

Overview of the epidemiologic studies on the health effects of ELF magnetic and electric fields published in the second trimester of 2017

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1. Reviews

EXTREMELY LOW-FREQUENCY MAGNETIC FIELDS AND RISK OF CHILDHOOD LEUKEMIA: A RISK ASSESSMENT BY THE ARIMMORA CONSORTIUM.

Schüz J, Dasenbrock C, Ravazzani P, Rösli M, Schär P, Bounds PL, Erdmann F, Borkhardt A, Cobaleda C, Fedrowitz M, Hamnerius Y, Sanchez-Garcia I, Seger R, Schmiegelow K, Ziegelberger G, Capstick M, Manser M, Müller M, Schmid CD, Schürmann D, Struchen B, Kuster N.

Bioelectromagnetics. 2016 Mar 15.

The authors conducted a hazard assessment using available scientific evidence published before March 2015, with inclusion of new research findings from the Advanced Research on Interaction Mechanisms of electroMagnetic exposures with Organisms for Risk Assessment (ARIMMORA) project. The IARC Monograph evaluation scheme was applied to hazard identification. In ARIMMORA for the first time, a transgenic mouse model was used to mimic the most common childhood leukemia: new pathogenic mechanisms were indicated, but more data are needed to draw definitive conclusions. Although experiments in different animal strains showed exposure-related decreases of CD8+ T-cells, a role in carcinogenesis must be further established. No direct damage of DNA by exposure was observed. Overall in the literature, there is limited evidence of carcinogenicity in humans and inadequate evidence of carcinogenicity in experimental animals, with only weak supporting evidence from mechanistic studies. New exposure data from ARIMMORA confirmed that if the association is nevertheless causal, up to 2% of childhood leukemias in Europe, as previously estimated, may be attributable to ELF-MF.

Conclusions: ARIMMORA concludes that the relationship between ELF-MF and childhood leukemia remains consistent with possible carcinogenicity in humans. While this scientific uncertainty is dissatisfactory for science and public health, new mechanistic insight from ARIMMORA experiments points to future research that could provide a step-change in future assessments.

COMPARATIVE ANALYSES OF STUDIES OF CHILDHOOD LEUKEMIA AND MAGNETIC FIELDS, RADON AND GAMMA RADIATION.

Kheifets L, Swanson J, Yuan Y, Kusters C, Vergara X.

J Radiol Prot. 2017; 37(2):459-491.

In this paper the authors compare the findings of epidemiologic studies of childhood leukemia that examined at least two of ELF magnetic fields and/or distance to power lines, and exposure to radon and gamma radiation or distance to nuclear plants. Many of the methodologic aspects are common to studies of non-ionising (i.e. ELF-MF) and ionising radiation. A systematic search and review of studies with more than one exposure under study identified 33 key and 35 supplementary papers from ten

countries that have been included in this review. Examining studies that have looked at several radiation exposures, and comparing similarities and differences for the different types of radiation, through the use of directed acyclic graphs, the authors evaluate to what extent bias, confounding and other methodological issues might be operating in these studies. Some indication of bias was found, although results are not clear cut.

Conclusions: There is little evidence that confounding has had a substantial influence on results. Influence of the residential mobility on the study conduct and interpretation is complex and can manifest as a selection bias, confounding, increased measurement error or could also be a potential risk factor. Other factors associated with distance to power lines and to nuclear power plants should be investigated. A more complete and consistent reporting of results in the future studies will allow for a more informative comparison across studies and integration of results.

2. Residential exposure

MAGNETIC FIELDS EXPOSURE FROM HIGH-VOLTAGE POWER LINES AND RISK OF AMYOTROPHIC LATERAL SCLEROSIS IN TWO ITALIAN POPULATIONS.

Vinceti M, Malagoli C, Fabbi S, Kheifets L, Violi F, Poli M, Caldara S, Sesti D, Violanti S, Zanichelli P, Notari B, Fava R, Arena A, Calzolari R, Filippini T, Iacuzio L, Arcolin E, Mandrioli J, Fini N, Odone A, Signorelli C, Patti F, Zappia M, Pietrini V, Oleari P, Teggi S, Ghermandi G, Dimartino A, Ledda C, Mauceri C, Sciacca S, Fiore M, Ferrante M.

