methods: The authors performed a systematic search for relevant studies published to August 2021 in the medical databases of PubMed, CINAHL, Scopus, Web of Science, Google Scholar and Cochrane Library. The following key terms were used: 'electromagnetic field,' 'mobile phones,' 'mobile phone base stations,' 'watching TV,' 'using Internet,' 'miscarriage,' 'abortions,' 'spontaneous abortion,' 'early abortion' and 'late abortion'. All case–control and cohort studies that investigated the effect of EMF exposure on the risk of miscarriage were included without any restriction of language or time. Statistical analyses were done using Comprehensive Meta-Analysis software (version 2.0). A random effects model was performed to calculate the overall effect size.

Results: A primary search revealed a total of 982 relevant studies; six articles (N = 3,187 participants) met the inclusion criteria for the meta-analysis. The results of the random-effects meta-analysis indicated that EMF exposure had a significant effect on miscarriage: rate ratio (RR) = 1.699; 95% confidence interval (CI): 1.121, 2.363 (P < 0.001); and heterogeneity (I2) = 84.55% (P < 0.001).

Conclusion of the authors: The findings showed that pregnant woman who were exposed to high levels of EMF had an increased risk of miscarriage.

Comment dr. Els De Waegeneer: Methodologically it is very uncommon and advised against to make no distinction between the different types of non-ionizing electromagnetic fields, such as extremely

low frequency fields or radiofrequency fields, given their different characteristics and diverse effects on the human body. Moreover the exposure measurement and its possible biases are not discussed transparently in the study.

#### 1.3 Risk factors for childhood brain tumours: A systematic review and metaanalysis of observational studies from 1976 to 2022

Onyije, F.M., Dolatkhah, R., Olsson, A. et al. (2024). Risk factors for childhood brain tumours: A systematic review and meta-analysis of observational studies from 1976 to 2022. Cancer Epidemiology, 88, 102510. <u>https://doi.org/10.1016/j.canep.2023.102510</u>

Background and objective: Childhood brain tumours (CBTs) are the leading cause of cancer death in children under the age of 20 years globally. Though the aetiology of CBT remains poorly understood, it is thought to be multifactorial. This study aimed to synthesize potential risk factors for CBT to inform primary prevention.

Methods: A systematic review and meta-analysis of epidemiological studies indexed in the PubMed, Web of Science, and Embase databases from the start of those resources through 27 July 2023. The authors included data from case-control or cohort studies that reported effect estimates for each risk factor around the time of conception, during pregnancy and/or during post-natal period. Random effects meta-analysis was used to estimate summary effect sizes (ES) and 95% confidence intervals (CIs). They also quantified heterogeneity (I2) across studies.

Results: A total of 4040 studies were identified, of which 181 studies (85 case-control and 96 cohort studies) met our criteria for inclusion. Of all eligible studies, 50% (n = 91) were conducted in Europe, 32% (n = 57) in North America, 9% (n = 16) in Australia, 8% (n = 15) in Asia, 1% (n = 2) in South America, and none in Africa. Associations were found for some modifiable risk factors including childhood domestic exposures to insecticides (ES 1.44, 95% CI 1.20–1.73) and herbicides (ES 2.38, 95% CI 1.31– 4.33). Maternal domestic exposure to insecticides (ES 1.45, 95% CI 1.09–1.94), maternal consumption of cured meat (ES 1.51, 95% CI 1.05–2.17) and coffee ≥ 2 cups/day (ES 1.45, 95% 95% CI 1.07–1.95) during pregnancy, and maternal exposure to benzene (ES 2.22; 95% CI 1.01-4.88) before conception were associated with CBTs in case-control studies. Also, paternal occupational exposure to pesticides (ES 1.48, 95% CI 1.23–1.77) and benzene (ES 1.74, 95% CI 1.10–2.76) before conception and during pregnancy were associated in case-control studies and in combined analysis. On the other hand, assisted reproductive technology (ART) (ES 1.32, 95% CI 1.05–1.67), caesarean section (CS) (ES 1.12, 95% CI 1.01–1.25), paternal occupational exposure to paint before conception (ES 1.56, 95% CI 1.02– 2.40) and maternal smoking > 10 cigarettes per day during pregnancy (ES 1.18, 95% Cl 1.00–1.40) were associated with CBT in cohort studies. Maternal intake of vitamins and folic acid during pregnancy was inversely associated in cohort studies. Hormonal/infertility treatment, breastfeeding, child day-care attendance, maternal exposure to electric heated waterbed, tea and alcohol consumption during pregnancy were among those not associated with CBT in both case-control and cohort studies.

