Overview of the epidemiologic studies on the health effects of ELF magnetic and electric fields published in the fourth trimester of 2015

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1. Residential exposure

RESIDENTIAL EXPOSURE TO EXTREMELY LOW-FREQUENCY MAGNETIC FIELDS AND RISK OF CHILDHOOD LEUKAEMIA, CNS TUMOUR AND LYMPHOMA IN DENMARK.
Pedersen C, Johansen C, Schüz J, Olsen JH, Raaschou-Nielsen O.
Br J Cancer. 2015;113(9):1370-1374.

The authors previously reported that children exposed to elevated extremely low-frequency magnetic fields (ELF-MF) had a five to six times higher risk of leukaemia, central nervous system (CNS) tumour and malignant lymphoma. Here they extend the study from 1968 to 1986 through 2003.

They included 3277 children with leukaemia, CNS tumour or malignant lymphoma during 1968-2003 recorded in the Danish Cancer Registry and 9129 controls randomly selected from the Danish childhood population. ELF-MF from 50 to 400 kV facilities were calculated at the residences.

For recently diagnosed cases (1987-2003), the relative risk (RR) was 0.88 (95% confidence interval (CI): 0.32-2.42), while for the total period (1968-2003) it was 1.63 (95% CI: 0.77-3.46) for leukaemia, CNS tumour and malignant lymphoma combined for exposures $\geqslant 0.4\,\mu T$ compared with $<0.1\,\mu T$. These results were based on five cases (recent period) and 11 cases (total period) in the highest exposure group.

Conclusions: This study did not confirm the previous finding of a five- to six-fold higher risk for leukaemia, CNS tumour and malignant lymphoma when including data from the more recent time period. For the total time period, the results for childhood leukaemia were in line with large pooled analyses showing RRs between 1.5 and 2.

ELECTRIC BLANKET USE AND RISK OF THYROID CANCER IN THE WOMEN'S HEALTH INITIATIVE OBSERVATIONAL COHORT.
Kato I, Young A, Liu J, Abrams J, Bock C, Simon M.
Women Health. 2015;55(7):829-841.

Thyroid cancer disproportionally affects more women than men. The aim of this study was to assess whether exposure to extremely low frequency electric magnetic fields from electric blankets (EBs) was associated with the development of thyroid cancer. Data were analyzed from 89,527 women who participated in the Women's Health Initiative Observational Study and who responded to questions concerning prior use of EBs. During a mean follow-up of 12.2 years, 190 incident cases of thyroid cancer were identified. The hazard ratio (HR) and 95 percent confidence interval (CI) of incident thyroid cancer associated with EB use was estimated by Cox's proportional hazard model, adjusted for selected covariates. A majority, 57 percent, of the women in the cohort reported the use of EBs while sleeping and/or for warming the bed before sleep. No association was found between use of EBs and subsequent risk of thyroid cancer (HR = 0.98, 95 percent CI 0.72-1.32). Duration of EB use measured in years, months, or

hours had no effect on risk. These results did not change when the cases were limited to papillary thyroid cancer, the most frequently occurring histologic type.

Conclusions: The results of this study do not support possible health hazards of EBs in regards to thyroid cancer risk.

2. Occupational exposure

OCCUPATIONAL EXPOSURE TO ELECTRIC SHOCKS AND MAGNETIC FIELDS AND AMYOTROPHIC LATERAL SCLEROSIS IN SWEDEN.
Fischer H, Kheifets L, Huss A, Peters TL, Vermeulen R, Ye W, Fang F, Wiebert P, Vergara XP, Feychting M.
Epidemiology. 2015;26(6):824-830.

Amyotrophic lateral sclerosis (ALS) has been consistently related to "electric occupations," but associations with magnetic field levels were generally weaker than those with electrical occupations. Exposure to electric shock has been suggested as a possible explanation. Furthermore, studies were generally based on mortality or prevalence of ALS, and studies often had limited statistical power.

Using two electric shock and three magnetic field job-exposure matrices, the authors evaluated the relationship of occupational magnetic fields, electric shocks, electric occupations, and incident ALS in a large population-based nested case-control study in Sweden. Sub-analyses, specified a priori, were performed for subjects by gender and by age (less than and more than 65 years).

