Title
Occupational Electric Shocks, Electromagnetic Fields and Amyotrophic Lateral Sclerosis

Author
Vergara, Ximena Patricia

Publication Date
2012

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

Occupational Electric Shocks, Electromagnetic Fields and Amyotrophic Lateral Sclerosis

A dissertation submitted in partial satisfaction of the

requirements for the degree Doctor of Philosophy

in Epidemiology

by

Ximena Patricia Vergara

2012

ABSTRACT OF THE DISSERTATION

Occupational Electric Shocks, Electromagnetic Fields and

Amyotrophic Lateral Sclerosis

by

Ximena Patricia Vergara

Doctor of Philosophy in Epidemiology

University of California, Los Angeles, 2012

Professor Leeka Kheifets, Chair

This dissertation examines the association of neurodegenerative diseases and electric occupations and evaluates electric shocks and magnetic fields exposures. First, we conducted a meta-analysis of occupational electromagnetic fields (MF) and neurodegenerative diseases (NDD) to systematically explore methodological differences between studies. Second, we developed an electric shocks job exposure matrix (JEM) to characterize occupations exposed to electric shocks. Finally, we examined the association between occupational electric shocks, MF and amyotrophic lateral sclerosis (ALS) mortality.

We conducted a meta-analysis of epidemiologic studies on occupational MF exposure and NDD. We found weak associations of occupational MF exposures with both AD and MND, but not with Parkinson's disease, dementia, and multiple sclerosis. Risk of developing MND was associated with electric occupations, while AD risk was associated with estimated MF levels. Nonetheless, there is extensive result variation related to aspects of study design, with dissimilarity in this variation across diseases. Our results do not support MF as the explanation for the observed electric occupation and MND association. Misclassification of disease, particularly for AD, and imprecise exposure assessment affected most studies.

To evaluate a consistent association between jobs in “electric” occupations and ALS, we developed a comprehensive JEM that includes electric shocks and MF. Electric shocks were based on two data sources along with expert judgment. Main occupational groups experiencing the electric shocks were precision production, craft and repair occupations. Specific jobs with high electric shock exposure were electrical apprentices, mechanic and repairer helpers, hoist and winch operators and electrical power installers. Examples of job titles with low electric-shock exposures were administrative support occupations, data-key entry operators, and waiters and waitresses.

The relationship between occupational electric shocks, MF and ALS was investigated using cases identified in 1991-1999 U.S. mortality data. For each ALS death, 10 sex-, age-, year- and region-matched controls were selected. We linked the usual occupation reported on the death certificate to a JEM with electric shocks and MF. Increased odds ratios were observed for ALS among those in electric occupations (OR=1.23, 95% confidence interval (CI): 1.04, 1.47). For electric shocks, ALS mortality odds ratios were 0.73 (95% CI: 0.67, 0.79) for high exposure and 0.90 (95% CI: 0.84, 0.97) for medium exposure compared to low exposure. For MF, ALS mortality odds ratios were 1.09 (95% CI: 1.00, 1.19) for high exposure and 1.09 (95% CI: 0.96, 1.23) for medium exposure as compared to low. However, ALS mortality increased only in electric occupations with medium and low electric shocks exposures. Current results support an association between electric occupations and ALS, but provide no evidence that this association is explained by occupational exposure to electric shocks or MF.

The dissertation of Ximena Patricia Vergara is approved.

Sander Greenland

William C. Hinds

Beate Ritz

Leeka Kheifets, Committee Chair

University of California, Los Angeles

2012

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ACKNOWLEDGMENTS

I would like to thank my advisor, Dr. Leeka Kheifets, for the support and sustained scientific counsel. I would also like to thank Dr. Sander Greenland for his scientific input and years of thought provoking teaching and members of my committee, Drs. William Hinds and Beate Ritz, who have devoted time to teach, review and comment.

Chapter 2 is a version of an analysis to be submitted, other researchers who have contributed to the analysis, and review of this work include Drs. Leeka Kheifets, Sander Greenland, Sona Oksuzyan and Yong-Sung Cho of University of California, Los Angeles Fielding School of Public Health and Dr. Gabor Mezei of the Electric Power Research Institute (EPRI). Chapter 3 is a version of "New Electric Shocks Job Exposure Matrix" published in the March 2012 American Journal of Industrial Medicine Volume 55, Issue 3, pages 232-40. The following co-authors contributed to the job exposure matrix analysis and review: Dr. Leeka Kheifets, Dr. Michael Yost of the University of Washington, School of Public Health, Dr. Dan Bracken of T. Dan Bracken, Inc., and Michael Silva of Enertech Consultants. Chapter 5 is a version of an article in preparation for publication with co-authors with Drs. Leeka Kheifets and Gabor Mezei who consulted on analysis and review.

Research funding for the neurodegenerative disease meta-analysis work was provided by EPRI (P31 1801/C14 763). The electric shocks job exposure matrix work was funded through a National Institute for Occupational Safety and Health (NIOSH) Training Grant (T42 OH 008412) awarded by the UCLA Southern California Education and Research Center. Support for the occupational electric shocks and ALS mortality analysis was partially provided through a NIOSH grant (R21 EP 31374).

I would like to thank the U.S. Bureau of Labor Statistics for providing us with data on occupational electric shocks. I am grateful to the National Vital Statistics System and the National Bureau of Economic Research for maintaining accessible public health data available for researchers. Lastly, I would like to thank all of the educators and support staff who work to create a nurturing learning environment for UCLA students.

VITA

1990	A.B., Chemistry University of Chicago Chicago, Illinois
2000-2004	Research Associate Public Health Institute California Department of Public Health Occupational Health Branch Oakland, California
2006	M.P.H., Environmental Health Sciences Specialized in Industrial Hygiene University of California, Los Angeles
2007	Graduate Student Researcher Department of Epidemiology University of California, Los Angeles
2007-2008	California Wellness Foundation Fellowship University of California, Los Angeles
2008-2009	School of Public Health Endowment Scholarship University of California, Los Angeles
2009-present	Senior Project Scientist Electric Power Research Institute Palo Alto, California

PUBLICATIONS AND PRESENTATIONS

Vergara XP, Kheifets L, Silva M, Bracken TD, Yost M. New electric-shock job exposure matrix. Am J Ind Med. 2012 Mar;55(3):232-40. doi: 10.1002/ajim.21027. Epub 2011 Nov 8.

Kheifets L, Monroe J, Vergara X, Mezei G, Afifi AA. Occupational electromagnetic fields and leukemia and brain cancer: an update to two meta-analyses. J Occup Environ Med. 2008 Jun;50(6):677-88. Review.

Sutton PM, Vergara X, Beckman J, Nicas M, Das R. Pesticide illness among flight attendants due to aircraft disinsection. Am J Ind Med. 2007 May;50(5):345-56.

1. Occupational Electric Shocks, Electromagnetic Fields and Amyotrophic Lateral Sclerosis

Introduction

Over the past forty years, researchers have investigated neurodegenerative diseases and occupational extremely low frequency magnetic fields (MF) and certain occupations. In these investigations, researchers primarily focused on Alzheimer’s disease, Parkinson’s disease and amyotrophic lateral sclerosis (ALS). To a lesser extent, investigators pursued these exposures with multiple sclerosis and other dementias as outcomes. Early occupational AD studies provide weak evidence of an association with MF. Within occupational ALS studies, investigators observe a consistent association between “electric” occupations and ALS [1-5]. Although, they do not understand which job exposures might be responsible for the observed association.

A loss of neuron structure or function characterizes neurodegenerative diseases. Dementias cover a broad spectrum of cognitive-related diseases, including Alzheimer’s disease [6]. Tangles and plaques in the brain typify Alzheimer’s disease, the most common dementia. After Alzheimer’s disease, Parkinson’s disease is the second most common neurodegenerative disease [7]. Involving cell loss in the neural pathway of the substantia nigra and presence of Lewy bodies, Parkinson’s disease causes uncontrolled body tremors. Among the motor neuron diseases, ALS is the most common. The invariably fatal disease causes the progressive loss of function of both upper and lower motor neurons [8]. The group of neurodegenerative diseases place undue economic and social burden on caregivers, family members and society [9]. None of these idiopathic diseases can be cured and risk factors to prevent them are important to pursue.

Electromagnetic fields are one of the most common, rapidly growing environmental exposures. Scientists designate electromagnetic field radiation as non-ionizing, possessing insufficient photon energy to ionize atoms or molecules within human tissue. Affected by distance, shape of the source, and wavelength, scientists define electromagnetic fields by frequency ranges. The EMF spectrum covers a wide range of frequencies, including sub-categories extending from 30Hz to 300GHz [10]. Electric power system sources mainly produce fields in the lower part of MF range while at the opposite end of the spectrum is radar, satellite communications, and microwave relay sources, which dominate high frequency field ranges [11]. Electric fields, are measured in volt per meter, and magnetic fields are measured in Tesla. People can easily shield electric fields, present whether or not equipment has power; whereas, shielding magnetic fields is difficult.

Worker populations are often highly exposed compared to the general population or residential exposures. Many chemical human carcinogens (e.g., aromatic hydrocarbons) identified in the occupational arena, were later recognized as more general environmental hazards. With important clues garnered from occupational exposures, advances in methods and new approaches to epidemiology provide valuable input to understanding the associations between workplace exposures and neurodegenerative diseases.

Workforce demographics have shifted over the last fifty years. The United States Bureau of Labor Statistics (U.S. BLS) projects a rise in active workers aged 55 years or more, reaching nearly 42.8 percent in 2016 [12]. A combination of higher average worker age and increased time to retirement will lead to rise in age-related degenerative diseases, impacting workforce productivity and the economy. Longer human lifespan lead to increased prevalence of neurodegenerative diseases, in particular. The culmination of these factors motivates public health professionals to pursue the etiology of neurodegenerative diseases and assess the literature to date.

Exposure assessment—including the use of job exposure matrices (JEMs)—remains a major challenge in occupational EMF epidemiology. Over the past 15 years, researchers improved assessment by creating JEMs. To create a MF JEM, researchers combine resultant MF data with activity records, to calculate either the time-weighted average (TWA) of the magnetic field or use other metrics. Investigators consolidate personal measurements as TWA MF by occupational titles. Thus far, researchers have constructed MF JEMs for electric utility workers [13, 14] and for the general population [15, 16] using extensive full-shift measurements recorded with MF meters, sampling an approximated "resultant" field every few seconds.

Spatial and temporal MF variations and lack of biological mechanism challenge investigators in finding an appropriate exposure metric for electromagnetic field studies. Usually, MFs are averaged over a period of time such as a full shift. Electrical workers, persons working near machines with electric motors, and welders have MF TWA measurements between 0.1 – 4.0 μT [17]. Industrial hygienists classify these workers as highly exposed to MF. However, workers may change physical positions, altering exposures perhaps causing spikes or peaks. Physical location may place typically low exposed workers in higher MF. For example, an office worker working above a transformer may actually have high MF exposure. Even though physical movement may alter exposures, e.g. causing peaks, the full-shift TWA measurements have been used to represent MF exposure in the workplace.

Magnetic fields, electric fields, contact currents, microshocks, and perceptible electric shocks contribute to the extremely low frequency electromagnetic field environment, of which MF are only one aspect. An electrical shock is a "physiopathological effect resulting from direct or indirect passage of an external electrical current through the body" [18], which may over-stimulate the nervous system or damage organs [19]. Unlike MF, electric shocks are not directly measurable in a worker population. Gleaned from the electric utility environment, elevated electric fields induce greater internal body currents than elevated magnetic fields. Electric shocks induce far greater internal body currents than elevated electric fields, albeit very briefly. Medical scientists and engineers describe electric shocks circumstances differently in the literature. Medical researchers separate injuries into low and high voltage; whereas, engineers may describe additional factors such as source frequency [19, 20]. Primary to understanding potential harm to human tissue and workplace injury prevention, public health scientists must define electric shocks and identify characteristics such occupations, tasks, and circumstances of injury.

Complex circumstances surround electric shocks. Severity and perception affect the capture of workplace shock injury reports. Shock severity depends on the following factors:

- voltage level,
- current passing through a person's body,
- the body's resistance,
- the path through the body,
- the shock duration
- the source frequency [21].

Electric current (Alternating Current (AC) or Direct Current (DC)) and skin tissue electrical properties, altered by tissue damage, sweat and personal protective equipment, partly determine the physiological effects of electric shocks [22]. At 60Hz frequencies, effects of AC passing through the human body range from imperceptible to producing "not let go" responses or cardiac arrest (2 A) [19]. Injury reports likely capture the most severe, primary shock cases. Conceivably, a worker may not report an electric shock event at lower currents or perceived physical effects. Mild to moderate workplace accidents may be completely missed, if a worker had mild pain or no direct physical harm. Given the ranges in severity and shock perception, reported injuries available at the national level likely underestimate the full extent of electric shocks in the workplace.

Currently, the biological mechanisms of action for electric shocks and MF are just hypotheses. Electroporation, Joule heating, and electroconformational protein changes are three posited mechanisms through which high electric fields (60 V/cm – 160 V/cm strength) cause damage to skeletal and peripheral nerve membranes [23, 24]. In electroporation, an electric field creates pores within the membrane lipid bilayer. The pores allow ions and DNA fragments to pass. In Joule heating, the tissue converts current to thermal energy. In the last posited mechanism, electroconformational change, strong electric fields realign the charged amino acids within membrane proteins. The realignment makes potassium channels and other charged membrane structures vulnerable. Scientists have postulated several biological mechanisms for MF including reactive oxygen species, disruption of melatonin levels and calcium channels [25]. In particular, biological mechanisms for neurodegenerative diseases and electric shocks and MF remain theories.

For study of neurodegenerative diseases, epidemiologists have used observational study designs such as proportionate mortality studies, for hypothesis generation, to cohort, for evaluating relationships between exposures and disease. Due to the rarity of neurodegenerative diseases like ALS, investigators used case-control design to ensure adequate number of cases within strata, despite the often-cited limitations. Unlike countries with disease registries, the United States (U.S.) has no concerted nationwide effort to track diseases, only recently initiating an ALS disease registry [26]. Publicly available death records present the best source information for fatal diseases in the U.S. However, death records contain limited information on occupation and industry, which are a proxy for many workplace exposures. Changes in diagnostic criteria and disease duration make death records problematic for investigating relationships for Alzheimer's and Parkinson's disease.

Dissertation Topics

Within this research context, I will direct my dissertation toward three objectives to advance the field of occupational MF epidemiology. In Chapter 2, I present a meta-analysis of occupational EMF and neurodegenerative diseases and to systematically explore epidemiologic methodological differences between studies. In Chapter 3, I describe an electric shock JEM created to characterize occupations exposed to electric shocks. I examine the association between occupational electric shocks, MF and ALS mortality in Chapter 4.

References

1. Johansen, C. and J.H. Olsen, *Mortality from amyotrophic lateral sclerosis, other chronic disorders, and electric shocks among utility workers.* Am J Epidemiol, 1998. 148(4): p. 362-8.

2. Davanipour, Z., et al., *Amyotrophic lateral sclerosis and occupational exposure to electromagnetic fields.* Bioelectromagnetics, 1997.

3. Deapen, D.M. and B.E. Henderson, *A case-control study of amyotrophic lateral sclerosis.* Am J Epidemiol, 1986. 123(5): p. 790-9.

4. Gunnarsson, L., et al., *A case-control study of motor neurone disease: its relation to heritability, and occupational exposures, particularly to solvents.* British Journal of Industrial Medicine, 1992: p. 791-8.

5. Gunnarsson, L.G., et al., *Amyotrophic lateral sclerosis in Sweden in relation to occupation.* Acta Neurol Scand, 1991. 83(6): p. 394-8.

6. Kukull, W.A. and J.D. Bowen, *Dementia epidemiology.* Med Clin North Am, 2002. 86(3): p. 573-90.

7. de Lau, L.M. and M.M. Breteler, *Epidemiology of Parkinson's disease.* Lancet Neurol, 2006. 5(6): p. 525-35.

8. Murray, B. and H. Mitsumoto, *The spectrum of motor neuron disorders*, in *Amyotrophic lateral sclerosis*, R.H. Brown, M. Swash, and P. Pasinelli, Editors. 2006, Informa Healthcare: London.

9. Lopez-Bastida, J., et al., *Social economic costs and health-related quality of life in patients with amyotrophic lateral sclerosis in Spain.* Amyotrophic Lateral Sclerosis, 2008: p. 1-7.

10. Mild, K. and B. Greenebaum, *Environmental and Occupationally Encountered Electromagnetic Fields*, in *Bioengineering and Biophysical Aspects of Electromagnetic Fields*, F. Barnes and B. Greenebaum, Editors. 2007, Taylor & Francis: Boca Raton, FL.

11. Chadwick, P., *Non-ionizing radiation: electromagnetic fields and optical radiation*, in *Occupational Hygiene*, K. Gardiner and J. Harrington, Editors. 2005, Blackwell Publishing: Birmingham, UK.

12. Toossi, M., *Labor force projections to 2016: more workers in their golden years.* Monthly Labor Review, 2007. 130(11): p. 33-52.

13. Sahl, J.D., et al., *Exposure to 60 Hz magnetic fields in the electric utility work environment.* Bioelectromagnetics, 1994. 15(1): p. 21-32.

14. Johansen, C., et al., *Validation of a job-exposure matrix for assessment of utility worker exposure to magnetic fields.* Appl Occup Environ Hyg, 2002. 17(4): p. 304-10.

15. Forssen, U.M., et al., *Occupational magnetic field exposure among women in Stockholm County, Sweden.* Occup Environ Med, 2004. 61(7): p. 594-602.

16. Bowman, J.D., J.A. Touchstone, and M.G. Yost, *A population-based job exposure matrix for power-frequency magnetic fields.* J Occup Environ Hyg, 2007. 4(9): p. 715-28.

17. NIEHS, *Health Effects from Exposure to Power-Line Frequency Electric and Magnetic Fields*, National Institute of Environmental Health Science (NIEHS), Editor. 1999, National Institutes of Health: Research Triangle Park. p. 80.

18. Folliot, D., *Electricity - Physiological Effects*, in *Encyclopaedia of Occupational Health and Safety*, J. Stellman, Editor. 1998, International Labour Office: Geneva.

19. NIOSH, *Worker Deaths by Electrocution: A Summary of NIOSH Surveillance and Investigative Findings*. 1998, US Department of Health and Human Services. p. 51.

20. Wright, R.K. (2008) *Electrical Injuries*. e-Medicine Environmental Emergency Medicine Volume, 1-19

21. El-Sharkawi, M., *Electrical Safety*, in *Electrical Energy: An Introduction,*. 2005, CRC Press: Boca Raton, FL.

22. Conrad, A., *Effects of Electricity on Living Tissue*, in *The Ohio State Engineer (April).* 1939.

23. Capelli-Schellpfeffer, M. and R.C. Lee, *Electric Shocks*, in *Wiley encyclopedia of electrical and electronics engineering*, J.G. Webster, Editor. 1999, John Wiley: New York.

24. Lee, R.C., D. Zhang, and J. Hannig, *Biophysical injury mechanisms in electrical shock trauma.* Annu Rev Biomed Eng, 2000. 2: p. 477-509.

25. Savitz, D.A., H. Checkoway, and D.P. Loomis, *Magnetic field exposure and neurodegenerative disease mortality among electric utility workers.* Epidemiology, 1998. 9(4): p. 398-404.

26. CDC, *National Amyotrophic Lateral Sclerosis (ALS) Registry Available Online.* MMWR CDC Surveillance Summaries, 2010. 59(45): p. 1492-1493.

27. Garcia, A., A. Sisternas, and S. Hoyos, *Occupational exposure to extremely low frequency electric and magnetic fields and Alzheimer disease: a meta-analysis.* International journal of epidemiology, 2008. 37(2): p. 329.

2. Occupational Exposure to Extremely Low Frequency Electromagnetic Fields and Neurodegenerative Disease: A Meta-Analysis

Introduction

Populations are aging and neurodegenerative diseases are becoming more prevalent. By 2040, neurodegenerative diseases are projected to become the second most common cause of death [1]. Research investigating extremely low frequency magnetic fields (EMF) and risk of neurodegenerative diseases has focused mainly on Alzheimer's disease (AD), and amyotrophic lateral sclerosis (ALS, a type of motor neuron disease (MND)), and to a lesser extent on Parkinson's (PD), multiple sclerosis (MS) and more broadly defined dementias.

According to several scientific review committees, occupational AD studies provide weak evidence of an association with MF [2] [3]. The strongest associations were reported by two clinic-based studies from one group of investigators [4, 5], whereas evidence from four population-based studies [6-9] taken together does not appear to support an association between MF and AD. Later studies appear inconsistent with relative risk estimates ranging from below one to four [10-14].

Strong associations among those employed in "electrical occupations" and ALS have been noted in several clinic- and population-based studies, especially among the early studies [15] [16-20]. In a 2003 review, authors recommended improved exposure assessment to aid interpretation of the association observed between occupational power frequency electromagnetic fields and ALS [21]. Studies of EMF exposure estimated from job exposure matrices (JEMs) [10, 11, 22] have been less consistent. More recently, two studies [10] [23] reported MF exposure associated with ALS, but possible confounding due neurotoxins for welders in one study was proposed as an explanation. Thus, increased ALS risk has been consistently observed among “electrical occupations”, but less so for estimated MF. Lastly, epidemiologic studies have not provided evidence of a connection between high occupational MF exposures and PD [8-13, 22-24].

A systematic review of eight occupational MF studies published between 2000 and 2005 concluded that there is evidence for an association between MF exposure and neurodegenerative disease risk [25]. A 2008 meta-analysis examined 14 studies on occupational MF and AD, reporting elevated risks, but with heterogeneity in subgroup analyses and possibility of publication bias [26]. Since then, six new occupational studies on MF and neurodegenerative diseases have appeared in the literature [13, 14, 23, 27-29].

