

Occupational Exposure to Extremely Low-Frequency Magnetic Fields and Risk of Amyotrophic Lateral Sclerosis: Results of a Feasibility Study for a Pooled Analysis of Original Data

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Previous meta-analyses have suggested an increased risk of amyotrophic lateral sclerosis (ALS) associated with occupational exposure to extremely low-frequency magnetic fields (ELF-MF). However, results should be interpreted with caution since studies were methodologically heterogeneous. Here, we assessed the feasibility of a pooling study to harmonize and re-analyze available original data. A systematic literature search was conducted. Published epidemiological studies were identified in PubMed and EMF-Portal from literature databases' inception dates until January 2019. The characteristics of all studies were described, including exposure metrics, exposure categories, and confounders. A survey among the principal investigators (PI) was carried out to assess their willingness to provide their original data. The statistical power of a pooling study was evaluated. We identified 15 articles published between 1997 and 2019. Studies differed in terms of outcome, study population, exposure assessment, and exposure metrics. Most studies assessed ELF-MF as average magnetic flux density per working day; however, exposure categories varied widely. The pattern of adjustment for confounders was heterogeneous between studies, with age, sex, and socioeconomic status being most frequent. Eight PI expressed their willingness to provide original data. A relative risk of ≥ 1.14 for ALS and occupational exposure to ELF-MF can be detected with a power of more than 80% in a pooled study. The pooling of original data is recommended and could contribute to a better understanding of ELF-MF in the etiology of ALS based on a large database and reduced heterogeneity due to a standardized analysis protocol with harmonized exposure metrics and exposure categories. *Bioelectromagnetics*. 2021;42:271–283. © 2021 Bioelectromagnetics Society.

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INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease with an incidence of 1.7–2.3 per 100,000 person-years in the general population [Logroscino and Piccininni, 2019]. ALS, the most common motor neuron disease (MND) comprising over 90% of all MND, affects the upper and lower motor neurons and is so far incurable [Gordon, 2011; Bozzoni et al., 2016]. About 10% of ALS cases are hereditary, while the majority are sporadic [Rowland and Shneider, 2001]. The etiology of the disease is still unknown, although

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a number of environmental factors are discussed [Belbasis et al., 2016].

A meta-analysis on ALS and residential exposure to extremely low-frequency magnetic fields (ELF-MF) [Röösli and Jalilian, 2018] included 5 studies, which evaluated the risk of ALS in association with exposure to overhead power lines. No increased risk was found for participants with the highest exposure. In contrast, a meta-analysis on occupational exposure to ELF-MF of Zhou et al. [2012] indicated a moderate statistically significant increased relative risk (RR: 1.45; 95% confidence interval [CI]: 1.15–1.84). This meta-analysis combined the results from 12 studies with an exposure estimation based on job titles. However, when quantitative data of ELF-MF were analyzed, estimated, e.g., by job-exposure matrices (JEM), the RR was not statistically significant (RR: 1.09; 95% CI: 0.82–1.43). An extended meta-analysis of Vergara et al. [2013], including four additional studies, showed similar results. The most recent meta-analysis of Huss et al. [2018] included further newly published studies from Sweden [Fischer et al., 2015], Switzerland [Huss et al., 2015], Denmark [Pedersen et al., 2017], the United States [Vergara et al., 2015a], and the Netherlands [Koeman et al., 2017]. The pooled estimate indicated a slightly increased risk (RR: 1.14; 95% CI: 1.00–1.30), comparing individuals with high exposure to ELF-MF to those with average or low exposure. However, Huss et al. [2018] identified high heterogeneity ($I^2 = 74.9\%$, $P = 0.000$) between studies. Zhou et al. [2012] also observed heterogeneity between the included studies ($I^2 = 58.9\%$, $P = 0.001$), and Vergara et al. [2013] hypothesized that methodological differences like different exposure assessment methods could be attributed to heterogeneity. Furthermore, heterogeneous cut-off points and thus different definitions of exposure categories could attribute to this heterogeneity [Zhou et al., 2012]. Therefore, the interpretation of meta-analyses with combined risk estimates based on different exposure categories is limited.

Huss et al. [2018] additionally concluded that the observed risks for ALS in analyses of “electrical occupations” might be related to electric shocks (ES) rather than ELF-MF exposure. The role of ES as a confounder for the observed association of ELF-MF and ALS is still not clear [Zhou et al., 2012]. Specific workplaces, namely in electrical occupations, seem to be associated with high exposure to ELF-MF and are accompanied by an increased risk for ES [Huss et al., 2013]. So far, it has been difficult to disentangle both exposures [Huss et al., 2018] because ES occurs unexpectedly [Huss et al., 2013].

The aim of this study was (i) to identify relevant studies on occupational exposure to ELF-MF and the risk of ALS with a systematic literature search, (ii) to describe characteristics of the included studies, and (iii) to evaluate the feasibility of a pooled analysis on occupational ELF-MF and ALS. For the feasibility of a pooling study, 2 major questions were addressed: (i) Is it possible to harmonize exposure data and confounders of the individual studies? (ii) Is it feasible to disentangle the effects of ELF-MF and ES on ALS? We conducted a survey among the principal investigators (PI) of the identified studies and evaluated the potential power of a pooled analysis based on the original data of previous studies provided by the PIs.

METHODS

Systematic Search

The systematic search was conducted according to the PRISMA statement [Moher et al., 2009]. The eligibility criteria were defined using the *Population, Exposure, Comparison, Outcome, Study design* (PECOS) strategy [National Toxicology Program, 2015]. Peer-reviewed articles published in English were included for the feasibility approach when they reported on men or women ≥ 18 years (P). Exposure was defined as exposure to occupational ELF-MF, especially in the power frequency range of 50 and 60 Hz, as quantitative exposure estimates in magnetic flux density in Tesla or Gauss (E). Exposed individuals were compared with a non- or low-exposed control group (C) for the risk of ALS or MND (O). Eligible study designs were epidemiological studies like case-control studies, cohort studies, or cross-sectional studies (S). Studies that reported ALS risks for job titles or residential exposure were excluded.

We conducted a systematic literature search in PubMed and the EMF-Portal (www.emf-portal.org), a specific database for studies on the health-related effects of electromagnetic fields. The search covered a timeframe from the literature databases' inception dates up to November 2018. A detailed description of the search terms is included in the Supplementary Appendix. After our initial systematic search, we updated our search in January 2019 by a nonsystematic screening for further potentially relevant studies in the EMF-Portal.

In the first stage of assessment, the titles and abstracts of the identified and potentially relevant articles were independently screened and assessed by two reviewers. Articles that failed to meet the inclusion criteria were excluded. For the abstracts that met the inclusion criteria, the full-text was retrieved and independently reviewed by the same reviewers in the second

stage of assessment. The two reviewers made a final decision about the inclusion of the articles. Whenever subgroups or overlaps of study populations were investigated in different publications, only the most recent publication with a complete follow-up was included. The data of relevant articles were extracted independently by two reviewers. The extraction protocol was defined and agreed upon before the start of the project. Extracted data included bibliographic data, country, study type, study size, study population, outcome information, information on exposure assessment, exposure metrics, and categories and information on confounders and risk estimates.