Overall, the authors did not observe any associations between occupational magnetic field or electric shock exposure and ALS. For individuals less than 65 years old, high electric shock exposure was associated with an odds ratio (OR) of 1.22 (95% confidence interval [CI] = 1.03, 1.43). The corresponding result for the age group 65 years or older was OR = 0.92 (95% CI = 0.81, 1.05). Results were similar regardless which job exposure matrices, exposure definitions, or cut-points were used. For electric occupations, ORs were close to unity, regardless of age. For welders, no association was observed overall, although for welders <65 years the OR was 1.52 (95% CI = 1.05, 2.21).

Conclusions: In this very large population-based study based on incident ALS case subjects, the authors did not confirm previous observations of higher risk of ALS in electrical occupations, and provided only weak support for associations between electric shocks and ALS.

3. Exposure assessment

PRELIMINARY BACKGROUND INDOOR EMF MEASUREMENTS IN GREECE.
Kottou S, Nikolopoulos D, Yannakopoulos PH, Vogiannis E, Petraki E, Panagiotaras D, Koulougliotis D.
Phys Med. 2015;31(7):808-816.

The main purpose of this work was to investigate the fluctuation of Greek indoor electromagnetic field (EMF) intensity values and identify peaks that might occur. The scientific interest is mainly focused on the bands of extremely low-frequency (ELF) magnetic fields and radiofrequency (RF) electric fields which have been suggested to be possibly carcinogenic to humans by the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Electromagnetic radiation (EMR) measurements

were performed in a variety of indoor dwellings, in Attica and in the islands of Zakynthos and Lesvos. A total number of 4540 measurements were taken in a wide frequency range (50 Hz-2100 MHz) of which 3301 in Attica, 963 in Lesvos and 276 in Zakynthos. Statistical analysis of the data revealed specific statistically significant differences between the mean values of the electric (ELF and RF) but not the magnetic (ELF) field strengths measured at different distances from the EMF source, as well as between some of the mean values of the RF electric field at different bands. Some statistically significant differences between mean electric field values at different geographic locations were also identified. As far as the RF electric field is concerned, the maximum values, in most cases, were below 0.5 V/m, however increased values above 1 V/m and up to 5.6 V/m were occasionally observed. The ELF magnetic field values were lower than 1 µT.

Conclusions: It may be concluded that overall, the observed indoor EMF intensity values remained well below domestic and European established limits.

4. <u>Leukemia studies</u>

RESIDENTIAL PROXIMITY TO HEAVY-TRAFFIC ROADS, BENZENE EXPOSURE, AND CHILDHOOD LEUKEMIA-THE GEOCAP STUDY, 2002-2007.
Houot J, Marquant F, Goujon S, Faure L, Honoré C, Roth MH, Hémon D, Clavel J.
Am J Epidemiol. 2015;182(8):685-693.

Childhood leukemia may be associated with traffic-related environmental exposure to benzene, and additional data are needed. The Géolocalisation des Cancers Pédiatriques (GEOCAP) Study, a nationwide French case-control study, was designed to avoid selection bias due to differential participation and misclassification. The study compared the 2,760 childhood leukemia cases diagnosed in France between 2002 and 2007 (including 2,275 cases of acute lymphoblastic leukemia (ALL) and 418 cases of acute myeloblastic leukemia (AML)) with 30,000 contemporaneous child population controls. The residence addresses were precisely geocoded, and 3 indicators of residential proximity to traffic were considered. Estimates of benzene concentrations were also available for the Île-de-France region (including Paris). A 300-m increase in major road length within 150 m of the geocoded address was significantly associated with AML (odds ratio = 1.2, 95% confidence interval: 1.0, 1.4) but not with ALL (odds ratio = 1.0, 95% confidence interval: 0.9, 1.1), and the association was reinforced in the Île-de-France region when this indicator was combined with benzene estimates. These results, which were free from any participation bias and based on objectively determined indices of exposure, showed an increased incidence of AML associated with heavy-traffic road density near a child's home.

Conclusions: The results support a role for traffic-related benzene exposure in the etiology of childhood AML.

CHILDHOOD CANCER AND RESIDENTIAL EXPOSURE TO HIGHWAYS: A NATIONWIDE COHORT STUDY.
Spycher BD, Feller M, Röösli M, Ammann RA, Diezi M, Egger M, Kuehni CE.
Eur J Epidemiol. 2015;30(12):1263-1275.