We conducted a meta-analysis of occupational MF exposure and neurodegenerative-diseases (including AD, MND, PD, MS and dementias). In an attempt to evaluate the difference between different exposure proxies we also included in our meta-analysis occupational title studies that did not specifically examine MF but that examined occupations with potentially high magnetic fields, based on the recently developed comprehensive JEM [30].

Methods

Literature Search

We identified relevant peer-reviewed published articles using bibliographic search engines in PubMed prior to January 12, 2012. Our initial search criteria included combinations of "neurodegenerative", "alzheimer", "amyotrophic lateral sclerosis", "parkinson", "dementia", "multiple sclerosis", or "motor neuron" and "EMF", "magnetic field", "electric field", "occupation", "electromagnetic", "job", "welders", "workplace exposure", or "work-related exposure". We also searched using specific two-word keyword combinations, included other reviewed studies based on our personal files and on references cited in the articles identified from PubMed. A total of 197 potentially relevant articles on neurodegenerative disease were identified through our literature search, and 3 were added from references noted in identified articles.

Inclusion Criteria

We selected the final articles for analysis based on these *a priori* inclusion criteria: 1) related to well-defined occupations or tasks exposed to extremely low frequency magnetic fields or 2) an assessment of MF exposure via job exposure matrix, historic measurements, or personal exposure measurements or 3) both and the following neurodegenerative diseases: motor neuron disease including amyotrophic lateral sclerosis, multiple sclerosis, Parkinson’s disease, Alzheimer’s disease and other dementias. We included any observational epidemiologic articles written in the English language that provided estimates of association of occupational titles or tasks with high magnetic field exposures and/or occupational magnetic field exposures. In case of studies with overlapping populations, we included articles with the most detailed report of the study population.

Exclusion Criteria

Upon further review, we excluded articles with the following issues: 1) poorly or broadly defined occupational groups, e.g. manual workers, or unrelated to MF exposures, e.g. pesticides, 2) unrelated to prevalence, mortality or incidence of disease, 3) review articles, 4) laboratory mechanisms, 5) clinical applications or 6) non-epidemiologic studies e.g. focused on caregiver roles or practitioner considerations. We found two residential exposure studies [31] [32] , one of which also examined occupational exposures.

Search results

Of all articles, 158 were excluded because they were not epidemiologic studies (n=25), they did not include any outcome of interest (n=11), did not include relevant occupations with MF exposure (n=50) (Figure 2-1.). Forty published articles were included in the final meta-analysis; one article [4] was treated as 3 different studies because it contained three different study populations. Table 2-1 summarizes 44 studies that were considered for the final analysis [4-11, 14, 16-19, 22-24, 27-29, 32-54]. The cross-sectional study [32] and proportionate mortality study [38] were examined in separate analyses, only case-control and cohort studies are presented below.

Data Extraction

Standardized procedures were developed to extract both study characteristics and relative-risk estimates. Based on these procedures, we extracted publication year, study location, study design, type of outcome (mortality, prevalence or incidence), source of the outcome information (death certificates or clinical pathology/diagnostic information), basis of occupational information (representative job or several jobs), source of occupational information (registry/census, interview or work history), exposure assessment methods (not done, industrial hygiene (IH)/ JEM or MF measurements), covariate adjustment, and funding source (government/foundation, industry or not mentioned) from the selected studies. We also coded additional bases of estimates, such as gender specificity, types of controls used (not applicable, relatives or friends, other neurological diseases included in controls, other neurological diseases excluded, or population-based), whether the estimate was MF level- or occupational title-based, and whether only selected results were reported in the article. After an independent coding by several co-authors, we compared and discussed extracted information, to build consensus on each coded characteristic used in the analysis.

When possible, we coded covariate adjustment (age, sex, race, socioeconomic status or education, calendar period, residence or region, or other covariates). We extracted more than one type of relative risk if the study reported several exposure metrics, e.g. estimates for occupational titles and MF levels. Estimation of magnetic field exposure varied between studies from career exposure or cumulative exposure in (µT-years) to average MF exposure during occupation (µT)). We combined separate estimates based on two expert judgments for one study [6]. The highest exposure levels were used for each exposure metric reported when more than one estimate was given. For studies reporting results for many occupations [16, 32], we extracted estimates for all occupations with high MF exposure, defined as occupations with MF time-weighted averages (TWA) greater than 0.3 µT in the Bowman et. al JEM [30]. We examined studies to include MF exposure proxies specified as well-defined groups of workers (e.g. welders), specific tasks (e.g. welding) or exposures (e.g. welding fumes) and with more than five observed deaths/cases. We extracted numbers of exposed cases and controls, person-time or persons for each of the exposure levels.

Because ALS makes up 90% motor neuron disease and numerous studies report ALS synonymously with MND, we grouped ALS into MND for our analysis. Where possible, we examined AD as a distinct outcome, but study definitions of dementia varied.

Statistical Analysis

For each outcome, we used inverse-variance weighting under both fixed- and random-effects models to estimate summary relative risk [55]. For each outcome, we analyze heterogeneity of log relative risks using test of homogeneity, stratification on study characteristic, and meta-regression methods [56, 57].

We analyzed publication bias using the Egger regression asymmetry test for funnel plots, based on weighted regression, and Begg-Mazumdar test, based on ranked correlation [58]. We examined the influence of each specific study on the overall estimate by omitting one study at a time.

To combine multiple risk estimates per study, we used generalized least squares in the Stata glst command [59] [60]. We created one dose variable per "occupation" and three or four categorical doses for each MF level. For studies with several occupational titles, we examined each reference level and inputted the maximum of exposed cases and controls, person-time or persons for each risk estimate. Fourteen studies did not contain enough basic data counts to include in these analyses [8, 9, 13, 14, 18, 19, 24, 35, 37, 44, 47, 48, 52, 61]. We used Stata12 (StataCorp, College Station, TX) for all statistical analyses.

Results

Study Overview

Of the 42 analyzed studies in Table 2-1, 20 were of Alzheimer's disease, 21 of motor neuron disease (MND) including ALS, 18 of Parkinson's disease (PD), 9 of dementia and 5 of multiple sclerosis (MS). The earliest published study year was 1983 and the latest 2011. All included studies were either case-control (n=27) or cohort design (n=15). Nineteen occupational studies came from the United States (U.S.), 15 from Nordic countries, with additional studies from Germany, Switzerland, Netherlands, South Korea and the UK. All reported estimates were adjusted for age and sex. Additional adjustments were made for socio-economic status or its proxy (education or schooling) in 24 studies, for residence or region in 21, for calendar period in 15, and for race in 7 studies. Sixteen studies adjusted for miscellaneous covariates such as employment duration, alcohol use, exposure to solvents or polychlorinated benzenes, vascular disease, and parental dementia. Nearly 40% of studies examined prevalence and about 30% examined mortality, with most diagnoses from clinical pathology/diagnostic criteria (n=30). Of the 22 MND or AD case-control studies, few excluded other neurodegenerative diseases from the controls (n=8) and few used population controls (n=5). Over half of the studies collected information on several jobs, of these only 3 used MF measurements. Exposure in 15 studies was based on a representative job classified MF levels by JEM or industrial hygiene assessment (n=9).

Small associations for MND (RR_{RE} = 1.26, 95% CI: 1.10 – 1.44) and AD (RR_{RE} = 1.27 (1.15 – 1.40) were present in both fixed and random effects models, which are higher for random effects models, as expected given the large heterogeneity [62]. There were no associations for dementia, MS and PD (data not shown). Of these, only for dementia and PD had a sufficient number of studies to allow more in depth analysis. Information on study characteristics for the 18 PD studies and 9 dementia studies (Table 2-2) reveals no patterns of interest. Thus for the remainder of this paper we focus on random-effects analyses of MND and AD. The forest plot (Figure 2-2) presents the relative risks and 95% confidence intervals for 21 MND and 20 Alzheimer's disease studies.

Study Characteristics

As seen in Table 2-3, there was consistent variation in relative-risk estimates with type of outcome measures, basis of occupational coding and exposure assessment methods for determination of MF levels. Estimates were highest for prevalence measures for both MND (RR

= 2.03, 95% CI: 1.22-3.37) and AD (RR = 2.15, 95% CI: 1.52-3.06), respectively, and for estimates based on either occupational titles or MF levels. For MND, studies with controls selected from relatives and friends had the highest estimates (RR = 2.23, 95% CI: 1.10-4.51). Sex differences could not explain this heterogeneity because few studies focused on women.

We examined magnitude and direction of associations using multiple meta-regression, particularly for type of outcome, source of occupational information, exposure assessment methods and basis of occupation. Meta-regressions (Table 2-4) exhibited decreases in MND and AD associations for exposure assessment methods after individually adjusting for occupational information and source of disease outcome. Adjustment for study design reduced both MND and AD associations for both source of outcome and type of outcome. Prevalence remained strongly associated with both MND and AD regardless of adjustment for study design or exposure assessment. Source of study funding accounted for some degree of heterogeneity between studies and decreased AD associations for exposure assessment and source of occupational information. Meta-regressions increased MND and AD associations for basis of occupation with adjustment for source of the occupational information.

Exposure Estimation

Of all studies, 57% occupational information came from interview data. Associations derived from interview and work records were similar. About half of the studies had no MF exposure assessment, 43% used classification tables or JEM, and 12% industrial hygiene review. Studies with industrial hygiene exposure evaluation exhibited higher relative risk estimates (RR=2.5, 95% CI: 0.63-9.97 for MND RR=2.21, 95% CI: 1.19-4.11 for AD).

We stratified estimates by either specific electric occupations or MF levels. Overall, we observed no association between MND and MF levels, but elevated relative risks for MND and occupational titles. The opposite was observed for AD elevated relative risks for AD and MF levels, but not for specific occupational titles. The same pattern was observed using generalized least squares trend (Table 2-5).

Publication Bias and Influence Analysis

There was some asymmetry in the funnel plots, with smaller studies tending to have positive associations for both MND and AD (Figure 2-3) and by Egger's test (p=0.005); Begg's test gave p =0.157 for MND and p = 0.018 for AD. These results suggest that some portion of the positive associations observed is due to publication bias favoring positive studies. When stratified by exposure assessment methods, we found publication bias among AD studies based on industrial hygiene/JEM (p=0.004) and MND studies with no MF exposure assessment (p=0.048) by Egger's test. Within subgroups of occupational information, we found publication bias in AD studies using interview/questionnaire (p=0.006) and MND studies using registry/census/death certificates (p=0.052) (Table 2-6). When we excluded selectively reported estimates, evidence supporting publication bias in AD studies diminished (data not shown). We detected no especially influential individual studies for MND or AD. (Figure 2-4).

Discussion

We observed moderate associations between indicators of occupational MF exposure and both MND and AD, and no association between MF and other neurodegenerative outcomes, such as dementia, MS and PD. We found relatively few dementia and MS studies, however. We observed increase in risk for MND in studies using occupational titles but increased risk for AD in studies using MF levels. Our results suggest that AD results might be due to publication bias.

Complete occupational exposure assessment consists of full work history with personal MF exposure measurements within each job held [63]. Because this is not feasible for all studies, researchers use alternative methods such as industrial hygiene judgment or job exposure matrices to assess exposure. Positive AD studies, using these methods, tended to be published. We found evidence of publication bias among MND studies without measurements or expert evaluation. Since NDD affect memory and cognition, we would expect recall bias in retrospective occupational histories based on subject interviews. Although we found similarly elevated associations for both MND and AD in interview- and work records-based studies, we found the possibility of publication bias in AD interview/questionnaire-based studies. Examination of exposure-related study characteristics suggests publication bias with AD studies. In light of these findings, efforts should be made to encourage publication of well-described occupational epidemiology studies including those with null results.

Disease classification and definition likely contribute to heterogeneity between studies. Lacking NDD registries, most occupational studies rely on mortality records, which underreport AD [64, 65]. Only severe AD is likely to appear on a death certificate [64]. The distinction between AD and dementia may differ between clinical studies [66]. In general, AD may be more susceptible to disease misclassification than MND. Another weakness in NDD studies is control selection, diagnoses made in hospital-based settings can potentially including patients with vascular or senile dementias among controls.

Prevalence was most associated with both MND and AD. Because ALS has short average disease duration and high fatality rate, we expected mortality rates would provide a reasonable proxy for ALS incidence. We noted similarly increased relative risks between MND and both incidence and mortality. With wide-spectrum AD, long disease duration would lead to higher population prevalence. Outcome measures explained some of the variability between studies.

Stronger associations in studies with MF measurements, complete work history records and clinical pathology/diagnostic information, respectively, lend some support for an association between AD and MF. Lower risk in incidence studies, on the other hand, argue for bias as an explanation for high prevalence estimates. Reporting and publication bias likely explains the clinical pathology/diagnostic criteria information observation for AD.

MND associations were stronger for electric occupations compared to estimates for MF levels. Positive associations using occupational title proxies may be confounded by co-exposure to neurotoxic agents or potential NDD risk factors, e.g. welding fumes for PD or polychlorinated benzenes (PCBs) for PD or ALS [67]. Electric shocks are suspected risk factors for ALS in electric occupations. Unfortunately, no MND study accounted for electric shocks and one study accounted for exposure to PCBs.

Our review was limited to English-language publications. It is possible that this limitation contributed to the publication bias we noted, since studies finding no association might well be more likely to be rejected from journals in this pool and eventually appear in unindexed or non-English journals. Another limitation of our study and any meta-analysis is that decisions about variable definitions, reference groups, metrics and cutpoints made by authors in the original studies may have introduced some bias. Some of these limitations could be speculatively addressed via sensitivity or bias analysis, which would largely expand the interval estimates for the associations [68, 69]. Such analyses require considerable labor to implement and space to report, however, and may not be justifiable given the large uncertainty already present, at least until the publication bias issue is resolved.

Conclusions

We provided a systematic summary of the literature on occupational MF and neurodegenerative diseases, which included a large number of occupational studies with and without measurements. Overall, we observed moderately increased risk estimates for MND and AD studies, but considerable heterogeneity, which appears to be at least partially attributable to methodologic differences among the studies. MND associations were stronger using occupational titles, while AD associations were higher using MF levels. Our results suggest that AD finding is due to publication bias for AD. Misclassification of disease coupled with imprecision related to exposure assessment likely affected all studies.

In light of these problems, we believe that conclusions about the relations of occupational MF exposure to neurologic disease will require improvement in exposure assessment (for example inclusion of female worker measurements, examination of electric shocks and disease classification), as well as more complete reporting of results regardless of association observed. Such improvements will be expensive, but until these improvements are made, the literature will remain too heterogeneous and potentially biased to draw reliable inferences about effects of occupational MF exposure. Because the associations we observed indicate potential risks, we suggest that improved studies are needed.

Table 2-1. Main characteristics of occupational epidemiological studies included in meta-analyses of MF and neurodegenerative diseases

Author [Ref]	Year	Type of measure	Diagnosis[1]	Country	Study design	Covariates[2]	Funding source	Exposure metrics	Type of outcome	Source of outcome information	Basis of occupational exposure	Source of the occupational exposure information	Occupational exposure assessment	Selective reporting	Control selection[3]
Andel [29]	2010	OR	AD, DEMENTIA	Sweden	case-control	1, 2, 3, 8	Gov't/Found.	MF level	Prevalence	Clin. pathology or dx	Represent. job	Interview/Quest.	Class. Table/JEM	No	1
Buckley [44]	1983	SMR	MND	UK	cohort	1, 2, 4, 5	Gov't/Found.	Occ. Title	Mortality	Clin. pathology or dx	Represent. job	Registry/Death Cert.	Not done/Unk./N.A.	No	0
Davanipour [14]	2007	OR	AD	USA	case-control	1, 2, 5, 8	Gov't/Found.	MF level	Prevalence	Clin. pathology or dx	Represent. job	Registry/Death Cert.	Class. Table/JEM	Yes	2
Davanipour [16]	1997	OR	ALS	USA	case-control	1, 2	Not mentioned	MF level	Prevalence	Clin. pathology or dx	Several jobs	Interview/Quest.	IH review	Yes	1
Deapen [17]	1986	OR	ALS	USA	case-control	1, 2	Gov't/Found.	Occ. Title	Prevalence	Clin. pathology or dx	Represent. job	Interview/Quest.	Not done/Unk./N.A.	No	1
Dick [34]	2007	OR	PD	Multi-country	case-control	1, 2, 5, 8	Gov't/Found.	Occ. Title	Prevalence	Clin. pathology or dx	Several jobs	Interview/Quest.	Not done/Unk./N.A.	No	3
Fang [41]	2009	OR	ALS	USA	case-control	1, 2, 3, 5, 8	Gov't/Found.	Occ. Title	Prevalence	Clin. pathology or dx	Several jobs	Interview/Quest.	Not done/Unk./N.A.	No	4
Feychting [7]	1998	OR	DEMENTIA, AD	Sweden	case-control	1, 2, 3	Gov't/Found.	MF level	Prevalence	Clin. pathology or dx	Several jobs	Interview/Quest.	Class. Table/JEM	No	1
Feychting [22]	2003	RR	AD, ALS, MS, PD, DEMENTIA	Sweden	cohort	1, 2, 3	Gov't/Found.	Both	Mortality	Death cert.	Several jobs	Registry/Death Cert.	Class. Table/JEM	No	0
Firestone [45]	2010	OR	PD	USA	case-control	1, 2, 5, 7, 8	Gov't/Found.	Occ. Title	Incidence	Clin. pathology or dx	Several jobs	Interview/Quest.	Not done/Unk./N.A.	No	3
Fored [42]	2005	RR	PD	Sweden	cohort	1, 2, 3, 4, 5	Industry	Occ. Title	Incidence	Clin. pathology or dx	Several jobs	Registry/Death Cert.	Not done/Unk./N.A.	No	0
Fryzek [52]	2005	SIR	PD	Denmark	cohort	1, 2, 4	Industry	Occ. Title	Prevalence	Clin. pathology or dx	Several jobs	Work history records	Not done/Unk./N.A.	No	0
Graves [6]	1999	OR	AD	USA	case-control	1, 2, 3	Gov't/Found.	MF level	Incidence	Clin. pathology or dx	Several jobs	Interview/Quest.	IH review	No	3
Gunnarsson [18]	1992	OR	MND	Sweden	case-control	1, 2	Gov't/Found.	Occ. Title	Prevalence	Clin. pathology or dx	Several jobs	Interview/Quest.	Not done/Unk./N.A.	No	4
Gunnarsson [19]	1991	OR	ALS	Sweden	case-control	1, 2, 4	Gov't/Found.	Occ. Title	Mortality	Death cert.	Represent. job	Registry/Death Cert.	Not done/Unk./N.A.	No	4
Hakansson [10]	2003	RR	AD, ALS, MS, PD	Sweden	cohort	1, 2, 3	Industry	MF level	Mortality	Death cert.	Several jobs	Registry/Death Cert.	Class. Table/JEM	No	0
Harmanci [32]†	2003	OR	AD	Turkey	cross-sectional	2, 3, 6, 8	Industry	MF level	Prevalence	Clin. pathology or dx	Represent. Job	Interview/Quest.	Class. Table/JEM	Yes	0
Johansen_a [24]	2000	RR	PD, DEMENTIA, MND	Denmark	cohort	1, 2, 4, 8	Industry	Both	Incidence	Clin. pathology or dx	Several jobs	Work history records	Class. Table/JEM	No	0
Johansen_b [37]	1999	SIR	MS	Denmark	cohort	1, 2, 4	Industry	Occ. Title	Incidence	Clin. pathology or dx	Several jobs	Work history records	Class. Table/JEM	No	0
Kirkey [46]	2001	OR	PD	USA	case-control	1, 2, 4, 5, 7	Gov't/Found.	Occ. Title	Prevalence	Clin. pathology or dx	Several jobs	Interview/Quest.	Not done/Unk./N.A.	No	3
Li [47]	2008	SIR	MS	Sweden	cohort	1, 2, 3, 4, 5	Gov't/Found.	Occ. Title	Incidence	Clin. pathology or dx	Several jobs	Registry/Death Cert.	Not done/Unk./N.A.	No	0
Li [48]	2009	SIR	PD	Sweden	cohort	1, 2, 3, 4, 5	Gov't/Found.	Occ. Title	Incidence	Clin. pathology or dx	Several jobs	Registry/Death Cert.	Not done/Unk./N.A.	No	0
McGuire [49]	1997	OR	ALS	USA	case-control	1, 2, 3, 5, 8	Gov't/Found.	Occ. Title	Incidence	Clin. pathology or dx	Several jobs	Interview/Quest.	Not done/Unk./N.A.	No	4
Noonan [11]	2002	OR	AD, ALS, PD	USA	case-control	1, 2, 3, 7	Not mentioned	Both	Mortality	Death cert.	Represent. job	Registry/Death Cert.	Class. Table/JEM	No	3
Park [12]	2005	MOR	AD, MND, PD, DEMENTIA	USA	case-control	1, 2, 3, 5, 7	Not mentioned	Both	Mortality	Death cert.	Represent. job	Registry/Death Cert.	Class. Table/JEM	Yes	3
Park [54]	2005	OR	PD	South Korea	case-control	1, 2, 3, 5, 8	Gov't/Found.	Occ. Title	Incidence	Clin. pathology or dx	Several jobs	Interview/Quest.	Not done/Unk./N.A.	No	3
Parlett [28]	2011	HR	MND	USA	cohort	1, 2, 3	Not mentioned	MF level	Mortality	Death cert.	Represent. job	Interview/Quest.	Class. Table/JEM	No	0
Qiu [33]	2004	RR	AD, DEMENTIA	Sweden	cohort	1, 2, 3, 8	Gov't/Found.	MF level	Incidence	Clin. pathology or dx	Several jobs	Interview/Quest.	EMF Measurements	No	0
Roosli [23]	2007	HR	AD, ALS, MS, PD, DEMENTIA	Swiss	cohort	1, 2, 4	Gov't/Found.	Both	Mortality	Death cert.	Several jobs	Work history records	EMF Measurements	No	0
Salib [53]	1996	OR	AD	UK	case-control	1, 2, 4, 5, 8	Not mentioned	Occ. Title	Incidence	Clin. pathology or dx	Several jobs	Interview/Quest.	Not done/Unk./N.A.	No	3
Savitz_a [9]	1998	OR	AD, ALS, PD	USA	case-control	1, 2, 3, 4, 7	Not mentioned	Occ. Title	Mortality	Death cert.	Represent. job	Registry/Death Cert.	Not done/Unk./N.A.	Yes	3
Savitz_b [8]	1998	RR	AD, ALS, PD	USA	cohort	1, 2, 3, 4, 5, 8	Industry	MF level	Mortality	Death cert.	Several jobs	Work history records	EMF Measurements	No	0
Schulte [38]†	1996	PMR	DEMENTIA, MND, PD	USA	PM study	1, 2, 7	Not mentioned	Occ. Title	Mortality	Death cert.	Represent. Job	Registry/Death Cert.	Not done/Unk./N.A.	Yes	0
Seidler [27]	2007	OR	AD, DEMENTIA	Germany	case-control	1, 2, 5, 8	Gov't/Found.	Both	Prevalence	Clin. pathology or dx	Several jobs	Interview/Quest.	Class. Table/JEM	Yes	3
Sobel [5]	1996	OR	AD	USA	case-control	1, 2, 3	Gov't/Found.	MF level	Prevalence	Clin. pathology or dx	Represent. job	Interview/Quest.	Class. Table/JEM	Yes	2
Sobel_1 [4]	1995	OR	AD	Finland	case-control	1, 2, 3, 5	Gov't/Found.	MF level	Prevalence	Clin. pathology or dx	Represent. job	Interview/Quest.	IH review	Yes	2
Sobel_2 [4]	1995	OR	AD	Finland	case-control	1, 2, 3, 5	Gov't/Found.	MF level	Prevalence	Clin. pathology or dx	Represent. job	Interview/Quest.	IH review	Yes	3
Sobel_3 [4]	1995	OR	AD	USA	case-control	1, 2, 3, 5	Gov't/Found.	MF level	Prevalence	Clin. pathology or dx	Represent. job	Interview/Quest.	IH review	Yes	4
Sorahan [13]	2007	RR	AD, MND, PD	UK	cohort	1, 2, 3, 4	Industry	MF level	Mortality	Death cert.	Several jobs	Work history records	Class. Table/JEM	No	0
Stampfer [50]	2009	MOR	PD, AD, MND, DEMENTIA	USA	case-control	1, 2, 4, 5, 7	Industry	Occ. Title	Mortality	Death cert.	Represent. job	Registry/Death Cert.	Not done/Unk./N.A.	No	2
Strickland [39]	1996	OR	ALS	USA	case-control	1, 2, 5, 8	Gov't/Found.	Occ. Title	Prevalence	Clin. pathology or dx	Several jobs	Interview/Quest.	Not done/Unk./N.A.	Yes	3
Sutedja [43]	2007	OR	ALS	Netherland	case-control	1, 2, 3, 8	Gov't/Found.	Occ. Title	Incidence	Clin. pathology or dx	Several jobs	Interview/Quest.	Not done/Unk./N.A.	No	1
Tanner [51]	2009	OR	PD	USA	case-control	1, 2, 5, 7, 8	Industry	Occ. Title	Prevalence	Clin. pathology or dx	Several jobs	Interview/Quest.	Not done/Unk./N.A.	No	1
Weisskopf [40]	2005	RR	ALS	USA	cohort	1, 2, 3, 8	Not mentioned	Occ. Title	Mortality	Death cert.	Represent. job	Interview/Quest.	Not done/Unk./N.A.	No	0

