



Potential health impacts of residential exposures to extremely low frequency magnetic fields in Europe



James Grellier^{a,b,c,*}, Paolo Ravazzani^d, Elisabeth Cardis^{a,b}

^a Centre for Research in Environmental Epidemiology (CREAL), PRBB, Doctor Aiguader, 88, 08003 Barcelona, Spain

^b CIBER Epidemiología y Salud Pública (CIBERESP), PRBB, Doctor Aiguader, 88, 08003 Barcelona, Spain

^c Department of Epidemiology and Biostatistics, Imperial College, St. Mary's Campus, Norfolk Place, London W2 1PG, UK

^d CNR National Research Council of Italy, Institute of Electronics, Computer and Telecommunication Engineering (IEIT), Piazza Leonardo da Vinci, 32, 20133 Milan, Italy

ARTICLE INFO

Article history:

Received 16 March 2013

Accepted 25 September 2013

Available online 24 October 2013

Keywords:

Cancer

Childhood leukaemia

Electromagnetic fields

Low frequency

Magnetic fields

Risk assessment

ABSTRACT

Over the last two decades residential exposure to extremely low frequency magnetic fields (ELF MF) has been associated with childhood leukaemia relatively consistently in epidemiological studies, though causality is still under investigation.

We aimed to estimate the cases of childhood leukaemia that might be attributable to exposure to ELF MF in the European Union (EU27), if the associations seen in epidemiological studies were causal.

We estimated distributions of ELF MF exposure using studies identified in the existing literature. Individual distributions of exposure were integrated using a probabilistic mixture distribution approach. Exposure–response functions were estimated from the most recently published pooled analysis of epidemiological data. Probabilistic simulation was used to estimate population attributable fractions (AF_p) and attributable cases of childhood leukaemia in the EU27.

By assigning the literature review-based exposure distribution to all EU27 countries, we estimated the total annual number of cases of leukaemia attributable to ELF MF at between ~50 (95% CIs: –14, 132) and ~60 (95% CIs: –9, 610), depending on whether exposure–response was modelled categorically or continuously, respectively, for a non-threshold effect. This corresponds to between ~1.5% and ~2.0% of all incident cases of childhood leukaemia occurring annually in the EU27. Considerable uncertainties are due to scarce data on exposure and the choice of exposure–response model, demonstrating the importance of further research into better understanding mechanisms of the potential association between ELF MF exposure and childhood leukaemia and the need for improved monitoring of residential exposures to ELF MF in Europe.

© 2013 The Authors. Published by Elsevier Ltd. Open access under [CC BY-NC-SA license](http://creativecommons.org/licenses/by-nc-sa/4.0/).

1. Introduction

For over 30 years there has been concern that exposure to electromagnetic fields (EMF) may impact on human health. Extremely low frequency magnetic fields (ELF MF)—alternating fields generated by distribution and supply of household electricity—have drawn particular attention due to their ubiquity in the environment (Schüz and Ahlbom, 2008). In addition to the electricity supply infrastructure within and near houses, domestic electrical and electronic devices contribute to residential ELF exposure, with sources ranging from overhead power lines (Vulevic and Osmokrovic, 2011) and step-down transformers (Huss et al., 2013; Ilonen et al., 2008; Mezei et al., 2010; Röösli et al., 2011; Thuróczy et al., 2008), domestic appliances and alarm clocks

(Behrens et al., 2004; Leitgeb et al., 2008; Mills et al., 2000), to trams and hybrid vehicles (Halgamuge et al., 2010). As a result, the entire population of the developed world is exposed non-occupationally to ELF MF in some form.

In Europe, alternating currents used in domestic mains electrical power circuits operate at around 50 Hz. Average residential exposures to such fields probably vary relatively little among developed countries; geometric means of residential ELF MF have been reported to vary between 0.025 and 0.07 μT in Europe, and between 0.055 and 0.11 μT in the USA (WHO, 2007). Surveys have been carried out in a selection of European countries including France (Bédja et al., 2010a,b), Belgium (Decat et al., 2008, 2009) and Germany (Bavaria) (Brix et al., 2001) with differing degrees of coverage. However, as there is little routine monitoring of ELF MF in Europe—most measurement is done ad hoc, subsequent to changes in infrastructure or citizen requests (Dürrenberger, 2012)—exposure is currently poorly characterised.

Potential associations between exposure to ELF MF and various health outcomes have been investigated in several epidemiological studies (reviewed most recently in EFHRAN Consortium (2012), EMF-NET (2008), IARC (2002), SCENIHR (2009), and WHO (2007)).

* Corresponding author at: Centre for Research in Environmental Epidemiology, PRBB, C/Doctor Aiguader, 88, 08003 Barcelona, Spain. Tel.: +34 932 147 331.

E-mail address: jgrellier@creal.cat (J. Grellier).

Consistent evidence of an association has been demonstrated only with childhood leukaemia (Kheifets et al., 2010b). Typically, odds ratios (ORs) of 1.5–2.0 have been found for exposures greater than 0.3 or 0.4 μT (Kheifets et al., 2006). Although similar results have been found using a diversity of approaches, chance or confounding cannot be ruled out in explanation of these observations, and given that the majority of epidemiological studies have used case–control designs, it is possible that selection bias might also contribute to the results observed.

Childhood leukaemia (that occurring in those aged <15 years) is the most common childhood malignancy. In Europe, annual incidence of childhood leukaemia is ~2–6 cases per 100,000 (IARC, 2008). Previously, epidemiological studies had shown increases in risk of childhood leukaemia (ORs of 1.5–2) above an inferred threshold at 0.3 or 0.4 μT (IARC, 2002; WHO, 2007), although a pooled analysis of the most recent epidemiological data provides no evidence of such a threshold (Kheifets et al., 2010b). Linear non-threshold functions—as well as others—have therefore been postulated and explored (Kheifets et al., 2010a; Schüz et al., 2007).

Several hypothetical mechanisms are being investigated (reviewed in Lagroye et al. (2011), SCENIHR (2009) and WHO (2007)) but available evidence does not appear to explain the response seen in epidemiological studies. Considering the epidemiologic evidence, inadequate evidence in animal studies, and a lack of relevant mechanistic data, the IARC Monographs Working Group evaluated ELF MF as *possibly carcinogenic* (Group 2B) (IARC, 2002). Similar evaluations have been done more recently (EFHRAN Consortium, 2012; SCENIHR, 2009; WHO, 2007). In general, animal experiments have produced positive results for all known human carcinogens, where *adequate* testing has been done (IARC, 2006). Although the aforementioned weight of evidence evaluations took into account a wealth of cancer bioassay studies (mostly negative with a few exceptions), we would argue that testing thus far may not be “adequate”. For example, very few studies have been done with specific models of acute lymphoblastic leukaemia (ALL), which represents the overwhelming majority of childhood leukaemia cases. A novel mouse model of childhood ALL has recently been developed (Li et al., 2013), which may prove useful in exploring mechanisms of action of environmental exposures such as ELF on development of the disease. In addition, none of the studies available considered exposure in utero, which is when the first hit of ALL is assumed to occur (Lagroye et al., 2011). It is notable that childhood leukaemia is the only cancer outcome for which this association has been consistently found using epidemiological methods. Currently, one possible mechanistic explanation for bioeffects of weak EMF MF is the radical pair mechanism (WHO, 2007). Although well understood theoretically, hypotheses relating to the radical pair mechanism have yet to be adequately tested in mammalian models, and insufficient mechanistic research has been carried out in vivo or in vitro regarding the roles of the cryptochrome molecule behind potential bioeffects of ELF MF (Lagroye et al., 2011). Furthermore, a limited number of in vivo and in vitro studies have demonstrated that ELF MF enhances the effects of known carcinogens (IARC, 2002; WHO, 2007). In two systematic reviews of the evidence (Juutilainen et al., 2000, 2006), it has been hypothesised that experiments designed following the classical two-step initiator-promoter concept of carcinogenesis may not be appropriate for understanding bioeffects of ELF MF, which may result from complex interactions of genotoxic and non-genotoxic carcinogens (Juutilainen, 2008).