Assessment of the Feasibility of a Pooled Analysis

The PIs of the eligible studies were contacted in May 2019 to evaluate their willingness to provide their original data for pooling. We carried out a sample size calculation for a pooled nested case-control study, thus enabling the inclusion of participants from cohort studies and case-control studies within a joint pooling approach using the two different study designs available. The cases in the cohort and case-control studies sum up to the total of all cases in a pooled nested case-control study, whereas the controls are recruited in the cohort populations and control groups of the case-control studies. The required sample size was calculated to detect an effect size of ≥ 1.14 , which was reported in the meta-analysis of Huss et al. [2018], with a power of 80% ($\alpha = 0.05$, one-sided). For the sample size calculation of a pooled nested case-control study, we assumed that 5.25% of the controls are highly exposed [Peters et al., 2019]. We compared the results of the sample size calculation to the number of cases in all identified studies and to the number of cases from studies, where the PI had indicated a willingness to pool their data. The sample size calculation was not further stratified for additional subgroups (e.g., for methods of exposure assessment), as the overall study base for a pooled analysis was expected to be limited. Sample size calculations were conducted in R using the package *epiR* [Stevenson et al., 2020]. For the sample size calculations, we excluded a Swedish cohort study on ALS mortality by Feychting et al. [2003] due to potential overlap with cases in a newer Swedish cohort on ALS incidence by Fischer et al. [2015].

RESULTS

Study Selection and Description

The systematic search yielded 473 articles that matched the search criteria (Fig. 1). After the removal of duplicates, 396 articles were screened based on the

title and abstract, of which 317 studies were excluded because they did not match the basic eligibility criteria; among them, 34 articles were not written in English. Despite fulfilling our inclusion criteria of study design, exposure, and outcome, we excluded one article that was published in Danish [Johansen, 2001] as this study was also published in English [Johansen, 2000] and was included in our full-text screening. The full text of the remaining 79 articles was examined. Of these, 62 further articles were excluded, most of them due to the lack of quantitative exposure estimates. We identified 3 publications from Denmark [Johansen and Olsen, 1998a; Johansen, 2000; Pedersen et al., 2017] and 2 publications from the United Kingdom based on the same study population [Sorahan and Kheifets, 2007; Sorahan and Mohammed, 2014]. Therefore, we only considered the most recent publication from Denmark [Pedersen et al., 2017] and the most recent publication from the United Kingdom [Sorahan and Mohammed, 2014], both of which reported results from the longest follow-up. Due to the additional nonsystematic screening in the EMF-Portal after November 2018, we identified one additional relevant article published online in January 2019 [Peters et al., 2019]. Finally, 15 studies fulfilled the eligibility criteria and were included in the feasibility assessment.

The 15 studies were published between 1997 and 2019 and were based on study populations from 8 different countries. They included 10 cohort studies, of which one was analyzed as a nested case-control study [Fischer et al., 2015], and 5 case-control studies (Table 1). In total, 8,230,768 participants with 7,357 cases were investigated in the cohort studies. In the case-control studies, 13,896 cases and 61,651 controls were considered overall. An overview of risk estimates for the included studies is shown in the Appendix. Most studies (13/15) reported adjusted risk estimates. Two cohort studies reported both crude and adjusted risk estimates. Of them, no difference in the study results was seen in one cohort study [Fischer et al., 2015], while a lower risk estimate was observed after adjustment for age, sex, and education compared with the crude risk estimate in the other cohort study [Parlett et al., 2011].

The majority of all studies (11/15) investigated “mortality” as the outcome of interest (Table 1). One cohort study [Pedersen et al., 2017] and one case-control study reported on “incident cases” [Fischer et al., 2015], whereas 2 case-control studies reported on “prevalent cases” [Davanipour et al., 1997; Peters et al., 2019].

From a total of 10 cohort studies, 5 investigated occupational cohorts (Swiss railway employees

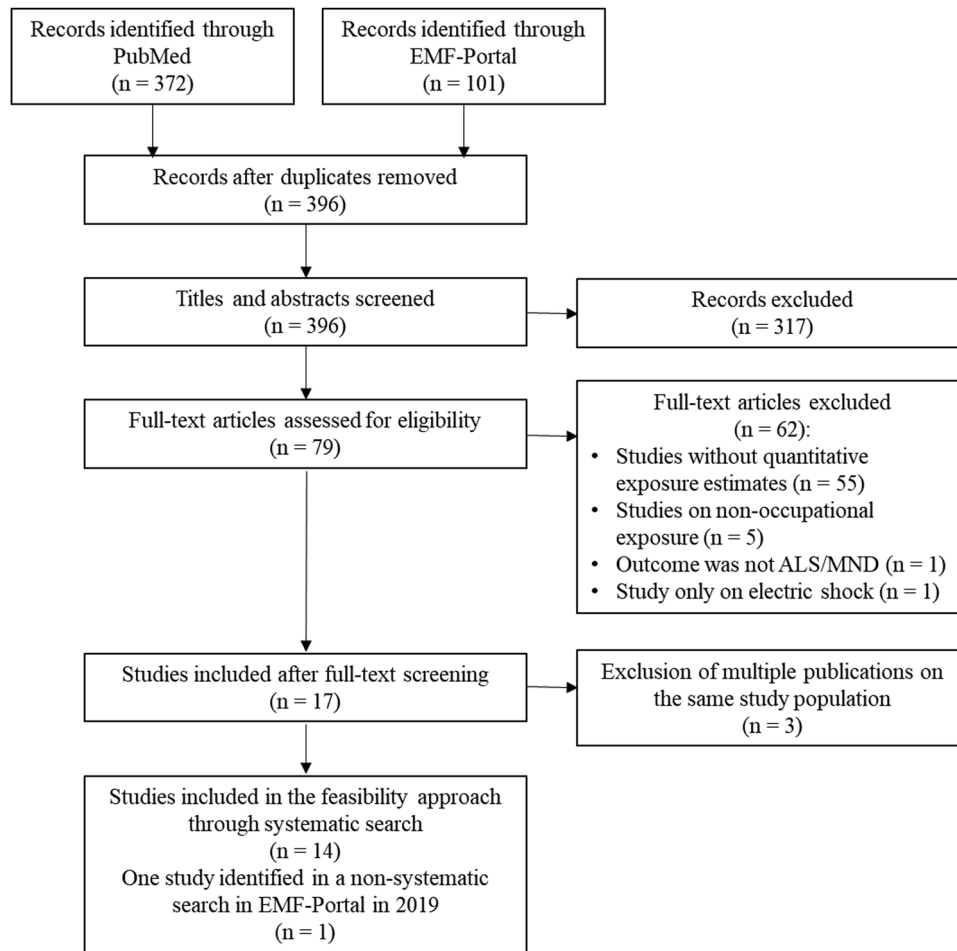


Fig. 1. PRISMA flow diagram of literature search, eligibility, and inclusion process (adapted from Moher et al., 2009). ALS = amyotrophic lateral sclerosis; MND = motor neuron disease.

