HHS Public Access
Author manuscript
J Occup Environ Med. Author manuscript; available in PMC 2015 December 04.

Published in final edited form as:
J Occup Environ Med. 2011 December ; 53(12): 1447–1451. doi:10.1097/JOM.0b013e318237a1d0.

Evaluation of Occupational Exposure to Magnetic Fields and Motor Neuron Disease Mortality in a Population-Based Cohort

Lauren E. Parlett, BS, **Joseph D. Bowman, PhD, CIH**, and **Edwin van Wijngaarden, PhD**
Department of Community and Preventive Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY (Ms Lauren and Dr Wijngaarden); and Engineering and Physical Hazards Branch, National Institute for Occupational Safety and Health, Cincinnati, Ohio (Dr Bowman)

Abstract

Objective—Epidemiologic evidence for the association between electromagnetic fields and amyotrophic lateral sclerosis, the most common form of motor neuron disease (MND), has been inconclusive. We evaluated the association between electromagnetic fields and MND among workers in occupations potentially exposed to magnetic fields.

Methods—MND mortality (ICD-9 335.2) was examined in the National Longitudinal Mortality Study using multivariable proportional hazards models. Occupational exposure to magnetic fields was determined on the basis of a population-based job-exposure matrix. Age at entry, education, race, sex, and income were considered for inclusion as covariates.

Results—After adjusting for age, sex, and education, there were no increased risks of MND mortality in relation to potential magnetic field exposure, with hazard ratios around the null in all magnetic field exposure quartiles.

Conclusions—Our study does not provide evidence for an association between magnetic field exposure and MND mortality.

Over the past several decades, there has been continuing concern over whether exposure to extremely-low-frequency magnetic fields can adversely affect health. A recent review of the epidemiologic literature concluded that although occupational magnetic fields may increase the risk for some health outcomes, the evidence is not strong or consistent enough to draw firm conclusions.[1] Nevertheless, continued research of the impact of magnetic field exposure on amyotrophic lateral sclerosis (ALS), which comprises more than 90% of all motor neuron disease (MND),[2] was recommended on the basis of consistent evidence linking electrical occupations to an increased risk of ALS but weaker evidence based on measured magnetic field.[1,3]

The etiology for ALS is still largely unknown,[4] but primarily animal studies have pointed toward oxidative damage, protein aggregation, mitochondrial dysfunction, and caspase-

Address correspondence to: Edwin van Wijngaarden, PhD, Department of Community and Preventive Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 (edwin_van_wijngaarden@urmc.rochester.edu)..

The authors declare no competing interests.

mediated apoptosis as possible causative mechanisms in the disease.[5-8] Therefore, it is important to pursue leads regarding potential risk factors, including magnetic field exposure. It has been suggested that magnetic field exposure can result in neurological damage through increasing oxidative stress and inducing DNA breaks. The association between magnetic fields and oxidative DNA stress has been demonstrated in some studies[9,10] but not others.[11] A study by Falone and colleagues[12] showed an interaction between rat age and magnetic fields in the decreasing activity levels of antioxidant enzymes, suggesting a susceptibility to oxidative stress from magnetic fields as the rats mature. As oxidative damage is thought to be involved in toxicity targeting motor neurons,[13] it is possible that magnetic field exposure may result in motor neuron degeneration through this pathway. Nevertheless, the biological mechanism responsible for an association between magnetic fields and ALS, or the broader group of MND, remains unclear.

We evaluated the association between quantitative levels of occupational magnetic field exposure and MND mortality in a population-based cohort representative of the general US population.

METHODS

Study Population

We examined the association between magnetic fields exposure and MND mortality in the National Longitudinal Mortality Study (NLMS). The NLMS is a population-based cohort study that uses a random sample of noninstitutionalized persons in the United States from the Census Population Survey of the Bureau of Census (BOC) in March 1979, April 1980, August 1980, December 1980, and March 1981. For confidentiality reasons, a representative subset of five of the original twelve Census Population Survey cohorts is available for public use. In these files, all personal, geographic, cohort, and time identifiers have been removed. Of the more than 637,000 participants in the NLMS, about half had occupational codes, resulting in 307,012 eligible individuals for our analysis. Occupational or industry codes were missing for those not in the workforce (44%), which include those looking for work (4%), housekeepers/homemakers (19%), students (7%), those unable to work (1%), and retirees (11%). Figure 1 shows the final sample size used in our analyses after considering available information on job codes and relevant covariates.