If, despite the lack of mechanistic information, we consider the observed epidemiological association between exposure to ELF magnetic fields and childhood leukaemia to be causal, we might expect ubiquitous exposure to translate the relatively low relative risks reported in epidemiological studies into non-negligible population attributable fractions (AF_p). Concerns, therefore, about the public health implications of ELF MF exposure have resulted in several assessments of AF_p being carried out e.g. for the populations of Italy (Grandolfo, 1996), of the US (Greenland, 2001b; Greenland et al., 2000; NIEHS, 1999), of

several industrialised countries (Greenland and Kheifets, 2006), and of the world (Kheifets et al., 2006; WHO, 2007). Reported estimates of AF_p for the US vary, although the most methodologically sound studies found ~3% of childhood leukaemia to be attributable to ELF MF exposure, with 95% confidence intervals (CIs) including zero (Greenland, 2001b; Greenland et al., 2000). European estimates were lower, with only 0.6% reported for the Italian population (Grandolfo et al., 1996). Reasons presented for discrepancies between higher estimates of AF_p in the US compared to Europe include differences in power systems (more overhead wires, low household voltages) and grounding practices between the two regions, and higher per capita power consumption in the US (Greenland et al., 2000). The studies of several more economically developed countries reported AF_p of around 3% with confidence intervals including zero (Greenland and Kheifets, 2006), and the worldwide study reported AF_p ranging from <1% to ~2.5%; the three European countries included all had lower AF_p than Canada or the US. These estimates corresponded to between ~100 and ~2400 cases worldwide depending on the exposure data and exposure–response model used. No detailed assessment of the cases attributable to exposure in Europe has been carried out to date.

The objectives of this study were to estimate—using up-to-date epidemiological data and exposure information together with probabilistic simulation—the proportion of childhood leukaemia cases attributable to current non-occupational ELF MF exposure in the 27 European Union Member States (EU27), if associations observed in epidemiological studies are causal. We also aimed to investigate the effects of selecting different models of exposure–response on the distributions of health impacts. Such information is highly sought after by regulatory bodies and policy makers, for whom it represents a key input to risk assessment and management (European Commission, 2013).

2. Material and methods

The exposure–response function (ERF) was regarded as the primary link between all other assessment data. As no primary continuous epidemiological data were available, it was necessary to estimate the ERF from summary data as reported in published studies. A review was undertaken to identify the most recent relevant meta-analyses and pooled analyses of epidemiological data. Several studies have been published over the last fifteen years (Ahlbom et al., 2000; Angelillo and Villari, 1999; Greenland et al., 2000; Kheifets and Shimkhada, 2005; Kheifets et al., 2010b; Pelissari et al., 2009; Schüz and Ahlbom, 2008; Schüz et al., 2007); the most recent of these was identified as the most up-to-date and appropriate for deriving ERF data. This pooled analysis comprised primary data from six matched case–control studies published after 2000 from Germany, Italy, UK, Japan and Tasmania. Sensitivity analyses were conducted, moreover, using exposure–response data derived from sub-analyses of the same study (including an additional Brazilian study which differed from the others in various ways, and with different exposure category cut-offs), and from two other pooled analyses (Ahlbom et al., 2000; Greenland et al., 2000).

A causal diagram was constructed in Analytica software (Version 4.4, Lumina Decision Systems Inc. 2012) relating exposure to ELF MF with estimates of health impacts (AF_p and the attributable cases (AC) of incident childhood leukaemia) via an ERF, incorporating data on population and incidence. Childhood leukaemia was defined as in the recent pooled analysis (Kheifets et al., 2010b): any leukaemia occurring in individuals aged 0 ≤ 15 years at time of diagnosis.

Estimates of exposure were needed that were congruent with exposure metrics used in the epidemiologic studies from which the ERF was obtained i.e. time-averaged (≥24 h) residential magnetic fields at power frequency (i.e. ~50 Hz) that were measured or calculated inside a typical home, provided in units of magnetic flux density (microTesla, μT). An initial review of existing data in the EU27 found

that sufficiently detailed exposure data was not available for most countries (Thuróczy et al., in press).

A measurement campaign was out of the scope of our study; in the absence of adequate data, we carried out a systematic review of available data describing residential exposure measurements of ~50 Hz magnetic fields in any of the EU27 countries to identify relevant exposure distributions (details of search presented in Supplemental material A, p1). Studies were excluded if they were non-European, only presented reviews of previously published studies, did not present exposure data in sufficient detail for fitting PDFs, presented results using inappropriate units, only measured exposure in specific sub-populations (e.g. children living close to power lines), had a purely occupational focus, did not sufficiently explain measurement methods, relied on one-off spot measures rather than time-integrated measurements, measured close to particular EMF sources, or focused on non-domestic environments. We assumed that the most reliable and representative exposure data were those based on personal and stationary household measurements. A PDF was generated from descriptive statistics of exposure presented in each identified study. We assumed that exposure was log-normally distributed (Swanson and Kaune, 1999). Where insufficient statistics were supplied to define a distribution, parameters were inferred from tabulated or plotted data presented in the paper, or were extracted from a summary tabulation presented elsewhere (Swanson and Kaune, 1999).

In the first phase of the literature review, eighty four studies were identified, including epidemiologic studies, ELF MF measurement studies, and both quantitative and qualitative reviews. The 14 studies which remained after applying our exclusion criteria (Table 1) provided measurements of exposure in Austria (Tomitsch et al., 2010), Belgium (Decat et al., 2009), Denmark (Skotte, 1994), Finland (Juutilainen et al., 1989), France (Bédja et al., 2010b), Germany (Brix et al., 2001; Michaelis et al., 1997; Schüz et al., 2000), Italy (Gobba et al., 2011), and the UK (Coghill et al., 1996; Merchant et al., 1994; Preece et al., 1996; UK Childhood Cancer Study Investigators, 2000a; van Tongeren et al., 2004). Since log-normal distributions are better characterised by the geometric mean (GM) and geometric standard deviation (GSD) than the arithmetic mean (AM) and standard deviation (SD), the following formulae were used to convert where necessary:

$$GM = \frac{AM^2}{\sqrt{AM^2 + SD^2}}$$

$$GSD = e^{\sqrt{\ln\left(1 + \left(\frac{SD}{AM}\right)^2\right)}}$$

Log-normal exposure distributions assembled from the data presented in the studies were similar (Fig. 1A). As exposure data were