[Röösli et al., 2007] and Swedish resistance welders [Hakansson et al., 2003], and electric utility workers from Denmark [Pedersen et al., 2017], the United Kingdom [Sorahan and Mohammed, 2014], and the United States [Savitz et al., 1998]. The remaining 5 cohorts were based on occupational information from the general population. Four of 5 case-control studies were population-based. One case-control study used clinical-based cases and blood and nonblood relatives as controls [Davanipour et al., 1997]. The most recent case-control study was a pooled study, combining data from Italy, Ireland, and the Netherlands [Peters et al., 2019].

The main method to assess occupational ELF-MF exposure was the application of JEMs (Table 2). Overall, 13 studies used different JEMs: the JEM by Bowman et al. [2007] ($n = 6$), the JEM developed by Floderus et al. [1996] ($n = 4$), and other JEMs ($n = 3$) [Kromhout et al., 1995; Johansen and

Olsen, 1998b; Renew et al., 2003]. Furthermore, in 2 studies, alternative approaches were used: measurements and modeling of the exposure for Swiss railway employees under real service conditions [Röösli et al., 2007] and the evaluation of the occupational history interrogated by an industrial hygienist [Davanipour et al., 1997]. Exposure was assessed by job titles from census data [Feychting et al., 2003; Hakansson et al., 2003; Parlett et al., 2011; Fischer et al., 2015; Huss et al., 2015], occupational history of employees from company records [Savitz et al., 1998; Röösli et al., 2007; Sorahan and Mohammed, 2014; Pedersen et al., 2017], job titles on death certificates [Noonan et al., 2002; Park et al., 2005; Vergara et al., 2015a], or questionnaires [Davanipour et al., 1997; Koeman et al., 2017; Peters et al., 2019].

Two different exposure metrics were used to quantify exposure to ELF-MF (Table 2). In 12 studies, average magnetic flux density in μT per working day

TABLE 1. Characteristics of the Included 15 Studies on Occupational Exposure to ELF-MF and ALS Sorted by Study Type

Author [publication year]	Country	Study type	Total and cases; number of cases and controls	Study population	Outcome
Pedersen et al. [2017]	Denmark	Retrospective cohort	Total: 32,006; cases: 44	Electric utility workers	Incidence
Fischer et al. [2015]	Sweden	Retrospective cohort ^a	Total: 28,044; cases: 4,709	General population	Incidence
Huss et al. [2015]	Switzerland	Retrospective cohort	Total: 2,167,046; cases: 237	General population	Mortality
Sorahan and Mohammed [2014]	United Kingdom	Retrospective cohort	Total: 73,051; cases: 86	Electric utility workers	Mortality
Röösli et al. [2007]	Switzerland	Retrospective cohort	Total: 20,141; cases: 15	Railway employees	Mortality
Håkansson et al. [2003]	Sweden	Retrospective cohort	Total: 646,694; cases: 97	Resistance welders	Mortality
Feychting et al. [2003]	Sweden	Retrospective cohort	Total: 4,812,646; cases: 1,965	General population	Mortality
Savitz et al. [1998]	United States	Retrospective cohort	Total: 139,905; cases: 28	Electric utility workers	Mortality
Koeman et al. [2017]	Netherlands	Prospective cohort	Total: 4,344; cases: 136	General population	Mortality
Parlett et al. [2011]	United States	Prospective cohort	Total: 306,891; cases: 40	General population	Mortality
Peters et al. [2019]	Netherlands/Ireland/Italy	Pooled case-control	Cases: 1,323; controls: 2,704	General population	Prevalence
Vergara et al. [2015a]	United States	Case-control	Cases: 5,886; controls: 57,667	General population	Mortality
Park et al. [2005]	United States	Case-control	Cases: 6,347; controls: not reported	General population	Mortality
Noonan et al. [2002]	United States	Case-control	Cases: 312; controls: 1,248	General population	Mortality
Davanipour et al. [1997]	United States	Case-control	Cases: 28; controls: 32	Clinical-based cases and family controls	Prevalence

ALS = amyotrophic lateral sclerosis; ELF-MF = extremely low-frequency magnetic field.

^aAnalyzed as a nested case-control study.

was provided. Three studies reported a cumulative exposure in μT -years [Savitz et al., 1998; Röösli et al., 2007; Sorahan and Mohammed, 2014]. Most of the studies reported the geometric mean (8/15) [Noonan et al., 2002; Feychting et al., 2003; Håkansson et al., 2003; Park et al., 2005; Fischer et al., 2015; Vergara et al., 2015a; Koeman et al., 2017; Peters et al., 2019], one study used the arithmetic mean [Parlett et al., 2011], and no information on the specification of the mean value was provided in 6 studies [Davanipour et al., 1997; Savitz et al., 1998; Röösli et al., 2007; Sorahan and Mohammed, 2014; Huss et al., 2015; Pedersen et al., 2017]. The exposure categories varied between the included studies. Whereas in studies that estimated the average exposure per working day, the reference categories ranged from <0.10 to $<0.2 \mu\text{T}$, and the highest exposure categories varied from >0.26 to $>1.0 \mu\text{T}$ (Fig. 2). In 2 studies that estimated the cumulative exposure, the reference categories varied from ≤ 0.59 to $<2.5 \mu\text{T}$ -years (>1.14 to $>20.0 \mu\text{T}$ -years for the highest exposure, respectively) (Table 2). For the study on Swiss railway employees, the mean cumulative lifetime exposure was reported. Station masters served as the reference category (median: $5.7 \mu\text{T}$ -years), and train drivers were defined as highly exposed (median: $120.5 \mu\text{T}$ -years) [Röösli et al., 2007].

Overall, we identified 11 different confounders, of which each was considered in at least 2 studies (Table 3). In all studies, results were adjusted for age and sex (however, in 4 studies, only men were included). The definition of socio-economic status (SES), the most frequent confounder after age and sex, varied largely between studies. For example, in one study, the SES was based on 2 categories only: blue-collar workers or others [Håkansson et al., 2003]. Another study used 3 broad occupational categories, without further information on the categories, to adjust for SES [Noonan et al., 2002]. A further study used 5 different categories for SES: white-collar, blue-collar, farmers, self-employed, and unclassified/missing, based on the occupational position stated in the census [Fischer et al., 2015].