Notes:
[1] Disease Abbrevations: AD = Alzheimer's Disease, ALS = Amyotrophic Lateral Sclerosis, MND = Motor Neuron Disease, PD = Parkinson's Disease
[2] Covariates: 1 = Age, 2= Sex, 3 = SES or Education; 4 = Calendar period/year, 5 = Residence/region, 6 = Urban/Rural, 7 = Race, 8 = Other Covariates
[3] Control Selection: 1 = N/A (cohort study), 2 = Relatives or friends, 3 = Other neurological diseases included, 4 = Other neurological diseases excluded, 4 = Population-based
Abbreviations: Clin. = Clinical; Dx = Diagnosis; Found. = Foundation; IH = Industrial hygiene; JEM = Job Exposure Matrix; N.A. = Not applicable; Quest. = Questionnaire; Unk. = Unknown
† These studies are presented for completeness, not included in the final analysis.

Table 2-2. Pooled risk estimates for Dementia and Parkinson's disease (PD) by study characteristics

Study Characteristics	Coding Description	Dementia				PD			
		No.[1]	Combined RR_{RE}	p-value[2]	95 % Range[3]	No.[1]	Combined RR_{RE}	p-value[2]	95 % Range[3]
Location	US	5	1.07 (0.95 – 1.19)	0.456	1.29	20	1.00 (0.92 – 1.10)	0.022	1.43
	Europe	18	0.98 (0.88 – 1.09)	0.133		15	0.93 (0.83 – 1.03)	0.636	
	Other	-	-	-		2	0.51 (0.23 – 1.11)	0.050	
Study design	Case-control	12	1.07 (1.00 – 1.16)	0.793	-	22	0.98 (0.90 – 1.12)	0.019	1.41
	Cohort	11	0.91 (0.86 – 0.96)	0.013		15	0.95 (0.84 – 1.05)	0.335	
Basis of occupation	Representative job	7	1.07 (0.99 -1.16)	0.477	-	16	1.02 (0.93 – 1.12)	0.045	1.46
	Several jobs	16	0.92 (0.86 -0.97)	0.178		21	0.91 (0.83 – 1.01)	0.168	
Occupational source	Registry or census or death certificate	7	1.00 (0.92 – 1.10)	0.004	1.41	22	0.99 (0.93 – 1.07)	0.039	1.38
	Interview	9	1.19 (0.93 – 1.52)	0.408		6	0.76 (0.59 – 0.98)	0.211	
	Work history records	7	1.20 (0.88 – 1.65)	0.369		9	0.92 (0.77 – 1.10)	0.518	
Exposure assessment	No exposure information	1	1.03 (0.77 – 1.39)	-	1.58	20	0.94 (0.85 – 1.03)	0.085	1.37
	Classification/JEM or IH	16	1.04 (0.92 – 1.16)	0.023		12	1.00 (0.90 – 1.10)	0.105	
	EMF measurement	6	1.19 (0.90 – 1.56)	0.126		5	1.00 (0.77 – 1.29)	0.330	
Type of outcome	Mortality	11	1.02 (0.95 – 1.12)	0.006	1.41	25	1.00 (0.93 – 1.09)	0.052	1.40
	Prevalence	7	1.35 (0.95 -1.91)	0.963		4	0.87 (0.65 – 1.15)	0.897	
	Incidence	5	1.04 (0.78 – 1.38)	0.063		8	0.87 (0.76 – 1.00)	0.122	
Outcome source	Death certificates	11	1.02 (0.92 -1.12)	0.006	1.44	25	1.00 (0.93 – 1.08)	0.052	1.38
	Clin., Path, dx info	12	1.16 (0.93 – 1.44)	0.351		12	0.87 (0.77 – 0.99)	0.360	
Funding source	Gov't or foundation	15	1.04 (0.90 – 1.20)	0.138	1.58	13	0.93 (0.83 – 1.04)	0.117	1.30
	Industry	4	1.02 (0.79 – 1.32)	0.304		9	0.89 (0.80 – 0.99)	0.445	
	None or unknown	4	1.10 (0.92 – 1.30)	0.327		15	1.05 (0.96 – 1.14)	0.303	
Selective reporting	Yes	8	1.09 (0.96 – 1.24)	0.669	1.33	13	1.02 (0.92 – 1.12)	0.725	1.34
	No	15	0.98 (0.89 – 1.09)	0.072		24	0.93 (0.86 – 1.01)	0.017	
Sex of risk estimates	Both	13	1.12 (0.99 – 1.26)	0.259	1.36	13	0.93 (0.83 – 1.05)	0.205	1.42
	Male	7	0.98 (0.86 – 1.23)	0.193		23	1.00 (0.92 – 1.09)	0.039	
	Female	3	0.92 (0.76 – 1.11)	0.701		1	0.80 (0.55 – 1.16)	-	
Basis of risk estimate	MF level	11	1.01 (0.90 – 1.14)	0.006	1.46	9	1.01 (0.89 – 1.14)	0.046	1.37
	Occupational title	12	1.09 (0.94 – 1.26)	0.458		28	0.95 (0.88 – 1.03)	0.152	
Control Selection	Not applicable	11	0.91 (0.86 – 0.96)	0.088	-	15	0.94 (0.86 – 1.05)	0.335	1.29
	Relatives or friends	3	1.31 (0.82 – 2.08)	0.615		1	1.01 (0.57 – 1.80)	-	
	Other neuro. diseases included	1	1.03 (0.86 – 1.24)	-		1	0.85 (0.71 – 1.02)	-	
	Other neuro excluded	8	1.08 (0.99 – 1.17)	0.669		20	1.01 (0.92 – 1.11)	0.068	
	Population-based	-	-	-		-	-	-	

Notes: Clin. Path./dx info. = Clinical, Pathology, RE = Random Effects

[1] Number of relative risk estimates extracted from studies

[2] Homogeneity p-value

[3] Estimated central residual range calculated as $e^{3.92\tau}$, assuming lognormality of residual RR

Table 2-3. Pooled risk estimates for motor neuron disease (MND) and Alzheimer's Disease (AD) by study characteristics

Study Characteristics	Coding Description	MND No.[1]	MND Combined RR_{RE}	MND p-value[2]	MND 95 % Range[3]	AD No.[1]	AD Combined RR_{RE}	AD p-value[2]	AD 95 % Range[3]
Location	US	23	1.39 (1.12-1.71)	0.000	4.07	26	1.23 (1.05-1.44)	0.007	2.95
	Europe	27	1.16 (0.95-1.42)	0.001		25	1.45 (1.19-1.77)	0.000	
Study design	Case-control	27	1.38 (1.13-1.68)	0.000	4.01	36	1.29 (1.11-1.50)	0.005	3.06
	Cohort	23	1.14 (0.92-1.42)	0.002		15	1.39 (1.10-1.75)	0.000	
Basis of occupation	Representative job	24	1.29 (1.05-1.58)	0.000	4.14	29	1.29 (1.10-1.52)	0.001	3.09
	Several jobs	26	1.24 (1.00-1.55)	0.000		22	1.36 (1.10-1.67)	0.000	
Occupational source	Registry or census or death certificate	31	1.19 (1.00-1.40)	0.000	3.90	27	1.24 (1.07-1.43)	0.000	3.05
	Interview	11	1.47 (1.00-2.14)	0.093		18	1.60 (1.20-2.14)	0.046	
	Work history records	8	1.62 (1.01-2.59)	0.929		6	1.60 (0.94-2.72)	0.471	
Exposure assessment	No exposure information	24	1.33 (1.07-1.65)	0.000	4.18	13	1.17 (0.94-1.46)	0.023	3.18
	Classification/JEM or IH	21	1.19 (0.95-1.47)	0.000		31	1.40 (1.18-1.66)	0.000	
	EMF measurement	5	1.53 (0.78-3.04)	0.742		7	1.44 (0.94-2.23)	0.133	
Type of outcome	Mortality	39	1.20 (1.03-1.40)	0.062	3.89	31	1.24 (1.09-1.42)	0.000	2.73
	Prevalence	6	2.03 (1.22-3.37)	0.000		16	2.15 (1.52-3.06)	0.480	
	Incidence	5	1.39 (0.81-2.39)	0.455		4	1.04 (0.67-1.60)	0.405	
Outcome source	Death certificates	36	1.20 (1.02-1.49)	0.000	3.97	31	1.25 (1.08-1.44)	0.000	3.09
	Clin., Path, dx info	14	1.49 (1.10-2.02)	0.122		20	1.64 (1.24-2.18)	0.063	
Funding source	Gov't or foundation	27	1.15 (0.93-1.41)	0.000	3.99	29	1.55 (1.28-1.89)	0.000	2.98
	Industry	6	1.29 (0.85-1.97)	0.001		4	1.18 (0.76-1.84)	0.075	
	None or unknown	16	1.46 (1.14-1.87)	0.001		18	1.18 (0.99-1.40)	0.194	
Selective reporting	Yes	14	1.56 (1.20-2.03)	0.000	3.89	28	1.40 (1.17-1.68)	0.005	3.18
	No	36	1.15 (0.97-1.37)	0.000		23	1.24 (1.17-1.68)	0.000	
Sex of risk estimates	Both	17	1.40 (1.11-1.78)	0.040	3.67	13	1.26 (0.98-1.62)	0.337	3.09
	Male	28	1.26 (1.05-1.52)	0.000		30	1.37 (1.16-1.60)	0.000	
	Female	4	0.75 (0.45-1.25)	0.616		8	1.19 (0.81-1.76)	0.005	
Basis of risk estimate	MF level	11	1.07 (0.78-1.46)	0.075	3.81	23	1.59 (1.28-1.99)	0.000	3.04
	Occupational title	39	1.32 (1.12-1.56)	0.000		28	1.21 (1.03-1.40)	0.000	
Control Selection	Not applicable	23	1.14 (0.93-1.40)	0.002	3.72	15	1.40 (1.09-1.80)	0.000	3.55
	Relatives or friends	4	2.23 (1.10-4.51)	0.614		3	1.19 (0.62-2.30)	0.633	
	Other neuro. diseases included	1	0.71 (0.35-1.46)	-		6	1.87 (1.13-3.07)	0.001	
	Other neuro excluded	15	1.51 (1.18-1.93)	0.000		25	1.25 (1.04-1.49)	0.141	
	Population-based	7	1.12 (0.75-1.65)	0.124		2	2.32 (0.52-10.3)	0.590	

Notes: Clin. Path./dx info. = Clinical, Pathology, RE = Random Effects

[1] Number of relative risk estimates extracted from studies

[2] Homogeneity p-value

[3] Estimated central residual range calculated as $e^{3.92\tau}$, assuming lognormality of residual RR

Table 2-4. Assessment of type of outcome, source of occupational information, exposure assessment and basis of occupation on risk estimates of occupational MF exposure in observational epidemiologic studies (results of multiple meta-regression)

	Additional study characteristics included in the model								
MND	RR	95% CI	95% Range**	RR	95% CI	95% Range**	RR	95% CI	95% Range**
Type of outcome	With study design		3.95	With exposure assessment		4.11	With funding		3.69
Prevalence	1.60	(0.92 - 2.78)		1.85	(0.97 - 3.52)		1.87	(1.10 - 1.77)	
Incidence	1.16	(0.66 - 2.30)		1.34	(0.75 - 2.39)		1.25	(0.70 - 2.24)	
Occupational source	With study design		3.77	With basis of occupation		3.86	With funding		3.65
Interview/Quest	-	-		0.86	(0.47 - 1.59)		1.27	(0.67 - 2.43)	
Registry or DC	0.85	(0.57 - 1.29)		0.66	(0.38 - 1.13)		1.00	(0.59 -1.68)	
Work hx records	1.35	(0.71 - 2.55)		-	-		1.59	(0.97 - 2.62)	
Exposure assessment	With basis of occupation		4.32	With outcome source		4.14	With funding		4.18
EMF Measurements	-	-		-	-		1.66	(0.78 - 3.53)	
IH/JEM	0.77	(0.37 - 1.60)		0.76	(0.37 - 1.55)		1.20	(0.77 - 1.90)	
Not done/unknown	0.86	(0.40 - 1.87)		0.80	(0.39 - 1.66)		1.34	(0.83 - 2.19)	
Basis of occupational information	With occupational source		3.86	With funding		4.07	With selective reporting		3.99
Representative job	1.92	(1.08 - 3.40)		1.16	(0.70 - 1.92)		0.87	(0.62 - 1.22)	
Several jobs	1.62	(1.01 - 2.59)		1.35	(0.87 - 2.10)		-	-	
AD									
Type of outcome	With study design		2.60	With exposure assessment		2.78	With funding		2.74
Prevalence	1.85	(1.27 - 2.70)		1.97	(1.34 - 2.90)		1.99	(1.13 - 3.50)	
Incidence	0.79	(0.50 - 1.24)		0.79	(0.45 - 1.41)		-	-	
Mortality	-	-		1.23	(1.03 - 1.47)		1.30	(0.80 - 2.10)	
Occupational source	With study design		3.13	With basis of occupation		3.20	With funding		3.07
Interview/Quest	-	-		0.98	(0.52 - 1.84)		1.32	(0.88 - 1.98)	
Registry or DC	0.77	(0.55 - 1.06)		0.74	(0.41 - 1.35)		1.17	(0.98 -1.40)	
Work hx records	0.95	(0.50 - 1.83)		-	-		1.43	(0.77 - 2.64)	
Exposure assessment	With basis of occupation		3.38	With outcome source		3.21	With funding		3.18
EMF Measurements	-	-		-	-		1.15	(0.60 - 2.19)	
IH/JEM	0.93	(0.56 - 1.54)		1.02	(0.64 - 1.65)		1.21	(0.73 - 2.01)	
Not done/unknown	0.75	(0.42 - 1.35)		0.90	(0.54 - 1.49)		1.19	(0.74 - 1.94)	
Basis of occupational information	With occupational source		3.20	With funding		3.04	With selective reporting		3.04
Representative job	1.68	(0.91 - 3.11)		1.36	(0.85 - 2.18)		1.38	(1.15 - 1.64)	
Several jobs	1.59	(0.93 - 2.73)		0.97	(0.59 - 1.60)		1.75	(1.20 - 2.54)	

Note: Additional study characteristics are defined as follows: study design (case-control or cohort), basis of occupation (representative job or several jobs), outcome source (death certificates or clinic pathology/diagnostic criteria) and funding (government/foundation, industry or unknown/not stated).

** Estimated central residual range calculated as $e^{3.92\tau}$, assuming lognormality of residual RR

Table 2-5. Pooled risk estimates of motor neuron disease and Alzheimer's disease and occupational MF exposure in observational epidemiologic studies using generalized least squares trend estimation

Outcome	**No. of Studies**	**No. of Estimates**	**Combined $RR_{Fixed\ effects}$**	**Combined $RR_{Random\ effects}$**	**df**	**p-value***	**95% Range****
Motor neuron disease							
Occupational title	10	13	1.02 (0.86-1.21)	1.53 (1.00-2.37)	12	0.0000	8.79
MF level	4	4	1.09 (0.95-1.24)	1.09 (0.95-1.24)	3	0.4579	0.000
Alzheimer's disease							
Occupational title	5	9	0.99 (0.90-1.08)	1.00 (0.89-1.12)	8	0.3911	1.16
MF level	11	15	1.04 (0.96-1.13)	2.14 (1.46-3.15)	14	0.0000	9.86

Notes: For occupational title, cases and controls with more than 5 exposed were extracted. Groups and occupations of high MF exposures as determined by MF job exposure matrix (Bowman et. al.) were included in analyses. For MF level, estimates were extracted from all exposed strata. Only studies publishing the number exposed cases and controls, person-time or persons for each exposure level were included in this analysis.