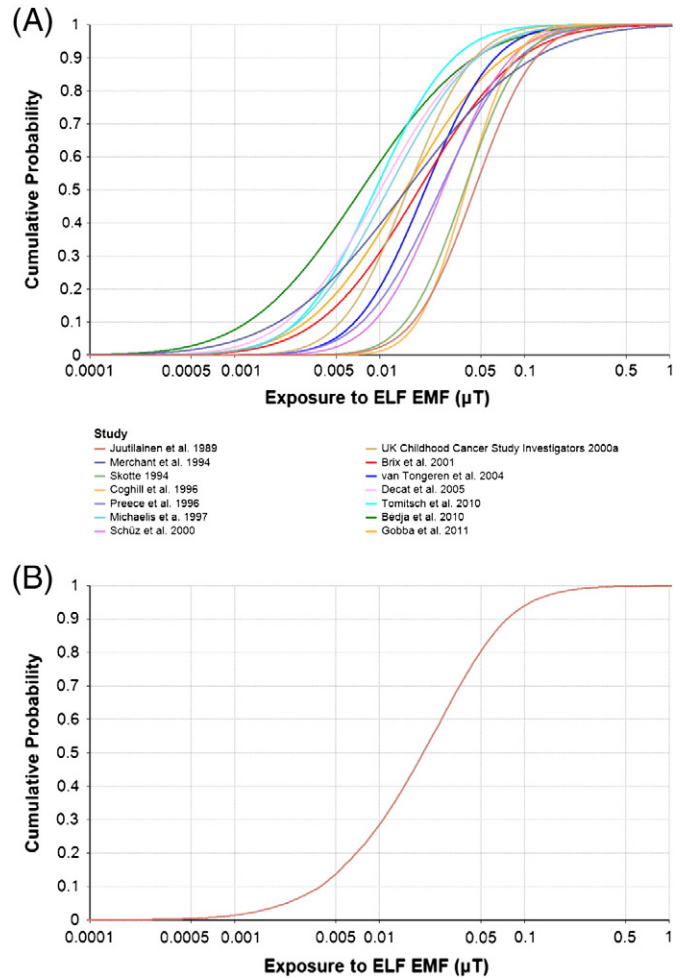


Fig. 1. Cumulative probability distribution functions of (A) estimates of residential exposure to ELF magnetic fields from the literature and (B) a mixture distribution of all literature-based exposure estimates to residential ELF magnetic fields.

not available for the remaining 19 EU27 Member States, estimating country-specific exposure was not practicable. Instead, exposure estimates from these studies were aggregated and assigned to the entire EU27 region. Averaging distributions would have led to undesirably precise estimates of exposure (the SD of the average distribution decreases in inverse proportion to number of distributions being averaged due to central limit theorem), so a pooled “mixture distribution” was generated by sampling from each exposure distribution, thereby

Table 1

List of included studies identified by literature review as providing information about exposure distribution in Europe. Where arithmetic means were provided in the original studies, these have been converted to geometric means. Where measures of variance other than the geometric mean were provided, distributions were fit using the original data and geometric means inferred.

Study	Country	Age	Timing	Stationary/personal	GM	GSD
Juutilainen et al. (1989) ^a	Finland	Adult	≥24 h time-weighted	Stationary	0.060	2.140
Merchant et al. (1994)	England and Wales	Adult	≥24 h time-weighted	Personal	0.054	4.900
Skotte (1994)	Denmark	Adult	≥24 h time-weighted	Personal	0.050	2.080
Coghill et al. (1996) ^a	UK	Child	≥24 h time-weighted	Stationary	0.047	1.830
Preece et al. (1996)	UK	Adult	≥24 h time-weighted	Personal	0.042	2.650
Michaelis et al. (1997)	Germany	Child	≥24 h time-weighted	Stationary	0.021	3.027
Schüz et al. (2000)	Germany	Child	≥24 h time-weighted	Stationary	0.039	2.355
UK Childhood Cancer Study Investigators (2000a)	UK	Child	≥24 h time-weighted	Stationary	0.022	2.299
Brix et al. (2001)	Germany	Adult	≥24 h time-weighted	Personal	0.041	3.518
van Tongeren et al. (2004)	UK	Adult	≥24 h time-weighted	Personal	0.030	2.390
Decat et al. (2009)	Belgium	Child	≥24 h time-weighted	Personal	0.020	3.226
Tomitsch et al. (2010)	Austria	Adult	Night	Stationary	0.015	2.654
Bédja et al. (2010b)	France	Adult and child	≥24 h time-weighted	Personal	0.020	4.086
Gobba et al. (2011)	Italy	Adult	≥24 h time-weighted	Personal	0.032	3.431

^a Statistical summary from Swanson and Kaune (1999).

generating a distribution encapsulating the range of variability represented by the individual distributions (Fig. 1B). This distribution provided a reasonable average of the medians of each of the distributions derived from the literature, while adequately representing the overall variability expressed by the complete set. Where more than one distribution was available for a single country, each was sampled in the same way. The literature-based distribution that was subsequently applied to the EU27 Member States was log-normal with a median of 0.02 μT and SD: 0.06 μT .

A number of sensitivity analyses relating to the definition of the literature review-based exposure distribution were carried out. Whereas the original literature review-based exposure was generated by inclusively pooling all studies that met our review criteria (preferentially including estimates of exposure measured for children, as time-averaged ≥ 24 h, and using personal monitoring equipment, where more than one type of exposure measure was provided), we also carried out sensitivity analyses in which we exclusively pooled studies meeting certain criteria regarding age of population (children vs. adults (or unspecified age)), timing of exposure measure (night time vs. time-averaged ≥ 24 h), and exposure measurement method (personal vs. stationary). We were also interested to see what impact using a pooled exposure distribution has on estimates of attributable cases relative to using country-specific exposure distributions, for those eight countries for which exposure estimates were available (Supplemental material C, p7). In addition, we carried out an expert elicitation exercise, wherein European experts were asked to provide their best estimates of residential exposure to ELF MF in their country of work (further details are provided in Supplemental material B, p2).

We investigated how assumptions related to ERF model affected estimates of AF_p , specifically: (1) a categorical threshold model, where only ORs for the uppermost category were applied to the appropriate proportion of the target population; (2) a categorical non-threshold model – where categorical ORs were applied proportionally across the range of exposures for which they are originally described in the pooled analysis article; and (3) a continuous non-threshold model – where a linear regression model was fit to the summary ORs for continuous application to the target population's entire exposure distribution. The first model was considered an important comparison with previous risk assessments that used a threshold ERF. The second model was warranted as the results of the most recent pooled analysis (Table 2) no longer indicate a threshold effect. Notably, this resulted in applying the reference category risk (OR = 1 (95% CI: 1, 1)) to the portion of the target population with exposures of less than 0.1 μT . The third approach was used as means of applying non-zero exposure–response across the entire target population exposure range. We fit a linear model to the categorical ORs, providing an estimate of the regression coefficient β and its standard error. However, the categorical log ORs are not independent of one another due to the common reference category. We therefore used generalized least-squares (GLS) regression, where approximate estimates of covariance were constructed for all non-reference adjusted log ORs from a fitted table that conforms to adjusted log ORs using the number of cases and controls in each exposure strata (Greenland and Longnecker, 1992), using the *gls* package (Orsini et al., 2006) in STATA (StataCorp, 2007).