Six of 15 studies provided information on the occurrence of ES among the study participants (Table 3). The study from Denmark [Pedersen et al., 2017] obtained data on occupation-related ES from the Danish Working Environment Authority and from an accident register. The other five studies used 3 different JEMs for estimating the risk of experiencing ES [Fischer et al., 2015; Huss et al., 2015; Vergara et al., 2015a; Koeman et al., 2017; Peters et al., 2019]. The risk for ES was categorized into low, medium, and high, depending on the occupation of the

TABLE 2. Exposure Information of the Included 15 Studies on Occupational Exposure to ELF-MF and ALS Sorted by Study Type as in Table 1

Author (publication year)	Exposure assessment	Information on occupation	Exposure metrics	Exposure categories (R/H)
Pedersen et al. [2017]	JEM	Occupational history from electric utility companies	Average per working day	R: < 0.1 μ T; H: \geq 1.0 μ T
Fischer et al. [2015]	JEM	Job title from the census in 1960, 1970, 1980, 1990	Average per working day	R: < 0.11 μ T; H: \geq 0.3 μ T
Huss et al. [2015]	JEM	Job title from the census in 1990 and 2000	Average per working day; Median intensity	R: 0.11 μ T; H: 0.52 μ T
Sorahan & Mohammed [2014]	JEM	Occupational history from electric utility companies	Cumulative lifetime exposure	R: < 2.5 μ T-years; H: > 20.0 μ T-years
Röösli et al. [2007]	Measurements and modeling	Occupational history from records of the Swiss railway company	Mean cumulative lifetime exposure	R: 5.7 μ T-years; H: 120.5 μ T-years
Hakanesson et al. [2003]	JEM	Job title from the census in 1980, 1985, 1990	Average per working day	R: < 0.16 μ T; H: > 0.53 μ T
Feychting et al. [2003]	JEM	Job title from the census in 1970 and 1980	Average per working day	R: < 0.11 μ T; H: \geq 0.5 μ T
Savitz et al. [1998]	JEM	Occupational history from electric utility companies	Cumulative exposure	R: \leq 0.59 μ T-years; H: > 1.14 μ T-years
Koeman et al. [2017]	JEM	Occupational history through a questionnaire	Average per working day	R: < 0.15 μ T; H: \geq 0.3 μ T
Parlett et al. [2011]	JEM	Job title from census	Average per working day	R: < 0.16 μ T; H: > 0.27 μ T
Peters et al. [2019]	JEM	Occupational history through a questionnaire	Average per working day	R: < 0.15 μ T; H: \geq 0.3 μ T
Vergara et al. [2015a]	JEM	Job title from death certificate	Average per working day	R: < 0.1 μ T; H: \geq 0.3 μ T
Park et al. [2005]	JEM	Job title from death certificate	Average per working day	R: < 0.10 μ T; H: > 0.9 μ T
Noonan et al. [2002]	JEM	Job title from death certificate	Average per working day	R: < 0.10 μ T; H: \geq 0.30 μ T
Davanipour et al. [1997]	By industrial hygienist	Occupational history through a questionnaire	Average per working day	R: < 0.2 μ T; H: > 1.0 μ T

ALS = amyotrophic lateral sclerosis; ELF-MF = extremely low-frequency magnetic field; H = lowest value of the highest exposure category; JEM = job-exposure matrix; R = highest value of the reference category.

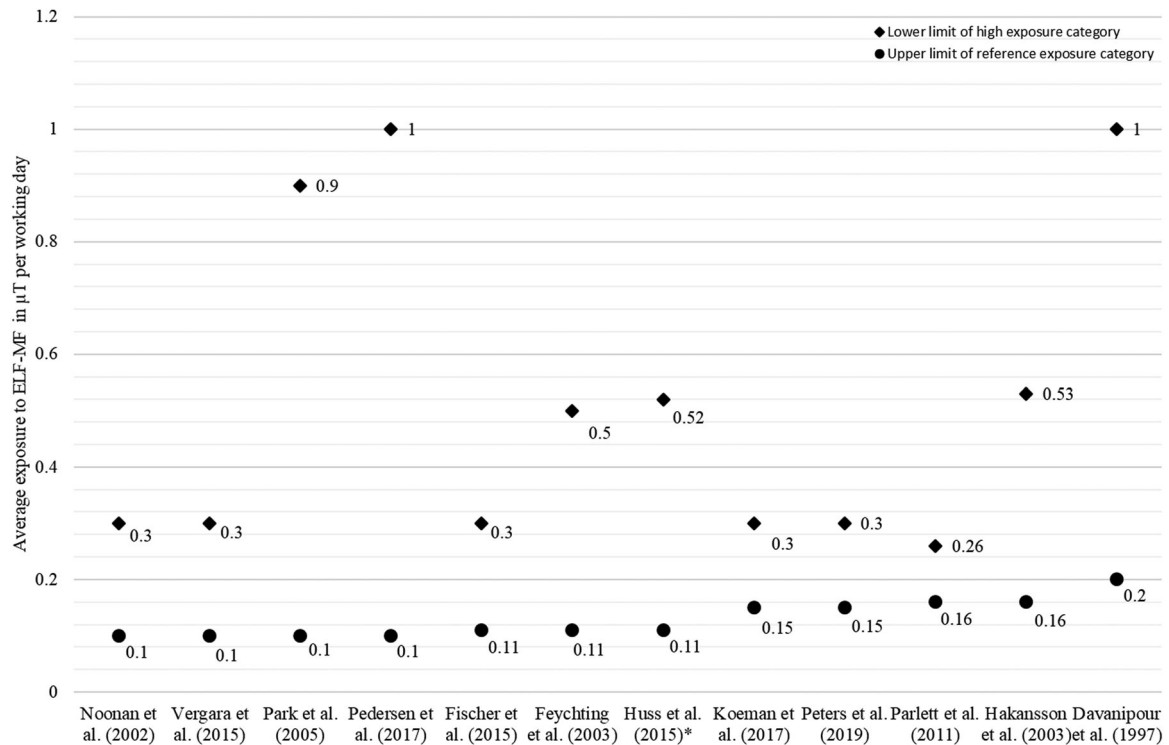


Fig. 2. Upper limit of reference exposure categories and lower limit of high exposure categories for the 12 studies on the risk of ALS using the metric average exposure to ELF-MF in μT per working day sorted by lowest to a highest reference category. ALS = amyotrophic lateral sclerosis; ELF-MF = extremely low-frequency magnetic field.

participant. Three studies [Fischer et al., 2015; Huss et al., 2015; Koeman et al., 2017] used the JEM by Huss et al. [2013], which considers 116 different occupations. One study [Vergara et al., 2015a] applied the JEM developed by Vergara et al. [2012], based on 501 different occupations, and Fischer et al. [2015] used an updated version of a JEM by Vergara et al [2015b].