Amyotroph Lateral Scler Frontotemporal Degener. 2017 Jun 1:1-7.

The etiology of amyotrophic lateral sclerosis (ALS), a rare and extremely severe neurodegenerative disease, has been associated with magnetic fields exposure. However, evidence for such a relation in the general population is weak, although the previous null results might also be due to exposure misclassification, or a relationship might exist only for selected subgroups. To test such a hypothesis the authors carried out a population-based case-control study in two Northern and Southern Italy regions, including 703 ALS cases newly diagnosed from 1998 to 2011 and 2737 controls randomly selected from the residents in the study provinces. Overall, they found that a residence near high-voltage power lines, within the corridors yielding a magnetic fields of $\geq 0.1 \mu\text{T}$, was not associated with an excess disease risk, nor did they identify a dose-response relationship after splitting the exposed corridor according to the 0.1, 0.2 and 0.4 μT cut-points of exposure. These results were confirmed taking into account age at onset, period of diagnosis, sex, geographical area, and length of exposure.

Conclusions: Overall, despite the residual possibility of unmeasured confounding or small susceptible subgroups not identified in this study, these results appear to confirm that the exposure to magnetic fields from power lines occurring in the general population is not associated with increased ALS risk.

RE-EXAMINING THE ASSOCIATION BETWEEN RESIDENTIAL EXPOSURE TO MAGNETIC FIELDS FROM POWER LINES AND CHILDHOOD ASTHMA IN THE DANISH NATIONAL BIRTH COHORT.

Sudan M, Arah OA, Becker T, Levy Y, Sigsgaard T, Olsen J, Vergara X, Kheifets L.

PLoS One. 2017 May 17;12(5):e0177651.

A study reported an increased risk of asthma in children whose mothers were exposed to magnetic field (MF) levels above 0.2 μ T during pregnancy. The authors re-examined this association using data from mothers and children in the Danish National Birth Cohort (DNBC). The study included 92,676 singleton-born children and their mothers from the DNBC. MF exposure from power lines was estimated for all residences where the mothers lived during pregnancy and for all children from birth until the end of follow up. Exposure was categorized into 0 μ T, 0.1 μ T, and \geq 0.2 μ T for analysis. Definitive and possible asthma cases were identified using data from three independent data sources: 1) mothers' reports, 2) a national hospitalization register, 3) a national prescription drug register. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated for the association between the highest level of exposure during pregnancy and asthma in children, adjusting for several potential confounding factors. The authors also examined the sensitivity of the risk estimates to changes in exposure and outcome definitions.

No differences or trends in the risk of asthma development were detected between children with different levels of MF exposure regardless of the asthma case definition or outcome data source. For definitive cases, the HR (95% CI) for those with any exposure was 0.72 (0.27-1.92), and it was 0.41 (0.06-2.92) for those exposed to \geq 0.2 μ T. Adjustments for confounding and variations in the exposure definition did not appreciably alter the results.

Conclusions: The authors did not find evidence that residential exposure to MF during pregnancy or early childhood increased the risk of childhood asthma. This interpretation is in line with the lack of an established biological mechanism directly linking MF exposure to asthma, but high exposure was very rare in this cohort.

3. Occupational exposure

CASE-CONTROL STUDY ON OCCUPATIONAL EXPOSURE TO EXTREMELY LOW-FREQUENCY ELECTROMAGNETIC FIELDS AND GLIOMA RISK.

Carlberg M, Koppel T, Ahonen M, Hardell L.

Am J Ind Med. 2017; 60(5):494-503.

Life time occupations were assessed in case-control studies during 1997-2003 and 2007-2009. An ELF-EMF Job-Exposure Matrix was used for associating occupations with ELF exposure (μ T). Cumulative exposure (μ T-years), average exposure (μ T), and maximum exposed job (μ T) were calculated.

Cumulative exposure gave for astrocytoma grade IV (glioblastoma multiforme) in the time window 1-14 years odds ratio (OR) = 1.9, 95% confidence interval (CI) = 1.4-2.6, p linear trend <0.001, and in the time window 15+ years OR = 0.9, 95%CI = 0.6-1.3, p linear trend = 0.44 in the highest exposure categories 2.75+ and 6.59+ μ T years, respectively.