The AF_p is the fraction by which total incidence would be reduced if the exposure of the population were reduced to the reference level

(Greenland, 2001a). It may be expressed in terms of incidence as follows:

$$AF_p = \frac{(I_p - I_r)}{I_p} = \frac{(R_p - 1)}{R_p}$$

where I_p is the actual population incidence, I_r is what this incidence would be if exposure followed the reference distribution, and $R_p = I_p / I_r$ is the population incidence ratio (Greenland, 2001b). We compared AF_p calculated using all three exposure–response models. For the first two, categorical ORs corresponding to ranges of the target population exposure distributions were applied directly to those proportions of population exposed within each category, and the AF_p was calculated according to the formula (Levin, 1953):

$$AF_p = \frac{\int_{x=0}^m P(x)OR(x) - 1}{\int_{x=0}^m P(x)(OR(x) - 1) + 1}$$

where $OR(x)$ is the OR at exposure level x , $P(x)$ is the population distribution of exposure, and m is the maximum exposure level. For the continuous non-threshold model, the AF_p was calculated using continuous distributions of exposure X and the distribution of the coefficient b , as follows:

$$AF_p = \frac{(\exp(b \cdot X) - 1)}{\exp(b \cdot X)}$$

where b is a probabilistic representation of the estimate of the coefficient, defined as a normal distribution with mean equal to the coefficient and standard deviation equal to the estimate of the standard error (SE) on that coefficient:

$$b = \text{Normal}(\beta, SE).$$

Numbers of age- and sex-stratified attributable cases (AC) in each of the EU27 countries—the number of cases childhood leukaemia that can be attributed to exposure to ELF MF—were calculated thus:

$$AC = \frac{AF_p \cdot N \cdot I}{100,000}$$

where N is the population and I is the incidence of the disease of interest (the rate per 100,000), both stratified by sex, age, and country. Annual incidence of childhood leukaemia (total cases in those between the ages of 0 and 15 years of age at the time of diagnosis) was extracted from published estimates in the GLOBOCAN database (IARC, 2008). Age- and sex-stratified population estimates for the EU27 Member States for 2008 were obtained from EUROSTAT (EUROSTAT, 2010). The GLOBOCAN database presents estimates for 2008 based on reported national-level incidence rates for each Member State of the EU27. Details of the probabilistic simulation methods used are provided in Supplemental material E (p16).

As sensitivity analyses, we also estimated AF_p and AC generating alternative estimates of exposure–response using risk estimates provided in Kheifets et al. (2010b) based on analyses including the Brazilian study, using 0.4 μT as the upper exposure category cut-off, as well as

Table 2
Summary odds ratios presented in Kheifets et al. (2010b) – pooled analysis excluding Brazilian study using a higher exposure category cut-off of 0.3 μT , and estimated percentages of the EU27 population exposed to those levels of residential ELF magnetic fields according to our literature review.

Exposure category (μT)	Exposure midpoint (μT)	Proportion of target population exposed	No. of cases	No. of controls	Odds ratio (adjusted for age, sex and SES) with 95% confidence intervals
<0.1	0	93.42%	10,571	12,085	1 (1.00, 1.00) Ref
0.1–0.2	0.15	5.08%	56	112	1.16 (0.83, 1.61)
0.2–0.3	0.25	0.96%	14	24	1.30 (0.67, 2.54)
≥ 0.3	0.35	0.54%	15	20	1.56 (0.78, 3.10)

estimating ERF for data reported in two previously published pooled analyses (Ahlbom et al., 2000; Greenland et al., 2000) (Supplemental material D, p10).

3. Results

Epidemiological studies investigating a potential association between exposure to ELF magnetic fields and childhood leukaemia have typically classified exposure as successive 0.1 μT exposure categories. We estimated the proportions of the population exposed at successive 0.1 μT increments for the pooled exposure distributions derived from the literature (Table 2). We estimated that 0.54% of the geometric mean exposures of the target population were in the $>0.3 \mu\text{T}$ category, lower than previous worldwide measurement surveys, which have reported between 1.2 and 10.7% of geometric mean exposures to be $>0.3 \mu\text{T}$, and 0.4–4.8% of $>0.4 \mu\text{T}$ (WHO, 2007). Our sensitivity analyses showed that the distribution of exposure in the target population was relatively stable according to the types of exposure measures included in the pooled distribution: exposures were, however, lower when only including studies focused on children, only measuring exposure at night, or when only using measurements from stationary monitors (Supplemental material C, Table S.4, p8). The exposure distribution derived from expert elicitation (median: 0.08 μT , SD: 0.74 μT) was very high in comparison with any estimates based on the literature (Supplemental material B, Fig. S.2, p5). Although differences in power supplies and wiring norms are known to account for some inter-country variation (Swanson and Kaune, 1999) we attributed the inflated expert-based distribution to poor calibration of a minority of experts, and therefore considered that using this distribution was not appropriate for use in this assessment (for comparison, the estimates of attributable cases resulting from its use are provided in Supplemental material B, Table S.3, p6).

The non-threshold model of exposure–response generated by GLS regression (Supplemental material D, p10) provided an OR slope estimate of 1.12 per 0.1 μT (95% CIs: 0.98, 1.27). Summary OR slopes based on exposure–response data from other sub-analyses presented in the Kheifets et al. (2010b) pooled analysis and from data derived from other pooled analyses differed little from this estimate (Supplemental material D, Table S.20, p14). For the categorical models, summary estimates of risk (ORs) were used as presented in the pooled analysis (Table 2).

The estimates of AF_p and the number of cases of childhood leukaemia attributable to ELF exposure was found to differ by a factor of ~ 6 depending on the exposure–response model used (Table 3): the largest differences were dependent on whether a threshold was assumed; only modest differences were observed between categorical and continuous exposure–response models. We considered non-threshold models to best represent the available epidemiological evidence. The overall variance in attributable cases was found to depend approximately equally on variance in distributions of exposure and ERF. When we assigned exposure distributions to those eight countries for which exposure estimates were available in the literature, we saw that the proportions of the target population exposed at each exposure level differed quite markedly (Supplemental material C, Table S.5, p8). However, we found that the overall impact of country-specific exposure distributions—rather than a pooled distribution applied to all eight countries—

on our total estimates of attributable cases for these countries was very small (Supplemental material C, Table S.6, p8).

4. Discussion

We estimated the annual number of cases of childhood leukaemia that could be attributed to estimates of domestic exposure to ELF magnetic fields in Europe in 2008, if associations in epidemiologic studies were causal. Estimates of the attributable cases were low, with relatively wide confidence intervals. Not including studies of highly-exposed population sub-groups probably resulted in underestimation. We showed that uncertainties due to the choice of methods for estimating exposure and ERF considerably impacted our results. Our study provides baseline estimates of health impacts attributable to ELF MF exposure, highlights gaps in available data, and addresses methodological issues relating to exposure estimation. In addition, carrying out the assessment was highly informative in ascertaining which areas of this potential public health issue are least well understood at the present time.

The use of epidemiological data in this assessment required a tacit assumption of causality, which is not currently supported by bioassay data and has not been explained by any of the proposed mechanisms. Since large numbers of cancer bioassays would be unlikely to return such consistently negative results, it is possible that there is no true effect, and that the epidemiological associations are the result of confounding or other biases. Clearly, the uncertainty bounds represented in the attributable fractions estimated for each exposure–response model do not take these kinds of uncertainty into account. As such, we recommend caution in the interpretation of these findings and the various uncertainties that are inherent to them.

If interactions due to other exposures such as chemicals were to account for the association seen in epidemiological studies, as might be postulated from some evidence in animals (Juutilainen, 2008), the nature of these in humans is as yet unknown and could not be taken account of in our assessment. In this light, the results might be viewed in terms of what the attributable burden would be if the target population of the EU had similar exposures to these unknown factors as the children in the epidemiological studies, which may or may not be a reasonable assumption. This highlights the need to carry out further work in clarifying the potential role of interactions in the pathway between ELF MF exposures and leukaemogenesis.