Assessment of the Feasibility of a Pooled Analysis

A total of 13 PIs responded to our survey. From these, the PIs of 6 cohorts (6/10) and 2 case-control studies (2/5) declared their willingness to provide the original data for a pooling study. Some PIs would prefer to be actively involved in a potential future project in terms of developing the study protocol for data analysis in addition to providing the original data. A few PIs pointed out that the relocation and transfer of data may be difficult due to the fact that some studies were conducted more than 15 years ago. A need for financial support was also emphasized.

The 8 studies with positive feedback about providing original data showed methodological differ-

ences. Nearly all studies used JEMs (7/8) to assess occupational exposure, whereas only one study used measurements and modeling. For those studies that investigated the risk for ALS in a specific occupational setting (e.g., electric utility workers), the occupational history from company records was used, while for population-based studies, information on occupation was retrieved from a few points in time (census data). Regarding confounders, all studies except one had available information on age, sex, and SES or education. Information on ES was assessed in 3 studies.

Our sample size calculation for a pooled nested case-control study showed that a total of 10,313 cases and 20,626 controls with a 1:2 matching must be included in a pooled nested case-control study to observe an effect size of ≥ 1.14 with a power of 80%. A 1:3 matching would result in 9,195 cases and 27,585 controls, and a 1:4 matching in 8,635 cases and 35,530 controls. When including data from all studies identified by our systematic search, 19,288 cases could be included in such a pooled analysis. In comparison, if only studies were considered for which the PIs would provide original data, 11,080 cases

TABLE 3. Reported Confounders^a in the 15 Included Studies on Occupational Exposure to ELF-MF and ALS Sorted by Study Type as in Table 1

Author (Year)	Age	Sex	SES	Education	ES	Ethnicity	Solvents	Pesticides	Metals	Marital status	Smoking
Pedersen et al. [2017]	✓	✓			✓						
Fischer et al. [2015]	✓	✓	✓	✓	✓						
Huss et al. [2015]	✓	✓	✓	✓	✓		✓	✓	✓	✓	
Sorahan and Mohammed [2014]	✓	✓	✓								
Rööslı et al. [2007]	✓	n.a.									
Hakansson et al. [2003]	✓	✓	✓								
Feychting et al. [2003]	✓	✓	✓								
Savitz et al. [1998]	✓	n.a.	✓			✓	✓				
Koeman et al. [2017]	✓	✓		✓	✓		✓	✓	✓		✓
Parlett et al. [2011]	✓	✓		✓	✓	✓				✓	
Peters et al. [2019]	✓	✓		✓	✓		✓	✓	✓		✓
Vergara et al. [2015a]	✓	n.a.		✓	✓	✓					
Park et al. [2005]	✓	✓	✓			✓		✓			
Noonan et al. [2002]	✓	n.a.	✓	✓		✓	✓				
Davanipour et al. [1997]	✓	✓	✓	✓							

ALS = amyotrophic lateral sclerosis; ELF-MF = extremely low-frequency magnetic field; ES = electric shock; n.a. = not applicable; SES = socio-economic status.

^aConfounders that were considered in at least 2 studies.

could be included. These results showed that there would be a sufficient number of participants for both scenarios to detect an effect of ≥ 1.14 with a power of $>80\%$, even if a pooling study is based on only those PIs with a positive attitude to such an analysis.

DISCUSSION

Brief Summary

Overall, 15 studies on occupational exposure to ELF-MF and ALS published between 1997 and 2019 were included in our feasibility assessment. The studies differed in terms of outcome, exposure assessment, exposure metrics, and categories as well as considered confounders. Based on the 8 studies whose PIs would agree to provide data for a combined analysis, it is feasible to detect an effect size of ≥ 1.14 with a power of 80% within the approach of a pooled nested case-control study.

Heterogeneity in a Pooled Analysis: Data Harmonization

All studies investigated the incidence, mortality, or prevalence. ALS is a disease with high case fatality rates and leads to death within 2–5 years after diagnosis [Mehta et al., 2014]. For this reason, combining these endpoints is a reasonable approach within a pooled nested case-control study.

The underlying mechanism by which ELF-MF might have an impact on health effects is still

unknown. Therefore, the definitive metric to estimate the exposure is still not certain [Kheifets et al., 2009]. The majority of the 15 studies estimated “exposure per working day” and 3 studies “cumulative exposure.” In a pooled analysis, the exposure metric “cumulative exposure” could be converted to “exposure per working day” if not already available in the original data. First, the ratio of exposure as cumulative $\mu\text{T-years}$ and the number of exposed years needs to be calculated. Second, the resulting value needs to be divided by, e.g., 250 days for the United Kingdom, which corresponds to the number of working days per year for a full-time job [Sorahan and Mohammed, 2014].

Compared with guidelines for limiting the exposure to time-varying electric and magnetic fields by the International Commission on Non-Ionizing Radiation Protection (ICNIRP), the observed exposure levels in the considered 15 epidemiological studies are, in general, rather low. The ICNIRP defined an exposure limit of $1,000 \mu\text{T}$ (50/60 Hz) for 8 h per working day for the occupational setting [International Commission on Non-Ionizing Radiation Protection, 2010]. The highest reported exposure category in the included studies started at $1.0 \mu\text{T}$, which is only 0.1% compared with the ICNIRP limits. However, exposure categories varied substantially in the identified studies, which is especially true for the highly exposed group. A meta-analysis is based on published risk estimates with varying exposure categories between the different studies. In contrast, a pooling study with

original data allows the exposure categories to be harmonized. This enables a more solid risk analysis based on a larger database [Vergara et al., 2013; Zhou et al., 2012; Huss et al., 2018]. Uniform exposure categories could be defined a priori in a protocol for a pooling approach, and the original data could be fitted to these categories. Another possibility to harmonize the original data is calculating the quantiles of exposure for all available data and using these quantiles as exposure categories for the pooled analysis.

In a pooling study, a basic adjustment for age and sex is possible. This is also feasible for other important information that was not explicitly mentioned as a confounder in the original studies, e.g., time of exposure. Adjusting for the time of exposure in a pooling study would account for possible general changes in exposure levels in the population over time, due to, e.g., the use of novel technical equipment and appliances at work. To cope with studies that used different definitions for the same confounder, standardized harmonization procedures should be applied. For example, SES (reported in 5 of the 8 studies with positive response) is defined differently in the included studies. The definitions vary in terms of complexity. The studies with the smallest number of categories for SES would define how complex the construct of SES could be. This means that SES would be harmonized as a dichotomous variable. In a study without data on SES, data on education could be transferred into an approximation of the SES to enlarge the set of studies adjusting for SES [Galobardes et al., 2006; Shavers, 2007]. However, adjusting for additional variables might be limited due to a lack of further overlapping confounders (Table 3).