* Homogeneity p-value

** Estimated central residual range calculated as $e^{3.92\tau}$, assuming lognormality of residual RR

Table 2-6. Assessment of publication bias in exposure-related study characteristics of occupational MF motor neuron disease and Alzheimer' disease studies (using linear regression of weighted log risk ratios on standard errors)

	MND			**AD**		
	Intercept (SE)	Slope (SE)	p-value*	Intercept (SE)	Slope (SE)	p-value*
Occupational source						
Interview/Questionnaire	1.13 (1.00)	-0.14 (0.44)	0.286	1.66 (0.52)	-0.35 (0.24)	0.006
Registry or DC	1.27 (0.63)	-0.17 (0.13)	0.052	0.87 (0.44)	0.04 (0.05)	0.060
Work history records	-0.30 (0.49)	0.64 (0.23)	0.558	0.74 (1.02)	-0.47 (1.79)	0.806
Exposure assessment						
EMF Measurements	0.90 (1.51)	-0.15 (0.96)	0.592	1.50 (0.82)	-0.31 (0.33)	0.126
IH/JEM	1.20 (0.71)	-0.18 (0.16)	0.109	0.99 (0.32)	0.05 (0.05)	0.004
Not done/unknown	1.19 (0.57)	-0.11 (0.15)	0.048	0.75 (0.56)	-.008 (0.07)	0.208
Basis of occupational information						
Representative job	1.17 (0.66)	-0.08 (0.15)	0.088	1.04 (0.29)	0.02 (0.03)	0.001
Several jobs	1.22 (0.47)	-0.22 (0.13)	0.017	0.32 (0.69)	0.21 (0.22)	0.652
Funding source						
Gov't/Foundation	1.13 (0.48)	0.24 (0.13)	0.027	0.93 (0.50)	0.09 (0.18)	0.072
Industry	2.27 (1.15)	-0.48 (0.27)	0.120	1.03 (0.95)	-0.08 (0.09)	0.393
Unknown or not stated	1.00 (0.68)	0.06 (0.16)	0.161	0.35 (0.38)	0.09 (0.04)	0.362
Type of outcome						
Incidence	-0.55 (0.93)	0.59 (0.38)	0.603	1.44 (1.15)	-0.43 (0.35)	0.336
Prevalence	1.08 (0.47)	-0.14 (0.11)	0.028	0.80 (0.39)	0.04 (0.05)	0.049
Mortality	1.69 (1.35)	0.09 (0.59)	0.281	0.92 (0.62)	0.20 (0.39)	0.162
Source of outcome information						
Death certificates	1.08 (0.50)	-0.14 (0.11)	0.037	0.79 (0.39)	0.04 (0.05)	0.049
Clinical diagnostic	0.90 (0.75)	0.05 (0.28)	0.252	1.61 (0.45)	-0.33 (0.22)	0.002

* p-value of null hypothesis, e.g. no small study effects

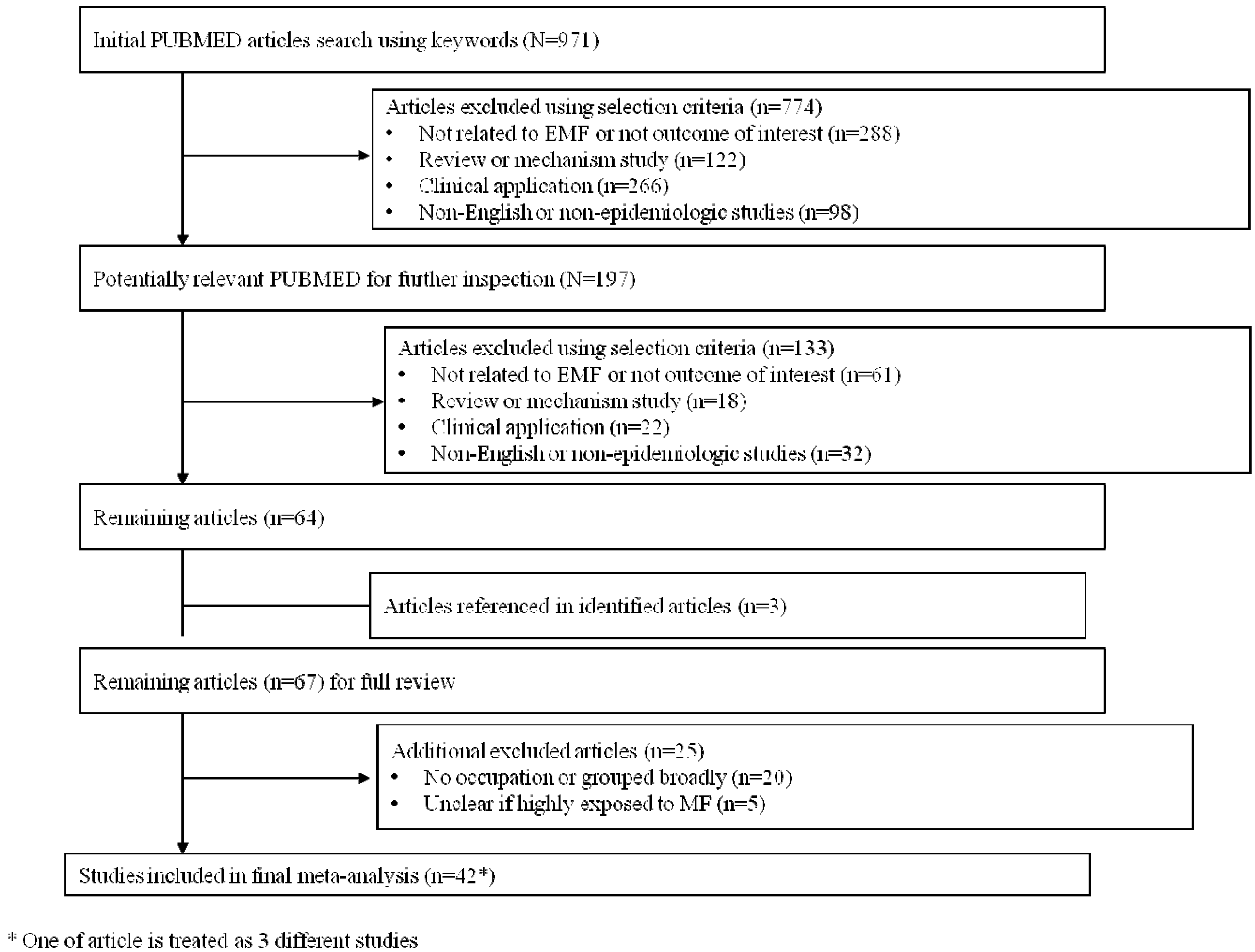


Figure 2-1. Flow of article selection and exclusion for final analysis of occupational MF and neurodegenerative diseases

Figure 2-2. Forest plot of occupational MF exposure and both motor neuron disease (MND) and Alzheimer's disease (AD)

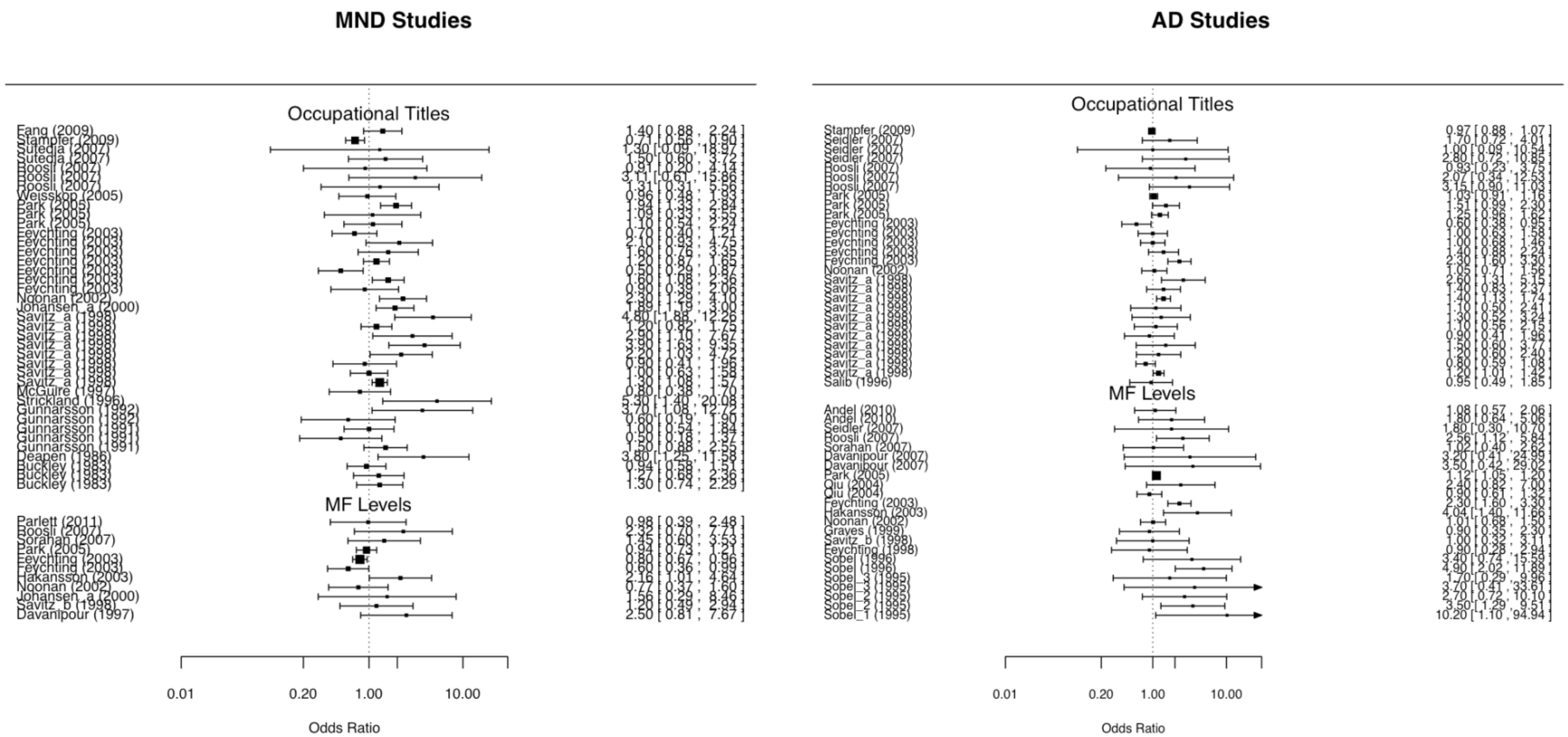
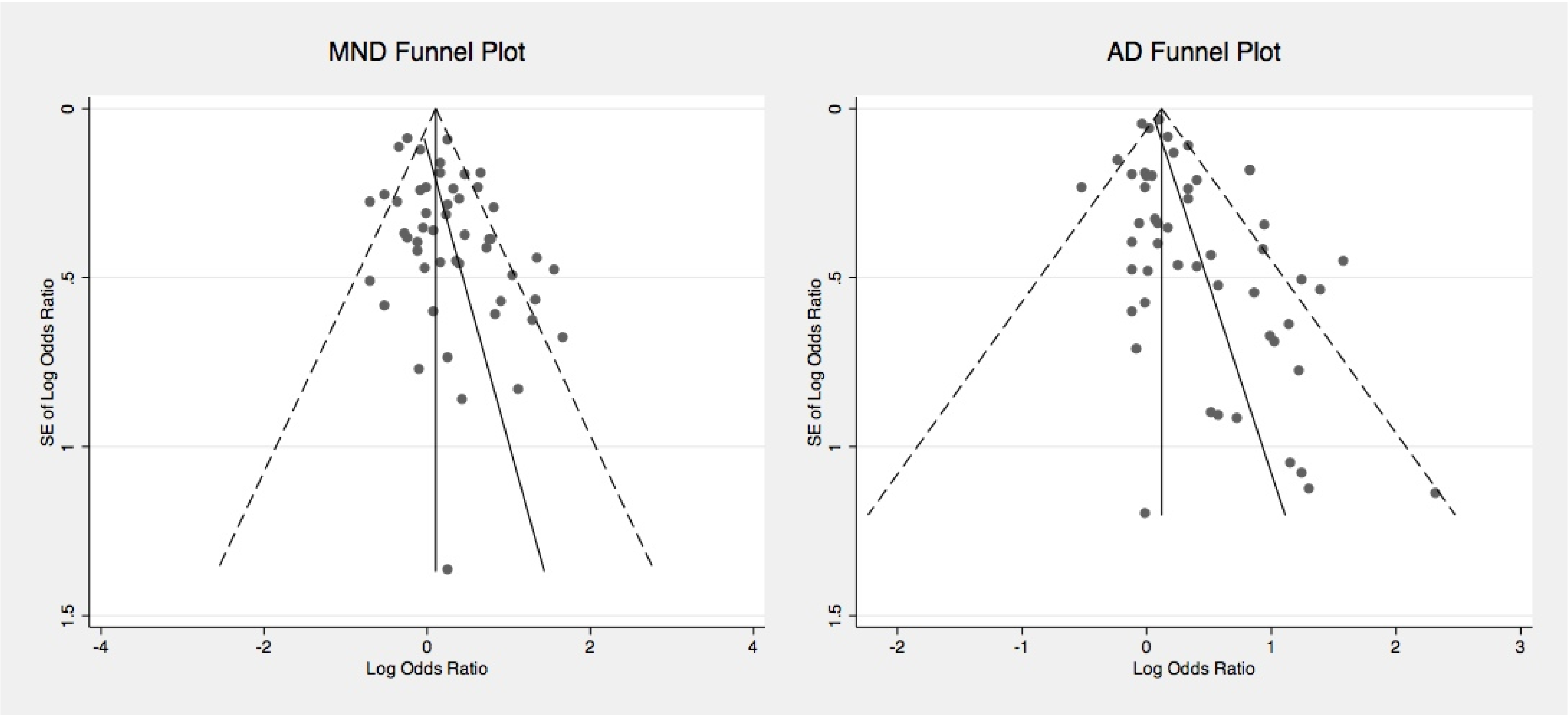
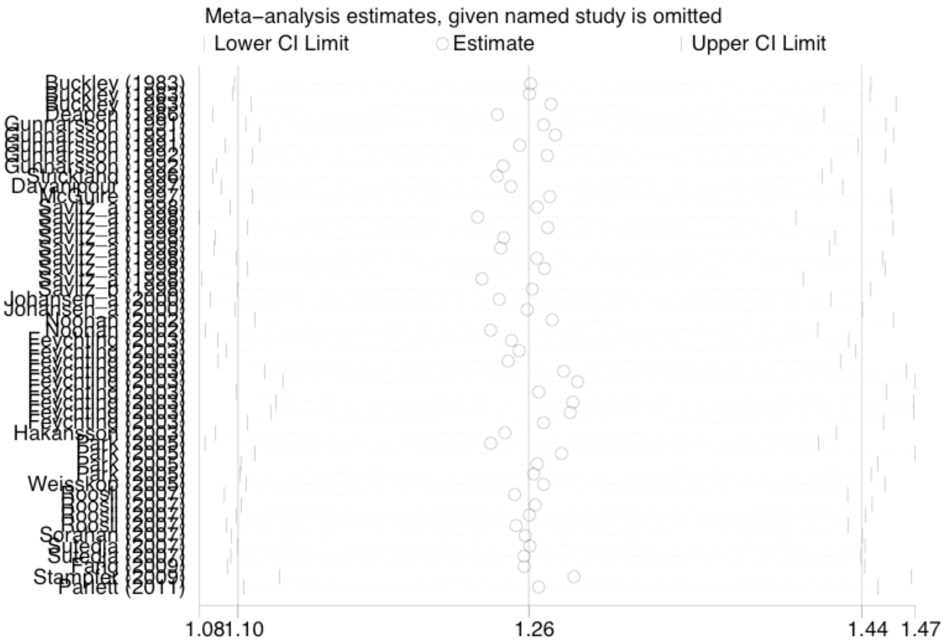


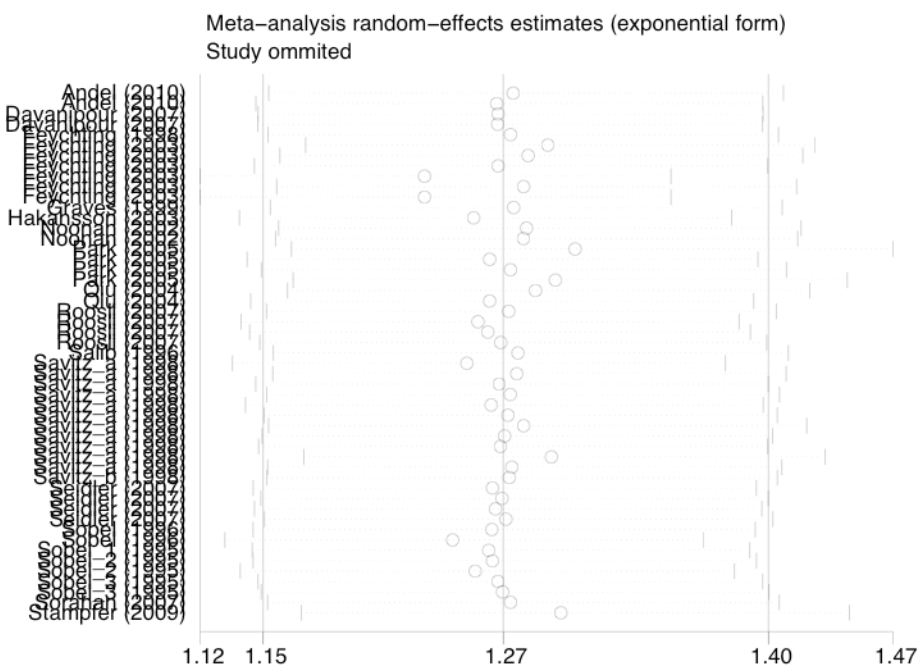
Figure 2-3. Funnel plot to display publication bias among studies of occupational EMF exposure and both motor neuron disease (MND) and Alzheimer's disease (AD), including the fitted regression line from Egger's test for small-study effects



Note: Dashed lines denote the pseudo 95% confidence limits

Figure 2-4. Influence plots of occupational MF exposure and both motor neuron disease (MND) and Alzheimer's disease (AD)





References

1. WHO and World Federation of Neurology, *Atlas: Country Resources for Neurological Disorders*, Programme for Neurological Diseases and Neuroscience, Editor. 2004, World Health Organization: Geneva, Switzerland.

2. Ahlbom, A., et al., *Review of the Epidemiologic Literature on EMF and Health.* Environmental Health Perspectives, 2001. 109(6): p. 911-933.

3. WHO, *Extremely Low Frequency Fields*, in *Environmental Health Criteria 238*. 2007, WHO: Geneva, Switzerland.

4. Sobel, E., et al., *Occupations with exposure to electromagnetic fields: a possible risk factor for Alzheimer's disease.* Am J Epidemiol, 1995. 142(5): p. 515-24.

5. Sobel, E., et al., *Elevated risk of Alzheimer's disease among workers with likely electromagnetic field exposure.* Neurology, 1996. 47(6): p. 1477-81.

6. Graves, A.B., et al., *Occupational exposure to electromagnetic fields and Alzheimer disease.* Alzheimer Dis Assoc Disord, 1999. 13(3): p. 165-70.

7. Feychting, M., et al., *Dementia and occupational exposure to magnetic fields.* Scand J Work Environ Health, 1998. 24(1): p. 46-53.

8. Savitz, D.A., H. Checkoway, and D.P. Loomis, *Magnetic field exposure and neurodegenerative disease mortality among electric utility workers.* Epidemiology, 1998. 9(4): p. 398-404.

9. Savitz, D.A., D.P. Loomis, and C.K. Tse, *Electrical occupations and neurodegenerative disease: analysis of U.S. mortality data.* Arch Environ Health, 1998. 53(1): p. 71-4.

10. Hakansson, N., et al., *Neurodegenerative diseases in welders and other workers exposed to high levels of magnetic fields.* Epidemiology, 2003. 14(4): p. 420-6; discussion 427-8.

11. Noonan, C.W., et al., *Occupational exposure to magnetic fields in case-referent studies of neurodegenerative diseases.* Scandinavian journal of work, environment & health, 2002. 28(1): p. 42-8.

12. Park, R., et al., *Potential occupational risks for neurodegenerative diseases.* Am. J. Ind. Med., 2005. 48(1): p. 63-77.

13. Sorahan, T. and L. Kheifets, *Mortality from Alzheimer's, motor neurone and Parkinson's disease in relation to magnetic field exposure: findings from the study of UK electricity generation and transmission workers, 1973-2004.* Occupational and Environmental Medicine, 2007: p. 8.

14. Davanipour, Z., et al., *A case-control study of occupational magnetic field exposure and Alzheimer's disease: results from the California Alzheimer's Disease Diagnosis and Treatment Centers.* BMC Neurol, 2007. 7: p. 13.

15. Kheifets, L., et al., *Future needs of occupational epidemiology of extremely low frequency (ELF) electric and magnetic fields (EMF): review and recommendations.* Occupational and Environmental Medicine, 2008. 66(2): p. 72-80.

16. Davanipour, Z., et al., *Amyotrophic lateral sclerosis and occupational exposure to electromagnetic fields.* Bioelectromagnetics, 1997. 18(1): p. 28-35.

17. Deapen, D.M. and B.E. Henderson, *A case-control study of amyotrophic lateral sclerosis.* Am J Epidemiol, 1986. 123(5): p. 790-9.

18. Gunnarsson, L.G., et al., *A case-control study of motor neurone disease: its relation to heritability, and occupational exposures, particularly to solvents.* Br J Ind Med, 1992. 49(11): p. 791-8.

19. Gunnarsson, L.G., et al., *Amyotrophic lateral sclerosis in Sweden in relation to occupation.* Acta Neurol Scand, 1991. 83(6): p. 394-8.

20. Johansen, C. and J.H. Olsen, *Mortality from amyotrophic lateral sclerosis, other chronic disorders, and electric shocks among utility workers.* Am J Epidemiol, 1998. 148(4): p. 362-8.

21. Li, C.Y. and F.C. Sung, *Association between occupational exposure to power frequency electromagnetic fields and amyotrophic lateral sclerosis: a review.* Am J Ind Med, 2003. 43(2): p. 212-20.

22. Feychting, M., et al., *Occupational Magnetic Field Exposure and Neurodegenerative Disease.* Epidemiology, 2003. 14(4): p. 413-419.

23. Roosli, M., et al., *Mortality from Neurodegenerative Disease and Exposure to Extremely Low-Frequency Magnetic Fields: 31 Years of Observations on Swiss Railway Employees.* Neuroepidemiology, 2007. 28(4): p. 197-206.

24. Johansen, C., *Exposure to electromagnetic fields and risk of central nervous system disease in utility workers.* Epidemiology, 2000. 11(5): p. 539-43.

25. Hug, K., M. Roosli, and R. Rapp, *Magnetic field exposure and neurodegenerative diseases--recent epidemiological studies.* Soz Praventivmed, 2006. 51(4): p. 210-20.

26. Garcia, A.M., A. Sisternas, and S.P. Hoyos, *Occupational exposure to extremely low frequency electric and magnetic fields and Alzheimer disease: a meta-analysis.* Int J Epidemiol, 2008. 37(2): p. 329-40.

27. Seidler, A., et al., *Occupational exposure to low frequency magnetic fields and dementia: a case-control study.* Occup Environ Med, 2007. 64(2): p. 108-14.

28. Parlett, L.E., J.D. Bowman, and E. van Wijngaarden, *Evaluation of occupational exposure to magnetic fields and motor neuron disease mortality in a population-based cohort.* J Occup Environ Med, 2011. 53(12): p. 1447-51.

29. Andel, R., et al., *Work-related exposure to extremely low-frequency magnetic fields and dementia: results from the population-based study of dementia in Swedish twins.* J Gerontol A Biol Sci Med Sci, 2010. 65(11): p. 1220-7.

30. Bowman, J.D., J.A. Touchstone, and M.G. Yost, *A population-based job exposure matrix for power-frequency magnetic fields.* J Occup Environ Hyg, 2007. 4(9): p. 715-28.