Exposure data were lacking for most EU countries and existing published data are limited in their representativeness. As such, we considered that exposure distributions provided in any individual study were unlikely to capture the variability anticipated across the EU. In particular, we were unable to explicitly take into account country- or region-specific differences in wiring configurations, proximity of buildings to power lines, and the presence of step-down transformers in apartment buildings, all of which have been demonstrated to affect exposure to ELF MF. We generated exposure estimates using a simple, transparent method that maximised variability as a means of accounting for these differences. Were more robust, country- or region-specific estimates of exposure available, we would be able to present more accurate estimates of the AF_p due to residential exposure to ELF magnetic fields in the EU27. The range of literature-based estimates of AF_p for the continuous and categorical non-threshold models (Table 3) were at the lower end of the range of estimates published previously e.g. Greenland and Kheifets (2006). Sensitivity analyses showed that

Table 3

Estimates of population attributable fraction (AF_p) and attributable cases (AC) in the EU27, for literature-based exposure of residential ELF magnetic fields.

Exposure estimation method	Model	AF_p % (95% CIs)	AC (95% CIs)
Literature review	Categorical threshold model	0.30 (–0.12, 1.12)	9.9 (–3.8, 36.7)
	Categorical non-threshold model	1.53 (–0.41, 4.03)	50.1 (–13.5, 132.1)
	Continuous non-threshold model	1.86 (–0.27, 18.61)	61.1 (–8.9, 609.7)

exposures—and consequently, estimates of attributable cases (Supplemental material, Table S.6, p8)—were lower when only those studies looking at children, measuring night time exposures, or using stationary monitoring equipment were incorporated into the pooled distribution. Differences among the attributable cases estimated using non-threshold models in the various sensitivity analyses were generally small, the maximum being a change of a factor of two. We might expect that exposures solely measured at night—when appliance usage and electrical power consumption are generally reduced—would be lower than 24- or 48-hour time-weighted average exposures. A pooled analysis based only on night time exposures to ELF MF and risk of childhood leukaemia found similar results to pooled analyses using 24- or 48-hour time-averaged exposures (Schüz et al., 2007), and reported that the use of night time measures was not more appropriate than such time-averaged, hence we ought not have any preference for using the night time exposure metric in this assessment. Measurements made using static monitoring equipment were also lower than personal measures of exposure, potentially because meters were often installed away from appliances, to which individuals may spend time in closer proximity. In addition, since it is plausible that prenatal exposure to ELF MF might be related to leukaemia risk, we consider it preferable not to use only the information based on children's exposure in this assessment. Overall, it is important to note that the effect of including or excluding various types of exposure studies had relatively small impacts on our estimates of attributable cases, particularly when viewed not only in terms of the median exposures, but considering also the large uncertainty/variability characterising the distributions: for either of the two non-threshold exposure–response models, median estimates of attributable cases varied by less than 2.5 times depending on how exposure was defined (Supplemental material, Table S.6, p8). In addition, it would be prudent to consider that in excluding more studies, the degree to which any resulting pooled exposure distribution might adequately represent variability across different European countries would only decrease.

Our pooled, literature-based exposure estimates were derived from measurements taken in western European countries. In order to be more “representative” of European exposures generally we included both studies of adults and children, which may introduce additional uncertainty. Overall, the pooled literature-based distribution should be considered as a current “best estimate”, indicative of the recent exposure situation in Europe.

The proportion of the general population exposed to magnetic fields of more than 0.3 μT according to our literature-based exposure estimates was, however, low compared to those published previously. In estimating the exposure of the *general* population, studies solely considering highly-exposed sub-populations (e.g. living close to power lines or in apartments above transformers) were excluded, as it was not possible to estimate the proportion of the general population in the EU27 countries that should be assigned high exposures. Better characterisation of the distribution of high exposures in EU populations would improve our exposure assessment. Attempts to use expert elicitation did not prove to be fruitful in addressing this issues in this case (Supplemental material B, p2). Although we recognise that our approach may have led to underestimation of the population exposed to high levels of EMF MF—and therefore attributable cases—we preferred not to introduce further uncertainties by attempting to estimate the proportion living in proximity to power lines or electrical transformers without access to any appropriate data available on for the vast majority of the EU27 population. Therefore, although our results may underestimate the true attributable risk, we consider that we have provided the best estimates that can be made with data available at the present time.

In contrast to the paucity of data generally available in the EU Member States, a few countries have collected comprehensive exposure data as part of large population-based epidemiological studies in representative childhood populations, most notably Germany (Schüz et al., 2000, 2001) and the UK (UK Childhood Cancer Study Investigators,

2000a,b). These data were included in our literature-based exposure estimate. For those two countries, attributable fractions of ~1% or lower have been estimated previously (Maslanyj et al., 2010; Schüz, 2007), aligning reasonably well with our estimates. We saw only small differences in estimates of attributable cases (~20%) when comparing country-specific exposure distributions assigned to those countries for which data were available against assigning the same pooled distribution to all countries (Supplemental material C, Table S.5, p8). While this does not provide us with any further information on the validity of applying a pooled exposure distribution to countries for which no exposure data were available, it does support the effectiveness of this method as a means of synthesising the characteristics of a number of distributions of exposure for use in this kind of assessment.

Since primary continuous epidemiological data were not available on which an ERF could be modelled, we used summary data derived from a published pooled analysis (ORs for several exposure categories). Where we assumed a non-threshold effect, the causal risk ratio at the exposure levels of relevance in the context of this assessment could be described either using a continuous relationship between exposure and risk derived through regression on summary data, or using the categorical ORs as reported. Using a continuous ERF derived from such data using regression techniques required us to make assumptions relating to the linearity of the model, its shape, the inclusion of an intercept term, and the choice of a representative value for each level of exposure (particularly for open-ended categories). Where exposure–response based on primary epidemiological data on ELF MF exposure and childhood leukaemia has been analysed previously, good fits have been found for log-linear quadratic-spline models (Greenland, 2001b), and threshold models (WHO, 2007). Using the most recent pooled dataset, quadratic and non-linear models have been shown to outperform both linear and threshold models, the best fit being obtained by representing risk as a logistic function of the geometric mean and its square (Kheifets et al., 2010a). Although these findings may appear to question our selection of an exponential-multiplicative model, we note that our regression analyses were based solely on summary epidemiological data. Fitting continuous non-linear models to such data was not considered appropriate, and we preferred to use more parsimonious linear models.

Not including an intercept term constrains the regression line to pass through the origin, thereby defining zero risk at zero exposure. This contrasts with the categorical epidemiological analysis, where zero risk is assigned to the entire reference category, to which most of the target population belongs. This resulted in somewhat higher estimates of the attributable cases for the continuous non-threshold model compared to the categorical non-threshold model. Additionally, the zero intercept has a zero standard error: variance in risk estimates for the portion of the population with very low exposures may therefore be underestimated when applying the continuous model. This is more than compensated for, however, by the variability that is introduced through applying the continuous model at higher exposures. For the threshold and non-threshold categorical models, where a large proportion of exposure in the assessment population is distributed within the reference category, the estimate of AF_p for that region is zero, and therefore probably underestimated. Sharp thresholds are biologically implausible, and result in sudden jumps in risk at category boundaries; these are artefacts of the epidemiological analysis, and have been considered an incorrect assumption in most settings (Maclure and Greenland, 1992). In contrast, although the continuous non-threshold ERF attempts to solve these problems, in using it we are forced to depart from the data presented in the pooled analysis and make somewhat arbitrary judgments regarding the shape and nature of the ERF.