Exposure Assessment

The assessment of magnetic field exposure in our cohort has been described elsewhere.[14] Briefly, participants were asked about the job worked during the week preceding the survey. For persons unemployed but actively looking for work within the 4 week period before the survey, information was obtained for the most recent job held (if any) within 5 years of the survey. Occupational codes in the NLMS were coded according to the 1970 BOC job classifications. To determine potential magnetic field exposure for each job reported in the NLMS, we first converted the 1970 BOC occupational codes to 1980 BOC occupational codes. Subsequently, these 1980 BOC codes were linked with a job-exposure matrix (JEM) developed previously by Bowman and colleagues.[15] Workplace magnetic field measurements were combined with supplemental data from other publications to create the

JEM. Because of the high correlation between the JEM geometric and arithmetic mean exposures,[14] the arithmetic mean was used because it allows for a more intuitive interpretation of the findings.

In the current analysis, magnetic field exposure was classified according to the 25th, 50th, and 75th percentiles based on the exposure distribution of the entire cohort. Exposure was treated as a nominal categorical variable to avoid assumptions as to the shape of its relationship to the dependent variable. The quartiles of exposure correspond to the following values: 0 μT to 0.1550 μT, 0.1550 μT to 0.2084 μT, 0.2084 μT to 0.2664 μT, and greater than 0.2664 μT.

Exposure assessment by job title and occupational category was also considered. Nevertheless, the small number of MND events precluded such an analysis because only one event happened in jobs typically associated with elevated magnetic field exposure, such as electricians, electrical engineers, welders, and power station operators.

OUTCOME

The mortality of cohort members was observed using the National Death Index to determine event and cause of death, indicated by International Classification of Diseases; ninth revision codes to one decimal point. The data set contains the following limited information about a death: up to two underlying causes of death, date and time of death, interval between cause onset and death, location of death, and coroner certification of death. Any underlying cause of death listed as 335.2 (MND) was used as the primary outcome in this study. Mortality follow-up information in the public-use NLMS was collected for the period 1979 to 1989. The maximum follow-up time was 9 years, or 3288 days.

Covariates

Health behaviors that could contribute to the risk of ALS, such as smoking,[16] physical activity,[17] and alcohol intake,[18] were not collected in the Census Population Survey and were therefore not available to the NLMS and our analysis. Nevertheless, these factors are unlikely to be associated strongly with magnetic field exposure and are therefore unlikely confounders. On the contrary, age at entry,[19] race, ethnicity, education,[16,18] adjusted income, urban living,[20] and marital status[21] were all considered as potential confounders on the basis of previous studies. An interaction between age and exposure was also considered. Missing data on any covariate resulted in removal of the observation from the preliminary model selection process (n = 285,120). After the final adjusted multivariable model was derived, only observations missing data from the model variables were then excluded from the analysis (n 306,891; see Figure 1). In all, 121 of 307,016 subjects (or 0.04%)=were excluded for missing educational data.

STATISTICAL ANALYSIS

Cox proportional hazards modeling using SAS PHREG (SAS, Inc, Cary, NC) was used to estimate hazard ratios (HRs) and 95% confidence intervals and incorporate the follow-up time of each cohort member from the time enumerated until the event of interest, defined as death from MND. Censoring occurred when a person died of another cause or was alive after 9 years of follow-up. The time scale used for the proportional hazards model was age of the cohort member, which was left censored before the study's start. Manual backward model reduction was used to determine confounders and independent risk predictors. Initial logit modeling was used to determine the appropriate scale (continuous, ordinal, or categorical) for the covariates in the model based on presence and strength of any linearity. Confounders were identified on the basis of a greater than 10% change in the HR for magnetic field exposure and independent risk factors were based on a significance level of $P < 0.10$.[22] Multivariate modeling allowed for control of demographic variables and socioeconomic position indicators. After examining exposure-stratified models, proportionality assumptions appeared to be met. Model building and confounding were based on complete case analysis only (Fig. 1). The final adjusted model includes all observations without missing values for the variables included. Crude and adjusted HRs and 95% confidenceintervals are presented. The NLMS sampling weights were not used because it was not the aim of this article to estimate risks for the US population. Analyses were performed in SAS v9.2 (SAS Institute, Cary, NC).