Conclusions: An increased risk in late stage (promotion/progression) of astrocytoma grade IV for occupational ELF-EMF exposure was found.

INTERACTIONS BETWEEN OCCUPATIONAL EXPOSURE TO EXTREMELY LOW FREQUENCY MAGNETIC FIELDS AND CHEMICALS FOR BRAIN TUMOUR RISK IN THE INTEROCC STUDY.

Turner MC, Benke G, Bowman JD, Figuerola J, Fleming S, Hours M, Kincl L, Krewski D, McLean D, Parent ME, Richardson L, Sadetzki S, Schlaefer K, Schlehofer B, Schüz J, Siemiatycki J, Tongeren MV, Cardis E.

Occup Environ Med. 2017 Jun 9. pii: oemed-2016-104080.

In absence of clear evidence regarding possible effects of occupational chemical exposures on brain tumour aetiology, it is worthwhile to explore the hypothesis that such exposures might act on brain tumour risk in interaction with occupational exposure to extremely low frequency magnetic fields (ELF).

INTEROCC is a seven-country (Australia, Canada, France, Germany, Israel, New Zealand and UK), population-based, case-control study, based on the larger INTERPHONE study. Incident cases of primary glioma and meningioma were ascertained from 2000 to 2004. Job titles were coded into standard international occupational classifications and estimates of ELF and chemical exposures were assigned based on job-exposure matrices. Dichotomous indicators of cumulative ELF (≥ 50 th vs < 50 th percentile, 1-4 year exposure time window) and chemical exposures (ever vs never, 5-year lag) were created. Interaction was assessed on both the additive and multiplicative scales. A total of 1939 glioma cases, 1822 meningioma cases and 5404 controls were included in the analysis, using conditional logistic regression. There was no clear evidence for interactions between ELF and any of the chemical exposures assessed for either glioma or meningioma risk. For glioma, subjects in the low ELF/metal exposed group had a lower risk than would be predicted from marginal effects. Results were similar according to different exposure time windows, to cut-points of exposure or in exposed-only analyses.

Conclusions: There was no clear evidence for interactions between occupational ELF and chemical exposures in relation to glioma or meningioma risk observed. Further research with more refined estimates of occupational exposures is recommended.

OCCUPATIONAL EXPOSURE TO EXTREMELY LOW-FREQUENCY MAGNETIC FIELDS AND RISK FOR CENTRAL NERVOUS SYSTEM DISEASE: AN UPDATE OF A DANISH COHORT STUDY AMONG UTILITY WORKERS.

Pedersen C, Poulsen AH, Rod NH, Frei P, Hansen J, Grell K, Raaschou-Nielsen O, Schüz J, Johansen C.

Int Arch Occup Environ Health. 2017 Apr 20.

Evidence of whether exposure to extremely low-frequency magnetic fields (ELF-MF) is related to central nervous system diseases is inconsistent. This study updates a previous study of the incidence of such diseases in a large cohort of Danish utility workers by almost doubling the period of follow-up. The authors investigated the risks for dementia, motor neurone disease, Parkinson disease, multiple sclerosis and epilepsy among 32,006 men employed at the 99 utility companies that supplied Denmark with electricity during the period 1900-1993. Cases were identified in the Danish National Patient Registry and the cohort was followed during 1982-2010. Exposure was estimated from a job-exposure matrix based on company records of job title and area of work and cohort members were allocated to one of three categories (< 0.1 , $0.1-0.99$ and ≥ 1.0 μT).

For dementia, multiple sclerosis and epilepsy the incidence rate ratios (IRR) were close to unity, but higher for motor neurone disease [IRR 1.24, 95% confidence interval (CI) 0.86-1.79] and lower for Parkinson disease (IRR 0.81, 95% CI 0.67-0.97) among workers exposed to $\geq 0.1 \mu\text{T}$ compared with the Danish population. For the highest level of exposure ($\geq 1.0 \mu\text{T}$), IRRs of 1.44, 1.78, 1.40 and 1.34 were observed for dementia, motor neurone disease, multiple sclerosis and epilepsy, respectively.