A major question of our feasibility study was the possibility of disentangling the effect of ELF-MF and ES. However, among those 8 PIs who would be willing to provide original data, only 2 cohorts and one case-control study assessed ES. A cohort study from Sweden [Pedersen et al., 2017] assessed ES as a dichotomous variable, giving information on whether a participant did or did not experience ES. Another cohort study [Fischer et al., 2015] and a case-control study [Vergara et al., 2015a] estimated the risk for ES via a JEM and classified the risk levels into low, medium, and high category. Data from the 2 studies that estimated the risk for ES via JEMs could be used for a stratified analysis among participants with a high risk versus participants with low risk for ES. Additionally, the risk for ES could be included as a confounder in regression analyses. Nevertheless, the general occurrence of ES is expected to be low. This can influence the specificity of a JEM in terms of

exposure classification [Vergara et al., 2012], which limits the precision of exposure estimation via a JEM for ES. Hence, an analysis to disentangle the effect of ELF-MF and ES does not seem promising within a pooling study due to a lack of studies with similar exposure assessment of ES and the limited precision of estimates via a JEM.

Strength and Limitations of a Pooled Analysis

The 15 studies included in our feasibility assessment have been carried out independently by different research groups and did not follow a standardized protocol. Therefore, data harmonization is a key element for a pooled analysis [Metayer et al., 2013; Tikellis et al., 2018] and a challenge at the same time [Schaap et al., 2011]. The process of data harmonization could be carried out in a data coordination center, similar to other international pooling projects [Schaap et al., 2011; Metayer et al., 2013; Tikellis et al., 2018]. Participating PIs would send all relevant data with variables and value labels to this data coordination center. The coordination center would be responsible for developing a harmonized data set based on a protocol agreed to by all PIs. The protocol should also contain an elaborated statistical analysis plan and data sharing and authorship agreements [Hofer and Piccinin, 2009]. Further important points in terms of data sharing that should be addressed early in the course of such a pooling project are the legal regulations in the cooperating countries and the General Data Protection Regulation (GDPR) [van Veen, 2018].

The main advantage of a pooled analysis is the increased statistical power due to the large sample size leading to more precise risk estimates [Lesko et al., 2018]. As differences in statistical risk analysis methods in the original studies can hamper the comparability of the results of the single studies, using a unified statistical analysis method for the pooled data is a further strength [Hofer and Piccinin, 2009].

After a harmonized data set has been established, information from potential future studies on ELF-MF and ALS could be added to enlarge the data set. All collaborative researchers who provide original data should have the opportunity to suggest new research questions. Therefore, a harmonized data set provides opportunities for reproducible research and validation [Munafò et al., 2017] and options to potentially develop a research platform for future projects based on established cooperation across different countries.

Despite extensive harmonization efforts in a pooled study, the data for analysis depends on the

quality of the original data. Seven out of 8 studies with a positive response regarding a pooled analysis used a JEM for exposure estimation. JEMs are in general superior to more simplistic approaches like the use of job titles, such as “electrical occupations” [Gobba et al., 2011], as a JEM is based on the time-weighted average (TWA) levels measured at work for specific occupations in a sample population and allows for a retrospective exposure assessment for large population size. A JEM provides a quantitative exposure estimate for certain jobs of interest, which enables the quantification of variation within and between job groups and the investigation of a potential dose-response relationship [Ahlbom et al., 2001]. Nevertheless, exposure estimates based on JEMs are at risk of misclassification in epidemiological studies due to several limitations: the individual occupational exposure to ELF-MF depends on various factors, including magnetic field sources, the average strength of the sources, and the proportion of time spent at different locations and sources. Hence, the individual exposure might differ compared with the average exposure in an occupational group [Kheifets et al., 2009]. Occupation might not be the main determinant of exposure to ELF-MF [Kheifets et al., 2009]. Therefore, misclassification might also be introduced due to exposures other than occupational exposure. Occupational exposure was reported to account for approximately 60% of 24-h exposure, while 40% of 24-h exposure was observed during periods spent at home or outside [Gobba et al., 2011]. Additionally, the accuracy of a JEM depends on the validity of the occupational information [Merletti et al., 2014]. In 2 of the 8 studies, information on occupation was derived from census data. In 2 further studies, information on the main occupation listed on death certificates was used. Complete occupational history, that is, information on all occupations held by the study participants from baseline to the end of the observational period, was assessed in the remaining 4 studies using occupational records. Information on a single point in time is thought to be less valid than a complete occupational history.

Furthermore, in addition to exposure to ELF-MF and ES, electric fields also might play a role in the occupational setting in the context of ALS [Kheifets et al., 2009]. Elevated electric field exposure can occur in the electricity supply sector close to unshielded high-voltage conductors or near high-voltage transmission lines or exposed busbars in substations [Kheifets et al., 2009]. The maximum electric field strength reported at the workplace can be as high as 47 kV/m [Korpinen et al., 2009]. These elevated electric fields induce a greater current in the

body than elevated magnetic fields; therefore, assessment of the TWA of these electric fields in the occupational setting would also be of interest [Kheifets et al., 2009], but none of the included studies assessed this exposure. The same applies to alternative magnetic field exposure metrics. All 8 studies relied on TWA. Other proposed metrics, which might be more biologically relevant, like, e.g., the induced current in the body or combinations of the alternating current and direct current [Kheifets et al., 2009], are not reported.

A further limitation might be that PIs of only 8 out of 15 studies would provide their original data. Not including all available data in a pooled analysis and therefore potentially missing out on essential scientific evidence could introduce bias to the results of such a pooling study. For this reason, sufficient methods for including published data from those studies that do not provide original data should be applied in sensitivity analyses.

Finally, our feasibility approach was limited to information published in articles. This involves some risk that the reported information could be misunderstood by us. At the same time, it is possible that the original data contain further important information and variables on, e.g., exposure characteristics, which we have not considered in this feasibility approach but could be included once the original data are available. Additionally, the comprehensiveness of the selection of studies for our feasibility approach might be affected by our language restriction in the systematic search. Also, a study by Morrison et al. [2012] found no evidence of a systematic bias when applying language restrictions for systematic reviews in the field of medicine.

CONCLUSION

Our systematic search yielded 10 cohort studies and 5 case-control studies on occupational exposure to ELF-MF and ALS. In a survey, the PIs of 6 cohorts, including 4 specific occupational cohorts and 2 case-control studies, expressed their willingness to provide original data for a pooled analysis. Based on the possibilities of data harmonization, a combined data set with a sufficient number of participants to show an effect size of 1.14 with a power of 80% on the association of occupational exposure to ELF-MF and ALS could be established. Therefore, we recommend conducting a pooled analysis of original data. However, a meaningful analysis to disentangle the effects of ES and ELF-MF on ALS does not seem feasible. Furthermore, in the context of a reproducibility crisis in science [Ioannidis, 2018], a pooled

analysis with original data using uniform methods to analyze the data is an important contribution to transparency and verifiability of study results. The next step toward such a pooled analysis is to establish a study protocol together with the PIs.