Children living near highways are exposed to higher concentrations of traffic-related carcinogenic pollutants. Several studies reported an increased risk of childhood cancer associated with traffic exposure, but the published evidence is inconclusive. The authors investigated whether cancer risk is associated with proximity of residence to highways in

a nation-wide cohort study including all children aged <16 years from Swiss national censuses in 1990 and 2000. Cancer incidence was investigated in time to event analyses (1990-2008) using Cox proportional hazards models and incidence density analyses (1985-2008) using Poisson regression. Adjustments were made for socio-economic factors, ionizing background radiation and electromagnetic fields. In time to event analysis based on 532 cases the adjusted hazard ratio for leukaemia comparing children living <100 m from a highway with unexposed children (≥500 m) was 1.43 (95 % CI 0.79, 2.61). Results were similar in incidence density analysis including 1367 leukaemia cases (incidence rate ratio (IRR) 1.57; 95 % CI 1.09, 2.25). Associations were similar for acute lymphoblastic leukaemia (IRR 1.64; 95 % CI 1.10, 2.43) and stronger for leukaemia in children aged <5 years (IRR 1.92; 95 % CI 1.22, 3.04). Little evidence of association was found for other tumours.

Conclusions: This study suggests that young children living close to highways are at increased risk of developing leukaemia.

HOME PESTICIDE EXPOSURES AND RISK OF CHILDHOOD LEUKEMIA: FINDINGS FROM THE CHILDHOOD LEUKEMIA INTERNATIONAL CONSORTIUM.
Bailey HD, Infante-Rivard C, Metayer C, Clavel J, Lightfoot T, Kaatsch P, Roman E, Magnani C, Spector LG, Th Petridou E, Milne E, Dockerty JD, Miligi L, Armstrong BK, Rudant J, Fritschi L, Simpson J, Zhang L, Rondelli R, Baka M, Orsi L, Moschovi M, Kang AY, Schüz J.
Int J Cancer. 2015;137(11):2644-2663.

Some previous studies have suggested that home pesticide exposure before birth and during a child's early years may increase the risk of childhood leukemia. To further investigate this, the authors pooled individual level data from 12 case-control studies in the Childhood Leukemia International Consortium. Exposure data were harmonized into compatible formats. Pooled analyses were undertaken using multivariable unconditional logistic regression. The odds ratio (ORs) for acute lymphoblastic leukemia (ALL) associated with any pesticide exposure shortly before conception, during pregnancy and after birth were 1.39 (95% confidence interval [CI]: 1.25, 1.55) (using 2,785 cases and 3,635 controls), 1.43 (95% CI: 1.32, 1.54) (5,055 cases and 7,370 controls) and 1.36 (95% CI: 1.23, 1.51) (4,162 cases and 5,179 controls), respectively. Corresponding ORs for risk of acute myeloid leukemia (AML) were 1.49 (95% CI: 1.02, 2.16) (173 cases and 1,789 controls), 1.55 (95% CI: 1.21, 1.99) (344 cases and 4,666 controls) and 1.08 (95% CI: 0.76, 1.53) (198 cases and 2,655 controls), respectively. There was little difference by type of pesticide used. The relative similarity in ORs between leukemia types, time periods and pesticide types may be explained by similar exposure patterns and effects across the time periods in ALL and AML, participants' exposure to multiple pesticides, or recall bias.

Conclusions: Although some recall bias is likely, until a better study design can be found to investigate the associations between home pesticide use and childhood leukemia in an equally large sample, it would appear prudent to limit the use of home pesticides before and during pregnancy, and during childhood.

MATERNAL AND CHILDHOOD CONSUMPTION OF COFFEE, TEA AND COLA BEVERAGES IN ASSOCIATION WITH CHILDHOOD LEUKEMIA: A META-ANALYSIS.
Thomopoulos TP, Ntouvelis E, Diamantaras AA, Tzanoudaki M, Baka M, Hatzipantelis E, Kourti M, Polychronopoulou S, Sidi V, Stiakaki E, Moschovi M, Kantzanou M, Petridou ET.

The objective of this study was to systematically review studies and meta-analyze the literature on the association of maternal and/or index child's coffee, tea, and cola consumption with subsequent development of childhood leukemia and its major subtypes. Eligible studies were identified through a detailed algorithm and hand-search of eligible articles' references; thereafter, summary-effect estimates were calculated by leukemia subtype and dose-response meta-analyses were performed.