Conclusion: These results should be interpreted with caution, especially as most associations between risk factors and CBT were discordant between cohort and case-control studies. At present, it is premature for any CBT to define specific primary prevention guidelines.

## 2. Residential exposure

#### 2.1 Public Exposure to Non-ionising Radiation from Major Electricity Infrastructure in Ireland

Mölter, A., Jalilian, H., Röösli, M, De Vocht, F., Pilla, F. (2024). Public Exposure to Non-ionising Radiation from Major Electricity Infrastructure in Ireland. EPA Research Report number 452. Environmental Protection Agency. <u>www.epa.ie</u>

Background and objective: The aim of the project was to review the published literature on extremely low-frequency (ELF) electromagnetic fields (EMFs) from major electricity infrastructure. This topic is highly relevant in Ireland, owing to the current expansion of the high-voltage network, including the construction of various interconnectors such as the Celtic Interconnector, which is a major electricity infrastructure project connecting the electricity grids of Ireland and France. Specific objectives of this project were to review international, and in particular European, publications on (1) ELF EMF exposure from electricity infrastructure, (2) potential health effects associated with this exposure, (3) current policies and monitoring strategies in Europe and (4) risk communication strategies for ELF EMF exposure.

Methods: (1) a systematic review of studies on exposure of the population to ELF EMFs from major electricity infrastructure; (2) an umbrella review of epidemiological studies on health risks associated with exposure to ELF EMFs from major electricity infrastructure; (3) a state-of-the-art review of current EU policies on ELF EMFs, monitoring strategies and methods to reduce public exposure; (4) a state-of-the art review of science communication strategies for ELF EMF exposure risks.

(1)The protocol for the systematic review of public ELF EMF exposure has been published via OSF (https://osf.io/b4cwx). In brief, four databases (Web of Science, PubMed, Embase and Xplore of IEEE) and the EMF-PORTAL (https://www.emf-portal.org/ en) were systematically searched from January 2007 to March 2022 for population exposure studies of ELF EMFs based in European countries. The title, abstract and keywords of identified documents were screened for eligibility; a list of eligibility criteria is provided in the protocol. From eligible studies the year of publication, country, sources of ELF EMF, ELF EMF assessment method, ELF EMF measurement instrument/model, population, covariates, study design and variability of exposure were extracted.

(2) The protocol for the umbrella review has been published via OSF (https://osf.io/bjpa4). In brief, three databases (Web of Science, PubMed and Embase) and the EMF-PORTAL (https://www.emf-portal.org/ en) were systematically searched from 2007 to 2022. The title and abstract of identified reviews were screened for eligibility; a list of eligibility criteria is provided in the protocol. From eligible reviews the following data items were extracted: first author, publication year, exposure unit/source, health outcome, study design, date range, quality instrument, population, number of studies included, type of effect size, summary meta-analytic estimates and corresponding 95% confidence intervals (CIs), random-effect p-value and heterogeneity measure. The methodological quality of each included review was assessed with the Assessment of Multiple Systematic Reviews (AMSTAR 2) Tool (Shea et al., 2017). This is a 16-item tool for quality assessment and risk of bias.

(3) The protocol for the systematic review has been published via OSF (https://osf.io/g3bew). In brief, three databases (Web of Science, PubMed, Embase) and the EMF-PORTAL (https://www.emf-portal.org/en) were systematically searched from 2015 to 2022. From eligible papers the following data items were extracted: authors, publication year, country, time period, number of cases, covariates,

study design, specific health outcome, source of health outcome data, the method of case ascertainment, source of exposure data, exposure assessment method, risk estimates [OR, risk ratio (RR), hazard ratio (HR) and 95% CI)]. The risk of bias in individual studies was assessed using a modified version of the method used by Repacholi (2012; Jalilian et al., 2018). This method considers seven sources of bias (funding source of study, reporting, data analysis, selection/ participation bias, confounding, exposure assessment and outcome misclassification) and three weights: full additional weight (two stars), partial weight (one star) and no weight (no stars). The sum of stars indicates the total risk of bias in individual studies, with zero stars indicating the highest risk of bias and 14 stars indicating the lowest risk of bias.