Conclusions: The authors observed elevated risks of dementia, motor neurone disease, multiple sclerosis and epilepsy and lower risks of Parkinson disease in relation to exposure to ELF-MF in a large cohort of utility employees.

OCCUPATIONAL EXPOSURE AND AMYOTROPHIC LATERAL SCLEROSIS IN A PROSPECTIVE COHORT.

Koeman T, Slottje P, Schouten LJ, Peters S, Huss A, Veldink JH, Kromhout H, van den Brandt PA, Vermeulen R.

Occup Environ Med. 2017; 74(8):578-585.

For this case-cohort analysis within the prospective Netherlands Cohort Study, 58 279 men and 62 573 women aged 55-69 years at enrolment in 1986 were followed up for 17.3 years on ALS mortality. Information on occupational history and potential confounders were collected at baseline through a self-administered questionnaire and entered for a random subcohort (2092 men and 2074 women) and ALS deaths (76 men and 60 women). Occupational exposure to solvents, pesticides, metals, extremely low frequency magnetic fields (ELF-MFs) and electrical shocks was estimated by means of job exposure matrices (JEMs). Associations between ever/never occupationally exposed and cumulative exposure and ALS mortality were analysed by gender using Cox regression.

Occupational exposure to ELF-MF showed a possible association with ALS mortality among men: HR for ever holding a job with high exposure versus background 2.19 (95% (CI): 1.02 to 4.73) and HR for the highest tertile of cumulative exposure versus background 1.93 (95% CI 1.05 to 3.55).

Conclusions: These results strengthen the evidence suggesting a positive association between ELF-MF exposure and ALS.

4. Human experimental studies

HUMAN EXPOSURE TO POWER FREQUENCY MAGNETIC FIELDS UP TO 7.6 mT: AN INTEGRATED EEG/fMRI STUDY.

Modolo J, Thomas AW, Legros A.

Bioelectromagnetics. 2017 Jun 19.

The authors assessed the effects of power-line frequency (60 Hz in North America) magnetic fields (MF) in humans using simultaneous electroencephalography (EEG) and functional magnetic resonance imaging (fMRI). Twenty-five participants were enrolled in a pseudo-double-blind experiment involving "real" or "sham" exposure to sinusoidal 60 Hz MF exposures delivered using the gradient coil of an MRI scanner following two conditions: (i) 10 s exposures at 3 mT (10 repetitions); (ii) 2 s exposures at 7.6 mT (100 repetitions). Occipital EEG spectral power was computed in the alpha range (8-12 Hz, reportedly the most sensitive to MF exposure in the literature) with/without exposure.

Brain functional activation was studied using fMRI blood oxygen level-dependent (BOLD, inversely correlated with EEG alpha power) maps. No significant effects were detected on occipital EEG alpha power during or post-exposure for any exposure condition. Consistent with EEG results, no effects were observed on fMRI BOLD maps in any brain region. These results suggest that acute exposure (2-10 s) to 60 Hz MF from 3 to 7.6 mT (30,000 to 76,000 times higher than average public exposure levels for 60 Hz MF) does not induce detectable changes in EEG or BOLD signals.

Conclusions: Combined with previous findings in which effects were observed on the BOLD signal after 1 h exposure to 3 mT, 60 Hz MF, this suggests that MF exposure in the low mT range (<10 mT) might require prolonged durations of exposure to induce detectable effects.

5. Exposure assessment

24-H PERSONAL MONITORING OF EXPOSURE TO POWER FREQUENCY MAGNETIC FIELDS IN ADOLESCENTS - RESULTS OF A NATIONAL SURVEY.

Eliyahu I, Hareuveny R, Riven M, Kandel S, Kheifets L.

Environ Res. 2017 Jun 29;158:295-300.

The aim of this exposure assessment study was to gain information about the exposure levels of adolescents in Israel to power frequency (50Hz) magnetic fields (MF) through personal monitoring, and to provide reliable data for national policy development. 84 adolescents, 6-10th grade students, carried an EMDEX II meter attached to their body for 24h. The meter recorded the MF every 1.5s. The students documented their activities and microenvironments, such as apartment (awake or asleep), school, transportation, open public areas and other indoor environments.