RESULTS

Over the 2.7 million years of follow-up time, there were 40 deaths due to MND (before excluding persons without information, the incidence for this cohort was 79 MND deaths for 5.5 million years of person-time). The death rate due to MND for our study is 1.47 per 100,000 person-years (compared with the weighted 1.395 per 100,000 person-years of the full cohort with NLMS weights). The median time to death from MND was 1685 days (or 4.6 years). Table 1 shows the characteristics of the NLMS population by both outcome and exposure. Some covariates had missing observations; the amended sample size for those variables is indicated in the footnote. The majority of MND deaths occurred in men, white and married individuals, and those more than 50 years old. Compared with the lowest quartile of magnetic field exposure, people in the highest quartile of magnetic field exposure were more likely to have less than a high school education, have an annual income of less than $25,000, and be male.

Table 2 presents the association between occupational magnetic field exposure and MND. Crude HRs were elevated for the increasing exposure quartiles relative to the lowest quartile. Nevertheless, after adjusting for age, education, and sex, there was no indication of an association between magnetic fields and MND death, with all HRs around the null. Hazard ratios and confidence intervals similar to the adjusted model were found after removing education to make use of the entire eligible sample (data not shown).

DISCUSSION

Epidemiologic studies have reported inconsistent associations between occupational magnetic field exposure and ALS, with some significant associations as well as absence of an effect in 13 ALS-MF studies recently reviewed by Kheifets and colleagues.[1] Previous studies were primarily of the case–control and cohort design and were conducted in the United States, Switzerland, Great Britain, Sweden, and Denmark. The evidence linking ALS to electrical occupations was more consistent than evidence for measured magnetic fields. Our study found no association between magnetic field exposure and MND, which may not be unexpected given the weak evidence presented by previous studies utilizing quantitative levels of exposure, and the challenges of studying this association in large population-based studies.

It may be particularly informative to contrast our findings with a previous study conducted by Park and colleagues,[19] who in a large death certificate–based case–control study in the United States reported an increased risk of MND mortality in relation to estimated magnetic field exposure among younger (aged <65 years) but not older (aged 65 + years) individuals. The discrepancy between the Park et al study and our study are not entirely clear, as both studies used the same JEM, controlled for similar covariates, and relied on the same data source for mortality assessment. Nevertheless, we were not able to stratify by age because of the relatively small number of events, which may have masked associations. Furthermore, inconsistent results may be due to differences in time spans between the two databases (1980–1989 for our study, 1992–1998 for the Park et al study) with potential changes in sources and levels of magnetic field exposures and in MND diagnosis over time. Finally, we used current or most recent occupation at the time of survey on the basis of subject self-report, whereas Park and colleagues relied on usual occupation on death certificates based on information reported by proxy respondents.

Exposure assessment across studies has been inconsistent, and has been based either on the occupation held longest,[16,18] a JEM,[19,23-27] occupational groups, magnetic field measurements, or exposure modeling.[19] Others have relied upon the expertise of industrial hygienists,[28] or have used self-reported occupational exposure.[29] In studies using quantitative levels of magnetic field exposure, cutoff values to create exposure categories vary from study to study, yet remain rather similar: low approximately 0.1 μT, medium approximately 0.25 μT, and high approximately 0.5 μT.

Our findings must be considered in light of several limitations. First, the exposure of interest, occupational exposure to magnetic fields, was measured neither directly nor for each individual but rather was based on a detailed but generic population-based JEM.[15] Much care was taken to ensure the quality of the exposure matrix. For example, the matrix was developed using seven data sources that had full-shift personal sampling and, in some cases, spot sampling.[15] The large amount of data from varied sources reduces the prospect of bias in the matrix. Job categories not covered by the data sources were investigated through a literature search for full-shift measurements.[15] One limitation of all generic JEMs is that they cannot adequately account for exposure variability within jobs, and they do not take into consideration specific job tasks of individuals in the cohort.

Given the data of the NLMS, we were unable to assess either lifetime or cumulative exposure to magnetic fields. The only occupational information provided in the data set refers to the subject’s last job and does not indicate length of employment in said position. Our analysis assumed that the most recent job is a proper indicator of lengthier magnetic field exposure, consistent with the finding that recent occupation is a relatively good surrogate for the longest-held job of an individual.[30] In addition, people who were unable to work or were retired did not have specific occupational information. Because of this, 39 cases of MND were excluded in our analysis because their magnetic field exposure could not be assessed from the given information.