Results: (1) During the database searches, 6231 unique peerreviewed articles were identified. After screening the titles and abstracts, 168 papers remained. After examination of the full texts, 26 studies were included in the review. Only four studies identified in the systematic review measured ELF EF exposure: one study measured ELF EFs at the power frequency (50Hz), while the other three studies covered a wider range of frequencies, from 5Hz to 400kHz. The overall mean ELF EF was 135.60V/m (n=19, range 0.82–637V/m). Three of these studies aimed to assess background ELF EF exposure levels in cities or for populations, rather than measuring close to emission sources. One study measured ELF EFs around overhead power lines; it found a mean ELF EF of 202V/m (n=7, range 0.82–637V/m, frequency range 5–32kHz) (Ztoupis et al., 2013).

(2) During the database searches, 3054 unique papers were identified. After screening the titles and abstracts 146 papers remained. After examination of the full texts, 38 reviews were included in the umbrella review. The umbrella review found that risk estimates for childhood leukaemia associated with ELF MF exposure presented in systematic reviews varied largely. The majority of systematic reviews analysing the association between ELF MF exposure and cancers other than childhood leukaemia found no significant increase in risk. The umbrella review identified two meta-analysis studies on the risk of ALS associated with public ELF MF exposure) and one meta-analysis study on the risk of dementia associated with public ELF MF exposure. Neither of these meta-analyses found a statistically significant risk among ELF MF-exposed subjects.

(3) During the database searches, 339 unique papers were identified. After screening the titles and abstracts, 31 papers remained. After examination of the full texts, seven papers were included in the systematic review. Pregnancy problems, including time to pregnancy, delayed pregnancy, total pregnancy loss, implantation, clinical pregnancy, live birth, total pregnancy loss, miscarriage and newborn death, were investigated in four studies. None of the studies found a statistically significant association between pregnancy outcomes and ELF MF exposure. Four studies examined a number of birth outcomes including small for gestational age, low birth weight, preterm births, fetal growth, any birth defect and multiple birth defects. Two studies, from Iran (Sadeghi et al., 2017) and Canada (Auger et al., 2019), with moderate or high quality scores, reported statistically significant risks for general birth outcomes and preterm births associated with residential distance to electricity infrastructure. However, misclassification must be considered. The reviewed studies did not confirm an association between small gestational age, low birth weight or multiple defects and ELF MF exposure.

(4) an overview of European science communication strategies on ELF MF exposure

- 3. Occupational exposure
- /
- 4. Exposure Assessment
- /

## 5. Leukaemia Studies

5.1 Environmental Pollution and Risk of Childhood Cancer: A Scoping Review of Evidence from the Last Decade

Navarrete-Meneses, M., Salas-Labadia, C., Gomez-Chavez, F., Perez-Vera, P. (2024). Environmental Pollution and Risk of Childhood Cancer: A Scoping Review of Evidence from the Last Decade. *International Journal of Molecular Science*, 25, 3284. <u>https://doi.org/10.3390/ijms25063284</u>

Background and objective: The long-term effects of environmental pollution have been of concern as several pollutants are carcinogenic, potentially inducing a variety of cancers, including childhood cancer, which is a leading cause of death around the world and, thus, is a public health issue. The present scoping review aimed to update and summarize the available literature to detect specific environmental pollutants and their association with certain types of childhood cancer.

Methods: Studies published from 2013 to 2023 regarding environmental pollution and childhood cancer were retrieved from the PubMed database.

