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

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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.

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)).

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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 $0 \leq 15$ 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 ($\geq$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