The geometric mean (GM) of the daily time weighted average (TWA) of all the participants was 0.059 μT (STD = 1.83). This result is similar to those of personal exposure surveys conducted in the UK (GM 0.042-0.054 μT), but lower than levels found in the US (GM 0.089 - 0.134 μT). The arithmetic mean was 0.073 μT , 23% higher than the GM. Fields were lowest at school (GM 0.033 μT), and average outdoor exposures were higher than indoor ones. 3.6% of the participants were exposed to daily TWA above 0.2 μT . The typical time spent above 0.2 μT ranged from few minutes to few hours. The time spent above 0.4 μT and 1 μT were much shorter, around 1-15min and from few seconds to 2min, respectively. Momentary peaks ever recorded were in the range of 0.35-23.6 μT .

Conclusions: Exposure of adolescents in Israel is similar to data reported in other countries, being below 0.1 μT for the vast majority, with very few average exposures above 0.2 μT . Analysis of the different microenvironments allows for a cost-effective and equitable policy development.

EXPOSURE TO EXTREMELY LOW AND INTERMEDIATE-FREQUENCY MAGNETIC AND ELECTRIC FIELDS AMONG CHILDREN FROM THE INMA-GIPUZKOA COHORT.

Gallastegi M, Jiménez-Zabala A, Santa-Marina L, Aurrekoetxea JJ, Ayerdi M, Ibarluzea J, Kromhout H, González J, Huss A.

Environ Res. 2017; 157:190-197.

Detailed assessment of exposure to extremely low frequency (ELF) and intermediate frequency (IF) fields is essential in order to conduct informative epidemiological studies of the health effects from exposure to these fields. There is limited information available regarding ELF electric fields and on both magnetic and electric field exposures of children in the IF range. The aim of this study was to characterize ELF and IF exposure of children in the Spanish INMA cohort. A combination of spot and fixed measurements was carried out in 104 homes, 26 schools and their playgrounds and 105 parks. Low levels of ELF magnetic fields (ELF-MF) were observed (with the highest 24-h time-weighted average (TWA) exposure being 0.15 μ T in one home). The interquartile range (IQR) of ELF electric fields (ELF-EF) ranged from 1 to 15V/m indoors and from 0.3 to 1.1V/m outdoors and a maximum value observed was 55.5V/m in one school playground. IQR ranges for IF magnetic and electric fields were between 0.02 and 0.23 μ T and 0.2 and 0.5V/m respectively and maximum values were 0.03 μ T and 1.51V/m in homes. Correlations between magnetic and electric fields were weak for ELF (Spearman 0.04-0.36 in different settings) and moderate for IF (between 0.28 and 0.75).

Conclusions: Children of INMA-Gipuzkoa cohort were exposed to very low levels of ELF-MF in all settings and to similar levels of ELF-EF compared to the range of previously reported levels, although somewhat higher exposures occurred at home. Children enrolled to this study were similarly exposed to IF in all settings.

EXPOSURE OF CHILDREN TO EXTREMELY LOW FREQUENCY MAGNETIC FIELDS IN FRANCE: RESULTS OF THE EXPERS STUDY.

Magne I, Souques M, Bureau I, Duburcq A, Remy E, Lambrozo J.

J Expo Sci Environ Epidemiol. 2016 Nov 9.

The assessment of magnetic field exposure in children is an important point in the context of epidemiological issues. EXPERS is the first study ever carried out measuring personal exposure to extremely low frequency magnetic fields at a national scale, involving 977 French children with 24 h personal measurements. Descriptive statistical analyses were performed for all the children, and only for children where no alarm clock was identified, as in some cases this requirement of the measurement protocol was not respected. The proportion of children with a 24 h arithmetic mean of $\geq 0.4 \mu$ T was 3.1% when considering all children and 0.8% when excluding alarm clocks. The alarm clocks were the main variable linked to the child exposure measurements. Magnetic field exposure increased when the home was located close to a high voltage power line. However, none of the 0.8% of children living at <125 m to a 225 kV line or <200 m to a 400 kV overhead line had a personal exposure of $>0.4 \mu$ T. A multiple correspondence analysis showed the difficulty to build a statistical model predicting child exposure.