We were not able to control for a variety of potential confounders, smoking, diet, and other health behaviors, because the information was unavailable in the NLMS. Nevertheless, it is unlikely that these factors are strongly related with our measure of magnetic field exposure.[14] In addition, our outcome of MND was based on mortality rather than morbidity. Nevertheless, given that ALS is a relatively fast progressing disease (with median survival around 3 years), death could be considered to be a fair surrogate for morbidity.[21,31]

Despite the limitations of both this study and the data set we used, this study has several important strengths. This study used a national sample representative of the noninstitutionalized US population. Therefore, the sampling of the NLMS allows for a wider generalizability of results. In addition, the prospective nature of our study ensured that occupational information was collected before event occurrence and is therefore less likely to be affected by inaccurate recall as compared with studies in which information is obtained from patients or their proxies after disease diagnosis or death.

In conclusion, our study showed no association between occupational magnetic field exposure and risk of MND. Future studies should focus on different exposures, such as electric shocks and contact currents, to explain the increased risk of ALS seen in some electrical occupations.[1]

ACKNOWLEDGMENTS

The findings and conclusions in this study have not been formally disseminated by the US National Institute for Occupational Safety and Health and should not be construed to represent any agency determination or policy.

No funding was received in support of this work.

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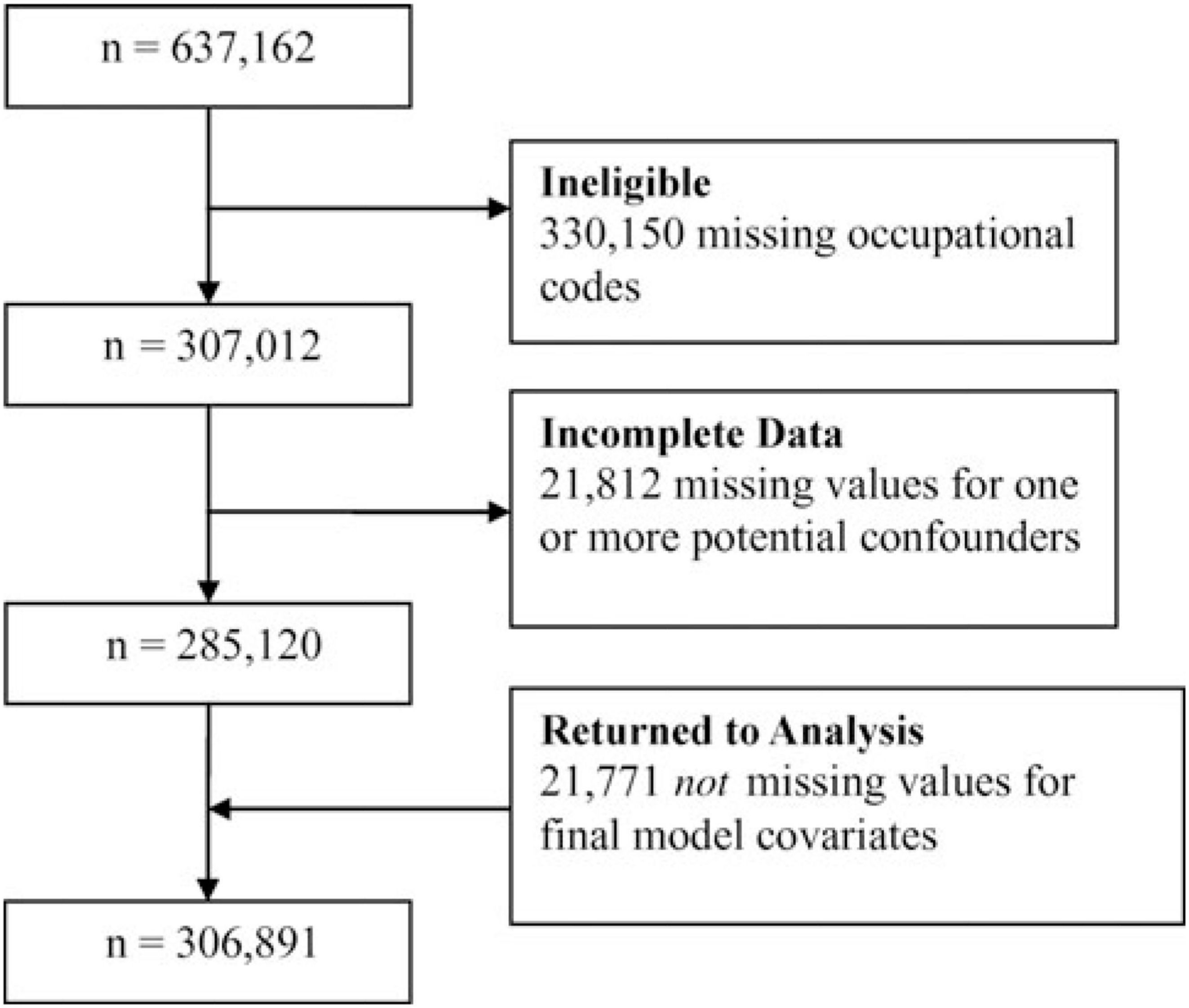

FIGURE 1.
Analysis sample size using National Longitudinal Mortality Study.