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REFERENCES

- Ahlbom IC, Cardis E, Green A, Linet M, Savitz D, Swerdlow A. 2001. Review of the epidemiologic literature on EMF and health. *Environ Health Perspect* 109(Suppl 6):911–933.
- Belbasis L, Bellou V, Evangelou E. 2016. Environmental risk factors and amyotrophic lateral sclerosis: An umbrella review and critical assessment of current evidence from systematic reviews and meta-analyses of observational studies. *Neuroepidemiology* 46:96–105.
- Bowman JD, Touchstone JA, Yost MG. 2007. A population-based job exposure matrix for power-frequency magnetic fields. *J Occup Environ Hyg* 4:715–728.
- Bozzoni V, Pansarasa O, Diamanti L, Nosari G, Cereda C, Ceroni M. 2016. Amyotrophic lateral sclerosis and environmental factors. *Funct Neurol* 31:7–19.
- Davanipour Z, Sobel E, Bowman JD, Qian Z, Will AD. 1997. Amyotrophic lateral sclerosis and occupational exposure to electromagnetic fields. *Bioelectromagnetics* 18:28–35.
- Feychting M, Jonsson F, Pedersen NL, Ahlbom A. 2003. Occupational magnetic field exposure and neurodegenerative disease. *Epidemiology* 14:413–419.
- Fischer H, Kheifets L, Huss A, Peters TL, Vermeulen R, Ye W, Fang F, Wiebert P, Vergara XP, Feychting M. 2015. Occupational exposure to electric shocks and magnetic fields and amyotrophic lateral sclerosis in Sweden. *Epidemiology* 26:824–830.
- Floderus B, Persson T, Stenlund C. 1996. Magnetic-field exposures in the workplace: Reference distribution and exposures in occupational groups. *Int J Occup Environ Health* 2:226–238.
- Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey, Smith G. 2006. Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 60:7–12.
- Gobba F, Bravo G, Rossi P, Contessa GM, Scaringi M. 2011. 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* 21:634–645.
- Gordon PH. 2011. Amyotrophic lateral sclerosis. *CNS Drugs* 25:1–15.
- Hakansson N, Gustavsson P, Johansen C, Floderus B. 2003. Neurodegenerative diseases in welders and other workers exposed to high levels of magnetic fields. *Epidemiology* 14:420–426.
- Hofer SM, Piccinin AM. 2009. Integrative data analysis through coordination of measurement and analysis protocol across independent longitudinal studies. *Psychol Methods* 14:150–164.
- Huss A, Peters S, Vermeulen R. 2018. Occupational exposure to extremely low-frequency magnetic fields and the risk of ALS: A systematic review and meta-analysis. *Bioelectromagnetics* 39:156–163.
- Huss A, Spoerri A, Egger M, Kromhout H, Vermeulen R. 2015. Occupational exposure to magnetic fields and electric shocks and risk of ALS: The Swiss national cohort. *Amyotroph Lateral Scler Frontotemporal Degener* 16:80–85.
- Huss A, Vermeulen R, Bowman JD, Kheifets L, Kromhout H. 2013. Electric shocks at work in Europe: Development of a job exposure matrix. *Occup Environ Med* 70:261–267.
- International Commission on Non-Ionizing Radiation Protection. 2010. Guidelines for limiting exposure to time-varying electric and magnetic fields (1 Hz to 100 kHz). *Health Phys* 99:818–836.
- Ioannidis JPA. 2018. Meta-research: Why research on research matters. *PLOS Biol* 16:e2005468.
- Johansen C. 2000. Exposure to electromagnetic fields and risk of central nervous system disease in utility workers. *Epidemiology* 11:539–543.
- Johansen C. 2001. [Exposure to electromagnetic fields and risk of central nervous system diseases among employees at Danish electric companies]. *Ugeskr Laeger* 164:50–54, in Danish.
- Johansen C, Olsen J. 1998a. Mortality from amyotrophic lateral sclerosis, other chronic disorders, and electric shocks among utility workers. *Am J Epidemiol* 148:362–368.
- Johansen C, Olsen JH. 1998b. Risk of cancer among Danish utility workers—A nationwide cohort study. *Am J Epidemiol* 147:548–555.
- Kheifets L, Bowman JD, Checkoway H, Feychting M, Harrington JM, Kavet R, Marsh G, Mezei G, Renew DC, van Wijngaarden E. 2009. Future needs of occupational epidemiology of extremely low frequency electric and magnetic fields: Review and recommendations. *Occup Environ Med* 66:72–80.
- Koeman T, Slotje P, Schouten LJ, Peters S, Huss A, Veldink JH, Kromhout H, van den Brandt PA, Vermeulen R. 2017. Occupational exposure and amyotrophic lateral sclerosis in a prospective cohort. *Occup Environ Med* 74:578–585.
- Korpinen LH, Elovaara JA, Kuisti HA. 2009. Evaluation of current densities and total contact currents in occupational exposure at 400 kV substations and power lines. *Bioelectromagnetics* 30:231–240.
- Kromhout H, Loomis DP, Mihlan GJ, Peipins LA, Kleckner RC, Iriye R, Savitz DA. 1995. Assessment and grouping of occupational magnetic field exposure in five electric utility companies. *Scand J Work Environ Health* 21:43–50.