Conclusions: The distribution of child personal exposure was significantly different from the distribution of exposure during sleep, questioning the exposure assessment in some epidemiological studies.

6. Leukaemia studies

ENVIRONMENTAL EXPOSURE AND RISK OF CHILDHOOD LEUKEMIA: AN OVERVIEW.

Schüz J, Erdmann F.

Arch Med Res. 2016; 47(8):607-614.

Childhood leukemia is the most common cancer diagnosed in children worldwide. However, only a few causes have been established so far, mainly some genetic syndromes and high doses of ionizing radiation. Major efforts have been undertaken to study the relationship between environmental factors and the risk of childhood leukemia, inspired by geographical variation in incidence rates. Some evidence has emerged for parental occupational exposures to pesticides, whereas there is less evidence for an association with postnatal pesticide exposure. Diagnostic radiation and radon exposure have been suggested but there remains a lack of convincing studies. Extremely low-frequency magnetic fields consistently showed a small increase in risk in numerous studies, but bias and confounding cannot be ruled out as possible explanations. From among factors other than environmental and radiation-related, the most promising candidate is abnormal patterns to common infections, but which children are most at risk and the pathways are not fully understood. In conclusion, although childhood leukemia shows some distinct incidence patterns by sex, age, and geography suggesting a role of the environment in its etiology, no major environmental risk factors including radiation have been established as major contributors to the global childhood leukemia burden.

Conclusions: Due to the young age at diagnosis and evidence of chromosomal damage before birth in many of the affected children, parental exposures remain of high interest. Although cure rates of childhood leukemia are high in economically developed countries, because of the adverse late effects of the disease and its treatment, identification of modifiable risk factors for implementing primary prevention remains the ultimate goal.

RESIDENTIAL EXPOSURE TO NATURAL BACKGROUND RADIATION AND RISK OF CHILDHOOD ACUTE LEUKEMIA IN FRANCE, 1990-2009.

Demoury C, Marquant F, Ielsch G, Goujon S, Debayle C, Faure L, Coste A, Laurent O, Guillevic J, Laurier D, Hémon D, Clavel J.

Environ Health Perspect. 2017; 125(4):714-720.

Exposures to high-dose ionizing radiation and high-dose rate ionizing radiation are established risk factors for childhood acute leukemia (AL). The risk of AL following exposure to lower doses due to natural background radiation (NBR) has yet to be conclusively determined.

AL cases diagnosed over 1990-2009 (9,056 cases) were identified and their municipality of residence at diagnosis collected by the National Registry of Childhood Cancers. The Geocap study, which included the 2,763 cases in 2002-2007 and 30,000 population controls, was used for complementary analyses. NBR exposures were modeled on a fine scale (36,326 municipalities) based on measurement campaigns and geological data. The power to detect an association between AL and dose to the red bone marrow (RBM) fitting UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation) predictions was 92%, 45% and 99% for exposure to natural gamma radiation, radon and total radiation, respectively.

AL risk, irrespective of subtype and age group, was not associated with the exposure of municipalities to radon or gamma radiation in terms of yearly exposure at age reached, cumulative exposure or RBM dose. There was no confounding effect of census-based socio-demographic indicators, or environmental factors (road traffic, high voltage power lines, vicinity of nuclear plants) related to AL in the Geocap study.

Conclusions: These findings do not support the hypothesis that residential exposure to NBR increases the risk of AL, despite the large size of the study, fine scale exposure estimates and wide range of exposures over France. However, the results at the time of diagnosis do not rule out a slight association with gamma radiation at the time of birth, which would be more in line with the recent findings in the UK and Switzerland.

BACKGROUND GAMMA RADIATION AND CHILDHOOD CANCER IN GERMANY: AN ECOLOGICAL STUDY.

Spix C, Grosche B, Bleher M, Kaatsch P, Scholz-Kreisel P, Blettner M.
Radiat Environ Biophys. 2017; 56(2):127-138.