TABLE 1

Demographic Variables by MF Exposure Category (n = 307,012) and MND Outcome (n = 40)

	MND		Exposure Level (μT)							
			<0.1550		0.1550–0.2083		0.2083–0.2664		>0.2664	
Covariate	**n**	**%**	**n**	**%**	***n***	**%**	***n***	**%**	***n***	**%**
Total	40	100	95,941	31	64,037	21	77,723	25	69,311	23
Sex										
Male	33	82.5	36,683	21.3	39,405	22.9	48,560	28.3	47,261	27.4
Female	7	17.5	59,258	43.9	24,632	18.2	29,163	21.6	22,050	16.3
Age (yr)										
<30	1	2.5	39,566	33.7	19,496	16.6	33,071	28.2	25,296	21.5
30–40	8	20	23,169	33.0	16,369	23.3	15,545	22.1	15,107	21.5
41–50	6	15	14,935	30.1	11,986	24.1	11,599	23.4	11,118	22.4
51–60	13	32.5	12,116	27.0	10,856	24.2	11,061	24.7	10,829	24.1
61–70	10	25	5,176	25.0	4,473	21.6	5,349	25.9	5,668	27.4
71–80	2	5	884	23.1	765	20.0	1,013	26.5	1,161	30.4
80+	0	0	95	23.5	92	22.8	85	21.0	132	32.7
Race										
White	36	90	84,523	31.1	58,508	21.6	68,480	25.2	60,045	22.1
Nonwhite	4	10	11,418	32.2	5,529	15.6	9,243	26.1	9,266	26.1
Marital Status*										
Married	32	80	55,991	29.4	44,015	23.1	45,937	24.1	44,677	23.4
Nonmarried	8	20	39,135	34.2	19,603	17.2	31,299	27.4	24,256	21.2
Adjusted Income ($)†										
>25,000	13	36	31,883	33.0	24,754	25.6	22,390	23.1	17,716	18.3
<25,000	23	64	59,780	30.6	36,015	18.4	51,510	26.3	48,217	24.7
Hispanic‡										
Yes	0	0	4,348	26.9	2,805	17.4	4,448	27.5	4,559	28.2
No	38	100	90,132	31.6	60,217	21.1	71,758	25.1	63,191	22.1
Education§										
Less than HS	7	17.5	17,702	23.1	10,653	13.9	24,382	31.8	23,923	31.2

	MND		Exposure Level (μT)							
			<0.1550		**0.1550–0.2083**		**0.2083–0.2664**		**>0.2664**	
Covariate	**n**	**%**	**n**	**%**	***n***	**%**	***n***	**%**	***n***	**%**
HS or more	33	82.5	78,213	34.0	53,364	23.2	53,306	23.2	45,348	19.7
Residence										
Urban	28	70	68,036	33.2	45,219	22.1	49,429	24.1	42,110	20.6
Rural	12	30	27,905	27.3	18,818	18.4	28,294	27.7	27,201	26.6

HS, high school; MF, magnetic field; MND, motor neuron disease.

[*] *n* = 304,913

[†] *n* = 292,265

[‡] *n* = 301,458

[§] *n* = 306,891

TABLE 2

Hazard Ratios and 95% Confidence Intervals for MND and MF exposure

Exposure Level (μT)	Population at Risk	MND Deaths	Crude Hazard Ratio (Confidence Interval)	Adjusted Hazard Ratio* (Confidence Interval)
<0.1550	95,941	10	1.00 (ref)	1.0 (ref)
0.1550–0.2083	64,037	10	1.51 (0.62–3.67)	0.98 (0.40–2.42)
0.2083–0.2664	77,723	10	1.24 (0.51–3.02)	1.02 (0.41–2.56)
>0.2664	69,311	10	1.40 (0.57–3.40)	0.98 (0.39–2.50)

MF, magnetic field; MND, motor neuron disease.

*Adjusted for age (continuous), sex, and education (< or > High school).