Overall, given the lack of convincing evidence for a particular exposure–response shape, we saw fit to present results of all three ERF models. As mentioned earlier, though previous studies have suggested a threshold effect, the most recent pooled analysis suggests a monotonic increase in risk with increasing levels of exposure. We

therefore believe that the two non-threshold models produce the most plausible estimates of attributable risk. Between the categorical and continuous non-threshold models, the difference in estimates of AF_p was relatively small, but the continuous model resulted in wider confidence intervals. Since non-linearity in exposure–response in relation to ELF MF and childhood leukaemia is increasingly not accepted (Kheifets et al., 2010a,b), non-threshold ERF were considered the most easily-interpretible and most suitable for informing policy decisions.

We were not able to adjust for covariates controlled for in the pooled analysis (sex, age, socioeconomic status and study) when applying the ERF to the target population. Although confounding is considered an unlikely candidate as an explanation of the association—chiefly because any such confounding factor would have to be a rather strong risk factor even when highly correlated with magnetic fields (Maslanyj et al., 2010)—adjusting for these covariates might alter our estimates in either direction. Selection bias in the epidemiological studies has been raised as a concern, as studies including measurements often only achieved response rates of around 50% or less. Its implications have been discussed extensively, and a review of the relevant epidemiological literature found evidence both for and against the existence of selection bias (Mezei and Kheifets, 2006). In the same study, the potential impact of such biases on risk estimates from any case–control study investigating the association between ELF MF and childhood leukaemia was demonstrated to be large. Selection bias has been reported as leading to overestimation of risk due to lower participation of controls living close to power lines (Maslanyj et al., 2010; Schüz, 2007). Non-differential exposure misclassification would probably lead to underestimation, however, and the net impact of these competing biases is unclear (Schüz, 2007).

Estimates of AF_p based on a combination of model-based incidence-ratio estimates with survey information on the US population exposures have been reported at 3.3% (median), with confidence intervals varying according to the calculation method used (–1.2 to –1.5% and 7.9 to 8.1%) (Greenland, 2001b). For all ERF models, we report lower estimates for the European population, chiefly due to the use of up-to-date exposure–response data and exclusion of exposure data in sub-populations living close to power lines, and the impact of differences in electrical supply mentioned previously. Our estimates of AC are relatively low compared to those reported for Western Europe (Kheifets et al., 2006) for the same reasons.

Since the associations observed are generally small, the public-health impacts have previously been considered to be low (Greenland and Kheifets, 2006; Kheifets et al., 2006). Previous health risk assessments have recommended precaution, stopping short of prescribing limits because potential risks are poorly characterised (SNBOSH, 1996), and mechanistic data are lacking (WHO, 2007). One US-wide health impact study recommended passive regulatory action, listing education of the public as the best means of reducing exposures and potential risks (NIEHS, 1999). Precautionary approaches have resulted in making similar recommendations (Kheifets et al., 2010c; Maslanyj et al., 2010); we would not necessarily alter this advice but recognise that with no mechanism and poor exposure characterisation, it is unclear what these measures might be. Since our assessment results are contingent on assuming causation, we recognise that the most appropriate focus of research at the present time is firstly to effectively control and carefully report on selection and other biases in any case-control studies that are done for this association (Mezei and Kheifets, 2006) and, upon establishing whether the associations are real or artefactual, in understanding mechanisms that might explain such epidemiological associations. Previously, Bayesian methods have been used to estimate the impact of a variety of possible sources of bias (Greenland and Kheifets, 2006) and these showed quantitative evidence that any new epidemiological study would have to be convincingly free of bias, make use of highly accurate measures of lifetime exposure, and contain large numbers of both cases and controls at high exposure levels; adding more small and problematic studies to

the existing body of evidence would at best only lead to very marginal improvements in precision of risk estimates (Greenland and Kheifets, 2006). Specifically concerning future research needs, mechanistic research has so far been inconclusive in elucidating whether and how ELF MF might cause leukaemia in children. The potential of novel methods such as proteomics and transcriptomics has been recognised as key to better understanding the effects of ELF MF on living systems, but this would require the application of these techniques to be better coordinated (Hardell and Sage, 2008; Leszczynski et al., 2012; Sinclair et al., 2006). In terms of improvements to epidemiological studies on ELF MF and childhood leukaemia, the rarity of both high exposures and health outcome have hampered research in this area. Well-designed case–control studies are currently being undertaken that focus specifically on children with very high exposures to ELF MF due to their residential proximity to indoor transformers. Through carrying out such studies in several large populations and pooling their results, we might anticipate the minimisation of biases in exposure, an increase in the power of the study to detect an effect, and thus an overall reduction in scientific uncertainty regarding the association between ELF MF and childhood leukaemia (Mezei et al., 2010).

5. Conclusions

We estimated that between 50.1 (95% CIs: –13.5, 132.2) and 61.1 (95% CIs: –8.9, 609.7) cases of childhood leukaemia could be attributed to current exposures to ELF magnetic fields annually, across the whole of the EU, if the association presented by epidemiological evidence is assumed to be causal, corresponding to between ~1.5% and ~2.0% of all childhood leukaemia cases in Europe. Our estimates assume no threshold effect, in line with recent epidemiological evidence. Estimates of exposure—and concomitantly, estimates of AF_p —could be improved if resources were invested in more extensive monitoring of ELF MF in the EU27. In conclusion, according to the current state of evidence, residential exposure to ELF MF may contribute to cases of leukaemia in children, but this contribution is relatively small and is characterised by considerable uncertainty.

Funding

This study was carried out as part of the European Health Risk Assessment Network on Electromagnetic Fields Exposure (EFHRAN) project (funded by the European Commission, Agreement Number 2008 11 06).

Conflicts of interest

All authors declare that they have no competing financial interests or other conflicts of interest.

Acknowledgements

We thank the EFHRAN Consortium—in particular Joachim Schüz, Zenon Sienkiewicz, and Isabelle Lagroye—and Jukka Juutilainen, all of whom provided useful comments in the preparation of this manuscript, and the many European EMF experts that assisted in the expert elicitation process.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.envint.2013.09.017>.