Results: A total of 174 studies were eligible for this review and were analyzed. The search strategy brought up most of the articles that evaluated air pollution (29%) and pesticides (28%). Indoor exposure to chemicals (11%), alcohol and tobacco use during pregnancy (16%), electromagnetic fields (12%), and radon (4%) were the subjects of less research. The authors found a particularly high percentage of positive associations between prenatal and postnatal exposure to indoor (84%) and outdoor (79%) air pollution, as well as to pesticides (82%), and childhood cancer. Positive associations were found between leukemia and pesticides and air pollution (33% and 27%); CNS tumors and neuroblastoma and pesticides (53% and 43%); and Wilms tumor and other rare cancers were found in association with air pollution (50%). Indoor air pollution was mostly reported in studies assessing several types of cancer (26%).

Conclusion: Further studies are needed to investigate the mechanisms underlying the potential associations between indoor/outdoor air pollution and pesticide exposure with childhood cancer risk as more preventable measures could be taken.

5.2 International study of childhood leukemia in residences near electrical transformer rooms

Crespi, C.M., Sudan, M., et al. (2024). International study of childhood leukemia in residences near electrical transformer rooms. *Environmental Research*, 249, 118459. https://doi.org/10.1016/j.envres.2024.118459

Background and objective: : New epidemiologic approaches are needed to reduce the scientific uncertainty surrounding the association between extremely low frequency magnetic fields (ELF-MF) and childhood leukemia. While most previous studies focused on power lines, the Transformer Exposure study sought to assess this association using a multi-country study of children who had lived in buildings with built-in electrical transformers. ELF-MF in apartments above built-in transformers can

be 5 times higher than in other apartments in the same building. This novel study design aimed to maximize the inclusion of highly exposed children while minimizing the potential for selection bias.

Methods: The authors assessed associations between residential proximity to transformers and risk of childhood leukemia using registry based matched case-control data collected in five countries. Exposure was based on the location of the subject's apartment relative to the transformer, coded as high (above or adjacent to transformer), intermediate (same floor as apartments in high category), or unexposed (other apartments). Relative risk (RR) for childhood leukemia was estimated using conditional logistic and mixed logistic regression with a random effect for case-control set.

Results: Data pooling across countries yielded 16 intermediate and 3 highly exposed cases. RRs were 1.0 (95% CI: 0.5, 1.9) for intermediate and 1.1 (95% CI: 0.3, 3.8) for high exposure in the conditional logistic model. In the mixed logistic model, RRs were 1.4 (95% CI: 0.8, 2.5) for intermediate and 1.3 (95% CI: 0.4, 4.4) for high. Data of the most influential country showed RRs of 1.1 (95% CI: 0.5, 2.4) and 1.7 (95% CI: 0.4, 7.2) for intermediate (8 cases) and high (2 cases) exposure.

Conclusion: Overall, evidence for an elevated risk was weak. However, small numbers and wide confidence intervals preclude strong conclusions and a risk of the magnitude observed in power line studies cannot be excluded.

5.3 Solar ultraviolet radiation exposure, and incidence of childhood acute lymphocytic leukaemia and non-Hodgkin lymphoma in a US population-based dataset

Little, M.P., Mai, J.Z., Fang, M. et al. (2024). Solar ultraviolet radiation exposure, and incidence of childhood acute lymphocytic leukaemia and non-Hodgkin lymphoma in a US population-based dataset. *British Journal of Cancer*, 130:1441–1452; <u>https://doi.org/10.1038/s41416-024-02629-3</u>

Background and objective: Acute lymphocytic leukaemia (ALL) and non-Hodgkin lymphoma (NHL) are among the commonest types of childhood cancer. Some previous studies suggested that elevated ultraviolet radiation (UVR) exposures increase ALL risk; many more indicate NHL risk is reduced.

Methods: The authors assessed age <20 ALL/NHL incidence in Surveillance, Epidemiology and End Results data using AVGLO-derived UVR irradiance/cumulative radiant exposure measures, using quasilikelihood models accounting for under dispersion, adjusted for age, sex, racial/ethnic group and other county-level socioeconomic variables.