Twelve case-control studies, comprising a total of 3649 cases and 5705 controls, were included. High maternal coffee consumption was positively associated with acute lymphoblastic leukemia (ALL; OR: 1.43, 95%CI: 1.22-1.68) and acute myeloid leukemia (AML; OR: 2.52, 95%CI: 1.59-3.57). Any or low to moderate maternal cola consumption was also positively associated with overall leukemia (AL) and ALL, A linear trend between coffee and cola consumption and childhood leukemia was observed in the dose-response analyses. On the contrary, low to moderate tea consumption was inversely associated with AL (OR: 0.85, 95%CI: 0.75-0.97), although the trend was non-significant. A null association between offspring's cola consumption and leukemia was noted.

Conclusions: These findings confirm the detrimental association between maternal coffee consumption and childhood leukemia risk and provide indications for a similar role of maternal cola intake. In contrast, an inverse association with tea was found, implying that other micronutrients contained in this beverage could potentially counterbalance the deleterious effects of caffeine. Further research should focus on the intake of specific micronutrients, different types of coffee and tea, specific immunophenotypes of the disease, and the modifying effect of genetic polymorphisms.

RISK FOR CHILDHOOD LEUKEMIA ASSOCIATED WITH MATERNAL AND PATERNAL AGE.
Sergentanis TN, Thomopoulos TP, Gialamas SP, Karalexi MA, Biniaris-Georgallis SI, Kontogeorgi E, Papathoma P, Tsilimidos G, Skalkidou A, Iliadou AN, Petridou ET.

The role of reproductive factors, such as parental age, in the pathogenesis of childhood leukaemias is being intensively examined; the results of individual studies are controversial. This meta-analysis aims to quantitatively synthesize the published data on the association between parental age and risk of two major distinct childhood leukemia types in the offspring. Eligible studies were identified and pooled relative risk (RR) estimates were calculated using random-effects models, separately for childhood acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). Subgroup analyses were performed by study design, geographical region, adjustment factors; sensitivity analyses and meta-regression analyses were also undertaken. 77 studies (69 case-control and eight cohort) were deemed eligible. Older maternal and paternal age were associated with increased risk for childhood ALL (pooled RR = 1.05, 95 % CI 1.01-1.10; pooled RR = 1.04, 95 % CI 1.00-1.08, per 5 year increments, respectively). The association between maternal age and risk of childhood AML showed a U-shaped

pattern, with symmetrically associated increased risk in the oldest (pooled RR = 1.23, 95 % CI 1.06-1.43) and the youngest (pooled RR = 1.23, 95 % CI 1.07-1.40) extremes. Lastly, only younger fathers were at increased risk of having a child with AML (pooled RR = 1.28, 95 % CI 1.04-1.59).

Conclusions: Maternal and paternal age represents a meaningful risk factor for childhood leukemia, albeit of different effect size by leukemia subtype. Genetic and socio-economic factors may underlie the observed associations. Well-adjusted studies, scheduled by large consortia, are anticipated to satisfactorily address methodological issues, whereas the potential underlying genetic mechanisms should be elucidated by basic research studies.

POVERTY AND THE RISK OF LEUKEMIA AND CANCER IN THE CENTRAL NERVOUS SYSTEM IN CHILDREN: A COHORT STUDY IN A HIGH-INCOME COUNTRY.
Del Risco Kollerud R, Blaasaas KG, Claussen B.
Scand J Public Health. 2015;43(7):736-743.

The association between childhood cancer and socioeconomic status is inconclusive. Family income has seldom been included in large population-based studies, and the specific contributions of it remain unknown.

A total of 712,674 children born between 1967 and 2009 in the Oslo region were included. Of these, 864 were diagnosed with leukemia or cancer in the central nervous system before the age of 15 years. The association between poverty and childhood leukemia or brain cancer was analyzed using logistic regression and Cox proportional hazards models. Family income was stratified according to poverty lines. Parents' educational level and several perinatal variables were also examined.

Family poverty during the first 2 years of life was associated with lymphoid leukemia before the age of 15 years: odds ratio 1.72, 95% confidence interval 1.11-2.64. In the same age group we found a significant dose response, with a 21% increased risk of lymphoid leukemia with increasing poverty. The risk for intracranial and intraspinal embryonal tumors in the whole study period was lower for children in the middle family income category. For astrocytomas there was a more than 70% increased risk in the medium income category when analyzing the two first years of life. The observed increase was reduced when all years each child contributed to the study were included. The risk of cancer in the central nervous system overall was 20% higher in the medium income category compared to the high-income category.

Conclusions: Being born into a household of low family income the first 2 years of life was found to be a risk factor for development of lymphoid leukemia. For astrocytomas an increased risk was observed among children born into the medium income category throughout the first two years of life.