References

- Ahlbom A, Day N, Feychting M, Roman E, Skinner J, Dockerty J, et al. A pooled analysis of magnetic fields and childhood leukaemia. *Br J Cancer* 2000;83:692–8. <http://dx.doi.org/10.1054/bjoc.2000.1376>.
- Angelillo IF, Villari P. Residential exposure to electromagnetic fields and childhood leukaemia: a meta-analysis. *Bull World Health Organ* 1999;77:906–15.
- Bédja M, Magne I, Souques M, Lambrozo J, Le Brusquet L, Fleury G, et al. Methodology of a study on the French population exposure to 50 Hz magnetic fields. *Radiat Prot Dosimetry* 2010a;142(2–4):146–52. <http://dx.doi.org/10.1093/rpd/ncq213>.
- Bédja M, Magne I, Souques M, Lambrozo J, Le Brusquet L, Fleury G, et al. Exposure of the French population to 50 Hz magnetic fields: EXPERS study. *Proceedings of Third European IIRPA Congress*; 2010b.
- Behrens T, Terschüren C, Kaune WT, Hoffmann W. Quantification of lifetime accumulated ELF-EMF exposure from household appliances in the context of a retrospective epidemiological case-control study. *J Expo Anal Environ Epidemiol* 2004;14(2):144–53. <http://dx.doi.org/10.1038/sj.jea.7500305>.
- Brix J, Wettemann H, Scheel O, Feiner F, Matthes R. Measurement of the individual exposure to 50 and 16 2/3 Hz magnetic fields within the Bavarian population. *Bioelectromagnetics* 2001;22:323–32.
- Coghill RW, Steward J, Philips A. Extra low frequency electric and magnetic fields in the bedpace of children diagnosed with leukaemia: a case-control study. *Eur J Cancer Prev* 1996;5:153–8.
- Decat G, Deckx L, Maris U. Persoonlijke exposimetrie voor het bepalen van de binnenhuisblootstelling van kinderen aan ELF. VLF en RF elektromagnetische velden afkomstig van interne en externe bronnen. Boerentang, Belgium: VITO - Flemish Institute for Technological Research NV; 2008. p. 114.
- Decat G, Deckx L, Wilczek D, Meynen G. Monitoring campaign of the 50 Hz magnetic field for the estimation of the proportion of Belgian children exposed to the epidemiological cut-off points of 0.2, 0.3, and 0.4 microTesla. *Final Report of the BBEMG Research Contract*; 2009. p. 1–62.
- Dürrenberger G. NIR-monitoring in Europe. FSM-report on country activities. FSM – Swiss Research Foundation on Mobile Communication; 2012. p. 1–7.
- EFHRAN Consortium. Deliverable report D2 of EFHRAN project: risk analysis of human exposure to electromagnetic fields (revised); 2012–13.
- EMF-NET. Health and electromagnetic fields; 2008–13.
- European Commission. Call for proposals: ENV.2013.6.4-2. Closing gaps of knowledge and reducing exposure to electromagnetic fields (EMF) – FP7-ENV-2013; 2013.
- EUROSTAT. Population estimates for EU27, 2008. Available: <http://epp.eurostat.ec.europa.eu/portal/page/portal/population/data/database>, 2010.
- Gobba F, Bravo G, Rossi P, Contessa GM, Scaringi M. Occupational and environmental exposure to extremely low frequency-magnetic fields: a personal monitoring study in a large group of workers in Italy. *J Expo Sci Environ Epidemiol* 2011;21:634–45. <http://dx.doi.org/10.1038/jes.2011.9>.
- Grandolfo M. Extremely low frequency magnetic fields and cancer. *Eur J Cancer Prev* 1996;5(5):379–81.
- Greenland S. Attributable fractions: bias from broad definition of exposure. *Epidemiology* 2001a;12:518–20.
- Greenland S. Estimation of population attributable fractions from fitted incidence ratios and exposure survey data, with an application to electromagnetic fields and childhood leukemia. *Biometrics* 2001b;57:182–8. <http://dx.doi.org/10.1111/j.0006-341X.2004.00236.x>.
- Greenland S, Kheifets LI. Leukemia attributable to residential magnetic fields: results from analyses allowing for study biases. *Risk Anal* 2006;26:471–82. <http://dx.doi.org/10.1111/j.1539-6924.2006.00754.x>.
- Greenland S, Longnecker MP. Methods for trend estimation from summarized dose-response data, with applications to meta-analysis. *Am J Epidemiol* 1992;135:1301–9.
- Greenland S, Sheppard AR, Kaune WT, Poole C, Kelsch MA. A pooled analysis of magnetic fields, wire codes, and childhood leukemia. *Epidemiology* 2000;11(6):624–34.
- Halgamuge MN, Abeyratne CD, Mendis P. Measurement and analysis of electromagnetic fields from trams, trains and hybrid cars. *Radiat Prot Dosimetry* 2010;141:255–68. <http://dx.doi.org/10.1093/rpd/ncq168>.
- Hardell L, Sage C. Biological effects from electromagnetic field exposure and public exposure standards. *Biomed Pharmacother* 2008;62(2):104–9.
- Huss A, Goris K, Vermeulen R, Kromhout H. Does apartment's distance to an in-built transformer room predict magnetic field exposure levels? *J Expo Sci Environ Epidemiol* 2013;1–5. <http://dx.doi.org/10.1038/jes.2012.130>, [October 2012].
- IARC. Non-ionizing radiation, Part 1, Static and extremely low-frequency (ELF) electric and magnetic fields (p. 429). Lyon, France: IARC Press; 2002.
- IARC. Preamble to IARC Monographs on the evaluation of carcinogenic risks to humans. Non-ionizing radiation, part 1. Static and extremely low-frequency (ELF) electric and magnetic fields. Lyon, France: IARC Press; 2006. <http://dx.doi.org/10.1007/s10350-006-0552-z>IARC 2002.
- IARC. GLOBOCAN crude and age-standardised cancer rates per 100,000. <http://globocan.iarc.fr/>, 2008.
- Ilonen K, Markkanen A, Mezei G, Juutilainen J. Indoor transformer stations as predictors of residential ELF magnetic field exposure. *Bioelectromagnetics* 2008;29(3):213–8. <http://dx.doi.org/10.1002/bem.20385>.
- Juutilainen J. Do electromagnetic fields enhance the effects of environmental carcinogens? *Radiat Prot Dosimetry* 2008;132(2):228–31. <http://dx.doi.org/10.1093/rpd/ncn258>.
- Juutilainen J, Saali K, Eskelinen T, Matilainen P, Leinonen A-L. Measurements of 50 Hz magnetic fields in Finnish homes. *Research Report IVO-A-02/89*; 1989.
- Juutilainen J, Lang S, Rytomaa T. Possible cocarcinogenic effects of ELF electromagnetic fields may require repeated long-term interaction with known carcinogenic factors. *Bioelectromagnetics* 2000;21(2):122–8.
- Juutilainen J, Kumlin T, Naarala J. Do extremely low frequency magnetic fields enhance the effects of environmental carcinogens? A meta-analysis of experimental studies. *Int J Radiat Biol* 2006;82(1):1–12. <http://dx.doi.org/10.1080/09553000600577839>.
- Kheifets LI, Shmikhada R. Childhood leukemia and EMF: review of the epidemiologic evidence. *Bioelectromagnetics* 2005;Suppl. 7:S51–9.
- Kheifets LI, Afifi AA, Shmikhada R. Public health impact of extremely low-frequency electromagnetic fields. *Environ Health Perspect* 2006;114:1532–7.
- Kheifets LI, Afifi AA, Monroe J, Swanson J. Exploring exposure-response for magnetic fields and childhood leukemia. *J Expo Anal Environ Epidemiol* 2010a;1–9. <http://dx.doi.org/10.1038/jes.2010.38>.
- Kheifets LI, Ahlbom A, Crespi CM, Draper G, Hagihara J, Lowenthal RM, et al. Pooled analysis of recent studies on magnetic fields and childhood leukaemia. *Br J Cancer* 2010b;103:1128–35. <http://dx.doi.org/10.1038/sj.bjc.6605838>.
- Kheifets LI, Swanson J, Kandel S, Malloy TF. Risk governance for mobile phones, power lines, and other EMF technologies. *Risk Anal* 2010c;30(10):1481–94. <http://dx.doi.org/10.1111/j.1539-6924.2010.01467.x>.
- Lagroye I, Percherancier Y, Juutilainen J, De Gannes FP, Veyret B. ELF magnetic fields: animal studies, mechanisms of action. *Prog Biophys Mol Biol* 2011;107:369–73. <http://dx.doi.org/10.1016/j.pbiomolbio.2011.09.003>.
- Leitgeb N, Cech R, Schröttner J, Lehofer P, Schmidpeter U, Rampetsreiter M. Magnetic emission ranking of electrical appliances. A comprehensive market survey. *Radiat Prot Dosimetry* 2008;129(4):439–45. <http://dx.doi.org/10.1093/rpd/ncm460>.
- Leszczynski D, De Pomerai D, Koczan D, Stoll D, Franke H, Albar JP. Five years later: the current status of the use of proteomics and transcriptomics in EMF research. *Proteomics* 2012;12(15–16):2493–509. <http://dx.doi.org/10.1002/pmic.201200122>.
- Levin ML. The occurrence of lung cancer in man. *Acta Unio Int Contra Cancrum* 1953;9:531–41.
- Li M, Jones L, Gaillard C, Binnewies M, Ochoa R, Garcia E, et al. Initially disadvantaged, TEL-AML1 cells expand and initiate leukemia in response to irradiation and cooperating mutations. *Leukemia* 2013;27(7):1570–3. <http://dx.doi.org/10.1038/leu.2013.15>.
- Maclure M, Greenland S. Tests for trend and dose response: misinterpretations and alternatives. *Am J Epidemiol* 1992;135:96–104.
- Maslanyj MP, Lightfoot T, Schüz J, Sienkiewicz Z, McKinlay A. A precautionary public health protection strategy for the possible risk of childhood leukaemia from exposure to power frequency magnetic fields. *BMC Public Health* 2010;10:1–10.
- Merchant CJ, Renew DC, Swanson J. Exposures to power-frequency magnetic fields in the home. *J Radiol Prot* 1994;14:77–87.
- Mezei G, Kheifets LI. Selection bias and its implications for case-control studies: a case study of magnetic field exposure and childhood leukaemia. *Int J Epidemiol* 2006;35(2):397–406.
- Mezei G, Kheifets LI, Breslow N, EPRI, TransExpo Study Group. TransExpo: international study of childhood leukemia and residences near electrical transformer rooms – protocol 2010; 2010148.
- Michaelis J, Schüz J, Meinert R, Menger M, Grigat JP, Kaatsch P, et al. Childhood leukemia and electromagnetic fields: results of a population-based case-control study in Germany. *Cancer Causes Control* 1997;8:167–74.
- Mills KM, Kheifets LI, Nelson LM, Bloch D, Takemoto-Hambleton R, Kelsey JL. Reliability of proxy-reported and self-reported household appliance use. *Epidemiology* 2000;11(5):581–8.
- NIEHS. NIEHS report on health effects from exposure to power-line frequency electric and magnetic fields. Prepared in response to the 1992 Energy Policy; 1999. p. 1–80.
- Orsini N, Bellocco R, Greenland S. Generalized least squares for trend estimation of summarized dose-response data. *Stata J* 2006;6:40–57.
- Pelissari DM, Barbieri FE, Wunsch Filho V. Magnetic fields and acute lymphoblastic leukemia in children: a systematic review of case-control studies. *Cad Saude Publica* 2009;25(Suppl. 3):S441–52.
- Preece AW, Grainger P, Golding J, Kaune WT. Domestic magnetic field exposures in Avon. *Phys Med Biol* 1996;41:71–81.
- Röösli M, Jenni D, Kheifets LI, Mezei G. Extremely low frequency magnetic field measurements in buildings with transformer stations in Switzerland. *Sci Total Environ* 2011;409(18):3364–9. <http://dx.doi.org/10.1016/j.scitotenv.2011.05.041>.
- SCENIHR – Scientific Committee on Emerging and Newly Identified Health Risks. Health effects of exposure to EMF; 20091–28.
- Schüz J. Implications from epidemiologic studies on magnetic fields and the risk of childhood leukemia on protection guidelines. *Health Phys* 2007;92:642–8.
- Schüz J, Ahlbom A. Exposure to electromagnetic fields and the risk of childhood leukaemia: a review. *Radiat Prot Dosimetry* 2008;132:202–11. <http://dx.doi.org/10.1093/rpd/ncm270>.
- Schüz J, Bernd J, Rippin G, Brinkmann K, Michaelis J, Grigat JP, et al. Extremely low frequency magnetic fields in residences in Germany. Distribution of measurements, comparison of two methods for assessing exposure, and predictors for the occurrence of magnetic fields above background level. *Radiat Environ Biophys* 2000;39:233–40.
- Schüz J, Grigat JP, Brinkmann K, Michaelis J. Residential magnetic fields as a risk factor for childhood acute leukaemia: results from a German population-based case-control study. *Int J Cancer* 2001;91:728–35.
- Schüz J, Svendsen AL, Linet MS, McBride ML, Roman E, Feychting M, et al. Nighttime exposure to electromagnetic fields and childhood leukemia: an extended pooled analysis. *Am J Epidemiol* 2007;166:263–9. <http://dx.doi.org/10.1093/aje/kwm080>.
- Sinclair J, Weeks M, Butt A, Worthington JL, Akpan A, Jones N, et al. Proteomic response of *Schizosaccharomyces pombe* to static and oscillating extremely low-frequency electromagnetic fields. *Proteomics* 2006;6(17):4755–64. <http://dx.doi.org/10.1002/pmic.200500861>.
- Skotte JH. Exposure to power-frequency electromagnetic fields in Denmark. *Scand J Work Environ Health* 1994;20:132–8.
- StataCorp. Stata Statistical Software: Release 10. College Station, TX: StataCorp LP; 2007.