- Lesko CR, Jacobson LP, Althoff KN, Abraham AG, Gange SJ, Moore RD, Modur S, Lau B. 2018. Collaborative, pooled and harmonized study designs for epidemiologic research: Challenges and opportunities. *Int J Epidemiol* 47:654–668.
- Logroscino G, Piccininni M. 2019. Amyotrophic lateral sclerosis descriptive epidemiology: The origin of geographic difference. *Neuroepidemiology* 52:93–103.
- Mehta P, Antao V, Kaye W, Sanchez M, Williamson D, Bryan L, Muravov O, Horton K. 2014. Prevalence of amyotrophic lateral sclerosis—United States 2010–2011. *MMWR Suppl* 63:1–14.
- Merletti F, Mirabelli D, Richiardi L. 2014. Occupational epidemiology. In: Ahrens W, Pigeot I, editor. *Handbook of Epidemiology*. New York, NY: Springer New York, pp 1577–1609.
- Metayer C, Milne E, Clavel J, Infante-Rivard C, Petridou E, Taylor M, Schüz J, Spector LG, Dockerty JD, Magnani C, Pombo-de-Oliveira MS, Sinnott D, Murphy M, Roman E, Monge P, Ezzat S, Mueller BA, Scheurer ME, Armstrong BK, Birch J, Kaatsch P, Koifman S, Lightfoot T, Bhatti P, Bondy ML, Rudant J, O'Neill K, Miligi L, Dessypris N, Kang AY, Buffler PA. 2013. The childhood leukemia international consortium. *Cancer Epidemiol* 37:336–347.
- Moher D, Liberati A, Tetzlaff J, Altman DG. 2009. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLOS Med* 6:e1000097.
- Morrison A, Polisen J, Husereau D, Moulton K, Clark M, Fiander M, Mierzwinski-Urban M, Clifford T, Hutton B, Rabb D. 2012. The effect of English-language restriction on systematic review-based meta-analyses: A systematic review of empirical studies. *Int J Technol Assess Health Care* 28:138–144.
- Munafò MR, Nosek BA, Bishop DVM, Button KS, Chambers CD, Percie du Sert N, Simonsohn U, Wagenmakers E-J, Ware JJ, Ioannidis JPA. 2017. A manifesto for reproducible science. *Nat Hum Behav* 1:0021.
- National Toxicology Program. 2015. Handbook for conducting a literature-based health assessment using OHAT approach for systematic review and evidence integration. Office of Health Assessment and Translation. Available from <https://ntp.niehs.nih.gov/whatwestudy/assessments/noncancer/handbook/index.html> [Last accessed 8 March 2021].
- Noonan CW, Reif JS, Yost M, Touchstone J. 2002. Occupational exposure to magnetic fields in case-referent studies of neurodegenerative diseases. *Scand J Work Environ Health* 28:42–48.
- Park RM, Schulte PA, Bowman JD, Walker JT, Bondy SC, Yost MG, Touchstone JA, Dosemeci M. 2005. Potential occupational risks for neurodegenerative diseases. *Am J Ind Med* 48:63–77.
- Parlett LE, Bowman JD, van Wijngaarden E. 2011. Evaluation of occupational exposure to magnetic fields and motor neuron disease mortality in a population-based cohort. *J Occup Environ Med* 53:1447–1451.
- Pedersen C, Poulsen AH, Rod NH, Frei P, Hansen J, Grell K, Raaschou-Nielsen O, Schüz J, Johansen C. 2017. Occupational exposure to extremely low-frequency magnetic fields and risk for central nervous system disease: An update of a Danish cohort study among utility workers. *Int Arch Occup Environ Health* 90:619–628.
- Peters S, Visser AE, D'Ovidio F, Beghi E, Chiò A, Logroscino G, Hardiman O, Kromhout H, Huss A, Veldink J, Vermeulen R, van den Berg LH. 2019. Electric shock and extremely low-frequency magnetic field exposure and the risk of ALS: Euro-motor. *Am J Epidemiol* 188:295–299.
- Renew DC, Cook RF, Ball MC. 2003. A method for assessing occupational exposure to power-frequency magnetic fields for electricity generation and transmission workers. *J Radiol Prot* 23:279–303.
- Röösli M, Jalilian H. 2018. A meta-analysis on residential exposure to magnetic fields and the risk of amyotrophic lateral sclerosis. *Rev Environ Health* 33:295–299.
- Röösli M, Lörtscher M, Egger M, Pfluger D, Schreier N, Lörtscher E, Locher P, Spoerri A, Minder C. 2007. Mortality from neurodegenerative disease and exposure to extremely low-frequency magnetic fields: 31 years of observations on Swiss railway employees. *Neuroepidemiology* 28:197–206.
- Rowland LP, Shneider NA. 2001. Amyotrophic lateral sclerosis. *N Engl J Med* 344:1688–1700.
- Savitz DA, Checkoway H, Loomis DP. 1998. Magnetic field exposure and neurodegenerative disease mortality among electric utility workers. *Epidemiology* 9:398–404.
- Schaap LA, Peeters GM, Dennison EM, Zambon S, Nikolaus T, Sanchez-Martinez M, Musacchio E, van Schoor NM, Deeg DJ, group Er. 2011. European Project on OsteoArthritis (EPOSA): Methodological challenges in harmonization of existing data from five European population-based cohorts on aging. *BMC Musculoskelet Disord* 12:272.
- Shavers VL. 2007. Measurement of socioeconomic status in health disparities research. *J Natl Med Assoc* 99:1013–1023.
- Sorahan T, Kheifets L. 2007. Mortality from Alzheimer's, motor neuron and Parkinson's disease in relation to magnetic field exposure: Findings from the study of UK electricity generation and transmission workers, 1973-2004. *Occup Environ Med* 64:820–826.
- Sorahan T, Mohammed N. 2014. Neurodegenerative disease and magnetic field exposure in UK electricity supply workers. *Occup Med (Lond)* 64:454–460.
- Stevenson M, Sergeant E, Nunes T, Heuer C, Marshall J, Sanchez J, Thornton R, Reiczigel J, Robison-Cox J, Sebastiani P, Solymos P, Yoshida K, Jones G, Pirikahu S, Firestone S, Kyle R, Popp J, Jay M, Reynard C 2020. epiR: Tools for the Analysis of Epidemiological Data. R package version 1.0-14. Available from <https://CRAN.R-project.org/package=epiR> [Last accessed 8 March 2021].
- Tikellis G, Dwyer T, Paltiel O, Phillips GS, Lemeshow S, Golding J, Northstone K, Boyd A, Olsen S, Ghantous A, Herceg Z, Ward MH, Håberg SE, Magnus P, Olsen J, Ström M, Mahabir S, Jones RR, Ponsonby AL, Clavel J, Charlés MA, Trevathan E, Min Qian Z, Maule MM, Qiu X, Hong YC, Brandalise S, Roman E, Wake M, He JR, Linet MS, International Childhood Cancer Cohort Consortium. 2018. The international childhood cancer cohort consortium (I4C): A research platform of prospective cohorts for studying the aetiology of childhood cancers. *Paediatr Perinat Epidemiol* 32:568–583.
- van Veen EB. 2018. Observational health research in Europe: Understanding the general data protection regulation and underlying debate. *Eur J Cancer* 104:70–80.
- Vergara X, Kheifets L, Greenland S, Oksuzyan S, Cho YS, Mezei G. 2013. Occupational exposure to extremely low-frequency magnetic fields and neurodegenerative disease: A meta-analysis. *J Occup Environ Med* 55:135–146.
- Vergara X, Mezei G, Kheifets L. 2015a. Case-control study of occupational exposure to electric shocks and magnetic fields and mortality from amyotrophic lateral sclerosis in the US, 1991-1999. *J Expo Sci Environ Epidemiol* 25:65–71.

- Vergara XP, Fischer HJ, Yost M, Silva M, Lombardi DA, Kheifets L. 2015b. Job exposure matrix for electric shock risks with their uncertainties. *Int J Environ Res Public Health* 12:3889–3902.
- Vergara XP, Kheifets L, Silva M, Bracken TD, Yost M. 2012. New electric-shock job exposure matrix. *Am J Ind Med* 55:232–240.
- Zhou H, Chen G, Chen C, Yu Y, Xu Z. 2012. Association between extremely low-frequency electromagnetic fields occupations and amyotrophic lateral sclerosis: A meta-analysis. *PLOS One* 7:e48354.

SUPPORTING INFORMATION

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