Results: There were 30,349 cases of ALL and 8062 of NHL, with significant increasing trends of ALL with UVR irradiance (relative risk (RR) = 1.200/mW/cm2 (95% CI 1.060, 1.359, p = 0.0040)), but significant decreasing trends for NHL (RR = 0.646/mW/cm2 (95% CI 0.512, 0.816, p = 0.0002)). There was a borderline-significant increasing trend of ALL with UVR cumulative radiant exposure (RR = 1.444/MJ/cm2 (95% CI 0.949, 2.197, p = 0.0865)), and significant decreasing trends for NHL (RR = 0.284/MJ/cm2 (95% CI 0.166, 0.485, p < 0.0001)). ALL and NHL trend RR is substantially increased among those aged 0–3. All-age trend RRs are most extreme (increasing for ALL, decreasing for NHL) for Hispanics for both UVR measures

Conclusions: The more novel finding, of excess UVR-related ALL risk, is consistent with some previous studies, but is not clear-cut, and in need of replication.. ALL and NHL trend RR is substantially increased among those aged 0–3. All-age trend RRs are most extreme (increasing for ALL, decreasing for NHL) for Hispanics for both UVR measures.

5.4 Evidence of spatial clustering of childhood acute lymphoblastic leukemia cases in Greater Mexico City: report from the Mexican Inter-Institutional Group for the identification of the causes of childhood leukemia

Duarte-Rodriguez, D.A., Flores-Lujano, J., McNally, R.J.Q. et al. (2024). Evidence of spatial clustering of childhood acute lymphoblastic leukemia cases in Greater Mexico City: report from the Mexican Inter-Institutional Group for the identification of the causes of childhood leukemia. Frontiers in Oncology, 14. <u>https://doi.org/10.3389/fonc.2024.1304633</u>

Background and objective: A heterogeneous geographic distribution of childhood acute lymphoblastic leukemia (ALL) cases has been described, possibly, related to the presence of different environmental factors. The aim of the present study was to explore the geographical distribution of childhood ALL cases in Greater Mexico City (GMC).

Methods: A population-based case-control study was conducted. Children <18 years old, newly diagnosed with ALL and residents of GMC were included. Controls were patients without leukemia recruited from second-level public hospitals, frequency-matched by sex, age, and health institution with the cases. The residence address where the patients lived during the last year before diagnosis (cases) or the interview (controls) was used for geolocation. Kulldorff's spatial scan statistic was used to detect spatial clusters (SCs). Relative risks (RR), associated p-value and number of cases included for each cluster were obtained.

Results: A total of 1054 cases with ALL were analyzed. Of these, 408 (38.7%) were distributed across eight SCs detected. A relative risk of 1.61 (p<0.0001) was observed for the main cluster. Similar results were noted for the remaining seven ones. Additionally, a proximity between SCs, electrical installations and petrochemical facilities was observed. Notably, six out of eight SCs were closed to high–voltage electric lines and high–voltage electric installations. Furthermore, it was also noted that the remaining two SCs were in proximity to areas where former petrochemical industrial facilities had been located (closed a decade before the beginning of the present study).

Conclusions: The identification of SCs in certain regions of GMC suggest the possible role of environmental factors in the etiology of childhood ALL. A possible limitation of the present investigation was the fact that a hospital-based recruitment of controls was followed instead of a random recruitment of controls from the source population, which has been recommended for this type of studies. Further investigations are required to elucidate the environmental hazards associated.

5.5 Residential exposure to magnetic fields from transformer stations and risk of childhood leukemia

Malavolti, M., Malagoli, M., Wise, L.A. (2024). Residential exposure to magnetic fields from transformer stations and risk of childhood leukemia. *Environmental Research*, 245. <u>https://doi.org/10.1016/j.envres.2023.118043</u>

Background and objective: Several studies have documented an increased risk of leukemia among children exposed to magnetic fields from high-voltage power lines, with some evidence of dose-

response relation. However, findings in some studies have been inconsistent, and data on the effects of different sources of exposure are lacking. In this study, the authors evaluated the relation of childhood leukemia risk to exposure to magnetic fields from transformer stations.