The relationship of low-dose background gamma radiation and childhood leukaemia was investigated in a number of studies. Results from these studies are inconclusive. Therefore, in the present study 25 years of German childhood cancer data were analyzed using interpolated background annual gamma dose rate per community in an ecological study. The main question was leukaemia; as exploratory questions the authors investigated central nervous system (CNS) tumours, thyroid carcinomas and diagnoses less likely to be related to radiation. A Poisson regression model was applied and a fractional polynomial model building procedure. As the main sensitivity analysis a community deprivation index was included as a potential confounder. It was found that outdoor background gamma annual dose rates in Germany range roughly from 0.5-1.5 mSv/a with an average of 0.817 mSv/a. No association of annual ambient gamma dose rates with leukaemia incidence was found. Amongst the exploratory analyses, a strong association was found with CNS tumour incidence [rate ratio for 1.5 vs 0.5 mSv/a: 1.35; 95% confidence interval (1.17, 1.57)]. The community level deprivation index was not a confounder.

Conclusions: It is concluded that the present study did not confirm an association of annual outdoor ambient gamma dose rate and childhood leukaemia, corresponding to some studies and contrasting others. An association with CNS incidence was found in the exploratory analyses. As this is an ecological study no causal interpretation is possible.

A TASK-BASED ASSESSMENT OF PARENTAL OCCUPATIONAL EXPOSURE TO PESTICIDES AND CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA.

Gunier RB, Kang A, Hammond SK, Reinier K, Lea CS, Chang JS, Does M, Scelo G, Kirsch J, Crouse V, Cooper R, Quinlan P, Metayer C.
Environ Res. 2017 Jul;156:57-62.

The authors assessed parental occupational pesticide exposure from the year before pregnancy to the child's third year of life for 669 children diagnosed with ALL and 1021 controls. They conducted expert rating using task-based job modules (JM) to estimate exposure to pesticides among farmer workers, gardeners, agricultural packers, and pesticide applicators. This method was compared to (1) partial JM using job titles and a

brief description, but without completing the task-based questionnaire, and (2) job exposure matrix (JEM) linking job titles to the International Standard Classifications of Occupation Codes. Unconditional logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (95% CI) for ALL cancer risk and pesticide exposure adjusting for child's sex, age, race/ethnicity and household income.

Compared to complete JMs, partial JMs and JEM led to 3.1% and 9.4% of parents with pesticide exposure misclassified, respectively. Misclassification was similar in cases and controls. Using complete JMs, an increased risk of ALL was observed for paternal occupational exposure to any pesticides (OR=1.7; 95% CI=1.2, 2.5), with higher risks reported for pesticides to treat nut crops (OR=4.5; 95% CI=0.9, 23.0), and for children diagnosed before five years of age (OR=2.3; 95% CI: 1.3, 4.1). Exposure misclassification from JEM attenuated these associations by about 57%. Maternal occupational pesticide exposure before and after birth was not associated with ALL.

Conclusions: The risk of ALL was elevated in young children with paternal occupational pesticide exposure during the perinatal period, using more detailed occupational information for exposure classification.

PARENTAL ALCOHOL CONSUMPTION AND RISK OF LEUKEMIA IN THE OFFSPRING: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Karalexi MA, Dessypris N, Thomopoulos TP, Ntouvelis E, Kantzanou M, Diamantaras AA, Moschovi M, Baka M, Hatzipantelis E, Kourti M, Polychronopoulou S, Stiakaki E, Mora AM, Wunsch-Filho V, Infante-Rivard C, Loutradis D, Petridou ET.

Eur J Cancer Prev. 2017 Apr 4.

Parental alcohol consumption before and during pregnancy has been linked to adverse outcomes in the offspring including leukemogenesis. The authors, therefore, aimed to systematically assess and quantitatively synthesize published data on the association of paternal consumption during preconception and maternal consumption during pregnancy with leukemia risk in childhood (0-14 years). Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, they searched PubMed (until February 2016) and the reference lists of the relevant studies. Observational studies examining the association between parental alcohol consumption and childhood leukemia were considered eligible. Data extracted from 39 case-control studies (over 16 000 leukemia cases and 30 000 controls) were pooled and summary-effect estimates were calculated. Subgroup analyses were carried out by main acute leukemia type (lymphoblastic or myeloid), cytogenetics/genetic polymorphisms, and specific alcohol beverages. A statistically significant dose-response association was found of any level of maternal alcohol consumption compared with nondrinking during pregnancy exclusively with acute myeloid leukemia (AML) [odds ratio (OR) moderate consumption: 1.64, 95% confidence intervals (CIs): 1.23-2.17 and OR high consumption: 2.36, 95% CI: 1.60-3.49]. In contrast, no association of paternal preconception consumption with any leukemia type was noted. In beverage-specific analyses, only a positive association of maternal wine drinking with childhood AML was found, which was more pronounced in analyses including only studies on infant leukemia (OR wine: 2.12, 95% CI: 1.16-3.90).