31. Huss, A., et al., *Residence near power lines and mortality from neurodegenerative diseases: longitudinal study of the Swiss population.* Am J Epidemiol, 2009. 169(2): p. 167-75.

32. Harmanci, H., et al., *Risk Factors for Alzheimer Disease: A Population-Based Case-Control Study in Istanbul, Turkey.* Alzheimer Disease & Associated Disorders, 2003. 17(3): p. 139-145.

33. Qiu, C., et al., *Occupational exposure to electromagnetic fields and risk of Alzheimer's disease.* Epidemiology, 2004. 15(6): p. 687-94.

34. Dick, S., et al., *Occupational titles as risk factors for Parkinson's disease.* Occup Med (Lond), 2007. 57(1): p. 50-6.

35. Park, R.M., et al., *Potential occupational risks for neurodegenerative diseases.* Am J Ind Med, 2005. 48(1): p. 63-77.

36. Sorahan, T. and L. Kheifets, *Mortality from Alzheimer's, motor neurone 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, 2007.

37. Johansen, C., et al., *Multiple sclerosis (MS) among utility workers.* Neurology, 1999. 52: p. 1279-82.

38. Schulte, P., et al., *Neurodegenerative diseases: occupational occurrence and potential risk factors, 1982 through 1991.* American Journal of Public Health, 1996. 86(9): p. 1281.

39. Strickland, D., et al., *Amyotrophic lateral sclerosis and occupational history. A pilot case-control study.* Archives of Neurology, 1996. 53(8): p. 730-733.

40. Weisskopf, M.G., et al., *Prospective study of occupation and amyotrophic lateral sclerosis mortality.* Am J Epidemiol, 2005. 162(12): p. 1146-52.

41. Fang, F., et al., *Workplace Exposures and the Risk of Amyotrophic Lateral Sclerosis.* 2009.

42. Fored, C.M., et al., *Parkinson's disease and other basal ganglia or movement disorders in a large nationwide cohort of Swedish welders.* Occup Environ Med, 2006. 63(2): p. 135-40.

43. Sutedja, N.A., et al., *Lifetime occupation, education, smoking, and risk of ALS.* Neurology, 2007. 69(15): p. 1508-14.

44. Buckley, J., et al., *Motor neuron disease in England and Wales, 1959-1979.* J Neurol Neurosurg Psychiatry, 1983. 46(3): p. 197-205.

45. Firestone, J.A., et al., *Occupational factors and risk of Parkinson's disease: A population-based case-control study.* Am J Ind Med, 2010. 53(3): p. 217-23.

46. Kirkey, K.L., et al., *Occupational categories at risk for Parkinson's disease.* Am J Ind Med, 2001. 39(6): p. 564-71.

47. Li, X., K. Hemminki, and K. Sundquist, *Regional, socioeconomic and occupational groups and risk of hospital admission for multiple sclerosis: a cohort study in Sweden.* Mult Scler, 2008. 14(4): p. 522-9.

48. Li, X., J. Sundquist, and K. Sundquist, *Socioeconomic and occupational groups and Parkinson's disease: a nationwide study based on hospitalizations in Sweden.* Int Arch Occup Environ Health, 2009. 82(2): p. 235-41.

49. McGuire, V., et al., *Occupational exposures and amyotrophic lateral sclerosis. A population-based case-control study.* Am J Epidemiol, 1997. 145(12): p. 1076-88.

50. Stampfer, M.J., *Welding occupations and mortality from Parkinson's disease and other neurodegenerative diseases among United States men, 1985-1999.* J Occup Environ Hyg, 2009. 6(5): p. 267-72.

51. Tanner, C.M., et al., *Occupation and risk of parkinsonism: a multicenter case-control study.* Arch Neurol, 2009. 66(9): p. 1106-13.

52. Fryzek, J.P., et al., *A cohort study of Parkinson's disease and other neurodegenerative disorders in Danish welders.* J Occup Environ Med, 2005. 47(5): p. 466-72.

53. Salib, E. and V. Hillier, *A case-control study of Alzheimer's disease and aluminium occupation.* Br J Psychiatry, 1996. 168(2): p. 244-9.

54. Park, J., et al., *Occupations and Parkinson's disease: a multi-center case-control study in South Korea.* Neurotoxicology, 2005. 26(1): p. 99-105.

55. DerSimonian, R. and N. Laird, *Meta-analysis in clinical trials.* Control Clin Trials, 1986. 7(3): p. 177-88.

56. Greenland, S. and K. O'Rourke, *Meta-Analysis*, in *Modern Epidemiology*, K.J. Rothman, S. Greenland, and T. Lash, Editors. 2008, Lippincott Williams & Wilkins: Philadelphia, PA. p. p. 652-682.

57. Bradburn, M., J. Deeks, and D.G. Altman, *sbe24 metan—an alternative meta-analysis command.* Stata Technical Bulletin, 1998. 8(44): p. 5-14.

58. Thompson, S.G., *Why and how sources of heterogeneity should be investigated*, in *Systematic Reviews in Health Care*, M. Egger, G.S. Smith, and D.G. Altman, Editors. 2001, BMJ Publishing Group: London.

59. Greenland, S. and M.P. Longnecker, *Methods for trend estimation from summarized dose-response data, with applications to meta-analysis.* Am J Epidemiol, 1992. 135(11): p. 1301-9.

60. Orsini, N., R. Bellocco, and S. Greenland, *Generalized least squares for trend estimation of summarized dose-response data.* The Stata Journal, 2006. 6(1): p. 40-57.

61. Feychting, M., et al., *Occupational magnetic field exposure and neurodegenerative disease.* Epidemiology, 2003. 14(4): p. 413-9; discussion 427-8.

62. Poole, C. and S. Greenland, *Random-effects meta-analyses are not always conservative.* Am J Epidemiol, 1999. 150(5): p. 469-75.

63. Checkoway, H., N. Pearce, and D. Kriebel, *Characterizing the Workplace Environment*, in *Research Methods in Occupational Epidemiology*. 2004, Oxford: New York, New York. p. 17-57.

64. Hoyert, D.L. and H.M. Rosenberg, *Alzheimer's disease as a cause of death in the United States.* Public Health Rep, 1997. 112(6): p. 497-505.

65. Phillips, N.J., J. Reay, and C.N. Martyn, *Validity of mortality data for Parkinson's disease.* J Epidemiol Community Health, 1999. 53(9): p. 587-8.

66. McKhann, G.M., et al., *The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease.* Alzheimers Dement. 7(3): p. 263-9.

67. Steenland, K., et al., *Polychlorinated biphenyls and neurodegenerative disease mortality in an occupational cohort.* Epidemiology, 2006. 17(1): p. 8-13.

68. Greenland, S. and T. Lash, *Bias Analysis*, in *Modern Epidemiology*, K.J. Rothman, S. Greenland, and T. Lash, Editors. 2008, Lippincott Williams & Wilkins: Philadelphia, PA.

69. Lash, T., M.P. Fox, and A.K. Fink, *Applying Quantitative Bias Analysis to Epidemiologic Data*. 2009, Boston, MA: Springer Publishing.

3. New Electric Shock Job Exposure Matrix

Introduction

A consistent association between jobs in "electric" occupations and amyotrophic lateral sclerosis (ALS) has been reported [1]. However, it is unclear which physical factor, if any, in the electrical environment of these jobs is important; electric shocks, electric fields and magnetic fields have all been proposed as potential causative agents. Exposures to all three factors are highly correlated in the well-studied electric utilities. Therefore, identification of a relationship between ALS and one or more of these electrical factors will require methodology for separating these exposures for occupations, both inside and outside the electric utility industry. The methodology described in this article produces a measure of occupational electric-shock exposure that is independent of magnetic field (MF) exposure, allowing for integration of both exposures into one JEM.

Numerous studies on occupational electromagnetic fields (EMF) and neurodegenerative disease, including several for ALS, have been published over the past 20 years. A detailed review is published in Kheifets et. al. 2008 [1]. The main epidemiologic limitations of these studies have been two-fold: 1) exposure misclassification based on job titles alone and/or limited EMF exposure data and 2) potential confounding due to other exposures, such as electric shocks. Moreover, electric-shock exposures have only been examined for occupations within select industries such as electric utility, railway and construction.

Two elements affecting capture of workplace shock events are severity and perception. Shock severity depends on voltage level, the current passing through a person's body, the body's resistance, the path through the body, the shock duration and the source frequency [2, 3]. The physiological effects of shocks are determined by the nature of electric current and electrical properties of the tissue, which may be altered by tissue damage, sweat and personal protection equipment [4]. Federal data sources will likely capture the most severe, primary shock cases while mild to moderate accidents might not get recorded; since it is unlikely a worker would report an event causing pain but not direct physical harm. Alternating current passing through the body at 60Hz, may be imperceptible at 1 milliamps (mA), noticeable (>1mA), produce “not let go” response (16mA), produce respiratory muscle paralysis (20 mA) or cardiac arrest (2 amps) [5]. Conceivably, the lower the perceived physical effects, the less likely a worker would report an event. Presently, only two studies have examined microshocks in workers [6] [7], in one analysis of 102 linemen, body mass index and painful sensations were inversely related [7]. Given the ranges in severity and shock perception, captured events would underestimate the full extent of electric shocks in an occupation, but could serve as sentinel events, allowing for relative ranking.

To date, data on occupational electric shocks remain fragmented; most articles using the U.S. Bureau of Labor Statistics (BLS) electrical injury, illnesses and fatalities data have focused either on industry or solely on occupational fatalities [8-10]. Between 1992 and 1998, nearly 35,000 workers sustained lost work time or died due to electrical shocks or burn injuries [9]. While these are rare occurrences, their potential to cause severe injury is high. Overall, 44% electrical fatalities occurred in the construction industry; many because of contact with power lines [9]. Aside from electricians, nearly 25% of construction industry fatalities were among construction laborers, carpenters and painters [11]. More recently, Lombardi et. al. found workers in services, manufacturing and retail had the largest number of worker compensation electrical injuries over a one-year period [12]. When Cawley and Homce examined 1992-2002

Census of Fatal Occupational Injuries data, they noted occupations, such as truck drivers, farmers and groundskeepers, as sustaining fatal electrical injuries [10]. These data underscore the need for full exploration of occupations outside of utility industries likely to experience electric shocks. As a result, nationally available fatal and non-fatal data are important to ensure broad coverage of occupations representative of many industries.

Job exposure matrices (JEMs) are tools used to classify exposures for occupations based on "what is generally known about exposures with particular tasks in particular industries" [13]. The purpose of our JEM is to develop and assign electric-shock exposure categories to job titles in the absence of direct electric shocks measures for individual workers [14]. To optimize the performance of any JEM used to evaluate the possible role of a factor in the development of neurodegenerative diseases, capturing contrasts in exposure is paramount [14].

Several factors contribute to the potential for electric-shock exposure. The factors include: types of energy sources, the physical work environment, availability of training and safeguards [15]. Injury and fatality data can be used to determine electric-shock exposure potential. If each factor was known for each occupation, then presumably one could assign electric-shock exposure potential based solely on statistical models using a set of outlined assumptions. However, given the number of unquantifiable factors in the work environment, the use of expert panel for exposure categorization of occupations is necessary, and more so because exposure is not directly measurable and no industrial hygiene standard is available. Consequently, we combine expert panel assessment with available U.S. data on occupational electric shocks and electrocutions, to develop probability of electric shocks in different occupations. We then incorporate these into an existing MF job exposure matrix [16].

Methods

We used existing data on incident electric shocks and electrocutions from two sources: the BLS Survey of Occupational Injuries and Illnesses (BLS SOII) and the Occupational Safety and Health Administration Integrated Management Information System (OSHA IMIS).

The BLS SOII provides estimates of the number and rates of workplace injuries and illnesses in the U.S. BLS solicits survey data from employers having 11 employees or more in agricultural production, and from all employers in agricultural services, forestry, and fishing; oil and gas extraction; construction; manufacturing; transportation and public utilities; wholesale trade; retail trade; finance, insurance, and real estate; and services (except private households). To assure consistent occupational coding with U.S. mortality data that we plan to use and the most relevant time period following implementation of the OSHA Electrical Standard CFR 1910, Subpart S, we requested from BLS all non-fatal injuries for 1992-1999 with nature of injury code 093x (electrocutions, electric shocks) by occupation. BLS SOII represented 22,858 workers involved in non-fatal electric shocks among 306 job titles, i.e.. 3-digit 1990 Bureau of Census (BOC) codes. Where occupations were reported and the number of events not reported for a given year, we assumed the minimum reportable number of four shock incidents per year. Then, we summed number of electric shocks across years to obtain total number of incidents in each detailed occupation (n_{BLS}).

We also accessed OSHA IMIS, an online accident investigation database that is used to manage resources within state agencies. OSHA state offices investigate and complete standardized forms (OSHA-170) for selected events, e.g. fatalities, serious injuries, explosions and those featured in media or newspapers [17]. These forms are subsequently logged into IMIS. We extracted 2470 records representing 155 occupations and 367 industries, primarily fatal occupational data, from OSHA IMIS online database using the keyword “electric” for the period of January 1, 1992 to December 31, 1999. For the records extracted from the specified time period, OSHA classified industries using the 1987 Standard Industrial Classification system [18]. We assumed that electrocutions or fatal electrical events are reasonable indicators of a potential for electric shocks within an occupation. Each record was evaluated to retain electric shock events only, to remove duplicate entries and to assign BOC code the given occupational title. We summed the number of electric shocks and electrocutions reported in OSHA IMIS across years by job titles (n_{OSHA}).

To assess the proportion of workers affected, we used both the Current Population Survey (CPS) and the 1990 Decennial Census (DC) for the number of workers. CPS is a monthly survey of households conducted by the BOC for the BLS [19] and it provides a comprehensive body of data on the labor force, employment, unemployment and persons not in the labor force. Persons captured in the labor force include all non-institutional civilian people age 16 years and older. We obtained the number of workers for each 3-digit 1990 BOC code in 1992-1999 CPS using the online data mining and extraction software, DataFerrett, N_{CPS} [19]. We used sample-based occupation data from the 1990 Equal Employment Opportunity (EEO) File [20], which was tabulated from civilian labor force data collected in the 1990 DC. The 1990 DC EEO file contained cross-tabulations for 512 job titles by sex, race, and Hispanic origin for the U.S. We extracted estimates by sex, summing female and male workers for each 3-digit 1990 BOC code to create N_{DC}.

While we have data on the incident cases of electrocution and electric shocks, we have imprecise information on the occupational population at risk. That is why we have defined the estimates as proportions constructed for the purpose of evaluating occupational groups at risk of electric shock for the specified time period. To create number of shocked or electrocuted, we assumed the BLS non-fatal electric shock (n_{BLS}) and OSHA IMIS electrocution data (n_{OSHA}) were independent sources and summed by occupation. Using two different worker population estimates, we created two proportions of injury by each occupation which are, $p_{CPS} = (n_{BLS} + n_{OSHA}) / N_{CPS}$ and $p_{DC} = [(n_{BLS} + n_{OSHA}) / 8] / N_{DC}$ (injury data were averaged to represent one year for the DC proportion).

Proportion distributions (p_{CPS} and p_{DC}) were positively skewed (mean > median). We assigned three interim exposure categories based on tertile cutoff points. Results using different population estimates (CPS and DC proportions) were compared.

For final exposure assignment, we assembled an expert panel with diverse backgrounds and with direct relevant and practical experience consisting of an industrial hygienist, a physicist with research experience with electric shocks and an electrical engineer with electric utility experience and research into magnetic fields and shocks. The expert panelists defined electric shock and devised a method for assignment of high exposure, to retain specificity. Clearly the general population experiences electric shocks, as there about 1000 deaths due to electric shocks occur each year [21]. However, in some occupations electric shocks will occur at a higher rate than those experienced by the general population. Panelists agreed painful events may occur at low currents, but that at levels at or exceeding 3 mA an electric shock could likely result in a reportable injury [22]. As a group, the experts assessed 322 job titles for the electric shock exposure, based on a proportion exposed along with consideration for potential electrical hazards and knowledge about jobs, according to the following three definitions: 1) low exposure (L) being very unlikely that exposure occurred among workers with this job title, 2) medium exposure (M) being a possibility that some of the workers with this job title had electric shock exposure (but the probability is fairly low), and 3) high exposure (H) with at least a proportion of the workers with this job title experienced electric shocks. Expert panelists considered workplace factors such as those affecting skin impedance, engineered protection and personal protection (Table 3-1). In addition, expert panelists independently reviewed exposure assignments for 179 occupations not captured by the data sources. The final assignment of these jobs was based on the exposure agreement of at least two experts. For summary descriptive analysis, occupations were categorized into thirteen major occupational groups defined in the 1990 BOC (Table 3-2).

We used the geometric mean of MF time-weighted averages (TWA) in the MF JEM by converting 1980 BOC codes (Appendix D) to 1990 BOC codes. We grouped occupations into three MF exposure categories using the following cut-points L ($\leq$ 0.1 microTesla (μT)), M (0.1μT- 0.3μT) and H ($\geq$ 0.3μT) [16].

Results

Exposure incidents

By occupational group. Main occupational groups with the highest number of electric shocks and electrocutions were precision production, craft and repair occupations, followed by service occupations and machine operators, assemblers and inspectors.

By job title. Electric shock and electrocution data were available for 322 job titles. Most occupations (83%) were exposed to on average less than 10 shocks per year, 16% of occupations had greater than 10 and less than 100 shocks per year, and 1% of occupations were exposed to at least 100 shocks per year. Occupations with the most frequent number of electric shocks and electrocutions were: electricians, cooks, janitors and cleaners, construction laborers and non-construction laborers.

Exposure proportions

By occupational group. Occupational groups such as sales occupations, professional specialty occupations, and executive, administrative and managerial occupations had consistently low electric-shock exposure, while other groups had more variability in electric-shock exposure.

By job title. The highest proportion of electric shocks and electrocutions per 100,000 workers per year included: electrician apprentices (99.7), mechanic and repairer helpers (74.0), hoist and winch operators (63.3) and electrical power installers (52.4). We obtained high agreement between proportion tertiles using CPS and BOC (Kappa statistic =0.86, $p<0.0001$). Of 30 occupations not in agreement, nine were in the machine operators, assemblers and inspectors group, six were in precision production, craft, and repair occupations group and three were in administrative support occupations, including clerical group. The expert panelist reviewed and assigned these 30 occupations an electric shock exposure.

By expert panel. Of the possible 501 classifiable BOC occupational titles, 179 occupations were not represented in BLS SOII and OSHA IMIS data (Table A-1). Of those without electric shocks information, over 40% (78/179) were in professional specialty occupations, followed by 10.6% (19/179) in administrative support occupations, including clerical, 9.0% (16/179) in precision production, craft, and in repair occupations and 7.8% (14/179) in executive, administrative and managerial occupations.

The overall distribution for the 501 occupations assigned probability electric-shock exposure was: 57% L, 22% M, and 21% H . High electric-shock exposure assignments were assigned mainly in four summary occupational groups: 1) handlers, equipment cleaners, helpers, and laborers, 2) machine operators, assemblers and inspectors, 3) transportation and material moving occupations and 4) precision production, craft, and repair occupations (Table 3-2). High electric-shock exposure included occupations such as electrical and electronic technicians, cooks, and construction laborers. Occupations assigned to the medium electric-shock exposure included: groundskeepers and gardeners, production inspectors, printing press operators, bus, truck and engine mechanics. As expected, low electric-shock exposures were among the broadly defined occupational groups: professional specialty, sales and protective service occupations. Examples of job titles with low electric-shock exposures were automobile mechanics, registered nurses, administrative support occupations, data-key entry operators, and waiters and waitresses.

Comparison of electric shock to magnetic field exposure. Most frequent occupations highly exposed to both electric shocks and magnetic fields were from the precision, craft and repair occupations. Occupations such as dressmakers and public relations specialists were not exposed to electric shocks but were exposed to magnetic fields (Table 3-3). With the expert assignment, shocks-MF exposure contrast resulted in 66 occupations with high exposure to electric shocks and not to MF (Table 3-4), including construction laborers, parking lot attendants, elevator installers and repairers and roofers. Occupations having high MF exposure and low or medium electric-shock exposure included dressmakers, tailors, and electrical and electronic equipment assemblers. With expert panel judgment, dental hygienists, camera, watch, and musical instrument repairers and metal patternmakers and model makers were assessed to have low electric-shock exposure.

Discussion

Our electric-shock classification is the first to capture these relatively low prevalence, but potentially important etiologically, workplace exposures in a systematic manner. This electric-shock JEM covers a wide range of occupations reflecting those held by many workers in the general population. Using data alone would have resulted in fewer jobs with electric-shock exposure assignments, but with the best available technique, i.e. data combined with expert judgment, we added 179 jobs to the matrix. A combination of injury data and expert panel assignment for 501 occupations resulted in several jobs not typically considered as highly exposed to electric shocks, e.g. janitors and cleaners and cooks, more likely to be found in services industries rather than utility or construction industries.

Occupational rates of electric shocks and electrocutions. Previous literature and regulations have included information about electric shocks rates by industry [10, 23], but literature on occupational electric shock rates is scarce [24-26]. A feasibility assessment of the 1990 OSHA Electrical Safety-related Work Practices Standard for General Industry [23], injury incidence rates (per 100,000 workers), derived from previously unpublished data, aided OSHA to determine which workers were at risk of injury and most in need of electrical training, based on actual and potential electric shock risks. OSHA determined a high-level training was required for electrical and machine assemblers (93.3) and stationary engineers (42.6). For non-routine work on live electrical parts, OSHA determined an average level training was required for home appliance and power tool repairers (10.1), and gas and petroleum operators (4.60). Finally, OSHA determined workers that needed minimal level training included welders and cutters (10.1), painters and paperhangers, and electrical engineers (1.0). In an analysis of 1992-1999 U.S. Census of Fatal Occupational Injuries, Taylor et al. found occupational electrocution rates ranged from 0.71 to 15.91 per 100,000 worker years [8]. The highest electrical fatality rates were among electrical power installers (15.9), earth drillers (8.75) and electrician apprentices (8.25). Within the electric utility industry, Bracken et. al. published electrical injury probabilities (per 100,000 workers) for a few grouped occupations, such as, electrical power installers (302), welders and cutters (355), and supervisors (12.8) [24]. The highest proportions calculated for the electric-shock JEM seemed comparable to rates captured in the literature; however, we found several "helper" occupations with high proportions of electric shocks.