- SNBOSH. Low-frequency electric and magnetic fields: the precautionary principle for national authorities. Guidance for decision-makers; 19961–8.
- Swanson J, Kaune WT. Comparison of residential power-frequency magnetic fields away from appliances in different countries. *Bioelectromagnetics* 1999;20:244–54.
- Thuróczy, G., Gajšek, P., Wiart, J., Grellier, J., Samaras, T., & Ravazzani, P. (n.d.). Electromagnetic field (EMF) exposure assessment in Europe – part I: Low frequency Fields (50 Hz – 10 MHz). In press.
- Thuróczy G, Jánossy G, Nagy N, Bakos J, Szabó J, Mezei G. Exposure to 50Hz magnetic field in apartment buildings with built-in transformer stations in Hungary. *Radiat Prot Dosimetry* 2008;131:469–73. <http://dx.doi.org/10.1093/rpd/ncn199>.
- Tomitsch J, Dechant E, Frank W. Survey of electromagnetic field exposure in bedrooms of residences in lower Austria. *Bioelectromagnetics* 2010;31:200–8. <http://dx.doi.org/10.1002/bem.20548>.
- UK Childhood Cancer Study Investigators. The United Kingdom Childhood Cancer Study: objectives, materials and methods. *Br J Cancer* 2000a;82:1073–102. <http://dx.doi.org/10.1054/bjoc.1999.1045>.
- UK Childhood Cancer Study Investigators. Childhood cancer and residential proximity to power lines. *UK Childhood Cancer Study Investigators. Br J Cancer* 2000b;83(11):1573–80. <http://dx.doi.org/10.1054/bjoc.2000.1550>.
- van Tongeren MJA, Mee TJ, Whatmough P, Broad L, Maslanyj MP, Allen SG, et al. Assessing occupational and domestic ELF magnetic field exposure in the UK Adult Brain Tumour Study: results of a feasibility study. *Radiat Prot Dosimetry* 2004;108:227–36. <http://dx.doi.org/10.1093/rpd/nch030>.
- Vulevic B, Osmokrovic P. Survey of ELF magnetic field levels in households near overhead power lines in Serbia. *Radiat Prot Dosimetry* 2011;145(4):385–8. <http://dx.doi.org/10.1093/rpd/ncq439>.
- WHO. *Environmental health criteria 238 – extremely low frequency fields*; 20071–543.