Methods: A population-based case-control study was conducted in a pediatric population of two Northern Italian provinces of Modena and Reggio Emilia. The authors included 182 registry-identified childhood leukemia cases diagnosed during 1998–2019 and 726 population controls matched on sex, year of birth, and province of residence. Exposure was assessed by calculating distance from childhood residence to the nearest transformer station within a geographical information system, computing disease odds ratios (ORs) and 95% confidence intervals (CIs) using conditional logistic regression, adjusting for potential confounders. The authors evaluated exposure using two buffers (15 m and 25 m radius) and assessed two case groups: leukemia (all subtypes) and acute lymphoblastic leukemia (ALL).

Results: Residing within 15 m of a transformer station (vs.  $\geq$ 15 m) was not appreciably associated with risk of leukemia (all subtypes) or ALL. Similar results were found using a less stringent exposure buffer (25 m). Among children aged  $\geq$ 5 years, the adjusted ORs were 1.3 (95% CI 0.1–12.8) for leukemia and 1.3 (95% CI 0.1–12.4) for ALL using the 15 m buffer, while they were 1.7 (95% CI 0.4–7.0) for leukemia and 0.6 (95% CI 0.1–4.8) for ALL using the 25 m buffer.

Conclusions: No overall association between residential proximity to transformer stations and childhood leukemia was found. However, there was some evidence for elevated risk of childhood leukemia among children aged  $\geq$ 5 years. Precision was limited by the low numbers of exposed children.

#### 5.6 Medically Assisted Reproduction and Risk of Cancer Among Offspring

Rios, P., Herlemont, P., Fauque, P. et al. (2024). Medically Assisted Reproduction and Risk of Cancer Among Offspring. JAMA Network Open, 7(5), 249429. https://doi.org/10.1001/jamanetworkopen.2024.9429

Background and objective: Cancer is a leading cause of death among children worldwide. Treatments used for medically assisted reproduction (MAR) are suspected risk factors because of their potential for epigenetic disturbance and associated congenital malformation. The objective of this study is to assess the risk of cancer, overall and by cancer type, among children born after MAR compared with children conceived naturally.

Methods: For this cohort study, the French National Mother-Child Register (EPI-MERES) was searched for all live births that occurred in France between January 1, 2010, and December 31, 2021 (and followed up until June 30, 2022). The EPI-MERES was built from comprehensive data of the French National Health Data System. Data analysis was performed from December 1, 2021, to June 30, 2023. Exposure: Use of assisted reproduction technologies (ART), such as fresh embryo transfer (ET) or frozen ET (FET), and artificial insemination (AI). The risk of cancer was compared, overall and by cancer type, among children born after fresh ET, FET, or AI and children conceived naturally, using Cox proportional hazards regression models adjusted for maternal and child characteristics at birth.

Results: This study included 8 526 306 children with a mean (SD) age of 6.4 (3.4) years; 51.2% were boys, 96.4% were singletons, 12.1% were small for gestational age at birth, and 3.1% had a congenital malformation. There were 260 236 children (3.1%) born after MAR, including 133 965 (1.6%) after fresh ET, 66 165 (0.8%) after FET, and 60 106 (0.7%) after AI. A total of 9256 case patients with cancer

were identified over a median follow-up of 6.7 (IQR, 3.7-9.6) years; 165, 57, and 70 were born after fresh ET, FET, and AI, respectively. The overall risk of cancer did not differ between children conceived naturally and those born after fresh ET (hazard ratio [HR], 1.12 [95% CI, 0.96 to 1.31]), FET (HR, 1.02 [95% CI, 0.78 to 1.32]), or AI (HR, 1.09 [95% CI, 0.86 to 1.38]). However, the risk of acute lymphoblastic leukemia was higher among children born after FET (20 case patients; HR 1.61 [95% CI, 1.04 to 2.50]; risk difference [RD], 23.2 [95% CI, 1.5 to 57.0] per million person-years) compared with children conceived naturally. Moreover, among children born between 2010 and 2015, the risk of leukemia was higher among children born after fresh ET (45 case patients; HR, 1.42 [95% CI, 1.06 to 1.92]; adjusted RD, 19.7 [95% CI, 2.8 to 43.2] per million person-years).

Conclusion: The findings of this cohort study suggest that children born after FET or fresh ET had an increased risk of leukemia compared with children conceived naturally. This risk, although resulting in a limited number of cases, needs to be monitored in view of the continuous increase in the use of ART.

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