Limitations of occupational data. Due to the nature of the collected information, only the most severe accidents are likely to be captured. For example, OSHA tends to investigate incidents that include fatalities and events where three or more employees are hospitalized [27]. Upon examination of 1999 data, BLS nonfatal injury and illness undercounting was estimated between 33% to 69% by Leigh et. al. [28]. Thus the number of accidents captured is likely to be an underestimate, but this will not have a major impact on our JEM. Capturing the full spectrum of electric shocks injuries is a well-recognized challenge in occupational health and remains as an important caveat of the developed electric-shock job exposure matrix.

More problematic is that these data may not be entirely representative of workforce electrical accidents: data may be skewed towards certain occupations and industries, excluding self-employed, private households and federal governments and agencies [29]. BLS data are from a two-stage design survey; first, randomly selecting from private sector establishments and, second, selecting cases involving lost work time [30], which would exclude small employers.

To capture expansive indicators of electric shocks, we combined both BLS SOII and OSHA IMIS data, despite their distinctly different methodology, i.e. survey estimates and actual count data, respectively. We could have included an indication for injury severity by weighting fatalities, using days away from work or considering lifetime risk [31]. However, we created the electric-shock JEM for application in neurodegenerative diseases study, for which non-fatal electric shocks may be equally, if not more relevant. While some researchers have observed progressive ALS occurring more among those electrical injuries of < 300 V [32], there are several case reports which describe onset of ALS following severe electrical injury [33, 34]. The temporality between injury and onset of disease makes electric shocks a plausible risk factor [35], but which type of electric shocks is less clear. Both data sources reflect electric shocks that result in lost time and, as expected, certain occupations are not captured by these data sources.

Determination of appropriate worker population denominators has continued to be problematic for construction of national occupational rates [36, 37] and we were faced with the same challenge. To address this we used to distinct data sources, which resulted in similar assignments for most occupations. Further, few differences due to population denominators were resolved by expert panel.

Regardless, the injury and illness data for each occupation were solely one factor in assessment of exposure, which also included consideration of the workplace environment. Limitations aside, national occupational injury and illness data shed light on occupations outside the well-studied electric utility, construction and railway industries, experiencing electric shocks and electrocutions.

Performance of the electric-shock JEM. JEMs are best suited to capture exposure prevalence greater than 10%, with dichotomous categories non-differential biases will be introduced as the specificity decreases [38]. In 1998, the injury rate for non-fatal electric shocks treated in emergency departments was 0.006 incidents per 100 full-time equivalent worker, representing 0.2% of total estimates [39]. Overall the expected shock prevalence is low;

consequently the positive predictive value will be low measured with imperfect specificity. Despite this, the electric-shock JEM may have sufficiently high specificity, decrease false positives and thus lead to less misclassification in future epidemiologic studies [40]. Since data presented and opinion of experts resulted in previously unobserved findings, repetition of the JEM methodology with new objective data such as worker's compensation may be advisable. However, these data may be limited given the scarcity of U.S. data sources and rarity of the exposure, e.g. 1.2% due to electric shocks in an analysis of 11,410 electrical worker compensation claims received by state of Washington between 1998 -2001 [41]. In addition, international comparisons can further enhance this JEM.

Unfortunately, there is no "gold standard" to quantify the specificity, nor is the exposure directly measurable, therefore electric-shock exposure assignments are the best determination, given the data.

Lack of industry or additional job task information within the JEM may limit its specificity. Using the MF JEM, authors from a recent study evaluated inclusion of detailed information about jobs, such as tasks and time spent working near electrical sources, affected MF categories; they noted a 3% increase in the number of jobs exposed to 0.3 μT or greater as compared to a JEM [42]. Future work incorporating industry or job task information may improve specificity of the MF exposure assessment component, in absence of source information and direct measurements. Though including industry will have a problem of its own, as it could result in unreliable estimates and consequently a need for stronger assumptions.

Due to sparse data and lack of solid estimates of numbers employed in specific occupations, our electric shock exposure categorization is somewhat uncertain, especially for specific occupations such as office machine repairers, vehicle washers and equipment cleaners, and non-nursing health-aides. We attempted to reduce this uncertainty, by using expert assessment, which incorporated employment data and workplace factors. Potential exposure to electric shocks in a workplace involves a number of variables, of which injury data are one factor [15]. Expert assessment, used in many fields including engineering and industrial hygiene, is the best manner to create informed exposure assignments. Errors in occupational coding of injury data could lead to exposure misclassification. For example, relying on data alone chief executive officers would be highly exposed to electric shocks, but with expert panel assessment are reassigned to medium exposed. Hence, examination by expert panelists would minimize these problems, assigning an appropriate exposure.

Strengths of the electric-shock JEM. The main strength of this work is the categorization of electric-shock exposures among non-utility occupations, previously not evaluated. These data have never been systematically compiled into a usable tool for population studies. Furthermore, we report occupations not classically recognized as exposed to electrical hazards. The present work illuminates the importance of tracking actual frequency of occupational injuries and combining expert panel opinion for exposure probability. Our approach may be reproduced for other workplace exposures that are not directly measured, where no data are available and for which occupational exposure limits do not exist.

The degree of certainty about the proportion of electric shocks within each occupation or relative rates within each occupation could be elicited to create a more quantified JEM. Actual quantification of each evaluator's degree of certainty has been done in a limited number of health-based studies. The field of industrial hygiene has only recently started incorporating Bayesian methods into the expert judgment arena [43]. The use of expert subject matter knowledge to assign electric-shock exposure offsets data limitations and allows for quantification of certainty during the creation of the JEM. In the future, the electric shocks-MF JEM can be enhanced by including the experts' degree of certainty to the assigned exposures and further incorporating this information in epidemiologic analyses.

Conclusions

Despite the numerous limitations of using publicly available data, construction of an electric-shock JEM is feasible. Combining such data with expert panel judgment results in an approach aimed at incorporating factors not reflected in injury data. The effort yielded a number of occupations with exposure only to electric shocks or only to magnetic fields needed for epidemiologic analyses capable of disentanglement of the potential associations between shocks, magnetic fields and neurodegenerative disease.

The largest number of electric shocks occurred among precision production, craft, and repair occupations. Occupations having the highest number of electric shocks not previously identified by the literature included: cooks, janitors and cleaners and miscellaneous laborers. Prevention efforts could be directed towards these worker groups including hazard education and training and/or workplace safety improvements. Future work should also account for uncertainties in the data sources and exposure assessment.

Table 3-1. Workplace conditions contributing to electric shocks

Types of energy sources

60 Hz power

Batteries

Environment

Dry and wet or damp conditions

Hot environments affecting perspiration

Un-insulated conductors present

Safeguards

Resistors, capacitors

Insulation

Grounding

Electrical training

None, some or skilled

Work Practices

Lock out/tag out procedure

Safety watchers or observers

Availability of protective measures

Fiberglass live line tools

Overshoe footwear

Non-conductive head protection, insulating blankets or covers, gloves

Table 3-2. Distribution of job titles within occupational groups by electric-shock exposure based on data and expert panel

Occupational Group		**Job Titles**		
	No.	**H**	**M**	**L**
Administrative Support Occupations, Including Clerical	55	3 (5.4%)	8 (14.5%)	44 (80%)
Executive, Administrative and Managerial Occupations	28	1 (3.6%)	3 (10.7%)	24 (85.7%)
Farming, Forestry and Fishing Occupations	19	3 (15.8%)	5 (26.3%)	11 (57.9%)
Handlers, Equipment Cleaners, Helpers, and Laborers	16	8 (50%)	4 (25%)	4 (25%)
Machine Operators, Assemblers and Inspectors	61	28 (45.9%)	27 (44.3%)	6 (9.8%)
Precision Production, Craft, and Repair Occupations	102	41 (40.2%)	32 (31.4%)	29 (28.4%)
Private Household Occupations	5	0 (0.0%)	0 (0.0%)	5 (100%)
Professional Specialty Occupations	106	0 (0.0%)	8 (7.5%)	98 (92.5%)
Protective Service Occupations	11	1 (9.1%)	0 (0.0%)	10 (90.9%)
Sales Occupations	23	0 (0.0%)	2 (8.7%)	21 (91.3%)
Service Occupations, Except Protective and Household	29	6 (20.7%)	8 (27.6%)	15 (51.7%)
Technicians and Related Support Occupations	22	2 (9.1%)	6 (27.3%)	14 (63.6%)
Transportation and Material Moving Occupations	24	10 (41.7%)	7 (29.2%)	7 (29.2%)

Table 3-3. Electric-shock and magnetic-field exposure assignments for selected job titles

1990 BOC Code	Job Title	Electric-shock Exposure	Magnetic-field Exposure
575	Electricians	H	H
783	Welders and cutters	H	H
676	Pattern makers, layout workers and cutters	M	H
538	Office machine repairers	M	H
869	Construction laborers	H	L
436	Cooks	H	M
804	Truck drivers	M	M
449	Maids and housemen	M	M
666	Dressmakers	L	H
744	Textile sewing machine operators	L	H
313	Secretaries	L	M
095	Registered nurses	L	L
447	Nursing aides, orderlies, and attendants	L	L

Note: BOC = Bureau of Census Occupational Code

Table 3-4. Exposure contrast frequencies for all job titles

Electric-shock		**Magnetic-field**	
		Yes (≥ 0.3 μT)	No (< 0.3 μT)
High	Yes	18	66
Medium Low	No	26	313

Note: Totals do not equal 501 as there was no MF exposure available for 78 1990 BOC job titles

References

1. Kheifets, L., et al., *Future needs of occupational epidemiology of extremely low frequency (ELF) electric and magnetic fields (EMF): review and recommendations.* Occupational and Environmental Medicine, 2008. 66(2): p. 72-80.

2. Capelli-Schellpfeffer, M. and R.C. Lee, *Electric Shocks*, in *Wiley encyclopedia of electrical and electronics engineering*, J.G. Webster, Editor. 1999, John Wiley: New York.

3. El-Sharkawi, M., *Electrical Safety*, in *Electrical Energy: An Introduction,*. 2005, CRC Press: Boca Raton, FL.

4. Conrad, A., *Effects of Electricity on Living Tissue*, in *The Ohio State Engineer (April).* 1939.

5. NIOSH, *Worker Deaths by Electrocution: A Summary of NIOSH Surveillance and Investigative Findings*. 1998, US Department of Health and Human Services. p. 51.

6. Fordyce, T., et al., *Thermal burn and electrical injuries among electric utility workers, 1995–2004.* Burns, 2007. 33(2): p. 209-220.

7. Ahmed, Y. and S.M. Rowland, *U.K. linesmen's experience of microshocks on HV overhead lines.* J Occup Environ Hyg, 2009. 6(8): p. 475-82.

8. Taylor, A., *Fatal occupational electrocutions in the United States.* Injury Prevention, 2002. 8(4): p. 306-312.

9. Cawley, J., *Occupational electrical injuries in the United States, 1992–1998, and recommendations for safety research.* Journal of Safety Research, 2003. 34(3): p. 241-248.

10. Cawley, J. and G. Homce, *Trends in Electrical Injury in the US, 1992–2002.* IEEE Transactions on Industry Applications, 2008. 44(4): p. 962-972.

11. Mccann, M., et al., *Causes of electrical deaths and injuries among construction workers.* American Journal of Industrial Medicine, 2003. 43(4): p. 398-406.

12. Lombardi, D.A., et al., *Etiology of work-related electrical injuries: a narrative analysis of workers' compensation claims.* J Occup Environ Hyg, 2009. 6(10): p. 612-23.

13. Armstrong, B.K., E. White, and R. Saracci, *Principles of exposure measurement in epidemiology*. Monographs in epidemiology and biostatistics. 1992, Oxford ; New York: Oxford University Press. ix, 351 p.

14. Goldberg, M., et al., *Job exposure matrices in industry.* Int J Epidemiol, 1993. 22 Suppl 2: p. S10-5.

15. Hintz, H. *Protection against Electric Shock*. in *Telecommunications Conference, 2005. INTELEC '05. Twenty-Seventh International*. 2005.

16. Bowman, J., J. Touchstone, and M. Yost, *A Population-Based Job Exposure Matrix for Power-Frequency Magnetic Fields.* J Occup Environ Hyg, 2007. 4(9): p. 715-728.

17. US DOL, *Occupational Safety & Health Administration, Fatality and Catastrophe Investigation Summaries*. 2009, US Department of Labor (US DOL).

18. US OMB, *Standard industrial classification manual, 1987.* 1987, Washington, DC: Executive Office of the President, Office of Management and Budget (US OMB).

19. US Census Bureau, *DataFerrett. Census Population Survey 1992-1999*. 2009.

20. US Census Bureau, *Detailed Occupation by Race, Hispanic Origin and Sex*. 1990, US Census Bureau.

21. Spies, C. and R. Trohman, *Narrative Review: Electrocution and Life-Threatening Electrical Injuries.* Annals of Internal Medicine, 2006. 145(7): p. 531.

22. OSHA, *Electrical Standards, Federal Register 29CFR1910. Vol. 46, No. 11. Friday, January 16, 1981. Supplementary Information - I. Background.* , in 1991, Occupational Safety and Health Administration (OSHA): Washington, DC.

23. US DOL, *Regulatory Impact and Regulatory Flexibility Analysis of the Electrical Safety-Related Work Practices Standard for General Industry (29 CFR 1910, Subpart S),* OSHA Office of Regulatory Analysis, Editor. 1990, US Department of Labor (US DOL): Washington, DC.

24. Bracken, T.D., et al., *An Integrated Job Exposure Matrix for Electrical Exposures of Utility Workers.* J Occup Env Hyg, 2009. 6(8): p. 499-509.

25. US Department of Labor, *Regulatory Impact and Regulatory Flexibility Analysis of the Electrical Safety-Related Work Practices Standard for General Industry (29 CFR 1910, Subpart S)*, OSHA Office of Regulatory Analysis, Editor. 1990, US Department of Labor (US DOL): Washington, DC.

26. Taylor, A.J., et al., *Fatal occupational electrocutions in the United States.* Inj Prev, 2002. 8(4): p. 306-12.

27. Froines, J., D. Wegman, and E. Eisen, *Hazard surveillance in occupational disease.* Am J Public Health, 1989. 79 Suppl: p. 26-31.

28. Leigh, J.P., J.P. Marcin, and T.R. Miller, *An estimate of the U.S. Government's undercount of nonfatal occupational injuries.* Journal of Occupational and Environmental Medicine, 2004. 46(1): p. 10-8.

29. Ruser, J.W., *Examining evidence on whether BLS undercounts workplace injuries and illnesses.* Monthly Labor Review, 2008. 131(8): p. 20-32.

30. US BLS, *BLS handbook of methods*. 2010, U.S. Bureau of Labor Statistics (US BLS): Washington, D.C.

31. Fosbroke, D.E., S.M. Kisner, and J.R. Myers, *Working lifetime risk of occupational fatal injury.* Am J Ind Med, 1997. 31(4): p. 459-67.

32. Abhinav, K., et al., *Electrical injury and amyotrophic lateral sclerosis: a systematic review of the literature.* Journal of Neurology, Neurosurgery & Psychiatry, 2006. 78(5): p. 450-453.

33. Zoccolella, S., et al., *Motoneuron disease after electric injury: a case report.* Neurol Sci, 2008. 29(1): p. 47-49.

34. Huynh, W., et al., *Corticospinal tract dysfunction and development of amyotrophic lateral sclerosis following electrical injury.* Muscle Nerve, 2010. 42(2): p. 288-92.

35. Panse, F., *Electrical Trauma,* in *Handbook of Clinical Neurology v. 23,* P.J. Vinken and G.W. Bruyn, Editors. 1975, North Holland Publishing Company: Amsterdam. p. 683-789.

36. Ruser, J., *Denominator choice in the calculation of workplace fatality rates.* American Journal of Industrial Medicine, 1998. 33(2): p. 151-156.

37. Richardson, D., et al., *The effect of rate denominator source on US fatal occupational injury rate estimates.* American Journal of Industrial Medicine, 2004. 46(3): p. 261-270.

38. Bouyer, J., *Studying the performance of a job exposure matrix.* International Journal of Epidemiology, 1993. 22(6 S2): p. 65-71.

39. CDC, *Work-Related Injury Statistics Query System (Work-RISQS)*. 2009, National Institute for Occupational Safety and Health.

40. Greenland, S. and T. Lash, *Bias Analysis*, in *Modern Epidemiology*, K.J. Rothman, S. Greenland, and T. Lash, Editors. 2008, Lippincott Williams & Wilkins: Philadelphia, PA.

41. Connon, C., C. Reeb-Whitake, and C. Curwick, *Electrical Contractors Industry Focus Group Report 2003*, Safety and Health Assessment and Research for Prevention (SHARP) Program, Editor. 2003, Washington Department of Labor and Industries: Olympia (WA).

42. Coble, J.B., et al., *Occupational exposure to magnetic fields and the risk of brain tumors.* Neuro Oncol, 2009. 11(3): p. 242-9.

43. Ramachandran, G., S. Banerjee, and J.H. Vincent, *Expert judgment and occupational hygiene: application to aerosol speciation in the nickel primary production industry.* Ann Occup Hyg, 2003. 47(6): p. 461-75.

4. Occupational Exposure to Electric Shocks, Magnetic Fields and Amyotrophic Lateral Sclerosis Mortality in the U.S., 1991-1999

Introduction

Amyotrophic lateral sclerosis (ALS), the most common of the motor neuron diseases, is a fatal, incurable disease striking nerve cells in the brain and the spinal cord. This rapidly progressive neurodegenerative disease has a worldwide incidence rate of 1.2 to 2.5/100,000 per year, peaking around 70 years of age and affecting people between 40 to 75 years of age [1-3]. Though rare, ALS is a devastating illness often limiting persons afflicted with it to palliative care. The disease dramatically alters the quality of life for the patients and family, both economically and socially [4]. With an etiology that is largely unknown, the opportunities for future prevention of disease remain unexplored. If implicated and modifiable workplace factors, such as magnetic fields and electric shocks, play a role in disease etiology, this work-related illness may be prevented.

Among the major neurodegenerative disorders, ALS has been most strongly and consistently related to electrical occupations, thus warranting further investigation [5-20]. However, only one of four recent studies reported an increased risk with extremely low frequency magnetic field (MF) exposure, which may be confounded by co-exposure to neurotoxic agents [7]. Four studies reporting no effect on ALS risk estimated magnetic field exposure through job exposure matrices (JEMs) [12, 17, 21, 22]; although, two of these studies found an increased risk for electrical occupations [12, 21]. Researchers reported broadly similar results for magnetic field exposure but found no risk increases in any job categories for motor neuron disease mortality among U.K. electricity generation and transmission workers compared to the general population [6]. Thus, the evidence linking electrical occupations to an increased risk of ALS is remarkably consistent, but the evidence of an association with measured magnetic field levels is weaker. Another risk factor may explain the observed increased risk in electrical occupations. Exposure to electric shock has been suggested as a possibility, [19, 20]. Feychting et. al. found that almost 50% of reported work-related electrical accidents in 1991 occurred in electricians [21]. In 2010, Milham hypothesized a link between electric currents and ALS, based on anecdotal use of electric stimulatory devices among athletes [23]. More recently, a retrospective cohort study examined the role of electric shocks in neurologic diseases, focusing mainly on peripheral nerve diseases, migraine, vertigo and epilepsy, due to small numbers for ALS [24]. Given the shortage of strong risk factors, public health epidemiologists should investigate consistent occupational associations using creative approaches [25, 26]. We have applied previously developed electric shock and MF JEMs, to U.S. mortality data to investigate whether increased risk of ALS among workers in electrical occupations can be explained by MF or electric shocks.

Methods

Data Source and Case Ascertainment

Multiple cause-of-death data (MCDD) collected annually were obtained from the National Center for Health Statistics (NCHS) (Centers for Disease Control and Prevention) through the National Bureau of Economic Research [27]. Our source population was all persons who died in the U.S. between the years of 1991 – 1999 (20,593,110 deaths). Occupational were coded for a select number of states limiting included observations to approximately 20%. To combine all years, we recoded the 1991 and 1992 occupation variable, which used 1980 Bureau of Census (BOC), to the 1990 BOC codes used for later years [28]. The study population was further limited to decedents of age 20 years or greater to potentially exclude familial ALS. We identified 40,820 deaths with any mention of motor neuron disease (International Classification of Diseases (ICD)-9 335.2, ICD-10 G12.2), which we will define as ALS.