Conclusions: The largest ever meta-analysis shows a sizeable, statistically significant dose-response association of maternal alcohol consumption during index pregnancy with

AML risk. Future research exploring the role of genetic polymorphisms is anticipated to shed light on the underlying pathophysiology.

ADVANCED PATERNAL AGE AND CHILDHOOD CANCER IN OFFSPRING: A NATIONWIDE REGISTER-BASED COHORT STUDY.

Urhoj SK, Raaschou-Nielsen O, Hansen AV, Mortensen LH, Andersen PK, Nybo Andersen AM.

Int J Cancer. 2017; 140(11):2461-2472.

Cancer initiation is presumed to occur in utero for many childhood cancers and it has been hypothesized that advanced paternal age may have an impact due to the increasing number of mutations in the sperm DNA with increasing paternal age. The authors examined the association between paternal age and specific types of childhood cancer in offspring in a large nationwide cohort of 1,904,363 children born in Denmark from 1978 through 2010. The children were identified in the Danish Medical Birth Registry and were linked to information from other national registers, including the Danish Cancer Registry. In total, 3,492 children were diagnosed with cancer before the age of 15 years. The adjusted hazard ratio of childhood cancer according to paternal age was estimated using Cox proportional hazards regressions. A 13% (95% confidence interval: 4-23%) higher hazard rate was found for every 5 years advantage in paternal age for acute lymphoblastic leukemia, while no clear association was found for acute myeloid leukemia (hazard ratio pr. 5 years = 1.02, 95% confidence interval: 0.80-1.30). The estimates for neoplasms in the central nervous system suggested a lower hazard rate with higher paternal age (hazard ratio pr. 5 years = 0.92, 95% confidence interval: 0.84-1.01). No clear associations were found for the remaining childhood cancer types.

Conclusions: These findings suggest that paternal age is moderately associated with a higher rate of childhood acute lymphoblastic leukemia, but not acute myeloid leukemia, in offspring, while no firm conclusions could be made for other specific cancer types.

BENZENE AND CHILDHOOD ACUTE LEUKEMIA IN OKLAHOMA.

Janitz AE, Campbell JE, Magzamen S, Pate A, Stoner JA, Peck JD.

Environ Res. 2017; 158:167-173.

The goal of this study was to evaluate the association between benzene, a known carcinogen, and childhood acute leukemia. The authors conducted a case-control study including cases diagnosed with acute leukemia between 1997 and 2012 (n = 307) from the Oklahoma Central Cancer Registry and controls matched on week of birth from birth certificates (n = 1013). Conditional logistic regression was used to evaluate the association between benzene, measured with the 2005 National-Scale Air Toxics Assessment (NATA) at census tract of the birth residence, and childhood acute leukemia.

No differences were observed in benzene exposure overall between cases and controls. However, when stratified by year of birth, cases born from 2005 to 2010 had a three-fold increased unadjusted odds of elevated exposure compared to controls born in this same time period (4th Quartile OR: 3.53, 95% CI: 1.35, 9.27). Furthermore, the estimates for children with acute myeloid leukemia (AML) were stronger than those with acute lymphoid leukemia, though not statistically significant.

Conclusions: While an association between benzene and childhood leukemia overall was not observed, the results suggest that acute leukemia is associated with increased benzene exposure among more recent births, and children with AML may have increased benzene exposure at birth. Using the NATA estimates allowed to assess a specific pollutant at the census tract level, providing an advantage over monitor or point source data. This study, however, cannot rule out the possibility that benzene may be a marker of other traffic-related exposures and temporal misclassification may explain the lack of an association among earlier births.