Control Selection

For each year, up to ten controls per ALS cases were individually matched on sex, 5-year age groups and four major regions using modified SAS 9.1 SQL code from among other deaths likely not related to electric shocks and magnetic field exposures. Of the 3,929,545 potential study subjects, a total of 1,828,522 records with any mention of the following diseases possibly related to electric shocks or electromagnetic fields in the underlying or contributing cause of deaths were excluded: leukemias (ICD-9: 204-208; ICD-10: C900, C901, C887, C910-912, C917, C919, C920-C923, C927, C929, C930-C932, C937, C939, C940-C942, C947, C950-C952, C957, C959), Parkinson's disease (ICD-9: 332; ICD-10: G20, G211-G213, G218, G219), brain tumors (ICD-9: 191, 225; ICD-10: C71, D320, D321, D332-D334, D337, D339), cerebral degenerations including Alzheimer's disease (ICD-9: 331; ICD-10: G309-G311 G318, G319, G910, G911, G937), seniledementias (ICD-9; 290; ICD-10 F03, F051), cardiovascular diseases (ICD-9: 4100-4149, 426-427, 430-434.91, 437-438; ICD-10: I20-25, I44-49, I60-69), accidental causes of death due to electrical current, and/or falls or suicides (ICD-9 E880-888, 950-959, 925; ICD-10: W00-W19, X60-X84, Y870 W86-W87).

Exposure assessment

Based on "usual occupation" as recorded on the death certificate, we linked occupational titles to a previously developed JEM for electric shocks integrated with another JEM of MF exposure [29, 30]. Using an a priori cut-off, we categorized exposures using MF time-weighted average (geometric mean) into a reference group less than 0.1 μT, medium (0.1 μT-0.3 μT), and high (0.3 μT or greater). For electric shock, three categories were used: low, medium and high, based on the probability of incurring electric shocks on the job. When examining high exposure categories for specific occupations, we grouped medium and low into a reference group for each exposure, MF and electric shocks, to have sufficient numbers in each category.

Data analysis

We conducted univariate and multivariate conditional logistic analyses of the data, using a matching variable based on sex (male or female), 5-yr age groups (20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, 95-99, 100-104 or 105-109 year) and region (Northeast, Midwest, South, West). Data are presented as percentages and adjusted odds ratios (OR) with 95% confidence intervals (95% CI), unless otherwise noted. We analyzed the associations of ALS with occupational electric shock and MF exposures using conditional logistic regression modeling with additional adjustment for education (none -8 years (reference), 9-12 years or 13-17 years), ethnicity (non-Hispanic (reference) or Hispanic), and race (White (reference), Black, Native American or Asian). We omitted cases and controls with unknown or missing information for MF, education, and ethnicity, which resulted 5,886 cases and 57,667 controls in the analytic sample.

We examined occupations as thirteen aggregate occupational groups as defined by BOC, as well as, for 15 electric occupations and 7 welding occupations previously defined in the literature (Table 4-1.) [17, 31]. We further examined electric and welding occupations separately, stratified by age less than 65 years, and by subsets of high exposure categories of electric shocks and MF. All analyses were performed using SAS software version 9.1 (SAS Institute, Inc., Cary, North Carolina).

Results

Of the 7419 ALS cases and their matched controls, 63% were male and 61% were between 60 and 79 years of age at death, with an average of 67.0 years. Table 4-2 shows the demographic characteristics of the study sample. Decedents were mainly located in the Midwest (35.6%) and South (32.2%) regions, with 35.3% cases and 37.0% controls occurring in New Jersey, North Carolina and Ohio, combined (data not shown). Educational information was missing for 11.7 % cases and 17.7% controls and ethnicity was missing for 3.2% cases and 2.7% controls. In the study population, the proportions of occupations in executive, administrative and managerial (14.0% vs 10.5%) and professional specialty groups (15.8% vs 10.6%) were higher among cases compared to controls. With industry, cases tended to work more in professional related services than controls (19.7% vs 16.6%).

Compared to those with education of 8 years of less, workers with 9-12 years of education had higher odds of ALS death (OR = 1.26, 95% CI: 1.16, 1.39) and workers with 13 or more years of education had the highest odds of death (OR = 1.85, 95% CI: 1.67, 2.04). Lower associations were detected for Blacks (OR=0.38, 95% CI: 0.33, 0.43), Native Americans (OR=0.50, 95% CI: 0.29, 0.86) and Asians (OR=0.64, 95% CI: 0.47, 0.89) compared to Whites.

When assessed by major occupational groups, we observed positive associations for professional specialty occupations (OR=1.47, 95% CI: 1.08, 2.01), executive administrative occupations (OR=1.34, 95% CI: 0.98, 1.83) and administrative support occupations (OR=1.27, 95% CI: 0.93, 1.73) as compared to private household occupations, for example. Associations were stronger for “white collar” occupations when no adjustment for education was made, particularly for professional specialty and executive administrative occupations.

Similarly to previous results in the literature, we detected positive associations for those who worked within electric occupations (OR=1.23, 95% CI: 1.04, 1.47), with stronger associations for unadjusted odds ratios (OR = 1.38, 95% CI: 1.15, 1.62). Among those occupations, we observed a stronger association among those less than 65 years of age, but not for those age 65 years or greater (Table 4-3).

Controlling for ethnicity, race and education, exposure to electric shocks were inversely associated with ALS. As compared to low exposure to electric shocks, the odds ratios were 0.73 (95% CI: 0.67, 0.79) for high exposure and 0.90 (95% CI: 0.84, 0.97) for medium exposure (Table 4-4). For MF, ALS mortality odds ratios were 1.09 (95% CI: 1.00, 1.19) for high exposure and 1.09 (95% CI: 0.96, 1.23) for medium exposure as compared to low (Table 4-4). We observed a weak positive association in those exposed to high levels of MF, after controlling for electric shocks (OR: 1.16, 95% CI: 1.02, 1.32). We did not detect appreciable changes in the odds ratios when the data were stratified by age less than 65 (data not shown).

Within the high MF exposure subgroup, the association approached the null for electric occupations as compared to non-electric occupations (Table 4-3). We observed inverse associations for those in electric occupations with high exposure to electric shocks; in contrast to positive associations for medium and low exposure to electric shocks (Table 4-5). Similarly, we observed inverse associations for those in electric occupations with high magnetic field exposure and positive associations for low and medium magnetic field exposure (Table 4-5).

We observed inverse associations within certain welding occupations (OR= 0.77, 95% CI: 0.55, 0.89), with stronger inverse associations in unadjusted odds ratios (OR=0.65, 95% CI: 0.52, 0.82). Among welding occupations, we observed an association similar in magnitude for those less than 65 years of age and age 65 years or greater (Table 4-3). For a group with high potential for electric shocks, the association approached the null for welding occupations as compared to non-welders, which was not observed for high MF group (Table 4-3). Analysis of welding occupations by electric shocks or magnetic fields did not reveal a consistent or remarkable pattern (data not shown).

Discussion

Among U.S. deaths occurring between 1991 -1999, we found increased associations between electric occupations and ALS. We found inverse associations between occupational electric shocks and ALS mortality and no consistent associations between occupational MF exposure and ALS mortality. In our analysis, electric shocks and MF did not account for the positive association observed for electric occupations. To our knowledge, this was the first attempt to disentangle two correlated exposures within the electric occupational environment in a large dataset. However, several potential biases must be addressed to understand the results of this study. For this analysis, we assumed that usual occupation was the longest held occupation and the electric shock-MF JEM captured information relevant to each individual who died. The main biases stem from potential exposure misclassification on at least two levels: first, the reliance on occupation in the death certificate and, second, the electric shock and magnetic field exposure assignment.

Electrical trauma injuries have been implicated in several ALS occupational case reports and case control studies, although differential reporting bias or the possibility that limb weakness led to the electrical injury (reverse-causation) was not investigated [32,] [19, 20, 32-36]. Electric shocks as a potential explanation for increased risk of ALS among “electric occupations” [19, 20, 37], has not been evaluated to date [38]. Thus, we focused on applying an electric shock JEM, with pre-categorized occupations, to mortality data.

Application of the electric shocks JEM has likely resulted in a large exposure misclassification and was dependent upon occupation denoted on death certificates. The developed electric shock JEM reflects severe electric shocks rather than barely perceptible shocks, and we acknowledge uncertainty as to etiologic relevance of either. Nonetheless, we expect the electric shocks JEM to perform better than a random assignment of exposure. Severe electric shocks may cause someone, to modify their work practices, or to seek a new job entirely and avoid repeated, perhaps less severe electric shocks. In a review of published case reports and studies, stronger shocks resulted in non-progressive motor neuron disease whereas mild events in ALS [39]. Severity should be added to an electric shocks JEM and associations examined across severe to mild electric shocks levels.

Death certificate occupation is a poor surrogate for lifetime occupational history [40]. People who live longer may have more than one occupation, leading to misclassification of occupation, consequently electric shocks and MF exposures. Type of occupation and SES may determine whether or not workers seek multiple jobs in a lifetime. One U.S. prospective ALS study reported more than 40% of the cohort held more than one job [16]. Low SES may require a person to have many jobs while high SES may not. Death certificates may serve as a better proxy for lifetime occupation among highly educated or trained workforce.

Past death certificate occupational coding could vary by state, for example, occupation at time of death, longest held occupation, or occupation/employer paying the insurance may be recorded rather than actual job [41]. Coding protocols have been developed to assist funeral directors and registrars and reduce inaccuracies with occupation [42]. Since only 16 to 21 states reported occupation for the study period, missing death certificate data on occupational title could create selection bias if “missingness” is dependent upon the outcome of interest, exposure and SES [43].

Suggestive potential ALS risk factors include: cigarette smoking and race [3, 44-46]. Smoking as a ALS risk factor is debated by researchers, a recent meta –analysis of 18 publications observed an odds ratio of 1.28 (95% CI: 0.97-1.68), for current versus never smokers [47]. Mortality rates have been observed to be higher among whites compared to blacks and other ethnicities [3]. We found limited support for “non-white” as protective from ALS. A study in the Netherlands identified lower socioeconomic status (SES) as a risk factor, using education level as a proxy [48] and other studies have been inconsistent [48, 49]. SES reflects occupation, education, income and household conditions, and is dependent upon the population. In our data, cases were higher educated than the controls, and to the extent education misclassifies SES [50] and underlying SES related to ALS, residual confounding due SES may be present in our analysis.

The association between electric occupations and ALS death was consistent, however, increased odds of ALS death were not observed for high electric shocks or MF exposure. This finding supports an alternative hypothesis that some factor unrelated to electric shocks and MF may account for this association. Positive associations between ALS and the following occupational exposures have been found: metals [51], such as lead [52-54], pesticides [55-57], solvents [49, 58], aspects of strenuous physical activity [15, 59, 60], and physical trauma, including head injury, and skeletal fractures [15, 20, 57, 61, 62], [45, 63]. We had no data on these other potential occupational risk factors.

Mortality data may be a reasonable substitute for ALS incidence, as disease is fatal and with an average duration of 1-3 years [64]. In Italy, accuracy of motor neuron disease as primary cause of death was examined and found to be underestimated [65]. A follow-up of ALS patients from a 1980s study found that death certificate data reporting accuracy was 72% to 92% [66]. Case ascertainment could reflect regional differences due to physician knowledge of ALS diagnosis [67, 68], changes in disease coding [69] and worker access to health care, which may vary by SES [67, 68]. Although disease misclassification is to some extent present, ALS mortality data is useful to explore the electric occupations, MF and electric shocks hypotheses. We present a first attempt to elucidate the relationship between electrical occupations, electric shocks, MF and ALS in a large set of data.

Conclusions

In the present study, we observed exposure to occupational electric shocks to be inversely associated with ALS deaths in the U.S. population, 1991-1999. However, there are no other studies that have evaluated electric shocks and ALS to compare results. Exposure misclassification of electric shocks is likely a large source of bias. Similar to past studies, we detected a positive association between electric occupations and death due to ALS. In our examination, neither electric shocks nor MF explained the association between electric occupations and ALS. Application of the electric shocks JEM to an alternate data source to assess electric occupations with complete job histories and information on SES would be informative. Future work should expand MF to occupations with no measurement data, quantify the degree of potential biases in the analyses, and incorporate new information on occupational electric shocks, such as industry-level data and degree of severity.

Table 4-1. Electric and welding occupational groups

Group	1990 BOC[a] Code	Occupational Title
Electric Occupations	55	Electrical and electronic engineers
	213	Electrical and electronic technicians
	228	Broadcast equipment operators
	523	Electronic repairers, communications and industrial equipment
	525	Data processing equipment repairers
	526	Household appliance and power tool repairers
	527	Telephone line installers and repairers
	529	Telephone installers and repairers
	533	Misc. electrical and electronic equipment repairers
	555	Supervisors, electricians and power transmission installers
	575	Electricians
	576	Electrician apprentices
	577	Electrical power installers and repairers
	695	Power plant operators
	773	Motion picture projectionists
Welding occupations	544	Millwrights
	557	Supervisors, plumbers, pipefitters, and steamfitters
	585	Plumbers, pipefitters, and steamfitters
	587	Plumber, pipefitter, and steamfitter apprentices
	597	Structural metal workers
	643	Boilermakers
	783	Welders and cutters

[a] U.S. Bureau of Census

Table 4-2. Characteristics of the study population, U.S. multiple cause of death data 1991-1999

		Cases		Controls	
		No.	%	No.	%
Sex	Male	4672	63.0	46720	63.0
Age	20-44 years	385	5.2	3850	5.2
	45-64 years	2359	31.8	23590	31.8
	65-74 years	2538	34.2	25380	34.2
	75 years or greater	2137	29.0	21370	29.0
Education	None to 8 years of school	712	9.6	10405	14.2
	9 – 12 years of school	3193	43.0	34616	46.6
	13 or more years of school	2345	31.6	16040	21.6
	Not stated	1169	11.7	13129	17.8
Ethnicity	Non-Hispanic	7080	95.5	70793	95.4
	Hispanic	98	0.3	1422	2.0
	Unknown	241	3.2	1975	2.7
Race	White	6977	94.0	63489	85.6
	Black	377	5.1	9612	13.0
	American Indian (includes Aleuts and Eskimos)	18	0.2	401	0.5
	Asian	47	0.6	688	0.9
Occupational Groups	Executive, Administrative and Managerial Occupations	1038	14.0	7994	10.5
	Professional Specialty Occupations	1175	15.8	7802	10.5
	Technicians and Related Support Occupations	170	2.3	1543	2.1
	Sales Occupations	787	10.6	6886	9.1
	Administrative Support Occupations, Including Clerical	898	12.1	7676	10.4
	Private Household Occupations	79	1.1	1291	1.7
	Protective Service Occupations	120	1.6	1182	1.6
	Service Occupations, Except Protective and Household	488	6.6	7307	10.0
	Farming, Forestry and Fishing Occupations	298	4.0	3587	4.7
	Precision Production, Craft, and Repair Occupations	1141	15.4	11799	16.2
	Machine Operators, Assemblers and Inspectors	591	8.0	7218	9.8
	Transportation and Material Moving Occupations	323	4.4	4449	5.9
	Handlers, Equipment Cleaners, Helpers, and Laborers	311	4.2	5456	7.6

Industry	Agricultural, Forestry, and Fisheries	302	4.1	3421	4.5
	Mining	110	1.5	937	1.4
	Construction	521	7.0	6659	9.0
	Manufacturing	1879	25.3	18960	25.5
	Transportation, Communications, and Other Public Utilities	656	8.8	6340	8.7
	Wholesale Trade	172	2.3	1564	2.1
	Retail Trade	898	12.1	9016	12.1
	Finance, Insurance and Real Estate	356	4.8	2842	3.7
	Business and Repair Services	228	3.1	2765	3.8
	Personal Service	259	3.5	3505	4.7
	Entertainment and Recreation Services	59	0.8	738	0.9
	Professional and Related Services	1463	19.7	12293	16.6
	Public Administration	443	6.0	4111	5.5
	Active Military Duty	8	0.1	69	0.1
	Retired; with no other industry reported	1	0.0	13	0.0
	Other, Blank, Unknown, NA	64	0.9	959	1.3

Source: National Center for Health Statistics

Table 4-3. Association of amyotrophic lateral sclerosis and electric and welding occupations within strata of age, high electric shocks and high magnetic fields, U.S. multiple cause of death data 1991-1999

	Electric Occupations		Welding Occupations	
	Adj. OR[a]	95% CI	Adj. OR[a]	95% CI
Overall	1.23	1.04, 1.47	0.70	0.55, 0.89
Age less than 65	1.64	1.28, 2.10	0.69	0.47, 1.02
Age 65 or greater	0.97	0.74, 1.34	0.70	0.53, 0.94
High electric shocks	1.48	1.05, 2.08	0.86	0.61, 1.23
Not high electric shocks	1.46	1.15, 1.85	0.68	0.36, 1.28
High MF ($\geq$ 3 μT)	1.05	0.65, 1.72	0.58	0.32, 1.04
Not high MF (< 3 μT)	1.34	1.07, 1.69	0.77	0.55, 1.08

[a] Conditional logistic regression models adjusted for education (none -8 years (reference), 9-12 years, 13-17 years), ethnicity (Hispanic or not (reference)), and race (White (reference), Black, Native American and Asian).
Source: National Center for Health Statistics

Table 4-4. Exposure distribution and association of amyotrophic lateral sclerosis and occupational magnetic fields and electric shocks, U.S. multiple cause of death data 1991-1999

	Cases		Controls		Adj. OR[a]	95% CI
	Number	%	Number	%		
Magnetic Fields						
High	503	8.5	5171	9.0	1.09	1.00, 1.19
Medium	4748	80.7	45517	78.9	1.09	0.96, 1.23
Low	635	10.8	6979	12.1	1.0	1.0
Electric shocks						
High	832	14.2	11941	20.7	0.73	0.67, 0.79
Medium	1356	23.0	14509	25.2	0.90	0.84, 0.97
Low	3698	62.8	31217	54.1	1.0	1.0

[a] Conditional logistic regression models adjusted for education (none -8 years (reference), 9-12 years, 13-17 years), ethnicity (Hispanic or not (reference)), and race (White (reference), Black, Native American and Asian).
Source: National Center for Health Statistics

Table 4-5. Association of amyotrophic lateral sclerosis and electric shocks, magnetic fields and electric occupations, U.S. multiple cause of death data 1991-1999

	Electric Shocks[a]				Magnetic fields[b]			
	High		Not High		High		Not High	
Electric Occupations	Adj. OR[c]	95% CI	Adj. OR[c]	95% CI	Adj. OR[c]	95% CI	Adj. OR[c]	95% CI
Yes	0.84	0.59, 1.20	1.48	1.17, 1.88	0.76	0.53, 1.08	1.40	1.11, 1.75
No	0.75	0.68, 0.81	1	-	1.00	0.90, 1.12	1	-

[a] One conditional logistic regression model containing electric shocks (ES) (high or not), electric occupations (yes or no) and ES x electric occupations
[b] One conditional logistic regression containing magnetic fields (MF) (high or not), electric occupations(yes or no) and MF x electric occupations
[c] Conditional logistic regression models adjusted for education (none -8 years (reference), 9-12 years, 13-17 years), ethnicity (Hispanic or not (reference)), and race (White (reference), Black, Native American and Asian).
[d] Crude ORs - Electric shocks: OR = 0.62, 95% CI: 0.58, 0.67; Magnetic Fields: OR = 0.94, 95% CI: 0.85, 1.04; Electric Occupations: OR =1.38, 95% CI: 1.15, 1.62
Source: National Center for Health Statistics

References

1. Shoesmith, C.L. and M.J. Strong, *Amyotrophic lateral sclerosis: update for family physicians.* Canadian family physician Médecin de famille canadien, 2006. 52(12): p. 1563-9.

2. Logroscino, G., et al., *Descriptive epidemiology of amyotrophic lateral sclerosis: new evidence and unsolved issues.* Journal of Neurology, Neurosurgery & Psychiatry, 2008. 79(1): p. 6-11.

3. Sejvar, J.J., et al., *Amyotrophic lateral sclerosis mortality in the United States, 1979-2001.* Neuroepidemiology, 2005. 25(3): p. 144-52.

4. Lopez-Bastida, J., et al., *Social economic costs and health-related quality of life in patients with amyotrophic lateral sclerosis in Spain.* Amyotrophic Lateral Sclerosis, 2008: p. 1-7.

5. Roosli, M., et al., *Mortality from Neurodegenerative Disease and Exposure to Extremely Low-Frequency Magnetic Fields: 31 Years of Observations on Swiss Railway Employees.* Neuroepidemiology, 2007. 28(4): p. 197-206.

6. Sorahan, T. and L. Kheifets, *Mortality from Alzheimer's, motor neurone and Parkinson's disease in relation to magnetic field exposure: findings from the study of UK electricity generation and transmission workers, 1973-2004.* Occupational and Environmental Medicine, 2007: p. 8.

7. Hakansson, N., et al., *Neurodegenerative diseases in welders and other workers exposed to high levels of magnetic fields.* Epidemiology, 2003. 14(4): p. 420-6; discussion 427-8.

8. Gunnarsson, L.G., et al., *A case-control study of motor neurone disease: its relation to heritability, and occupational exposures, particularly to solvents.* Br J Ind Med, 1992. 49(11): p. 791-8.

9. Gunnarsson, L.G., et al., *Amyotrophic lateral sclerosis in Sweden in relation to occupation.* Acta Neurol Scand, 1991. 83(6): p. 394-8.

10. Schulte, P., et al., *Neurodegenerative diseases: occupational occurrence and potential risk factors, 1982 through 1991.* American Journal of Public Health, 1996. 86(9): p. 1281.

11. Feychting, M., et al., *Occupational Magnetic Field Exposure and Neurodegenerative Disease.* Epidemiology, 2003. 14(4): p. 413-419.

12. Noonan, C.W., et al., *Occupational exposure to magnetic fields in case-referent studies of neurodegenerative diseases.* Scandinavian journal of work, environment & health, 2002. 28(1): p. 42-8.

13. Savitz, D.A., H. Checkoway, and D.P. Loomis, *Magnetic field exposure and neurodegenerative disease mortality among electric utility workers.* Epidemiology, 1998. 9(4): p. 398-404.

14. Davanipour, Z., et al., *Amyotrophic lateral sclerosis and occupational exposure to electromagnetic fields.* Bioelectromagnetics, 1997.

15. Strickland, D., et al., *Amyotrophic lateral sclerosis and occupational history. A pilot case-control study.* Archives of Neurology, 1996. 53(8): p. 730-733.

16. Weisskopf, M.G., *Prospective Study of Occupation and Amyotrophic Lateral Sclerosis Mortality.* American Journal of Epidemiology, 2005. 162(12): p. 1146-1152.

17. Park, R.M., et al., *Potential occupational risks for neurodegenerative diseases.* Am. J. Ind. Med., 2005. 48(1): p. 63-77.

18. Savitz, D.A., D. Loomis, and C. Tse, *Electrical occupations and neurodegenerative disease: analysis of US mortality data.* Arch Environ Health, 1998. 53(1): p. 71-4.

19. Johansen, C. and J.H. Olsen, *Mortality from amyotrophic lateral sclerosis, other chronic disorders, and electric shocks among utility workers.* Am J Epidemiol, 1998. 148(4): p. 362-8.

20. Deapen, D.M. and B.E. Henderson, *A case-control study of amyotrophic lateral sclerosis.* Am J Epidemiol, 1986. 123(5): p. 790-9.

21. Feychting, M., et al., *Occupational Magnetic Field Exposure and Neurodegenerative Disease.* Epidemiology, 2003. 14(4): p. 413-419.

22. Parlett, L.E., J.D. Bowman, and E. van Wijngaarden, *Evaluation of occupational exposure to magnetic fields and motor neuron disease mortality in a population-based cohort.* J Occup Environ Med. 53(12): p. 1447-51.

23. Milham, S., *Amyotrophic lateral sclerosis (Lou Gehrig's disease) is caused by electric currents applied to or induced in the body: it is an iatrogenic disease of athletes caused by use of electrotherapy devices.* Med Hypotheses. 74(6): p. 1086-7.

24. Grell, K., et al., *Risk of neurological diseases among survivors of electric shocks: A nationwide cohort study, Denmark, 1968-2008.* Bioelectromagnetics.

25. Sutedja, N., et al., *What we truly know about occupation as a risk factor for ALS: A critical and systematic review.* Amyotrophic Lateral Sclerosis, 2008: p. 1-19.

26. Kheifets, L., et al., *Future needs of occupational epidemiology of extremely low frequency (ELF) electric and magnetic fields (EMF): review and recommendations.* Occupational and Environmental Medicine, 2008: p. 27.

27. National Center for Health Statistics., *Multiple Cause of Death Data, 1991-1999,* in *National Center for Health Statistics*: Hyattsville, Maryland.

28. US Census Bureau, *1990 Census of Population and Housing. Classified index of industries and occupations*. 1992, Washington, DC: U.S. Dept. of Commerce, Economics and Statistics Administration. 1 v. .

29. Vergara, X.P., et al., *New electric-shock job exposure matrix.* Am J Ind Med, 2012. 55(3): p. 232-40.

30. Bowman, J., J. Touchstone, and M. Yost, *A Population-Based Job Exposure Matrix for Power-Frequency Magnetic Fields.* J Occup Environ Hyg, 2007. 4(9): p. 715-728.

31. Savitz, D., D. Loomis, and C. Tse, *Electrical occupations and neurodegenerative disease: analysis of US mortality data.* Arch Environ Health, 1998. 53(1): p. 71-4.

32. Gawel, M., Z. Zaiwalla, and F.C. Rose, *Antecedent events in motor neuron disease.* Journal of Neurology, 1983.

33. Sirdofsky, M.D., R.J. Hawley, and H. Manz, *Progressive motor neuron disease associated with electrical injury.* Muscle Nerve, 1991. 14(10): p. 977-80.

34. Gallagher, J.P. and M. Sanders, *Trauma and amyotrophic lateral sclerosis: a report of 78 patients.* Acta Neurol Scand, 1987. 75(2): p. 145-50.

35. Zoccolella, S., et al., *Motoneuron disease after electric injury: a case report.* Neurol Sci, 2008. 29(1): p. 47-49.

36. Jafari, H., *Motor neuron disease after electric injury.* Journal of Neurology, Neurosurgery & Psychiatry, 2001. 71(2): p. 265-267.

37. Ahlbom, A., et al., *Review of the Epidemiologic Literature on EMF and Health.* Environmental Health Perspectives, 2001. 109(6): p. 911-933.

38. Park, R., et al., *Potential occupational risks for neurodegenerative diseases.* Am. J. Ind. Med., 2005. 48(1): p. 63-77.

39. Abhinav, K., et al., *Electrical injury and amyotrophic lateral sclerosis: a systematic review of the literature.* Journal of Neurology, Neurosurgery & Psychiatry, 2006. 78(5): p. 450-453.

40. Schade, W.J. and G.M. Swanson, *Comparison of death certificate occupation and industry data with lifetime occupational histories obtained by interview: variations in the accuracy of death certificate entries.* Am J Ind Med, 1988. 14(2): p. 121-36.

41. Kaminski, R., et al., *Occupational information on death certificates: a survey of state practices.* Am J Public Health, 1981. 71(5): p. 525-6.

42. U.S. Department of Health and Human Services, *Guidelines for Reporting Occupation and Industry on Death Certificates*, CDC and NCHS), Editor. 1988: Hyattsville, MD.

43. National Institute for Occupational Safety and Health (NIOSH), *Mortality by Occupation, Industry, and Cause of Death: 24 Reporting States (1984-1988)* 1997, U.S. Department of Health and Human Services: Cincinnati, Ohio.

44. Armon, C., *Amyotrophic Lateral Sclerosis*, in *Neuroepidemiology: From Principles to Practice*, L.M. Nelson, et al., Editors. 2004, Oxford University Press: New York. p. 162-187.

45. Nelson, L.M. and V. McGuire, *Epidemiology of amyotrophic lateral sclerosis*, in *Amyotrophic lateral sclerosis*, R.H. Brown, M. Swash, and P. Pasinelli, Editors. 2006, Informa Healthcare: London.

46. Wang, H., et al., *Smoking and risk of amyotrophic lateral sclerosis: a pooled analysis of 5 prospective cohorts.* Arch Neurol. 68(2): p. 207-13.

47. Alonso, A., G. Logroscino, and M.A. Hernan, *Smoking and the risk of amyotrophic lateral sclerosis: a systematic review and meta-analysis.* J Neurol Neurosurg Psychiatry. 81(11): p. 1249-52.

48. Sutedja, N.A., et al., *Lifetime occupation, education, smoking, and risk of ALS.* Neurology, 2007. 69(15): p. 1508-14.

49. Chancellor, A.M., et al., *Risk factors for motor neuron disease: a case-control study based on patients from the Scottish Scottish Motor Neuron Disease Register.* Journal of Neurology, 1993.

50. Centers for Disease Control and Prevention (CDC), *Education Reporting and Classification on Death Certificates in the United States, DHHS* National Center for Health Statistics Division of Vital Statistics, Editor. 2010, U.S. Department of Health and Human Services: Hyattsville, MD.

51. Mitchell, J.D., *Heavy metals and trace elements in amyotrophic lateral sclerosis.* Neurol Clin, 1987. 5(1): p. 43-60.

52. Kamel, F., et al., *Lead exposure and amyotrophic lateral sclerosis.* Epidemiology, 2002. 13(3): p. 311-9.

53. Campbell, A.M., E.R. Williams, and D. Barltrop, *Motor neurone disease and exposure to lead.* J Neurol Neurosurg Psychiatry, 1970. 33(6): p. 877-85.

54. Fang, F., et al., *Association between blood lead and the risk of amyotrophic lateral sclerosis.* Am J Epidemiol, 2010. 171(10): p. 1126-33.

55. Holloway, S.M. and A.E. Emery, *The epidemiology of motor neuron disease in Scotland.* Muscle Nerve, 1982. 5(2): p. 131-3.

56. Kamel, F., et al., *Association of cigarette smoking with amyotrophic lateral sclerosis.* Neuroepidemiology, 1999. 18(4): p. 194-202.

57. Chio, A., et al., *Risk factors in motor neuron disease: a case-control study.* Neuroepidemiology, 1991. 10(4): p. 174-84.

58. Armon, C., et al., *Epidemiologic correlates of sporadic amyotrophic lateral sclerosis.* Neurology, 1991. 41(7): p. 1077-84.

59. Rosati, G., et al., *Studies on epidemiological, clinical, and etiological aspects of ALS disease in Sardinia, Southern Italy.* Acta Neurol Scand, 1977. 55(3): p. 231-44.

60. Longstreth, W.T., et al., *Risk of amyotrophic lateral sclerosis and history of physical activity: a population-based case-control study.* Arch Neurol, 1998. 55(2): p. 201-6.

61. Kondo, K. and T. Tsubaki, *Case-control studies of motor neuron disease: association with mechanical injuries.* Arch Neurol, 1981. 38(4): p. 220-6.

62. Chen, H., et al., *Head injury and amyotrophic lateral sclerosis.* Am J Epidemiol, 2007. 166(7): p. 810-6.

63. Cabanholt, A., et al., *Neurodegenerative Memory Disorders: A potential Role of Environmental Toxins.* Neurologic Clinics, 2005. 23(2): p. 485-521.

64. Marin, B., et al., *Can mortality data be used to estimate amyotrophic lateral sclerosis incidence?* Neuroepidemiology, 2011. 36(1): p. 29-38.

65. Chio, A., et al., *Accuracy of death certificate diagnosis of amyotrophic lateral sclerosis.* J Epidemiol Community Health, 1992. 46(5): p. 517-8.

66. Noonan, C.W., et al., *Temporal and geographic variation in United States motor neuron disease mortality, 1969-1998.* Neurology, 2005. 64(7): p. 1215-21.

67. Yeo, L., C. Lynch, and O. Hardiman, *Validating population-based registers for ALS: how accurate is death certification?* J Neurol, 2010. 257(8): p. 1235-9.

68. Coffman, C.J., et al., *Estimating the occurrence of amyotrophic lateral sclerosis among Gulf War (1990-1991) veterans using capture-recapture methods.* Neuroepidemiology, 2005. 24(3): p. 141-50.

69. Stickler, D.E., J.A. Royer, and J.W. Hardin, *Accuracy and usefulness of ICD-10 death certificate coding for the identification of patients with ALS: results from the South Carolina ALS Surveillance Pilot Project.* Amyotroph Lateral Scler, 2012. 13(1): p. 69-73.

5. Conclusions

The purpose of this dissertation was to evaluate potential role of occupational exposure to magnetic fields and electric shocks in the development of NDD. This was accomplished by first, conduct a meta-analysis of occupational magnetic fields (MF) exposure and neurodegenerative diseases, second, to develop a tool to evaluate electric shocks and amyotrophic lateral sclerosis (ALS) and, finally, to examine whether specific aspects of "electric" occupation environment are related to ALS mortality in the U.S. worker population between 1991-1999.

Several scientific reviews have evaluated the relationship of occupational MF and neurodegenerative diseases. Occupational MF studies that focused on Alzheimer's disease (AD) found weak associations. While occupational studies have found consistent associations between "electrical occupations" and ALS. No sufficiently powered research has examined electric shocks with, an often-cited potential risk factor for ALS, and motor neuron disease (MND). This dissertation attempts to examine: 1) the use of occupational titles as a proxy for MF exposure in existing occupational MF neurodegenerative disease literature, 2) occupations exposed to electric shocks, and 3) the association between electric shocks, MF and ALS deaths.

Chapter 2 examines the body of literature on occupational electromagnetic fields and neurodegenerative diseases, in addition to the differences between studies with and without measurements. We explored differences between the studies examining occupational EMF and motor neuron disease (MND) including ALS, AD, Parkinson's disease, multiple sclerosis, and dementia. We found weak associations of occupational MF exposures with both AD and MND. Risk of developing MND was associated with electric occupations, while AD risk was associated with estimated MF levels. Our results suggest that AD associations can be explained by publication bias. This finding is consistent with the current scientific reviews and supports the evaluation other exposures within the electric occupation environment and MND. Misclassification of disease coupled with imprecision related to exposure assessment likely affected all studies. Our findings suggest future work should incorporate improvements into exposure assessment, such as MF measurements of women and other electrically-related exposures.

Chapter 3 describes the creation of a population electric shocks job exposure matrix (JEM). Using expert judgment and available data on occupational electric shocks and electrocutions, we created a tool to evaluate the relationship between occupational electric shocks and amyotrophic lateral sclerosis. We found the largest number of electric shocks occurred among precision production, craft, and repair occupations groups. By occupational title, cooks, janitors and cleaners and miscellaneous laborers had the highest number of electric shocks. The final assessment of electric shocks into categories of low, medium and high exposure for 501 U.S. Bureau of Census occupational titles allows for further analysis. Future work should also account for uncertainties in the data sources and exposure assessment.

Chapter 4 investigates associations between occupational electric shocks, MF and amyotrophic lateral sclerosis among deaths occurring in the U.S. The results from this study demonstrated inverse associations between occupational electric shocks and ALS. We found no association between occupational MF and ALS, but we found weak associations between "electric occupations" and ALS. However, neither electric shocks nor MF explained the association between electric occupations and ALS. Given the limitations of using "usual occupation", application of electric shock JEM to an alternate data source with more complete or verified job histories would be informative. Future work should expand the MF JEM to occupations with no measurement data, incorporate new information on occupational electric shocks, such as industry-level data and degree of severity, and quantify the degree of potential biases in the analyses.

There are numerous strengths to the work conducted. First, we provide a review of published literature on occupational MF and neurodegenerative disease and, more importantly, highlight important study characteristics to improve upon for future studies. This expanded review included all relevant occupational titles with and without MF measurements appearing in PubMed through 2011. Our work indicates that, for MND, other exposures within the electric occupation environment be evaluated. As such, we created the first population-based electric shocks JEM for use in epidemiologic studies. Finally, we investigated occupational electric shocks and with a dataset containing more than 7000 ALS cases, our sample size was sufficiently powered to detect a possible association, should it exist.

Despite the strengths of the presented work, several limitations need to be mentioned. In the neurodegenerative meta-analysis, articles were sought from a peer-review journal database, which were English language-based, which could have contributed to the publication bias we noted. Studies finding no association might be more likely to be rejected from journals in this pool and eventually appear in unindexed or non-English journals. Biases may have been introduced by original study author decisions of variable definitions, reference groups, metrics and cutpoints and selective presentation of the results. These limitations could be addressed using sensitivity or bias analysis. The presence of publication bias needs to be addressed prior to embarking upon such a large effort.

With regards to the assessment of electric shocks exposure, improvements to reduce exposure misclassification are needed. The presented job exposure matrix was constructed using nationally available data on severe workforce accidents and expert knowledge of workplace risk factors contributing to those shocks. An absence of measures to judge these exposure assignments is a limitation to this work. Nonetheless, incorporating expert uncertainty into the JEM would assist in identifying to direct such improvements e.g. where the information is needed. Other aspects, which could inform our understanding of the role of electric shocks on ALS etiology, are the severity of the shock event, as well as, information on the type of industry. Both of these dimensions could be incorporated into the electric shock JEM using additional data and expert judgment.

In the analysis of electric shocks, MF and ALS mortality, we used “usual occupation” provided on the death certificate combined with two job exposure matrices for the basis of exposure. The assumptions we made were that “usual occupation” reported on the death certificate was accurate and, when applied, that the electric shocks job exposure matrix would result in a reasonable classification of exposure. Use of death certificates contributes to exposure misclassification, nonetheless, the mortality data provide a rich source of data to explore etiologic hypotheses.

Overall, we noted weak associations between occupational MF and MND and AD in published studies. The risk of MND was associated with occupational titles working exposed to MF, while AD risk was associated with estimated MF levels. Publication bias for AD may explain part of this observed association. Misclassification of disease coupled with imprecision related to exposure assessment likely affected all studies. Improvements in exposure assessment include disentangling the electric shocks and MF exposures in occupations. Our study found inverse associations between occupational electric shocks and ALS. We found no association between occupational MF and ALS, but found weak associations between “electric occupations” and ALS, which could not be explained by MF or electric shocks. Like in the meta-analysis, the findings are uncertain in light of the likelihood for electric shock exposure misclassification. However, it is important to continue work in the area of occupational exposure assessment given the aging workforce and large public health impacts of neurodegenerative diseases.

Appendix 1. 179 Occupational titles without electric shocks or electrocution information

BOC	Occupational Title	BOC	Occupational Title	BOC	Occupational Title	BO C	Occupational Title
3	Legislators	117	Natural science teachers, n.e.c.	227	Air traffic controllers	468	Child care workers, n.e.c.
5	Administrators and officials, public administration	118	Psychology teachers	233	Tool programmers, numerical control	473	Farmers, except horticultural
6	Administrators, protective service	119	Economics teachers	234	Legal assistants	474	Horticultural specialty farmers
8	Personnel and labor relations managers	123	History teachers	254	Real estate sales occupations	476	Managers, horticultural specialty farms
9	Purchasing managers	124	Political science teachers	255	Securities and financial services sales occupations	489	Inspectors, agricultural products
14	Administrators, education and related fields	125	Sociology teachers	263	Sales workers, motor vehicles and boats	494	Supervisors, forestry, and logging workers
15	Managers, medicine and health	126	Social science teachers, n.e.c.	265	Sales workers, shoes	497	Captains and other officers, fishing vessels
16	Postmasters and mail superintendents	127	Engineering teachers	283	Demonstrators, promoters and models, sales	498	Fishers
19	Funeral directors	128	Mathematical science teachers	284	Auctioneers	499	Hunters and trappers
24	Underwriters	129	Computer science teachers	285	Sales support occupations, n.e.c.	506	Automobile mechanic apprentices
26	Management analysts	133	Medical science teachers	305	Supervisors, financial records processing	535	Camera, watch, and musical instrument repairers
29	Buyers, wholesale and retail trade, except farm products	134	Health specialties teachers	309	Peripheral equipment operators	536	Locksmiths and safe repairers
34	Business and promotion agents	135	Business, commerce, and marketing teachers	314	Stenographers	553	Supervisors, brickmasons, stonemasons, and tile setters
35	Construction inspectors	136	Agriculture and forestry teachers	316	Interviewers	645	Patternmakers and model makers, metal
43	Architects	137	Art, drama, and music teachers	317	Hotel clerks	646	Lay-out workers
44	Aerospace Engineer	138	Physical education teachers	325	Classified-ad clerks	647	Precious stones and metals workers
46	Mining	139	Education teachers	326	Correspondence clerks	654	Sheet metal worker apprentices
47	Petroleum	143	English teachers	329	Library clerks	655	Miscellaneous precision metal workers
48	Chemical	144	Foreign language teachers	338	Payroll and timekeeping clerks	656	Patternmakers and model makers, wood
49	Nuclear	145	Law teachers	343	Cost and rate clerks	657	Cabinet makers and bench carpenters
53	Civil	146	Social work teachers	353	Communications equipment operators, n.e.c.	658	Furniture and wood finishers
54	Agricultural	147	Theology teachers	354	Postal clerks, except mail carriers	659	Miscellaneous precision woodworkers
58	Marine and naval architects	148	Trade and industrial teachers	355	Mail carriers, postal service	668	Upholsterers
63	Surveyors and mapping scientists	149	Home economics teachers	357	Messengers	678	Dental laboratory and medical appliance technicians
66	Actuaries	153	Teachers, postsecondary, n.e.c.	374	Material recording, scheduling, and distributing clerks, n.e.c.	687	Bakers
67	Statisticians	154	Postsecondary teachers, subject	377	Eligibility clerks, social welfare	705	Milling and planing machine operators

BOC	Occupational Title	BOC	Occupational Title	BOC	Occupational Title	BO C	Occupational Title
68	Mathematical scientists, n.e.c.	156	Teachers, elementary school	384	Proofreaders	729	Nailing and tacking machine operators
69	Physicists and astronomers	157	Teachers, secondary school	386	Statistical clerks	736	Typesetters and compositors
73	Chemists, except biochemists	158	Teachers, special education	387	Teachers' aides	784	Solderers and brazers
74	Atmospheric and space scientists	165	Archivists and curators	403	Launderers and ironers	809	Taxicab drivers and chauffeurs
75	Geologists and geodesists	166	Economists	404	Cooks, private household	829	Sailors and deckhands
76	Physical scientists, n.e.c.	167	Psychologists	405	Housekeepers and butlers	834	Bridge, lock, and lighthouse tenders
77	Agricultural and food scientists	168	Sociologists	406	Child care workers, private household	845	Longshore equipment operators
79	Forestry and conservation scientists	169	Social scientists, n.e.c.	407	Private household cleaners and servants	875	Garbage collectors
83	Medical scientists	176	Clergy	413	Supervisors, firefighting and fire prevention occupations	876	Stevedores
85	Dentists	177	Religious workers, n.e.c.	414	Supervisors, police and detectives		
86	Veterinarians	179	Judges	415	Supervisors, guards		
87	Optometrists	183	Authors	416	Fire inspection and fire prevention occupations		
88	Podiatrists	186	Musicians and composers	418	Police and detectives, public service		
89	Health diagnosing practitioners, n.e.c.	187	Actors and directors	423	Sheriffs, bailiffs, and other law enforcement officers		
96	Pharmacists	193	Dancers	425	Crossing guards		
99	Occupational therapists	194	Artists, performers, and related workers, n.e.c.	445	Dental assistants		
103	Physical therapists	195	Editors and reporters	457	Barbers		
104	Speech therapists	199	Athletes	461	Guides		
106	Physicians assistants	204	Dental hygienists	462	Ushers		
113	Earth, environmental, and marine science teachers	205	Health record technologists and technicians	464	Baggage porters and bellhops		
114	Biological science teachers	214	Industrial engineering technicians	466	Family child care providers		
115	Chemistry teachers	226	Airplane pilots and navigators	467	Early childhood teachers' assistants		

BOC: 1990 U.S. Bureau of Census Code